Circulation Journal
Circ J 2023; 87: 1410–1621
doi:10.1253/circj.CJ-22-0794

JCS/JSCVS/JATS/JSVS 2020 Guideline on Diagnosis and Treatment of Aortic Aneurysm and Aortic Dissection

Hitoshi Ogino; Osamu Iida; Koichi Akutsu; Yoshiro Chiba; Hiromitsu Hayashi; Hatsue Ishibashi-Ueda; Shuichiro Kaji; Masaaki Kato; Kimihiro Komori; Hitoshi Matsuda; Kenji Minatoya; Hiroko Morisaki; Takao Ohki; Yoshikatsu Saiki; Kunihiro Shigematsu; Norihiko Shiiya; Hideyuki Shimizu; Nobuyoshi Azuma; Hirooki Higami; Shigeo Ichihashi; Toru Iwahashi; Kentaro Kamiya; Takahiro Katsumata; Nobuyoshi Kawaharada; Yoshihisa Kinoshita; Takuya Matsumoto; Shinji Miyamoto; Takayuki Morisaki; Tetsuro Morota; Kiyonori Nanto; Toshiya Nishibe; Kenji Okada; Kazumasa Orihashi; Junichi Tazaki; Masanao Toma; Takuro Tsukube; Keiji Uchida; Tatsuo Ueda; Akihiko Usui; Kazuo Yamanaka; Haruo Yamauchi; Kunihiro Yoshioka; Takeshi Kimura; Tetsuro Miyata; Yutaka Okita; Minoru Ono; Yuichi Ueda on behalf of the Japanese Circulation Society, the Japanese Society for Cardiovascular Surgery, the Japanese Association for Thoracic Surgery and the Japanese Society for Vascular Surgery Joint Working Group

Table of Contents

J-STAGE Advance Publication released online September 1, 2023

This document is an English version of the JCS/JSCVS/JATS/JSVS 2020 Guideline on Diagnosis and Treatment of Aortic Aneurysm and Aortic Dissection reported at the 84th Annual Scientific Meeting of the Japanese Circulation Society held in 2020 (https://www.j-circ.or.jp/cms/wp-content/uploads/2020/07/JCS2020_Ogino.pdf).

Refer to **Appendix 1** for the details of members.

JCS Joint Working Groups: The Japanese Circulation Society; the Japanese Society for Cardiovascular Surgery, the Japanese Association for Thoracic Surgery, the Japanese Society for Vascular Surgery, Japan Radiological Society, Japanese College of Cardiology, Japanese College of Angiology

Mailing address: Guideline Committee of the Japanese Circulation Society, 6th Floor, Uchikanda Central Building, 1-18-13 Uchikanda, Chiyoda-ku, Tokyo 101-0047, Japan. email: jcsGL@j-circ.or.jp

All rights are reserved to the Japanese Circulation Society. For permissions, please email: cj@j-circ.or.jp

ISSN-1346-9843

Abbreviations and Acronyms

AAA	abdominal aortic aneurysm
ABF	aorto-bronchial fistula
ACC	American College of Cardiology
ADD-RS	Aortic Dissection Detection Risk Score
AEF	aorto-esophageal fistula
AHA	American Heart Association
BAV	bicuspid aortic valve
ESC	European Society of Cardiology
ESVS	European Society for Vascular Surgery
ET	elephant trunk
EVAR	endovascular aortic repair
FET	frozen elephant trunk
IMH	intramural hematoma
IRAD	International Registry of Acute Aortic Dissection
JACSM	Japanese Committee for Stentgraft Management
JCVSD	Japan Cardiovascular Surgery Database
NCD	National Clinical Database
PAU	penetrating atherosclerotic ulcer
SCI	spinal cord injury
STS	Society of Thoracic Surgeons
SVS	Society for Vascular Surgery
TAA	thoracic aortic aneurysm
TAAA	thoracoabdominal aortic aneurysm
TEVAR	thoracic endovascular aortic repair
ULP	ulcer-like projection
VSRR	valve-sparing [aortic] root replacement

Preface to the Revised Edition

Of the clinical practice guideline of the Japanese Circulation Society concerning aortic diseases, the Guidelines on Diagnosis and Treatment of Aortic Dissection (first edition) were published in 2000, followed by the Guideline for Diagnosis and Treatment of Aortic Aneurysm and Aortic Dissection (JCS 2006) with the addition of clinical practice guidelines for aortic aneurysm and their revised edition in 2011.[1] The present revision is the third and relatively extensive.

With aging of society, aortic diseases have increased, and the incidence of aortic dissection has been shown to be 10 or higher per 100,000 people annually according to its registry. Particularly, in Japan, under the high adoption rate of CT examination, aortic diseases can be diagnosed at many facilities and opportunities, and further improvements in the therapeutic results can be expected with further development of the diagnosis and treatment system including emergency transport. For this, transition from the conventional diagnosis and treatment system largely restricted to cardiovascular surgery to multidisciplinary approaches for the diagnosis and treatment participated in by cardiologists, radiologists, pathologists, clinical geneticists, general internists, clinical laboratory technicians, as well as cardiovascular/vascular surgeons, anesthesiologists, emergency care doctors, clinical engineers, and nurses is also necessary. Therefore, the present guideline was prepared by including a wide range of contents from basic matters to expert information to address the users' objectives.

The first of the major points of revision was that interpretations of conditions differently defined in Japan and abroad were explicitly described. One example is the interpretation of intramural hematoma (IMH) of aortic dissection. In Japan, it is defined as "intramural hematoma caused by bleeding in the tunica media of the aortic wall". However, as the term is interpreted more broadly and tends to be used to refer to all false lumen occlusion type aneurysms in Europe and the United States, IMH was approved as one of the terms by respecting the international consensus. On the other hand, of the concepts reported from Japan, the criteria of ulcer-like projection (ULP), which had been relatively unclear, were made explicit. In addition, the position of ULP and extension of

Table 1. Classes of Recommendation (COR)	
Class I	There is evidence and/or general agreement that a given procedure or treatment is effective and/or useful
Class II	There is conflicting evidence and/or a divergence of opinion about the efficacy/usefulness of a given procedure or treatment
Class IIa	There is a high probability of efficacy/usefulness based on evidence and opinion
Class IIb	Effectiveness/usefulness is not well established based on evidence and opinion
Class III	There is evidence and/or general agreement that the procedure or treatment is not effective and/or useful

Table 2. Level of Evidence (LOE)	
Level A	Demonstrated by multiple randomized clinical trials or meta-analyses
Level B	Demonstrated by a single randomized clinical trial or large non-randomized studies
Level C	Consensus from expert opinion and/or small clinical trials, sub-analyses

indications of open surgery for Stanford Type A aortic dissection with thrombosed false lumen were also described. Moreover, along with acute aortic dissection, penetrating atherosclerotic ulcer (PAU), an element of acute aortic syndrome (AAS), is separately outlined.

Concerning treatment methods, the percentage of stent grafting (thoracic endovascular aortic repair: TEVAR/endovascular aortic repair: EVAR) among all treatments for aortic diseases is increasing, and studies that serve as evidence have increased during the past 9 years with increases in reports about TEVAR/EVAR. New devices have been developed or improved, and many descending thoracic and abdominal aortic aneurysms (AAAs) are regarded as indications of TEVAR/EVAR at some institutions. Also, new techniques incorporating measures to cope with branch perfusion have been introduced for some aneurysms of the aortic arch or thoracoabdominal aorta, and favorable results have been confirmed. Regarding aortic dissection, also, indications of TEVAR have been extended during the past 9 years as devices for the treatment of dissection have been approved. TEVAR has come to be performed more aggressively not only for complicated type Stanford Type B acute/subacute dissections with complications but also for uncomplicated types at a high risk of complications, enlargement, or rupture based, in part, on the results of RCTs.

At the same time, the results of conventional open surgery have also been improved due to priority placed on TEVAR/EVAR for patients at a high risk in open surgery, such as older patients, in addition to technical improvements, procedural modifications, establishment of brain/spinal cord protection, improvements in artificial vessels, and accumulation of experience. However, because of the lack of new epoch-making techniques or treatments, there have been few novel studies that provide evidence, and no marked changes have been observed in the levels of recommendation. This must also be noted in comparing the level of recommendation between conventional open surgery and TEVAR/EVAR. Moreover, the establishment of hybrid treatment between the two approaches was a development during the past 9 years, and not only debranching with prior bypassing but also step-wise treatment for enlarging lesions is an important therapeutic strategy combining open surgery and TEVAR/EVAR.

One of the topics related to aortic dissection is that malperfusion as well as hemorrhagic complications has been shown to markedly affect the therapeutic outcome. Particularly, the mortality rate is high in patients with Type A dissection showing malperfusion of the coronary artery or carotid artery and those with Type A/B dissection showing malperfusion of the superior mesenteric artery, and prompt treatment is required. In this connection, commercial frozen elephant trunk (FET) devices (open stent grafts) also have become available in Japan since 2014, and are used for the treatment of extensive aneurysms of the aortic arch and distal anastomosis of Type A dissection complicated by malperfusion. This has resulted in improvements in early results and descending aorta remodeling (disappearance of false lumen) in a remote period, and the technique has gained wide acceptance in Japan and abroad.

Moreover, elucidation of the relationship between aortic diseases and gene abnormalities has been recently advancing. The importance of multidisciplinary treatment including gene diagnosis of "inherited aortic diseases" including hereditary connective tissue disorders was also overviewed.

However, the lack of evidence in this field has continued to be an obstacle in the preparation of the guideline. While many findings have been disclosed from international registries of aortic dissection, the lack of data of patients who died immediately after the onset and detailed data at times of emergency is considered to be preventing the accumulation of evidence. In addition, the treatments are primarily high-risk invasive procedures, which are often inappropriate to evaluate by RCTs. Moreover, the experience and technical factors of the surgeon and the protocols of the institutions also markedly affect the outcome, also leading to the lack of evidence including meta-analyses. Therefore, the conventional criteria for the adoption and grading of recommendation classes and evidence used in previous guidelines were adopted in this guideline (**Tables 1**,**2**).

Some of the recent guidelines adopt the Minds system and provide Mind style classes of recommendation along with conventional recommendation grades. However, as there have been few studies that can be regarded as evidence or included in systematic reviews, the Minds system was not adopted. However, as Minds style Clinical Questions are useful in that they immediately provide solutions to questions in routine clinical practice, similar questions were also added to the test of the present guideline as "Practical Questions (PQ)".

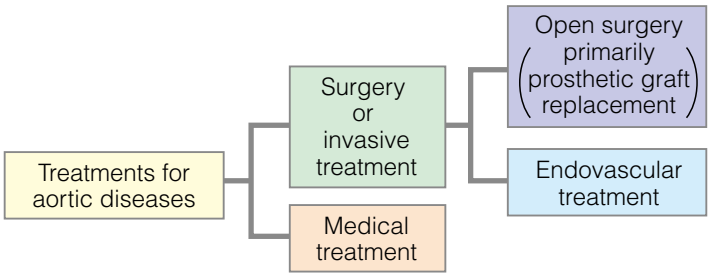
Finally, this guideline was compiled under the basic principle of multidisciplinary care as a comprehensive volume that includes many related phenomena such as definitions of aortic aneurysm/aortic dissection, diagnosis/examinations, internal treatment/invasive treatment, rehabilitation, prevention, and surveillance by a board of doctors of various specialties including cardiologists, radiologists, pathologists, clinical geneticists, and cardiovascular surgeons with support by related academic societies. We hope that they provide reliable standards for the diagnosis and treatment of aortic aneurysm/dissection, but as they are clinical guidelines prepared on the basis of the limited evidence available at present and many expert consensuses, they do not demand full compliance.

Instead, excellent doctors in this field may conduct other or novel treatments not mentioned in the guidelines with approval of the ethical review board at each institution with sufficient knowledge about the evidence or expert consensuses shown in the guidelines. The results of such attempts are expected to serve as evidence for the future. In addition, institutions and doctors differ in risk assessment, contents of treatment, and technical level, and, in this particular field, in which highly invasive treatments including emergency operations occupy a large portion, the guidelines do not address the contents of care, and actual clinical decisions are left entirely to the judgments of individual institutions and doctors. Especially, in invasive treatments for unruptured aortic aneurysms, the guidelines explicitly describe the indications, but the final judgments should be made not by medical experts alone but according to wishes and with the consent of the patients and their families after sufficient explanation.

However, for young doctors, primary care doctors, and doctors of other specialties, sufficient understanding of this guideline is the first step to provide care for aortic aneurysm/dissection of the current level. With strong awareness of this aspect, we arranged this guideline by selectively incorporating contents aimed to improve the outcomes of multidisciplinary care.

In Japan, the incidence of aortic diseases is high from a global perspective, but the care level including the emergency care system is also high, and the therapeutic results are considered excellent. On behalf of those who were involved in the revision of the guideline, I would like to express my sincere hope that they further improve the level of care for aortic diseases in Japan and contribute to survival and welfare of many patients.

In this guideline, terms describing treatments for aortic diseases are used in the meanings shown in the following chart. "Surgery" is synonymous to "invasive treatment" and means both open surgery and endovascular treatment. "Open surgery" means open chest/abdominal surgery and primarily refers to prosthetic graft replacement. On the other hand, "endovascular treatment" means techniques including stent-graft deployment (TEVAR, EVAR) and transcatheter stent placement.



Terms for treatments of aortic diseases in this guideline

I. Definition, Pathogenesis, and Epidemiology

1. Definition, Pathological Condition, and Classification of Aortic Aneurysm

1.1 Definition

Aortic aneurysm is defined as "the circumferential or local enlargement (in diameter) or thickening of a part of the entire circumference of the aortic wall." Overall enlargement of the aorta is called "aortomegaly." On the other hand, dilatation of the aortic root is also called "annuloaortic ectasia." Generally, the normal diameter of the aorta in adults has been reported to be 30 mm in the thoracic region and 20 mm in the abdominal region. A local dilatation of part of the wall (aneurysmal bulge, saccular dilatation), or aortic enlargement (the formation of fusiform aneurysms) with an aortic diameter of more than 1.5 times the normal diameter (45 mm in the thoracic area and 30 mm in the abdominal area) is called an "aneurysm", whereas a less severe aortic enlargement is called an "aneurysmal dilatation."[2,3]

An aortic aneurysm is a local enlargement (in diameter) or thickening of the aortic wall. An aortic aneurysm with a fusiform shape is called a "fusiform type aortic aneurysm" (**Figure 1**), whereas an aortic aneurysm with a saccular shape is called a "saccular type aortic aneurysm" (**Figure 2**) (see **PQ 1**). Additionally, the types of aortic aneurysm differ depending on the site of the aneurysm. For example, an aneurysm in the thoracic aorta is called a thoracic aortic aneurysm (TAA). An aneurysm extending from the thoracic aorta to abdominal aorta is called thoracoabdominal aortic aneurysm (TAAA). An aneurysm in the abdominal aorta is called an abdominal aortic aneurysm (AAA). The aneurysm has a smooth transition from the aortic wall to the aneurysmal wall. From a histopathological viewpoint, in many cases, the aortic wall structure, especially medial elastic fibers, remains in the aneurysmal wall (**Figure 3A**). Therefore, it is easy to detect dilatation of the aortic wall. However, further destruction of the aneurysmal wall leads to the destruction and loss of the media, and in some areas the fibrous structure is the only remnant (**Figure 3B**). Even in such a case, the aneurysmal wall shows a transition from the non-dilatated site; A close observation of the aneurysmal wall may show a part of medial elastic fibers at other sites. Such an aneurysm is called a "true aneurysm" to clearly differentiate it from a "pseudoaneurysm".

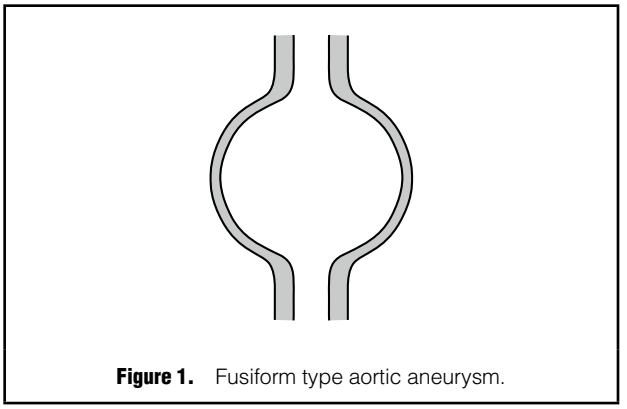


Figure 1. Fusiform type aortic aneurysm.

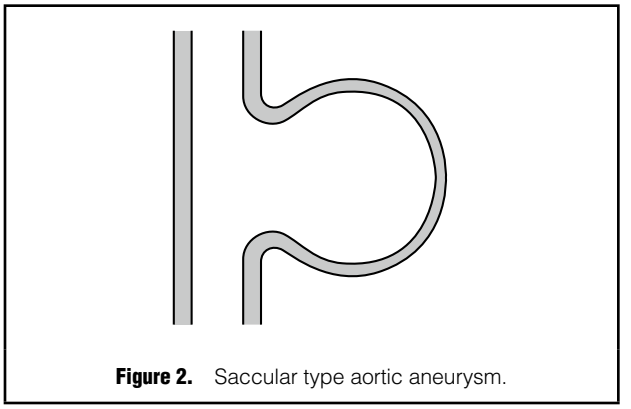


Figure 2. Saccular type aortic aneurysm.

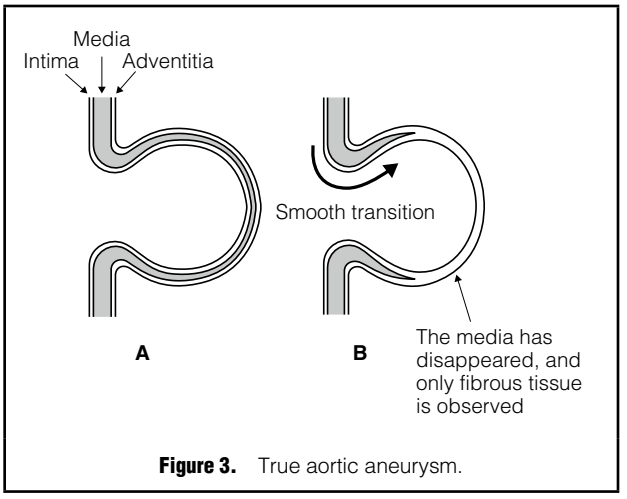


Figure 3. True aortic aneurysm.

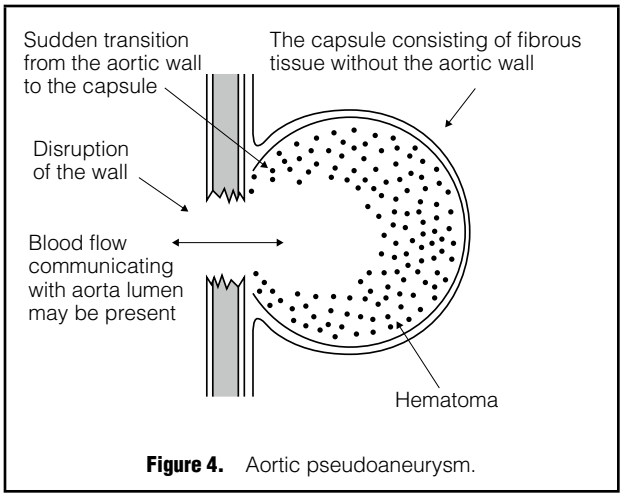


Figure 4. Aortic pseudoaneurysm.

On the other hand, a "pseudoaneurysm" leads to communication between the aortic lumen and the surrounding tissue due to damage to the aortic wall, resulting in the formation of a blood-filled cavity outside the aortic wall. In some cases, the blood leakage is ceased by thrombosis and hematoma formation (**Figure 4**). Therefore, not three layers but only a fibrous cap remains in the outermost layer, showing instability after aortic rupture. Aortic dissection with an increase in diameter and the subsequent formation of aneurysms is also called a "dissecting aneurysm."

The most important clinical problem with aortic aneurysms is aortic rupture. Although it is difficult to strictly define "rupture," extravascular blood leakage is generally called "rupture," whereas rupture with the site of pain in the location of aneurysms without blood leakage is called an "impending rupture." In some cases, an impending rupture shows a high attenuating crescent sign, which means influx of part of the contrast medium to atheroma due to rapid dilatation of aortic aneurysm. Aortic aneurysms have recently been classified according to the presence or absence of symptoms into "symptomatic" meaning unstable condition and "asymptomatic" aortic aneurysms. In many cases, invasive treatment is indicated for symptomatic aortic aneurysms.

Increased fragility of the aortic wall is deeply involved in the development of aortic aneurysms. The increased fragility is caused by structural abnormalities or destruction of the aortic wall due to heritable disorders of connective tissue[8,9] such as Bechet's disease,[4,5] Takayasu arteritis,[6,7] Marfan syndrome, and structural abnormalities or destruction of the aortic wall such as atherosclerosis.[10,11] AAA shows significant arteriosclerotic changes on the luminal side. The development of aneurysms is strongly associated with arteriosclerosis.[12] However, the following reports show that the development of AAA cannot be explained by arteriosclerosis alone, and suggests the involvement of other factors especially genetic factors and hypertension: (i) a lower association between AAA and arteriosclerosis obliterans;[13] (ii) the presence of familial aortic aneurysms;[14,15] (iii) findings that diabetes mellitus is not a risk factor for AAA, and reports on the inverse relationship between the incidence of AAA and diabetes mellitus;[16,17] and (iv) the absence of a significant association[18] between AAA and LDL cholesterol.[3,19] At the molecular level, previous studies have strongly suggested the involvement of the following factors on AAA: proinflammatory cytokines, such as interleukin and interferon gamma, and enzymes involved in the degradation of the extracellular matrix such as matrix metalloproteinase.[3,19,20]

1.2 Pathogenesis

Signs and symptoms of aortic aneurysm can be classified

into (1) "pain" and "hemorrhage" due to rupture; and (2) "compression symptoms" induced by aneurysms before rupture to surrounding organs. Details of symptoms are discussed in another section (See "**1. Symptoms**" in **Chapter III**).

Pain and hemorrhage: Generally, in most cases, aortic aneurysms before rupture are asymptomatic. However, rupture causes severe pain. Depending on the site of hemorrhage, symptoms, such as chest pain, back pain, abdominal pain, and low back pain occur. When a patient has relatively severe symptoms and CT scan shows no blood leakage from the aorta, the patient has "impending rupture" and is at risk of rupture. The hemorrhagic symptoms include disturbance of consciousness due to hemorrhagic shock, hemoptysis due to rupture to lung or bronchial tracts, hematemesis due to rupture to the esophagus, melena due to hemorrhage to colon, hemothorax due to rupture into the thoracic cavity leading to respiratory failure, and symptoms such as acute heart failure due to rupture to pulmonary artery. Compression symptoms: Pressure caused by aneurysms on surrounding tissues is seldom recognized as symptoms. Compression symptoms include hoarseness due to recurrent laryngeal nerve paralysis, bloody sputum due to compression of the lung, dysphagia due to compression of the esophagus, and obstruction due to compression of the gastrointestinal tract. Long-term compression leads to fistula formation, sometimes resulting in hemorrhage nearly rupture condition and sepsis.

1.3 Classification

Aneurysms are classified based on (1) the pathology (morphology) of the aneurysmal wall, (2) the site, (3) the cause, and (4) the shape of aneurysms (**Table 3**).[21]

1.3.1 Pathology (Morphology) of the Aneurysmal Wall

True aneurysm: Aneurysms in which the aneurysmal wall consists of the components of the aortic wall (three layers: intima, media, and adventitia) is a true aneurysm. However, a part of the wall can be composed without the three layers.

Pseudoaneurysm: "New cavity" formed outside the original aortic cavity with the aneurysmal wall that does not include components of the aortic wall (a fibrous cap and the adventitia can be included) is called a pseudoaneurysm. Such aneurysms communicate with the aortic lumen through an aneurysmal fistula. If thrombosis of damaged aortic wall occurs, it is called a "hematoma."

Dissecting aneurysm: Aortic dissection occurs when the aortic wall is dissected into two layers, resulting in the original aortic cavity (true lumen) and a newly formed cavity in the aortic wall (false lumen). Such an aneurysm with the saccular dilatation of the aorta (mainly dilatation of the false lumen) or an aneurysm with the entire circumference dilatation of the aorta (fusiform dilatation, extended dissection) is called a "dissecting aneurysm." The pathogenesis is observed in aortic dissection in the chronic phase.

1.3.2 Location of Aneurysms

Aneurysms are classified into thoracic, thoracoabdominal, and abdominal aneurysms, which are further classified as follows:

Thoracic: It is further classified into ascending, arch, and descending aortic aneurysms.

Thoracoabdominal: The Crawford classification based on the range of replacement in thoracoabdominal aneurysm surgery (**Figure 5**).

Abdominal: Abdominal aortic aneurysms are classified using the renal artery as the reference into the supra- and infra-renal segments.

Table 3. Classification of Aortic Aneurysms

Location:	Thoracic
	Thoracoabdominal
	Abdominal
Shape of aneurysm:	Saccular type
	Fusiform type
Morphology of the wall:	True
	Dissecting
	Pseudo
Cause:	Atherosclerotic
	Infected
	Traumatic
	Inflammatory
	Congenital
	Others

(Adapted from Matsuo H, 2004.[21])

1.3.3 Cause

Based on the cause of the aneurysm, aortic aneurysms are classified into atherosclerotic, traumatic, inflammatory, infected, congenital, etc. Most of them are atherosclerotic aortic aneurysms.

Etiology of Abdominal Aortic Aneurysm and Thoracic Aortic Aneurysm

The etiology of AAA has previously been considered as arteriosclerosis. However, a new etiology "degeneration" has been proposed. Therefore, the previous disease name, "atherosclerotic abdominal aortic aneurysm," does not reflect the pathogenesis. However, it cannot be denied that arteriosclerotic changes are always pathologically present in the intimal lesions in the aneurysmal wall. Regarding aortic aneurysm enlargement, it is an important factor contributing to the fragility of the aortic wall. In addition, inflammation due to arteriosclerosis and the destruction and recovery of vascular wall structure in response to immune reaction play an important role in the formation of dilatation lesions. Furthermore, other factors, such as developmental, hemodynamic, and genetic factors, have also been reported to contribute to the formation of dilatation lesions.

As described above, not only arteriosclerosis but also other factors are involved in the etiology of AAA. Therefore, it would be appropriate to refer to such lesions as "degenerative abdominal aortic aneurysms." On the other hand, in many cases, the etiology of TAA in the ascending aorta is medial lesions which are typical histological findings in patients with Marfan syndrome and vascular Ehlers-Danlos syndrome, characterized by a reduction in the number of elastic fibers in the aneurysmal wall. In contrast, atherosclerotic TAA is more commonly observed in the descending aorta. The findings are pathologically similar to AAA. In a broad sense, "degeneration" can be the etiology of an aneurysm.

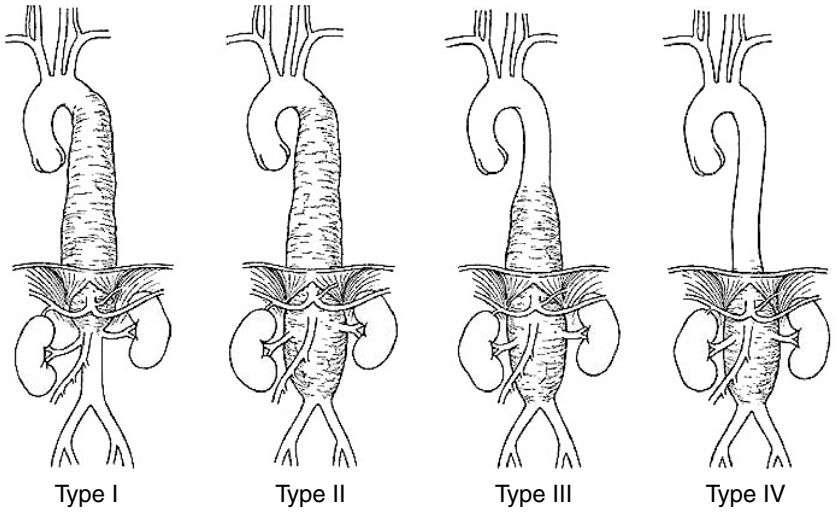


Figure 5. The Crawford classification of thoracoabdominal aortic aneurysms based on the extent of the prosthetic graft replacement.

1.3.4 Shape of Aneurysm

Aneurysms are classified into fusiform and saccular types based on the shape of aneurysms. The fusiform type is characterized by dilatation of the entire circumference of the aorta, whereas the saccular type has a saccular or a spherical shape due to unilateral and partial local dilatation (see **PQ 1**).

2. Definition, Pathogenesis, and Classification of Aortic Dissection

2.1 Definition

Aortic dissection is a dynamic pathology in which the aortic wall is dissected into two layers at the medial level. It has two-channel aortic lumen with a certain length along the aorta, and with blood flow or hematoma. Many cases of false lumen have blood flow, but some have thrombus without blood flow.[22,23] Although some studies set the length of the dissection at ≥1 cm,[24] there is no clear definition of it. Clinically, clear diagnostic imaging requires at least 1–2 cm of dissection for diagnosis of aortic dissection.

Aortic dissection consists of the original aortic lumen (true lumen) and the newly formed aortic lumen in the wall (false lumen) separated by the dissected flap composed of intima and part of media. The dissection flap usually has one or a few intimal tears that allow communication between the true lumen and the false lumen. However, some patients with no intimal tears have no communication between the two. The main intimal tear or primary tear that allows blood to flow from the true lumen into the false lumen is called 'the entry', whereas an intimal tear that allows resumption of blood flow from false lumen into the true lumen is called 'the re-entry'. The term "Re-dissection" is used in the case of a new dissection in a site other than the pre-existing false lumen or in the case of a new a 3-channel aortic dissection in the same site. In many cases, this disease does not lead to aneurysm formation just after onset of dissection. Therefore, it is usually called an "aortic dissection", not "dissecting aneurysm", which is used only if the diameter increases, leading to the formation of an aneurysm.

The onset mechanism of aortic dissection has not been fully elucidated. Aortic dissection is considered to be caused by a combination of "lesions in the media" and "hemodynamic load." is inferred that a decrease in the number of the elastic lamina[25,26] and interlaminar fibers interconnecting the elastic laminae[26,27] leads to the formation of lesions. They are supposed to be caused by heritable disorders of connective tissue[25] such as Marfan syndrome and hypertension.[27]

Previously reported "cystic medial necrosis" as a lesion in the media is often seen in patients with connective tissue diseases, such as Marfan syndrome. However, the findings cannot be generalized to other patients. Future studies should examine hemodynamic load mostly caused by shear stress due to hypertension[29,30] and aortic root motion.[31]

The most confusing terms related to dissection, as described below, are intramural hematoma (IMH), penetrating atherosclerotic ulcer (PAU), and ulcer-like projection (ULP). In Japan, aortic dissection has long been classified into two types: (i) aortic dissection with patent false lumen with blood flow; and (ii) aortic dissection with thrombosed false lumen without blood flow. On the other hand, in Western countries, "acute aortic syndrome (AAS)" has been classified into three types: classic dissection, IMH, and PAU[32] at first definition of AAS

IMH (intramural hematoma): In Western countries, it refers to aortic dissection with a thrombosed false lumen without blood flow because intramural hematoma (or intramural hemorrhage) has been recognized as a subtype of dissection. "Originally IMH" was pathologically defined as intramural hematoma (or intramural hemorrhage) without an intimal tear. However, with the advancement of diagnostic imaging, terms with a meaning different from the original term ("IMH with ulcer", "IMH with ULP", etc.) have been commonly used. Therefore, the term, IMH, was not used in the previous version (2011) of this guideline to avoid confusion. However, because the term, "IMH", is now common worldwide, IMH in this vision was interpreted

Table 4. Concept and Notations of Intramural Hematoma

Concept	Japanese notation	English notation
Thrombosed false lumen with no tears in the flap (Pathological concept, original concept of IMH)	Aortic dissection with thrombosed false lumen (**Figure 7A**)	IMH
Thrombosed false lumen with tears in the flap, which cannot be clinically identified (Clinical concept)	Aortic dissection with thrombosed false lumen (**Figure 7B**)	IMH
Thrombosed false lumen with ULP	ULP type aortic dissection (**Figure 7C**)	IMH with ULP IMH with ulcer Intimal defect with IMH
Patent false lumen with blood flow in the false lumen	Aortic dissection with patent false lumen (**Figure 7D–F**)	Aortic dissection or classic dissection

IMH, intramural hematoma; ULP, ulcer-like projection.

as a term with different perspectives and a meaning different from the original. The correspondence between terms in Japan and those in Western countries is summarized in **Table 4**.

PAU (penetrating atherosclerotic ulcer): PAU is defined as ulceration of the arteriosclerotic lesions extending below the internal elastic lamina and media.[33] PAU has a pathogenesis different from aortic dissection. PAU with extension to cephalocaudal direction in the medial direction becomes to be dissection, whereas PAU with progression toward the adventitia becomes to be saccular aneurysm or aortic rupture. A common problem with clinical practice is which is proper, progression of PAU into the media or dissection with limited extent. Another problem is a proper use of PAU and ULP (see **PQ 9**).

ULP (ulcer-like projection): ULP is "one of the findings of diagnostic images" of acute aortic dissection. ULP is defined as the contrast region of <15 mm in the cephalocaudal direction in a thrombosed false lumen evaluated by contrast-enhanced CT or angiography. ULP has been suggested as the primary entry in the ULP type dissection. Furthermore, ULP is an important observation point for the ULP type dissection because ULP enlargement (transition to aortic dissection with patent false lumen or leading to aneurysm formation) or loss (transition from shrinkage to aortic dissection with thrombosed false lumen) during clinical course can be used as a prognostic factor.

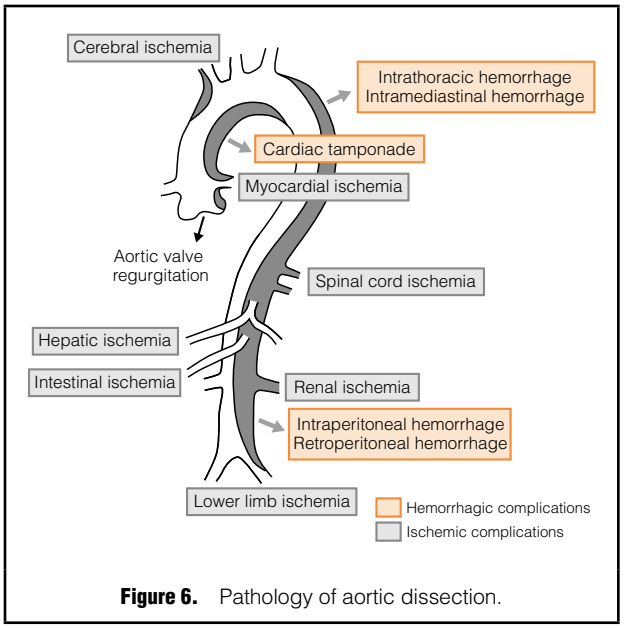


Figure 6. Pathology of aortic dissection.

2.2 Pathogenesis

Dissection of the aortic wall, which allows blood flow into the false lumen, shows temporal changes and has a dynamic pathology immediately after its onset. Furthermore, dissection progresses to distal aorta and branches in wide range, resulting in various pathogeneses (**Figure 6**). The pathogenesis of dissection is classified into, (1) rupture, (2) malperfusion, and (3) Other. For more details, see "**1. Symptoms**" in **Chapter III**.

Rupture: Rupture can be roughly classified into cardiac tamponade and rupture into the thoracic and abdominal cavities. Cardiac tamponade, one of the forms of aortic rupture, is the highest cause of death in Type A aortic dissection and accounts for about 85% of autopsy cases.[34] Cardiac tamponade can be caused by aortic wall rupture on the ascending aorta in a range until reflection point of pericardial cavity, resulting in aortic blood running into the pericardial cavity and rapid accumulation of blood (pericardial effusion) with collapse of hemodynamics. Rupture into the thoracic and abdominal cavities accounts for the remaining 15%.[34]

Malperfusion: Dissection leads to reduced blood flow into the aortic branch artery, resulting in organ ischemia. The mechanisms of malperfusion include: (i) static obstruction; in which blood flow in the true lumen of branch artery decreases due to direct dissection into branch artery, and (ii) dynamic obstruction in which blood flow of branch artery decreases due to the narrowing of the ostium of the branch artery by compression by intimal flap. In some cases, malperfusion in the coronary artery, the carotid artery, intercostal and lumbar arteries (the artery of Adamkiewicz), the celiac artery, the superior mesenteric artery, the renal artery, or the common iliac artery, leads to major organ failure such as myocardial infarction, cerebral infarction, paraplegia, liver disorder, bowel ischemia, renal dysfunction, hypertension, renal infarction, and lower limb ischemia, resulting in the cause of death of acute aortic dissection, respectively.

Others: Dissection of the aortic root may lead to aortic insufficiency, resulting in severe heart failure. Aortic dissection may lead to aortic dilatation in the chronic period, resulting in rupture of aortic aneurysm. The formation of

Table 5. Classification of Aortic Dissections

1. Classification based on the extent of dissection

Stanford Classification

Type A: Dissection is present in the ascending aorta

Type B: Dissection is absent in the ascending aorta

DeBakey Classification

Type I: A tear is present in the ascending aorta, and the dissection extends to the periphery from the aortic arch

Type II: A tear is present in the ascending aorta, and the dissection is localized to the ascending aorta

Type III: A tear is present in the descending aorta

Type IIIa: The dissection does not extend to the abdominal aorta

Type IIIb: The dissection extends to the abdominal aorta

The following subcategories can be added to the DeBakey Classification:

Arch type: A tear is present in the arch region

Arch localized type: The dissection is localized to the arch region

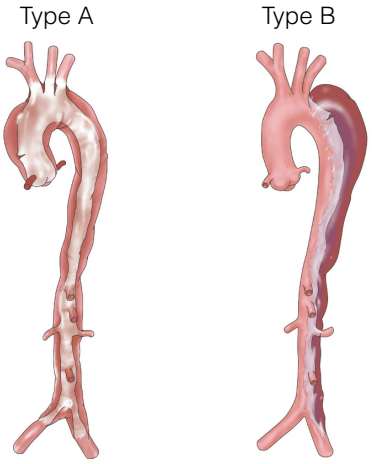
Arch extended type: The dissection extends to the ascending or descending aorta

Abdomen type: A tear is present in the abdominal region

Abdomen localized type: The dissection is present only in the abdominal aorta

Abdomen extended type: The dissection extends to the thoracic aorta

(The term "retrograde type III dissection" is not used)



2. Classification based on blood flow in the false lumen

Dissections with patent false lumen: Dissections with blood flow in the false lumen. In this type of lesion, the false lumen may show no thrombus, be partially thrombosed (partial thrombosis), or show more advanced thrombosis resembling the appearance of the ULP type

ULP type dissections: Dissections in which ULP (<15 mm) is observed even once in part of the thrombosed false lumen on contrast-enhanced CT examination within 2 weeks after the onset

Dissections with thrombosed false lumen: Dissections with a crescent-shaped false lumen with no influx of blood into the false lumen. This type of lesion has a thrombosed false lumen with no tears in flap or thrombosed false lumen with tears in flap, which cannot be clinically identified

3. Classification based on the disease phase

Acute phase: Dissections presenting within 2 weeks after onset, of which hyperacute phase refers to those presenting within 48 hours of onset

Subacute phase: Dissections presenting between 2 weeks and 3 months of onset

Chronic phase: Dissections presenting after more than 3 months of onset

ULP, ulcer-like projection.

massive thrombosis in the false lumen leads to disseminated intravascular coagulation (DIC) syndrome and inflammatory response.

2.3 Classification

Types of aortic dissection are classified based on three perspectives. Specifically, aortic dissections are classified based on (1) extent of dissection, (2) blood flow in the false lumen, and (3) disease phase (**Table 5**). To understand the pathogenesis and set the treatment strategy, these three factors should be considered to determine the disease type.

2.3.1 Classification Based on the Extension of Dissection

There are two classification methods: the Stanford classification and the DeBakey classification. The former method classifies aortic dissections based on whether the dissection extends to the ascending aorta (types A) or not (Type B) regardless of the site of entry.[35] In some cases, aortic dissections with entry or false lumen in aortic arch can be classified as "non-A non-B aortic dissection." The latter method classifies aortic dissections into type I, type II, type III (a, b) based on extension of dissection and the site of entry.[36]

2.3.2 Classification Based on Blood Flow in the False Lumen

Aortic dissections can be classified according to the status of blood flow in false lumen; aortic dissection with thrombosed false lumen, ULP type, and aortic dissection with patent false lumen.

Aortic dissection with thrombosed false lumen type: A crescent-shaped false lumen is observed, and there is no blood flow into the false lumen. Enhancement with contrast media in false lumen is not identified in the early phase of contrast-enhanced CT. However, in some cases, it is seen in the false lumen in the late phase. This type includes the cases without actual intimal tears (the original meaning of IMH) (**Figure 7A**) and cases with intimal tears but no observable blood flow in diagnostic imaging (**Figure 7B**). It is difficult to differentiate the two types.

ULP type: Aortic dissection is classified as ULP type if ULP in thrombosed false lumen is detected by contrast-enhanced CT within two weeks of after symptom onset (**Figure 7C**). Aortic dissection is not classified as ULP type if the size in the cephalocaudal direction is ≥15 mm (4 slice or more in 5-mm thick axial CT images). In such cases, it was not classified as ULP type but as an aortic dissection with a patent false lumen type. On the other hand, in cases

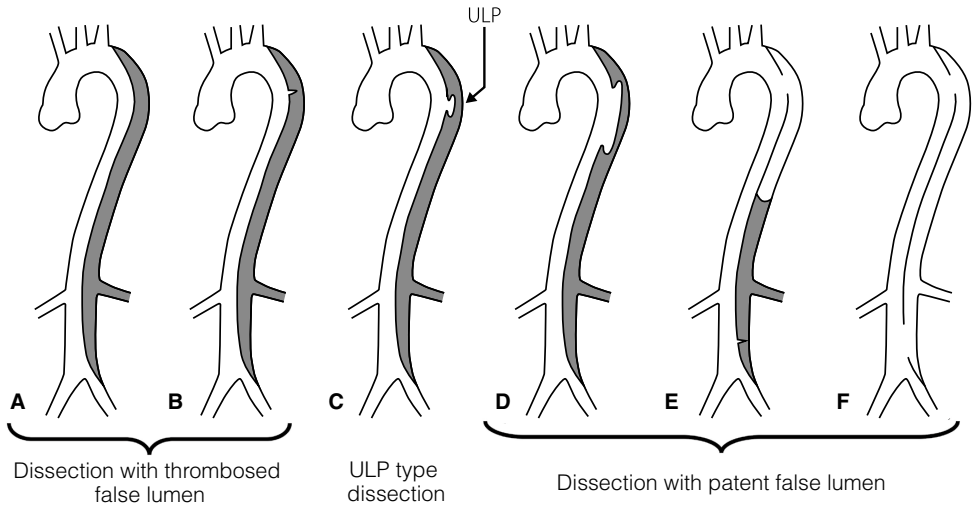


Figure 7. Classification of aortic dissections based on the condition of the false lumen.

Table 6. Regional Survey of the Incidence Rate of Acute Aortic Dissection

Year	Surveyed area	Surveyed population	Incidence/100,000 people/year
1997	North central region of Osaka Prefecture	6 million	3.12
1998	Mie Prefecture	1.6 million	3.7
1999	Hanshin area	10 million	2.67
1991–2000	Takatsuki City, Osaka Prefecture	0.37 million	2.62
1997–2005	Metropolitan area of Iwate Prefecture	1 million	5.2

(Adapted from Fukumoto H, 2002.[37])

of pooling of the contrast medium in intramural hematoma (IBP, which is due to injury of intercostal artery, described below), it is difficult to discriminate against ULP type. In case surely diagnosed with IBP based on its morphology, and it is not classified as ULP type.

Aortic dissection with patent false lumen type: If the false lumen is imaged by contrast-enhanced CT at the onset, it clearly differentiates between the true lumen and the false lumen by the dissection flap. This type includes three different conditions; no thrombus is seen in the false lumen (**Figure 7F**), partial thrombosis (**Figure 7E**) or progression of thrombosis (close to ULP type) (**Figure 7D**).

2.3.3 Classification Based on Disease Phase

Within the first two weeks of after symptom onset is classified as the acute phase. Between two weeks and three months after onset is classified as the subacute phase. While more than three months after onset is classified as the chronic phase. In emergency medical service, within 48 h after onset is classified as hyperacute phase.

3. Epidemiology

There is no Japanese national statistical data on aortic aneurysm and aortic dissection. Therefore, its accurate incidence is unknown. Statistical data from a small number of databases are shown below.

3.1 Annual Incidence

Although data of annual incidence from local area was rare, a few data was reported (**Table 6**).[37] Although annual incidence of acute aortic dissection was estimated to be approximately 3 per 100,000 population. According to the data from the Tokyo Acute Aortic Super-network, the annual incidence is 10 per 100,000 population.

According to the annual report by the Japanese Association for Thoracic Surgery (2011–2017), the estimates of the number of surgeries for both non-dissecting TAA and aortic dissection tend to increase (**Figure 8**).[38–43,43a] In addition, according to the annual report based on patients registered in the NCD by the Japanese Association for Vascular Surgery (2011–2014), the estimates of the number of surgeries for AAA also tend to increase (**Figure 9**).[43b]

3.2 Changes in the Incidence by Age

Based on estimations from autopsy cases, the age distribution of the onset of non-dissecting aortic aneurysm is

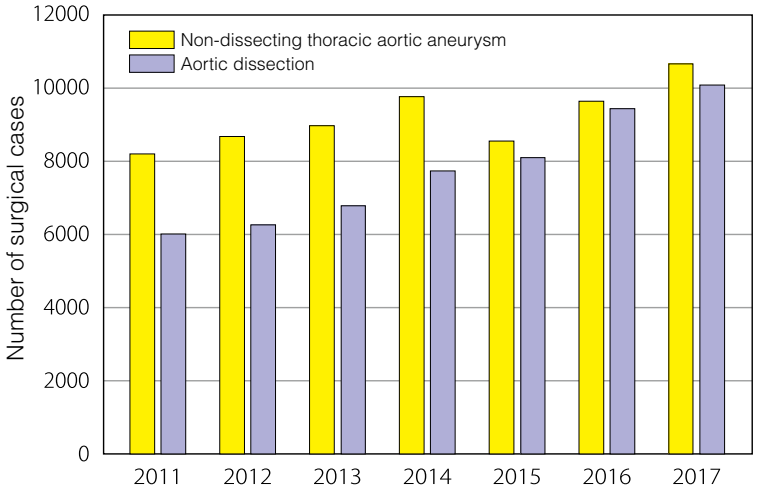


Figure 8. Annual changes in the number of surgical cases for non-dissecting thoracic aortic aneurysm and aortic dissection in Japan. (Source: Prepared based on Amano J, et al. 2013,[38] Masuda M, et al. 2014,[39] 2015,[40] 2016,[41] 2018,[42] Shimizu H, et al. 2019,[43] 2020.[43a])

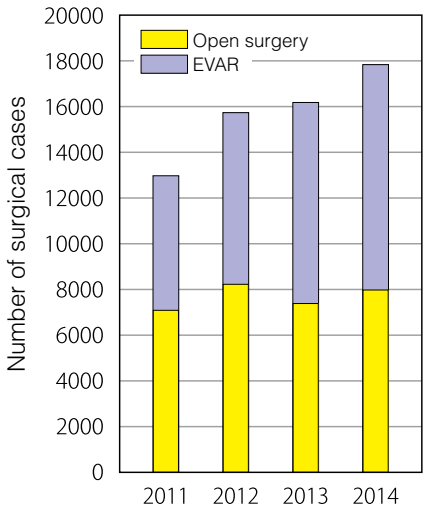


Figure 9. Annual changes in the number of surgical cases for non-dissecting abdominal aortic aneurysm in Japan. (Source: Prepared based on the Japanese Society for Vascular Surgery[43b])

shown in **Figure 10A**, in which those at the onset peak were men in their 70s and women in their 80s.[44] The higher incidence of non-dissecting aortic aneurysm in the elderly may be due to arteriosclerosis. As shown in **Figure 10B**, those who were at the onset peak of aortic dissection were in their 70s.[44]

3.3 Changes in the Incidents by Season, Time of Day, and Day of Week

The incidence of aortic dissection tends to be higher in winter than in summer.[34,45,46] In terms of time of day, the incidence was higher during the day especially at the most active time of the day (between 6:00 AM and 12:00 PM). In contrast, the incidence was lower between midnight and early morning.[45–47] There was no day-of-week effect.[34]

3.4 Aortic Dissection Based on Cases of Sudden Death

Because autopsy data from the Tokyo Medical Examiner's Office were mostly data with death soon after the onset, the following data are likely to be autopsy reports of sudden death. The incidence of death before reaching to the hospital was 61.4%. The incidence of death within less than 1h from the onset was 7.3%. The incidence of death within 1–6h from the onset was 12.4%. The incidence of death within 6–24h from the onset was 11.7%. The incidence of death within 24h (including death before reaching the hospital) was 93%. Regarding the time of onset of dissection, the incidence of dissection in acute phase was 94.5%. Of these cases, the incidence of DeBakey type II aortic dissection was 38.1%, the highest. In general autopsy, incidence of DeBakey type I aortic dissection was usually highest. The direct cause of death was aortic rupture in 98.5% of cases of sudden deaths. Of them, cardiac tamponade accounted for 86.6% and rupture into left or right thoracic cavity accounted for 8.1%. Cause of sudden death other than aortic rupture was only 1.5%, and was inferred to be myocardial ischemia due to the extension of the dissection to the coronary arteries. In general, the right coronary artery has been frequently reported to contribute to sudden death. However, in cases of sudden death, the incidence of the dissection of the left coronary artery was higher.

4. Glossary

4.1 Aortic Aneurysm

Thoracic aortic aneurysm (TAA): A term for aortic aneurysms in the thoracic cavity. The ascending aorta refers to the aorta extending from the aortic annulus to the brachiocephalic artery branches. The aortic arch refers to the aorta extending from the origin of the brachiocephalic artery to the T3–T4 thoracic levels (bifurcation of the pulmonary artery). The descending aorta refers to the aorta extending from the T3–T4 thoracic levels to the lower thoracic levels.

Thoracoabdominal aortic aneurysm (TAAA): A term for the

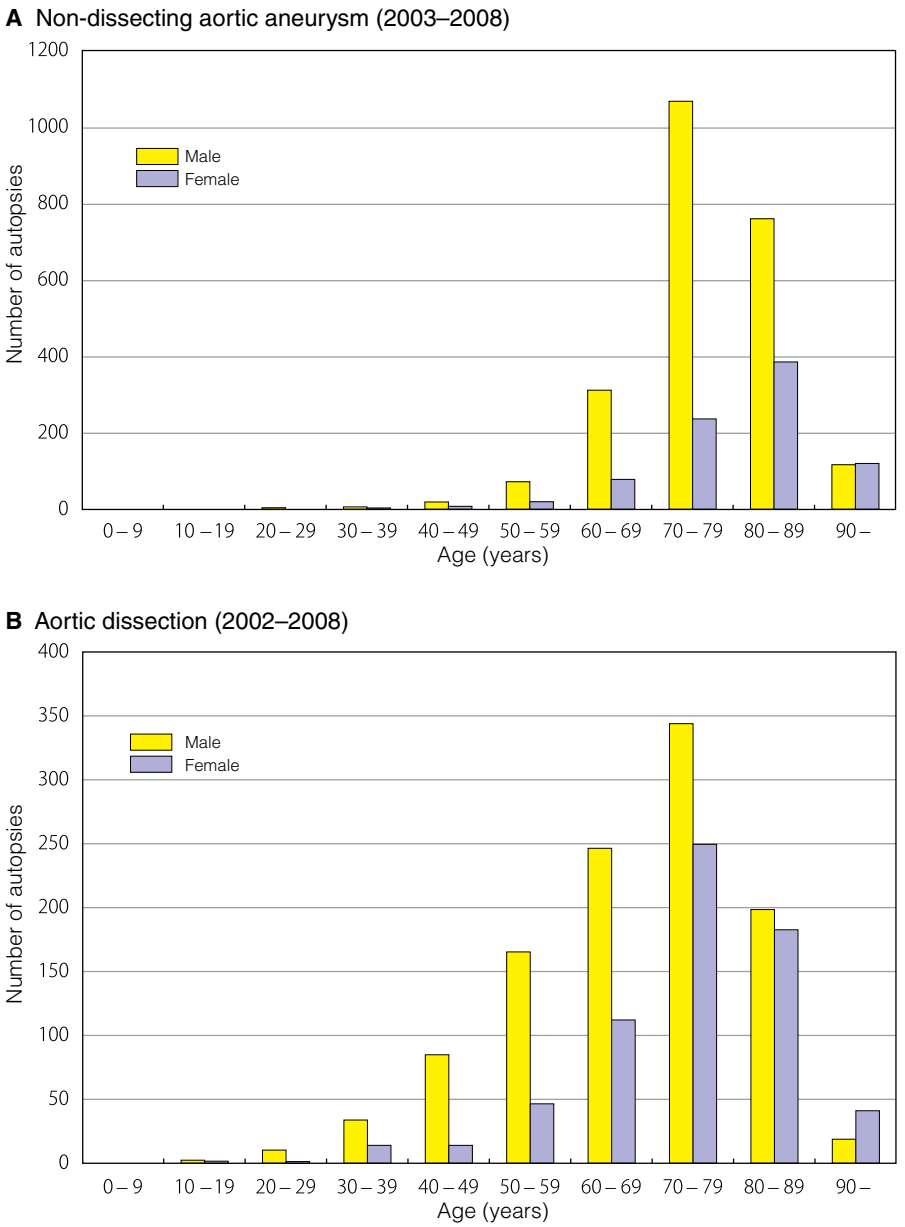


Figure 10. Age distribution of the number of autopsies for non-dissecting aortic aneurysm and aortic dissection in Japan. (Source: Prepared based on the Japanese Society of Pathology[44])

area extending from the thoracic cavity to the abdominal cavity. The aneurysm is classified based on the range of the replacement of vascular prosthesis into four types using the Crawford classification (**Figure 5**).

Abdominal aortic aneurysm (AAA): A term for an aneurysm that occurs in the abdominal aorta.

True aneurysm: In general, it is a synonym for so-called aortic aneurysm. It is used to clearly differentiate the aneurysm from a "dissecting aneurysm" or "pseudoaneurysm". Although the aneurysmal wall consists of the original arterial wall, the media may not be histologically confirmed when the aneurysm is enlarged.

Dissecting aneurysm: Aneurysm caused by aortic dissection.

Pseudo- (false aneurysm) aneurysm: Aneurysm without the aortic wall. It is mostly caused by trauma or infection.

Fusiform type aortic aneurysm: A type classified based on aortic aneurysmal morphology.

Saccular type aortic aneurysm: A type classified based on aortic aneurysmal morphology.

Fusiform or saccular type aneurysms: Fusiform aneurysm is defined as the circumferential dilatation of the vessel with a diameter of more than 1.5 times the normal diameter. A saccular aneurysm is defined as a partial aneurysmal bulge. When clear differentiation is difficult, the aneurysm is classified as a saccular aneurysm. Clinically, saccular aneurysms are unstable. Therefore, in many cases, surgery

is indicated for saccular aneurysms regardless of the size of the thickening (See **PQ 1**).

Inflammatory aortic aneurysm: Aneurysm caused by inflammation. Although, in general, "inflammation" is a concept that includes infection, however, inflammatory aortic aneurysm does not include the aortic aneurysm with infection.

Inflammatory periaortitis: A case with inflammation around the aorta but with less aortic dilation that does not meet the criteria of aneurysm.

Infected aortic aneurysm: Aneurysm caused by infection.

Rupture: Extravascular blood leakage due to damage to the arterial wall.

Impending rupture: The absence of damage to the arterial wall despite the presence of aneurysmal pain.

4.2 Aortic Dissection

Dissecting aneurysm: Aortic dissection with aneurysmal formation. A general term that was previously used for overall aortic dissection. However, because in many cases with aortic dissection in acute phase does not meet the criteria for an aneurysm, aortic dissection in acute phase is now called, "acute aortic dissection."

True lumen: The original arterial cavity.

False lumen: A new cavity formed in the arterial wall (the term "dissection cavity" is not appropriate).

Dissection flap: The (intima-media) septal wall. It used to be called "intimal dissection." However, it actually consists of intima and a part of the media.

Tear: Intimal and medial tears of aortic dissection which is the site of communication between the true lumen and the false lumen. "Intimal tear" is also regularly used as a synonym for "tear".

Entry: A site where blood flow enters from the true lumen to the false lumen.

Re-entry: A site where blood flow enters from the false lumen to the true lumen.

("communication window" that is also used as a term for both entry and re-entry)

Aortic dissection with patent false lumen: It is a synonym for "communicating aortic dissection", a type of aortic dissection in Europe classification. It is also called "classic dissection" or "double barrel aorta." One of the three types of aortic dissection in Japanese

Aortic dissection with thrombosed false lumen: It is a synonym for "noncommunicating aortic dissection", a type of aortic dissection in Europe classification. One of the three types of aortic dissection in Japan.

Ulcer-like projection (ULP): Protrusion in a part of the thrombosed false lumen detected by diagnostic imaging, such as angiography. Although the sensitivity varies by diagnostic imaging techniques, "image findings" show various pathogenesis (tear, artery branch injury, arteriosclerotic ulcer site, etc.) Due to unstable pathogenesis regardless of the size, it requires close monitoring. Therefore, to seek attention, it is recommended to treat "the ULP type dissection" described in the next section with the same procedure as for "aortic dissection with patent false lumen type" (For details, see **PQ 9**).

ULP type dissection: Dissection with ULP. One of the three types of aortic dissection in Japan.

Classic aortic dissection: Dissection with a tear or a flap. One of the three types of acute aortic syndrome in Western countries. It is almost equivalent to the Japanese term "aortic dissection with patent false lumen."

Intramural hematoma (IMH): Originally, dissection without a tear. One of the three types of acute aortic syndrome in Western countries. It is almost equivalent to the term "aortic dissection with thrombosed false lumen" used in Japan (for details, see **PQ 9**).

Intramural hemorrhage: It is a synonym for intramural hematoma.

Penetrating atherosclerotic ulcer (PAU): Ulceration of arteriosclerotic lesions, extending below the internal elastic lamina and media. One of the three types of acute aortic syndrome in Western countries.

Intramural blood pool (IBP): Blood pooling space in IMH, and they are often associated with an adjacent aortic branch artery, like the intercostal, bronchial and lumbar arteries. It needs to be discriminated from ULP.

Re-dissection: Aortic dissection at a site other than the pre-existing dissection site. Or a 3-channel aortic dissection at the same site.

Re-canalization: Blood flow recovery in aortic dissection with thrombosed false lumen without blood flow.

Retrograde dissection: It refers to an extensive retrograde dissection to the proximal aorta. Type A dissection with ULP distal to the left subclavian artery is strongly suggestive of the presence of retrograde dissection.

Extension of aortic dissection: Extension of dissection mainly in the longitudinal direction of the aorta. Re-progression of the completed dissection after some time can be classified as re-dissection.

Enlargement of the dissection (false lumen): Extension of the false lumen in the short axis direction.

PQ 1.
Is a Saccular Type Aneurysm an Indication for Early Surgery?

Recommendation

Saccular aneurysms, particularly those that are markedly protruded, are more likely to rupture, but the rupture risk assessment has not been established, and the surgical indication for saccular aneurysms must be carefully evaluated.

Aortic aneurysms are morphologically classified into fusiform and saccular. The surgical indication of fusiform aortic aneurysms is often determined according to the aortic diameter, but as the risk of rupture is considered high in saccular aneurysms, surgery is often indicated in an earlier stage despite a smaller aortic diameter compared with fusiform aneurysms. Therefore, whether the aneurysm is fusiform or saccular is one of the most important factors for making decisions. Generally, saccular aneurysms are defined as "focal or asymmetric aortic enlargement",[48] but this description is vague, and a more precise definition has been considered necessary.

Recently, the finite element analysis has shown that there are true saccular aneurysms at a high risk of rupture and "aneurysms that have been recognized as saccular aneurysms" at a low risk of rupture similarly to fusiform aneurysms. If, as shown in **Figure 11**, a sac depth/neck width of >0.8 is defined as the criterion for high-risk saccular aneurysms, saccular aneurysms with a sac depth/neck width of >0.8 have low wall shear stress[49] and, consequently, a high risk of rupture.[50] Also, if, as shown in

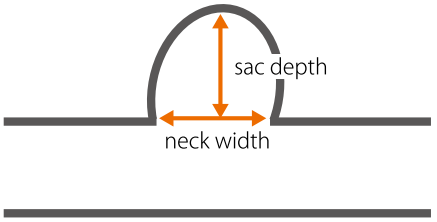


Figure 11. Definition of high-risk saccular aneurysm (1).

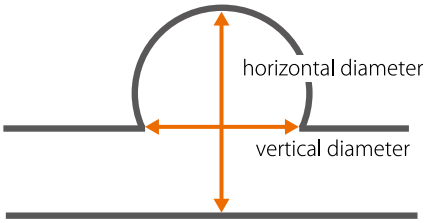


Figure 12. Definition of high-risk saccular aneurysm (2).

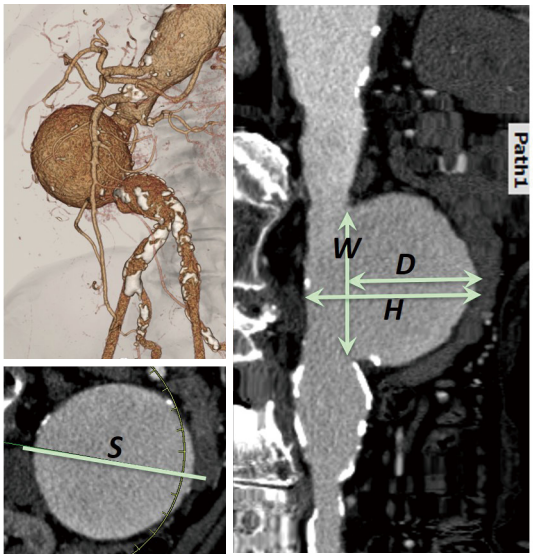


Figure 13. High-risk saccular aneurysm.
The right image was prepared by linearizing the sagittal section at the sagittal line (S).
sack depth (D)/neck width (W) = 1.03 > 0.8
neck width (W)/horizontal diameter (H) = 0.73 < 1.0
(D=54.8 mm, W=53.0 mm, H=72.2 mm)

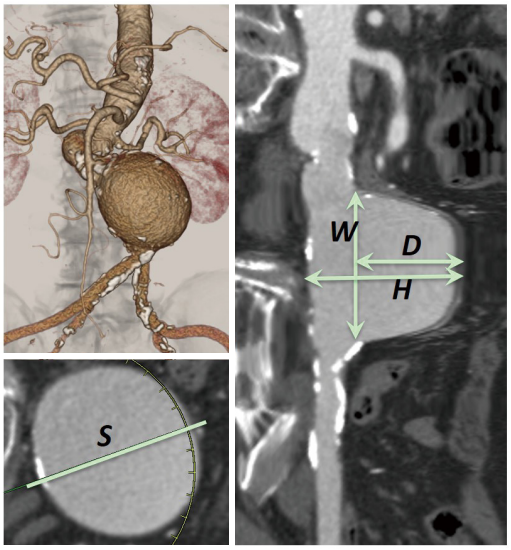


Figure 14. Low-risk saccular aneurysm.
The right image was prepared by linearizing the sagittal section at the sagittal line (S).
sac depth (D)/neck width (W) = 0.64 < 0.8
neck width (W)/horizontal diameter (H) = 1.01 ≥ 1.0
(D=36.0 mm, W=56.5 mm, H=55.8 mm)

Figure 12, an aspect ratio (vertical diameter/horizontal diameter) of <1.0 is defined as the criterion for high-risk saccular aneurysms, the maximum principle stress has been shown to be very high when the aspect ratio is <1.0.[51] As observed above, the definition of high-risk saccular aneurysms is not uniform, but it has been suggested that the sac depth/neck width increases, but the vertical/horizontal diameter decreases, as a saccular aneurysm is more markedly protruded and leads to high risk of rupture. Therefore, saccular aneurysms that fulfill the above criteria need to be considered at a higher risk of rupture compared with fusiform aneurysms and may be regarded as "true saccular aneurysms". However, caution is necessary in saccular aneurysms with a short protrusion (neck width or vertical diameter), because the risk is overestimated according to the above parameters.

Also, the assessment of saccular aneurysms is difficult if the aorta is curved at the site of the aneurysm. In such a case, it is possible to make evaluation by linearizing images by the technology also adopted in CT examination of the coronary artery. Although both the lesions in **Figures 13** and **14** appear saccular in 3D-CT images, calculation after linearization indicates that the lesions in **Figures 13** and **14** are a high-risk and low-risk saccular aneurysm, respectively.

There are also reports that the enlargement rate of saccular aneurysms is not different compared with fusiform aneurysms[52] and that the maximum wall pressure after correction for the aortic diameter does not differ between saccular and fusiform aneurysms.[53] Many "fusiform aneurysms that appear saccular aneurysms" as mentioned above are considered to have been included in the study population because of the vagueness of the definition of saccular aneurysms. The size that is an indication of invasive treatment for saccular aneurysms cannot be set precisely. However, in a cohort study that included a large number of AAA, rupture at the diameter <45 mm was 8.4% in the

saccular aneurysms and rupture at the diameter <55 mm was 8.1% in the fusiform aneurysms. These results are leading to the conclusion that "the indication size of fusiform aneurysm – 10 mm" is a recommendable indication of invasive treatment for saccular aneurysm.[54] If this view is adopted, an indication of invasive treatment for saccular aneurysms may be a horizontal diameter of ≥45 mm in AAA and ≥50 mm in TAA.

Unfortunately, the method for risk assessment of rupture of saccular aneurysms including definitions has not been established, and indications of treatment must be evaluated in consideration of this fact.

II. Pathology

1. Normal Aorta and Its Age-Related Changes, and Atherosclerosis

The aorta begins in the sinus of Valsalva/aortic sinus, including the aortic valve, and continues to the ascending, arch, thoracic descending, and abdominal aorta. A normal aorta consists of three layers: the intima, media, and adventitia. The intima is comprised of a single layer of endothelial cells and a subendothelial layer of loose fibroconnective tissue, while the media is composed of elastic laminae made of elastic fibers running in parallel, collagen fibers, and proteoglycan, as well as smooth muscle cells that produce them. The ascending aorta contains the largest number of medial elastic laminae, with 50–60 layers, while 30 or fewer layers are found in the descending aorta (**Figure 15**). An aneurysm occurs when the following three changes become excessive due to atherosclerosis, medial degeneration, or aging: (1) decrease in the medial smooth muscle cells, (2) fragmentation of elastic fibers, and (3) increase in the extracellular matrix, each of which results in dilatation, elongation, and meandering of the blood vessels (**Figure 16**). The adventitia is composed of sparse connective tissue, in which the vasa vasorum, peripheral nerves, and lymph nodes are diffusely present. The vasa vasorum of the adventitia supply oxygen to one-third of the outer layer of the media, and normally, blood vessels are not distributed further to the inner side. However, medial destruction by inflammation or degeneration leads to angiogenesis in the media. Aortic diseases are broadly divided into atherosclerosis, medial degeneration due to medial degenerative disease, and inflammatory diseases,

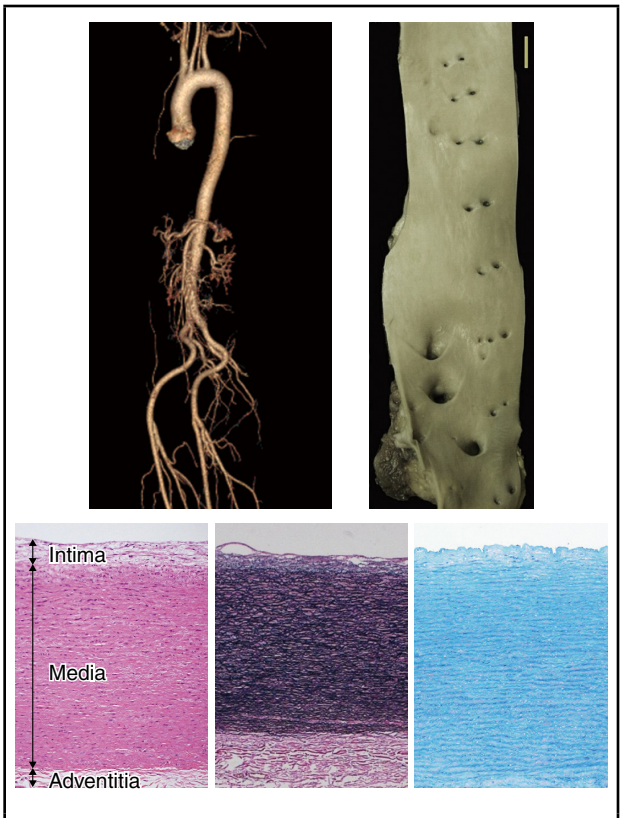


Figure 15. Structure of the normal aorta (Representative patients in their 20s; Non-identical cases). Lower photomicrographs of H&E, EVG, and Toluidine blue stainings.

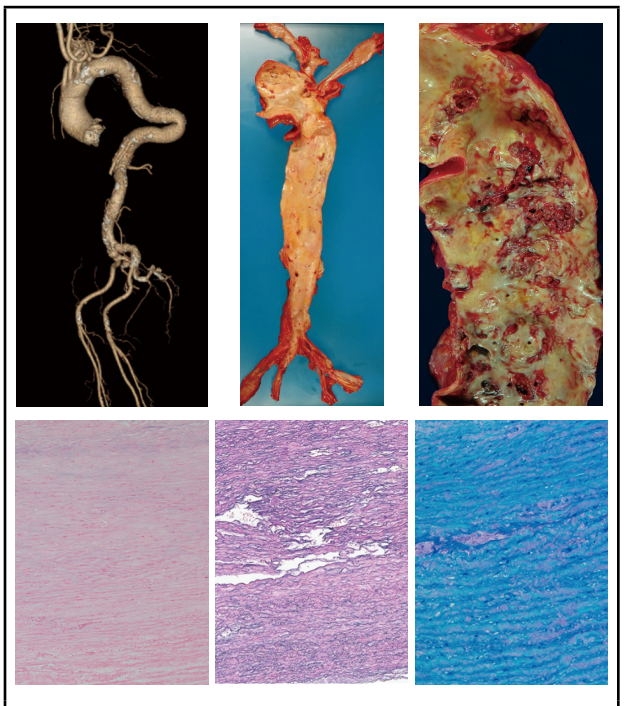


Figure 16. Age-related changes (tortuous, or atherosclerosis) of the aorta (Representative patients in their 80s; Non-identical cases). Lower photomicrographs of EVG, and Toluidine blue stainings show medial degeneration.

many of which result in aortic aneurysm, and the destruction of medial elastic laminae and hemodynamic effects lead to aortic aneurysm formation.[55]

2. Aortic Lesions

The histopathological changes of the aorta in the intima are mainly fibrocellular intimal thickening and atherosclerosis, and disorders that primarily affect the media include connective tissue diseases and inflammatory diseases, each of which is discussed in a separate section.

3. What Is Aortic Aneurysm?

Aortic aneurysm is a condition of localized or diffuse dilatation of the aortic wall and its protrusion toward the adventitia. However, a true aneurysm contains aortic aneurysmal wall composed of the intima, media, and adventitia, while a pseudoaneurysm has an aneurysmal wall lacking medial components and is composed of the adventitia or surrounding fibrous tissue (**Figure 17**). In a dissecting aneurysm, blood flows into the medial muscular layer through an intimal tear called entry, forming a false lumen, and dilatation of the false lumen increases the vascular diameter.[55]

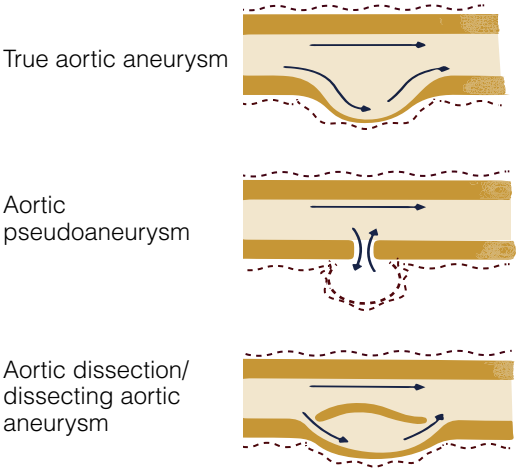


Figure 17. Classification of aortic aneurysm.

4. Atherosclerosis

Atherosclerosis is a change that impairs the vascular function due to the decreased elasticity of the arterial wall caused by inflammation, fibrosis, or calcification (**Figure 18**). It is caused by chronic pressure overload, such as age-related changes and hypertension. The aorta presents with dilatation and stenotic lesions, mainly due to advanced atherosclerosis with calcification. AHA has classified atherosclerotic lesions into early lesions (grades I, II), moderate lesions (grade III), and advanced/complicated lesions (grades IV, V, VI).[56–58]

Advanced/complicated lesions form atheroma consisting of collagen fiber proliferation and excessive lipid deposition (cholesterin deposition) under the fibrous thickened intima, along with inflammation by T-lymphocytes and macrophages. Additionally, calcification appears in the thickened area of the intima. Atheroma formation in the abdominal aorta is most prominent under the renal arteries. The iliac arteries often present with severe atherosclerotic stenosis. In the thoracic aorta and its branches, atheroma formation around the origins of the trifurcation of the arch to the carotid and subclavian arteries often precedes atherosclerosis. The surface of the atheroma exhibits ulcer formation due to endothelial cell injury, and it is called a complicated lesion if thrombosis is formed at the site, corresponding to grades IV to VI of the AHA classification[56–58] (**Figure 18**). At this stage, a large amount of atheroma spreads to the media, resulting in the thinning of the media. As a result, aneurysm formation and aortic dissection tend to occur.

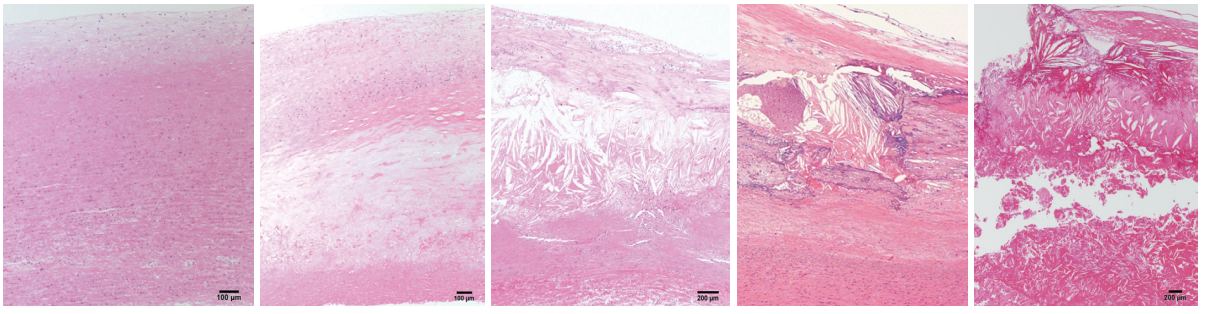


Figure 18. Grades of aortic atherosclerosis (AHA Classification). Grade IV or higher grades indicate complicated lesions.

5. Aortic Dissection Due to Atherosclerosis

Atherosclerosis-related aortic dissection occurs based on penetrating atherosclerotic ulcer (PAU), and the base of the ulcer of PAU ruptures, progressing to dissection.[59–64]

6. Aortic Dissection Due to Heritable Connective Tissue Disorders

Abnormal formation of the extracellular matrix, an important component of the media of the aorta, due to the genetic background causes abnormalities in the media, leading to dilatation and dissection. In Marfan syndrome, fibrillin-1 gene (FBN1) mutations destabilize the microfibril in the media, resulting in fragile connective tissue. Although there are histological differences among the sites, disruption and fragmentation of elastic fibers are notable, and the extracellular matrix (mainly proteoglycan) accumulates between the disrupted elastic fiber layers, presenting an image of so-called cystic medial necrosis (CMN). In addition to Loeys-Dietz syndrome, which is caused by mutations in the TGF-β receptor, genetic abnormalities of the TGF-β signaling pathway have been identified in other familial thoracic aortic aneurysms and dissections in recent years. Additionally, fibrillin-1, which is the causative protein of Marfan syndrome, was also shown to be a signal regulator of TGF-β. (See "**1. Hereditary Aortic Diseases**" in **Chapter VIII**.)

III. Symptoms, Examinations, and Diagnoses

1. Symptoms

1.1 Symptoms of Aortic Aneurysm

Thoracic aortic aneurysm (TAA) and abdominal aortic aneurysm (AAA) are mostly subclinical and often diagnosed unexpectedly during imaging examinations. However, aortic aneurysm should be considered as one of the differential diagnoses during examinations as it may cause comorbid symptoms depending on its site, size, and enlargement rate.

Patients with TAA may experience cough, shortness of breath,[65] odynophagia, dysphagia,[66] and hoarseness, while those with AAA may experience continuous or intermittent abdominal pulsating feeling, abdominal pain, and abdominal discomfort. Aneurysmal pressure may cause a feeling of fullness when eating, resulting in reduced appetite. On the other hand, patients often present with sudden pain in the chest, abdomen, back, or buttocks during rupture or impending rupture of an aortic aneurysm, and its rupture results in a collapse of vital signs. In rare cases, heart failure symptoms due to high output heart failure from aorto-caval fistula, hematemesis and melena from aortic gastrointestinal fistula, or hemoptysis from aortic tracheal fistula may occur.

1.2 Clinical Symptoms of Acute Aortic Dissection

The clinical symptoms of acute aortic dissection include pain/syncope caused by dissection itself and sequelae (complications) secondary to dissection. The sequelae due to dissection are divided into three types: rupture/hemorrhage, malperfusion, and others.

1.2.1 Pain and Syncope at the Time of Onset

a. Pain

Pain is the main symptom in the acute phase, and is listed as an important risk marker for aortic dissection detection risk score (ADD-RS) in Europe and the United States. The majority of the patients complain of intense pain in the chest or back during its onset, and it is often described as severe pain that they have never experienced. It is a sharp and tearing pain characterized by a sudden onset. Anterior chest pain is characteristic of Type A dissection, while back and abdominal pain is characteristic of Type B dissection. In addition, the pain may migrate with the extension of the dissection site, or conversely, it may temporarily disappear when its extension stops. On the other hand, it is also important to note that approximately 6% of acute aortic dissections are painless.[67]

b. Syncope

Syncope without typical pain is experienced by 9–20% of the patients.[68,69] Syncope occurs due to cardiac tamponade or cerebral ischemia when acute aortic dissection reaches the heart or cerebral blood vessels; however, it may also be caused by vagal reflex due to pain.

1.2.2 Sequelae of Dissection

a. Rupture

Rupture of the ascending aorta dissection in the pericardial sac results in cardiac tamponade. Cardiac tamponade is the most serious cause of death in the acute phase, and according to autopsy case reports, the cause of death in 70% of the cases is the perforation into the pericardial cavity.[70] In particular, cardiac tamponade may develop if the dissection extends to the ascending aorta covered by the pericardium. Cardiac tamponade is caused by the accumulation of hemorrhagic effusion due to perforation in the pericardial sac of the dissected aorta; however, the time course until its onset varies depending on the amount and accumulation rate of hemorrhagic effusion. Also, hemorrhage due to intrathoracic/celiac perforation is observed when rupture occurs from thoracic/abdominal aortic dissection. Based on aortic dissection autopsy cases, massive lethal hemorrhage is most commonly observed in the left thoracic cavity, followed by the mediastinum and retroperitoneal space.[71]

b. Malperfusion of Thoracic/Abdominal Aortic Branches

Stenosis or occlusion in an aortic branch due to dissection leads to malperfusion of the organ receiving blood from the branch, resulting in various symptoms. Malperfusion is classified into three types: (1) dynamic obstruction (blood that has entered the false lumen from the entry has no place to escape, and the blood collected in the false lumen presses on the true lumen, interfering with the branch perfusion),

(2) static obstruction (the dissected intima enters the branch and occludes it, interfering with the branch perfusion), and (3) a combination of (1) and (2). For details on the treatment for each malperfusion, see the section on treatment of "**3. Stanford Type B Aortic Dissection**" in **Chapter VI**.

i. Coronary Artery

According to autopsy case reports, 3–7% of all aortic dissections extend to the coronary arteries.[25,72] Myocardial ischemia, excluding shock cases, accounts for 3–9% of Type A dissection,[72,73] and it presents with various clinical symptoms found in coronary artery diseases, such as chest pain, atrioventricular block, and dyspnea. Since dissection often extends from the right coronary cusp to the non-coronary cusp at the base of the aorta, impaired blood flow due to dissection is more likely to occur in the right coronary artery than in the left coronary artery.

ii. Cerebral Blood Vessels

When the dissection reaches the carotid and vertebral arteries, various neurological symptoms are exhibited due to abnormal cerebrovascular perfusion, hypotension, distal thromboembolism, and nerve compression. Cranial nerve symptoms are divided into impaired consciousness and local neuropathy; however, the symptoms and their severity vary. Both are caused by an abnormal blood flow in the arch branches; however, impaired consciousness may also be caused by systemic circulatory failure due to myocardial ischemia or massive hemorrhage. The complication rate of cerebral ischemia is 3–7%. Cerebral infarction is most commonly caused by stenosis or occlusion of the brachiocephalic artery or left common carotid artery.

iii. Spinal Cord Ischemia

Lower limb paraplegia occurs in approximately 4% of the patients.[71,74] The upper part of the spinal cord is mainly nourished by the branched blood flow of the vertebral arteries, which is rarely damaged by aortic dissection. On the other hand, the main blood flow to the lower part of the spinal cord is maintained by the branches of the intercostal and lumbar arteries, which are directly branched from the aorta. In particular, the branch that connects to the anterior spinal artery between the lower thoracic spine and the upper lumbar spine (Adamkiewicz artery), which is called the arteria radicularis magna, is usually thicker than other spinal branches. Stenosis of the intercostal and lumbar arteries, their interruption from the true lumen, or occlusion of the false lumen by thrombosis due to descending aorta dissection results in an impaired blood flow of the Adamkiewicz artery, causing ischemia in the middle of the thoracic spinal cord, which divides the upper and lower parts of the spinal cord. Although transverse spinal symptoms may occur, the anterior part of the spinal cord, that is, the motor nerve region, can be easily damaged, causing paraplegia.

iv. Intestinal Ischemia

Intestinal ischemia occurs concomitantly due to stenosis or occlusion of the celiac and superior mesenteric arteries with a complication rate of 2–7%.[70,73,75,76] However, it is difficult to clarify its pathology, and it may appear abruptly after surgery. Also, its complication rate was reported to be higher in Type B dissection than in Type A dissection.[72] Aortic dissection with intestinal ischemia has a poor prognosis,[77] and the diagnosis should be made by paying attention to its symptoms, such as abdominal pain and melena, and elevated blood lactate and LDH levels.

v. Renal Ischemia

Impaired renal blood flow due to malperfusion occurs in approximately 7% of the patients[71] and presets with oliguria and hematuria. Hypertension may occur concomitantly due to renal artery stenosis. Some studies have reported that the left kidney is more susceptible to malperfusion-related ischemia than the right kidney, while others have reported that there is no laterality. Thus, there is no consensus on the difference between the left and right kidneys.

vi. Limb Ischemia

The disappearance of lower limb pulse due to stenosis/occlusion of the iliac artery, or due to aortic stenosis or thrombosis occlusion in some cases, and lower limb ischemia symptoms occur in 7–18% of the patients.[73,75] These often occur after extensive dissection, and are frequently complicated by multiple-organ ischemia. Invasive treatment intervention needs to be considered for lower limb ischemia. Severe ischemia may be complicated by myonephropathic metabolic syndrome (MNMS), which is an ischemia-reperfusion injury. On the other hand, upper limb ischemia is caused by stenosis/occlusion of the brachiocephalic and subclavian arteries, and is found in 2–15% of patients with Type A dissection.[75,76] Regardless of the presence or absence of clinical symptoms, upper limb ischemia, including the laterality of upper limb blood pressure (>20 mmHg), is found in approximately half of the cases.[68]

c. Other Pathological Conditions

i. Aortic Valve Regurgitation

Aortic valve regurgitation is exhibited when dissection is present in the ascending aorta, and approximately half of the dissection cases require surgery for the aortic valve.[75] When the dissection extends to the aortic valve annulus, the commissural region and annular ring are detached from the aortic wall and pushed medially and inferiorly, and regurgitation is caused as the valve leaflet droops in the left ventricle. In particular, the extension of dissection from the non-coronary cusp to the right coronary cusp results in the loss of support of the valve leaflet at the site, making it likely to droop. Its symptoms include chest pain followed by heart failure symptoms, such as respiratory discomfort.

ii. Acute Heart Failure

Aortic valve regurgitation, decreased coronary artery blood flow, and myocardial infarction often cause acute left heart failure, such as dyspnea. On the other hand, left heart failure symptoms may occur due to myocardial ischemia, existing dilatation dysfunction, and uncontrolled hypertension, even in Type B dissections.

iii. Coagulation Abnormalities, Fever, and Respiratory Impairment

Disseminated intravascular coagulation (DIC) due to aortic dissection often results from massive hemorrhage due to rupture or formation of a massive thrombus in the false lumen in the acute phase. However, it may develop in the chronic phase or postoperatively due to prolonged abnormal blood coagulation. DIC due to aortic dissection shows pathological features of enhanced fibrinolysis. In addition, regardless of the presence or absence of rupture, the accumulation of pleural effusion is relatively common, which may be serous or hemorrhagic. After the onset of acute aortic dissection, systemic inflammatory response syndrome (SIRS) may be induced by vascular inflammation or activation of the coagulation fibrinolytic system, and approximately 30% of the patients suffer from fever above 38°C.[77] Some cases show prolonged oxygenation disorders.

2. Sample Blood Examinations

Aortic aneurysm and dissection are diagnosed primarily by imaging examination, in which blood tests play a small role. However, blood tests are useful for differentiating them from other serious diseases and for diagnosing malperfusion that complicates aortic dissection. Furthermore, patients with aortic diseases often have atherosclerotic risk factors, such as hypertension, dyslipidemia, diabetes, hyperuricemia, obesity, and smoking, and blood tests are also important for the risk management for atherosclerotic diseases that extends to other areas.

2.1 Aortic Aneurysm

Various biomarkers specific for diagnosing unruptured aortic aneurysm have been investigated, including fibrinogen, D-dimer, CRP, IL-6, and matrix metallopeptidase 9.[78] Among those, a high sensitivity CRP (hs-CRP) and D-dimer level have been reported to correlate with aneurysm diameter of AAA, and are useful for predicting the growth rate and rupture of an aneurysm.[79–81]

The rupture of aortic aneurysm may cause marked anemia and acidosis associated with shock, and a sharp decrease in hematocrit, in particular, strongly suggests aortic aneurysm rupture. In addition, elevated lactic acid and LDH levels suggest malperfusion in each organ.

Abnormal coagulation tends to be more common in larger aortic aneurysms, and DIC with enhanced fibrinolysis may also develop due to aortic aneurysm. Although a hemorrhagic tendency is not necessarily observed, tooth extraction or trauma may trigger chronic DIC that makes hemorrhagic control difficult.[82–84] Thrombocytopenia in patients with DIC complicating aortic aneurysm is generally mild, and their prothrombin time and activated partial thromboplastin time are often in the normal range, while their fibrin degradation product (FDP) and D-dimer levels are elevated. Several patients with DIC with enhanced fibrinolysis have an elevated FDP/D-dimer ratio,[85,86] which is useful for its differentiation (See **PQ 2**).

Patients with inflammatory aortic aneurysm have elevated inflammatory markers, including white blood cell count, CRP, and erythrocyte sedimentation. In recent years, inflammatory aortic aneurysm has been suggested to be associated with IgG4-related diseases, and patients with IgG4-related diseases often show elevated IgE and positive antinuclear antibody, in addition to a high IgG4 level.[87] Additionally, while inflammatory aortic aneurysm needs to be differentiated from infected aortic aneurysm, it is often difficult.

2.2 Aortic Dissection

Prognosis in the treatment of acute aortic dissection is determined by rapid diagnoses, including diagnostic imaging. Thus, various biomarkers have been investigated, but none has been found to be specific, like troponin in acute myocardial infarction. However, many patients with acute aortic dissection have an elevated D-dimer level, and it is useful for diagnosis by exclusion as it has a specificity of 46.6% and a high sensitivity of 96.6% at a cut-off value of 500 ng/mL.[88–91] However, caution is needed since the D-dimer level may not be elevated in patients with aortic dissection with thrombosed false lumen or young patients.[92,93]

The guidelines in Europe and the United States recommend a diagnostic algorithm that combines the aortic dissection detection risk score (ADD-RS) and D-dimer level, which is thought to increase the probability of pretest diagnosis.[94–99] ADD-RS is a score derived from the patient background, symptoms, and physical findings, and patients with an ADD-RS of 0 or 1 and a D-dimer level of <500 ng/mL are diagnosed with acute aortic dissection by exclusion, allowing the omission of CT examination. On the other hand, CT examination is recommended for patients with ADD-RS of 2 or 3 without measuring their D-dimer levels. Further, a prospective study of 1,850 patients reported that, of the 924 patients with an ADD-RS of 0 or 1 and a D-dimer level of <500 ng/mL, only 3 patients (0.3%) had acute aortic dissection.[99] On the other hand, acute aortic dissection may be hidden in patients with cerebral ischemia symptoms without complaints of chest or back pain; however, a high D-dimer level was reported to be useful for their differential diagnosis.[100,101]

In addition, the D-dimer level is expressed in μg/mL or ng/mL, depending on the measurement method; nevertheless, μg/mL is widely used in Japan. Also, the cut-off value needs to be confirmed at each facility as it differs depending on the test reagent.

In acute aortic dissection, elevated CPK, lactic acid, and LDH values, in addition to repeated abdominal pain, are the basis for suspecting malperfusion of the celiac and mesenteric arteries. Also, approximately 1/3rd of the patients are known to suffer from fever, which can be a risk factor that leads to delayed diagnoses.[102] Furthermore, although its differentiation from bacterial infection is required in patients with fever, those without bacterial infection were reported to show no increase in the procalcitonin levels.[103]

The occurrence of DIC is not uncommon in patients with acute aortic dissection.[104] It is often due to massive hemorrhage caused by rupture or thrombosis formation in the false lumen. However, even without DIC, blood flow to the false lumen activates coagulation and secondarily enhances the fibrinolytic system in the acute phase, resulting in a decrease in the coagulation factors, fibrinogen, and platelets, which leads to exacerbation of the postoperative course and occurrence of complications.[105,106] In addition, as with aortic aneurysm, DIC with enhanced fibrinolysis may occur in aortic dissection with patent false lumen in the chronic phase.[107]

PQ 2.

How Should Disseminated Intravascular Coagulation (DIC) Complicating Aortic Diseases Be Treated?

Recommendation

Invasive treatment is primarily considered for underlying aortic diseases. For DIC with enhanced fibrinolysis, it is desirable to use anticoagulation therapy in combination with an antifibrinolytic agent upon consultation with a DIC specialist.

The complication of aortic aneurysm with DIC has long been reported.[108] Aneurysms with larger diameters are more likely to have abnormal coagulation, and the complication rate is said to be approximately 4%.[81,83] In fact, tooth extraction or trauma may trigger chronic DIC that

makes hemorrhagic control difficult in aortic aneurysm and aortic dissection with patent false lumen in the chronic phase. However, there are no clear diagnosis/treatment guidelines at present, and it is often difficult to respond.

DIC is classified into three types: suppressed fibrinolysis, balanced fibrinolysis, and enhanced fibrinolysis. While sepsis is a typical disease that causes DIC with suppressed fibrinolysis, diseases that cause DIC with enhanced fibrinolysis include some malignant tumors (acute promyelocytic leukemia and prostate cancer) and aortic aneurysm.[85] In aortic aneurysm and chronic aortic dissection, the formation and dissolution of parietal thrombosis inside the aneurysm or false lumen, as well as turbulent blood flow, are presumed to cause enhanced fibrinolysis; however, the details of this mechanism are yet to be elucidated.

In DIC with enhanced fibrinolysis associated with aortic aneurysm, thrombocytopenia may be mild with normal prothrombin time (PT) and activated partial thromboplastin time (APTT), and it may have been overlooked in several cases. Even in patients who have been diagnosed with aortic aneurysm, the values of these test items are in the normal range, and they do not show a hemorrhagic tendency. Thus, their conditions are not recognized as chronic DIC, and the manifestation of a hemorrhagic tendency is triggered by tooth extraction or trauma in some cases. In addition, patients who have not been diagnosed with aortic aneurysm may be misdiagnosed to have conditions, such as idiopathic thrombocytopenic purpura (ITP), and aortic aneurysm also needs to be differentiated in patients exhibiting thrombocytopenia of unknown cause.

As described above, thrombocytopenia of patients with DIC with enhanced fibrinolysis is mild, and even if their PT and APTT are in the normal range, other coagulation markers, such as fibrin degradation product (FDP) and D-dimer, show abnormal values. They exhibit a significant increase in the plasmin-α2 plasmin inhibitor (PI) complex (PIC), a decrease in α2PI and plasminogen, and an increase in the FDP and D-dimer levels. However, the test results of thrombin-antithrombin (TAT) complex, PIC, and α2PI are often not available immediately in the hospital, and an increase in the FDP/D-dimer ratio is useful in clinical practice.[86] This is because fibrinogen degradation (primary fibrinolysis) becomes the main component due to the local enhancement of fibrinolysis, resulting in lesser production of D-dimer in comparison to FDP.

The principle of DIC treatment is replacement therapy and anticoagulation therapy, in addition to the treatment of the underlying diseases. However, at present, there is no established treatment for DIC with enhanced fibrinolysis complicating aortic aneurysm or chronic aortic dissection. Invasive treatment is considered for the underlying diseases, and supplementation with fresh frozen plasma is considered in patients with a hemorrhagic tendency and a decreased fibrinogen. The drugs used in anticoagulation therapy include unfractionated heparin and heparins (low-molecular-weight heparin, fondaparinux, and danaparoid), nafamostat, and recombinant thrombomodulin; however, no regimen, including the dosage, has been established for chronic DIC caused by aortic aneurysm. On the other hand, there is concern that anticoagulation therapy may promote hemorrhage in patients with extremely strong fibrinolytic activation.[85,109]

In addition, antifibrinolytic agents, such as tranexamic acid, may be used in patients with DIC with enhanced fibrinolysis. However, because antifibrinolytic therapy for DIC suppresses the biological defense reaction that attempts to dissolve microthrombosis by fibrinolytic activation, it rather promotes thrombosis formation. Thus, when used alone, antifibrinolytic agents may cause serious complications, such as organ damage and systemic thrombosis, and there have been reports of deaths.[110] Therefore, the use of antifibrinolytic agents in combination with anticoagulation therapy is recommended.[85] Also, the use of direct oral anticoagulant (DOAC) as an anticoagulation therapy was recently reported,[111] and a further accumulation of knowledge is expected.

3. Diagnostic Imaging

3.1 Plain Radiography Images

Basically, aortic aneurysm and dissection in thoracic and abdominal regions are evaluated using radiographs of the front of the chest in a standing position (PA image) and the front of the abdomen in a supine position (AP image), respectively.

3.1.1 Aortic Aneurysm

TAA may be detected on plain radiographs, such as those taken during medical examinations. In the front view, it is often observed as a shadow that continuously protrudes to the right on the contour of the ascending aorta (**Figure 19A**). In arch aneurysm, a mass-like shadow is seen on the left first arch (**Figure 19B**), and it protrudes inferiorly in some cases. In the descending aorta, it is seen as a continuous fusiform-shaped or circular shadow on the contour of the aorta (**Figure 19C**). Although the significance of plain radiography is not high in the treatment of AAA, calcification of the aneurysm wall is occasionally observed, leading to the identification of the presence of an aneurysm (**Figure 19D**).

3.1.2 Aortic Dissection

In acute aortic dissection, an enlarged mediastinal shadow is observed in some cases; however, its diagnostic significance is controversial as the normal mediastinum may appear enlarged in the supine position. The medial deviation of intimal calcification of the aortic wall is a finding suggestive of dissection, which is highly reliable, especially if it shows a change compared to the photograph taken before the onset. The distance between the outer edge of the aortic wall and intimal calcification is usually 2–3 mm, and the presence of a dissection is suspected if it is 6 mm or greater.[112] However, caution is required as approximately 20% of the patients show no abnormal findings on plain radiographs despite the presence of a dissection.[113] Therefore, if its presence is suspected from clinical symptoms, other imaging examinations, including CT and MR examinations, should be actively performed, even without abnormal findings, such as an enlarged mediastinum. Also, secondary findings, such as pleural effusion and heart failure complicating dissection, can be evaluated on plain radiographs.

3.2 CT Examination

3.2.1 Methods

Unenhanced and early-phase contrast-enhanced imaging is

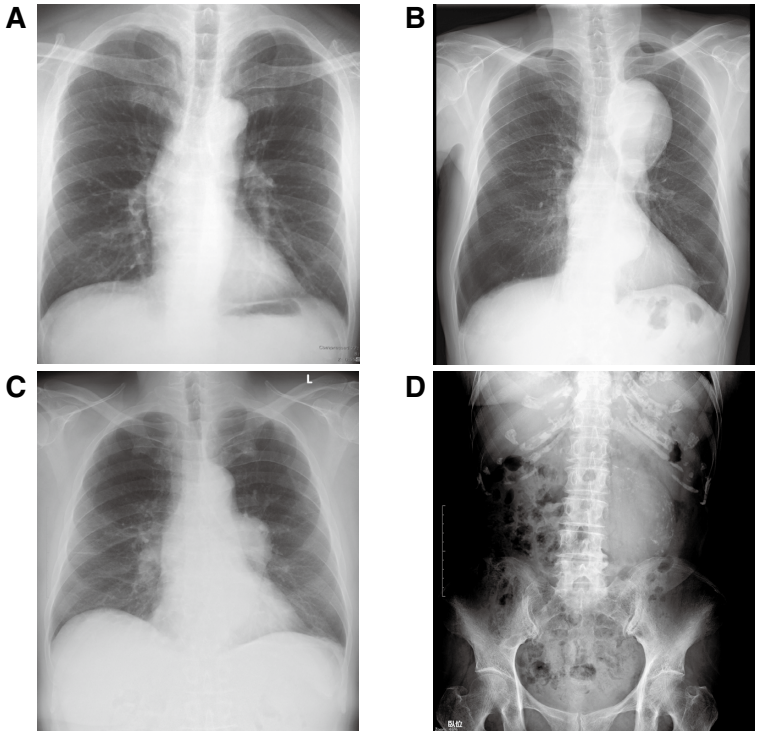


Figure 19. Front view of aortic aneurysm in a standing/supine position on plain radiograph. (**A**) A shadow protruding to the right continuously on the contour of the ascending aorta (PA image). (**B**) The left first arch protrudes to the left, suggesting aortic arch aneurysm (PA image). (**C**) In the descending aorta, an aneurysm is seen as a continuous fusiform-shaped or circular shadow on the contour of the aorta (PA image). (**D**) Calcification of the aneurysm wall may be seen in the abdomen, leading to the identification of presence of an aneurysm (AP image).

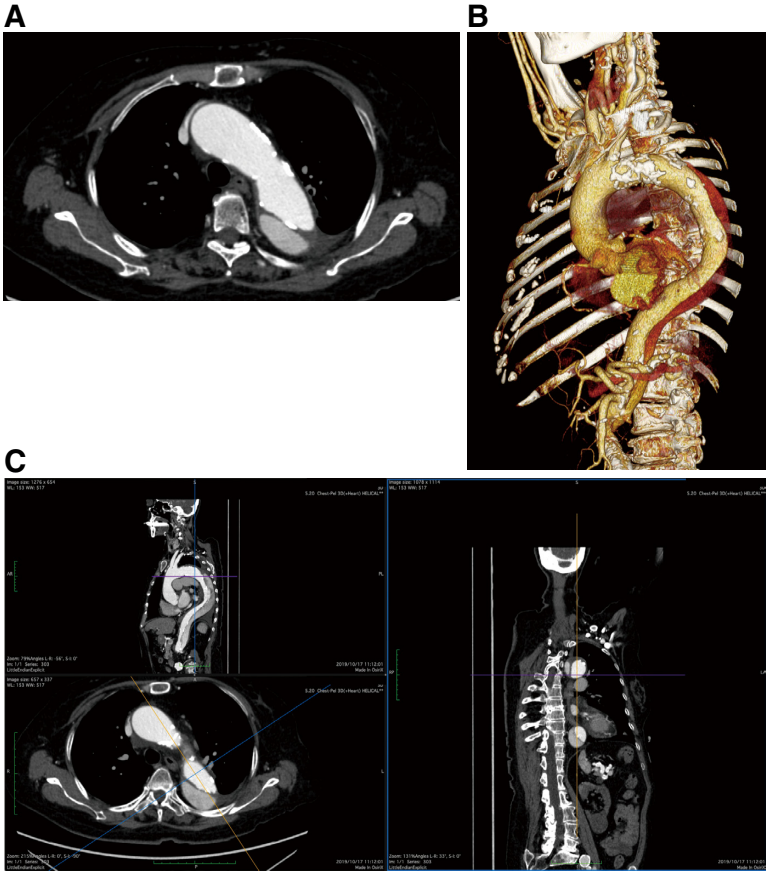


Figure 20. Early-phase contrast-enhanced CT images of aortic dissection. (**A**) Contrast-enhanced CT, transected image. (**B**) Contrast-enhanced CT, volume rendering (VR) image. (**C**) Contrast-enhanced CT, multi-planar image (MPR) image.

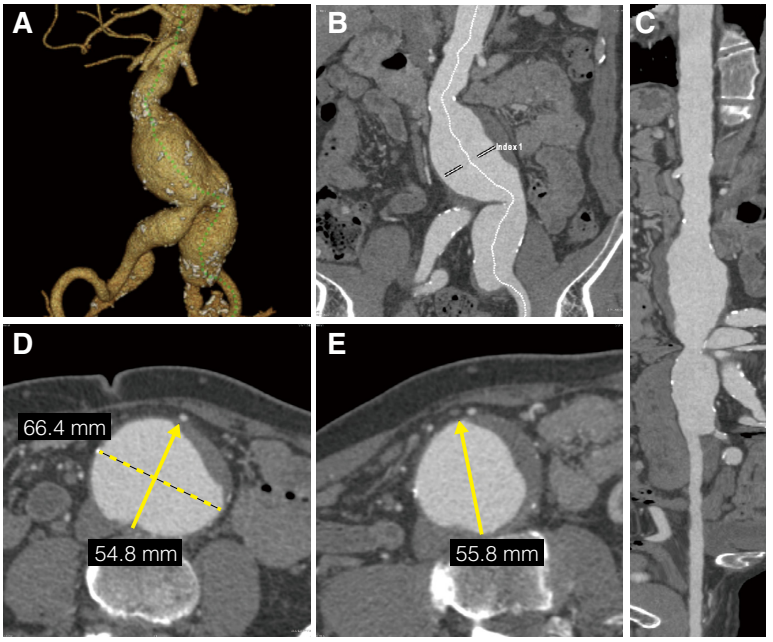


Figure 21. Measurement of the size of the aortic aneurysm. (**A**) VR (volume rendering) image. (**B**) CPR (curved planar reconstruction) image. (**C**) Stretched CPR image. (**D**) Measurements on a transected image (axial image). In transected images, the measurement of the maximum major axis (dotted line: 66.4 mm) leads to overestimation, while the measurement of the maximum minor axis (arrow: 54.8 mm) leads to underestimation. (**E**) Measurement on a vertical cross-sectional image with respect to the center line of the aorta (perpendicular image). The size of an aneurysm can be evaluated most accurately by the measurement on a vertical cross-sectional image perpendicular to the center line or axis of the aorta (55.8 mm).

essential, and the delayed-phase contrast-enhanced imaging is added as needed. Unenhanced CT examination is useful for the identification of hematoma in the false lumen of aortic dissection with thrombosed false lumen and the evaluation of a high concentration area in the parietal thrombosis suspected of impending rupture of an aneurysm, in addition to examining the degree of wall calcification and the presence or absence of medial deviation.[114]

In contrast-enhanced CT examination, clear early-phase contrast-enhanced images of the entire aorta are generally taken while injecting a nonionic contrast medium with a power injector at an injection rate of approximately 3 mL/s using a helical CT (**Figure 20A**). Multidetector row CT (MDCT), which is a helical CT with multiple rows of detectors, is highly useful for diagnosing aortic aneurysm and dissection as it can take a wide range of high-definition images with a short breath-holding time. With the obtained high-resolution data, stereoscopic images (**Figure 20B**) and tomographic images from various directions (**Figure 20C**) can be reconstructed using volume rendering (VR) and multi-planar reconstruction (MPR), allowing for precise diagnosis.

3.2.2 CT images of Aortic Aneurysms

In addition to diagnosing the presence of an aortic aneurysm, CT images provide a wide range of information, including the size and range of extension, calcification, and other conditions of the aneurysm wall (such as inflammatory aortic aneurysm), the amount and condition of parietal thrombosis, and positional relationship of an aneurysm with the surrounding organs and major branches. In fusiform type aneurysms, the aneurysm diameter is an important factor in determining surgical indication. Generally, TAA with a diameter of 55–60 mm or larger and AAA with a diameter 50–55 mm or larger are indicated for invasive treatment,[96] and their measurements require accuracy and objectivity.

a. Measurement of Aneurysm Diameter

i. Center Line Method

It is recommended that the aneurysm diameter be measured in a cross-section perpendicular to the center line of the aorta using a three-dimensional CT image reconstructed by MPR and curved planar reconstruction (CPR) (**Figure 21**). This allows the measurement of the diameter of craniocaudally extending or tortuously curved aortic aneurysm with high accuracy and reproducibility compared with the measurement in transected images.[115–117]

ii. Method Using the Maximum Minor Axis

In principle, the maximum minor axis is measured if three-dimensional reconstructed CT images are not available.[118] The minor axis of the aneurysm is measured with a few slices, and the largest diameter is regarded as the maximum minor axis, which has excellent objectivity. However, if the aorta meanders or runs diagonally, there is a risk of overestimation or underestimation of the aneurysm diameter (**Figure 21**).

b. Thoracic Aortic Aneurysm

i. Ascending Aortic Aneurysm

In the ascending aorta, the evaluation of an aneurysm is hindered by stepwise motion artifacts associated with the heartbeat; however, this problem does not occur with electrocardiogram gated imaging. It is recommended to be used for the evaluation of Valsalva sinus aneurysm and annuloaortic ectasia (**Figure 22**).

ii. Aortic Arch Aneurysm

In the invasive treatment of aortic arch aneurysms (open surgery and TEVAR), reconstruction of arch branches needs to be considered, and the range of extension of an aneurysm must be evaluated accurately. Three-dimensional images allow for observation from any direction. Thus, the morphology and spread of an aortic aneurysm can be grasped three-dimensionally, and the positional relationship between the aneurysm and arch branches can be evaluated.

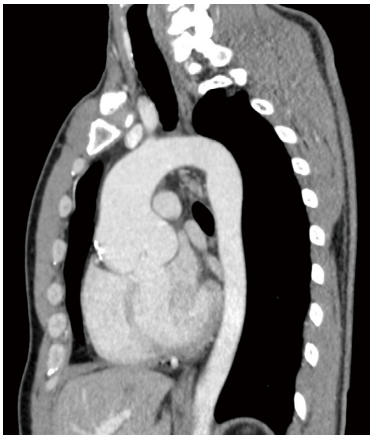


Figure 22. Aortic root dilatation (Annuloaortic ectasia. Electrocardiogram gated contrast-enhanced CT, MPR image).

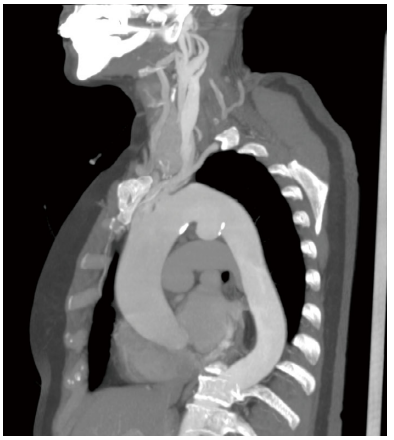


Figure 23. Aortic arch aneurysm (Contrast-enhanced CT, MPR image).

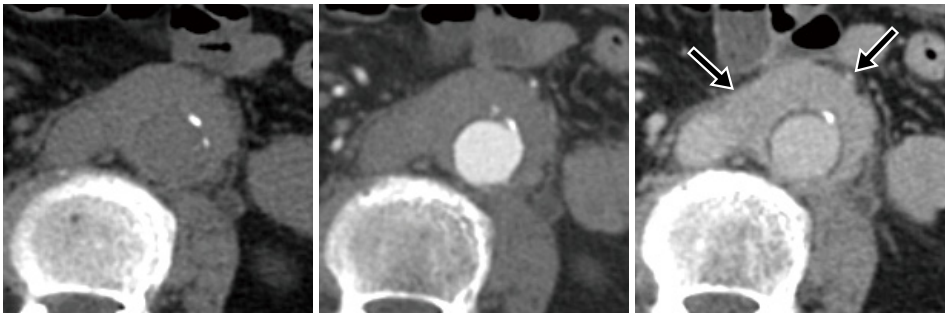


Figure 24. Inflammatory aortic aneurysm. A soft tissue shadow is observed anteriorly, covering the abdominal aortic aneurysm, and the area is faintly and deeply stained on the delayed-phase contrast-enhanced image (↑).

In addition to transected images, MPR images are useful for measuring the aneurysm diameter (**Figure 23**).

iii. Descending Aortic Aneurysm

For descending aortic aneurysm, the size, the presence or absence of parietal thrombosis, vertical extension, and its relationship with surrounding organs are evaluated. However, the extension of a proximal descending aortic aneurysm to the proximal side requires attention since its positional relationship with the arch branches poses a problem.

iv. Thoracoabdominal Aortic Aneurysm

The reconstruction of major abdominal branches may be required, and the positional relationship between the lower end of the aneurysm and these branches is clarified. Spinal cord ischemia is a complication of invasive treatment for TAAA or distal descending aortic aneurysm, and it is contributed by occlusion of the Adamkiewicz artery. The Adamkiewicz artery branches from the intercostal or lumbar artery of Th9-L2 at a frequency of 85–90%, which can be visualized non-invasively using MDCT.[119]

c. Abdominal Aortic Aneurysm

In addition to the diagnosis of its presence, the diameter of abdominal aortic aneurysm can be evaluated accurately, and calcification and surrounding condition of the aneurysm wall, amount and condition of parietal thrombosis, and the condition of surrounding organs is evaluated. It is important to understand the relationship between the aneurysm and the renal and iliac arteries, for which three-dimensional images are useful. In addition to the above, necessary information, such as the patency of the inferior mesenteric and internal iliac arteries, can be obtained.[120–122]

d. Special Aortic Aneurysms

i. Inflammatory Aortic Aneurysm

Inflammatory aortic aneurysm exhibits marked thickening of the aneurysm wall and inflammatory cell infiltrate of the adventitia, often with lymph follicles, in addition to aneurysmal dilatation in the aorta, and is characterized by fibrous thickening around the aneurysm and fibrous adhesions to the surrounding tissues. It often develops in the abdominal aorta and occurs in 3–10% of AAA.[123] Its

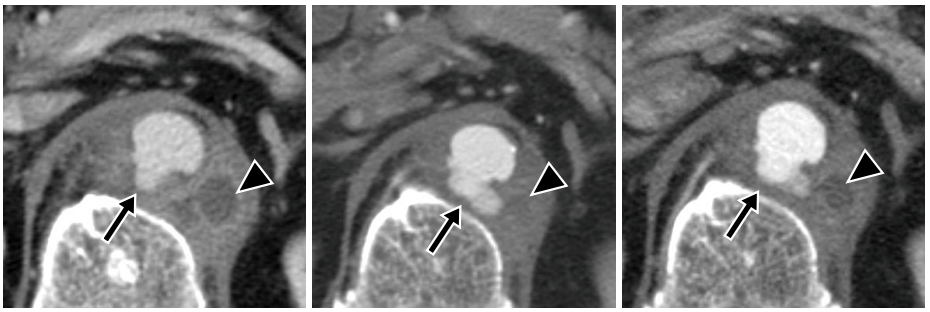


Figure 25. Mycotic aortic aneurysm. An irregularly shaped saccular aortic aneurysm (↑) rapidly expanded in a short period of time. Accumulation of encapsulated fluid, which appears to be an abscess, is observed in the vicinity (▲).

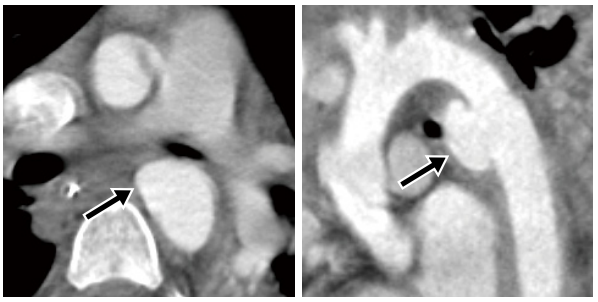


Figure 26. Traumatic aortic aneurysm. Saccular type aortic aneurysm is observed in the thoracic descending aorta, suggesting traumatic aortic aneurysm (↑).

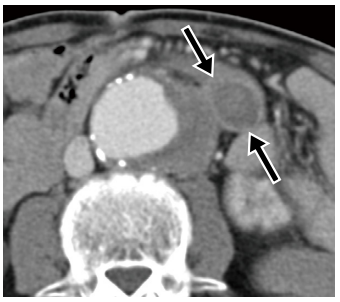


Figure 27. Aorto-enteric fistula. An abdominal aortic aneurysm perforates into the duodenal mucosal layer, forming submucosal hematoma (↑).

unenhanced CT examination shows a thick soft-tissue shadow from the anterior to anterolateral direction around the aneurysm, which is deeply stained in the delayed-phase contrast-enhanced CT[124] (**Figure 24**). Several inflammatory aortic aneurysms are of the fusiform type, and approximately 1/3rd of the patients have complications, such as hydronephrosis, adhesion to the intestinal tract, and fistula formation.

ii. Mycotic Aortic Aneurysm

Infected aortic aneurysm is caused by infection, and gram-positive coccus (mainly *Staphylococcus* bacteria) and gram-negative bacillus (mainly *Salmonella*) are the causative bacteria in many cases. The characteristics of its CT images include the formation of a localized saccular type aneurysm, accumulation of fluids, such as edema and abscess formation due to inflammation around the aneurysm, and rapid expansion in a short period of time[125] (**Figure 25**).

iii. Traumatic Aortic Aneurysm

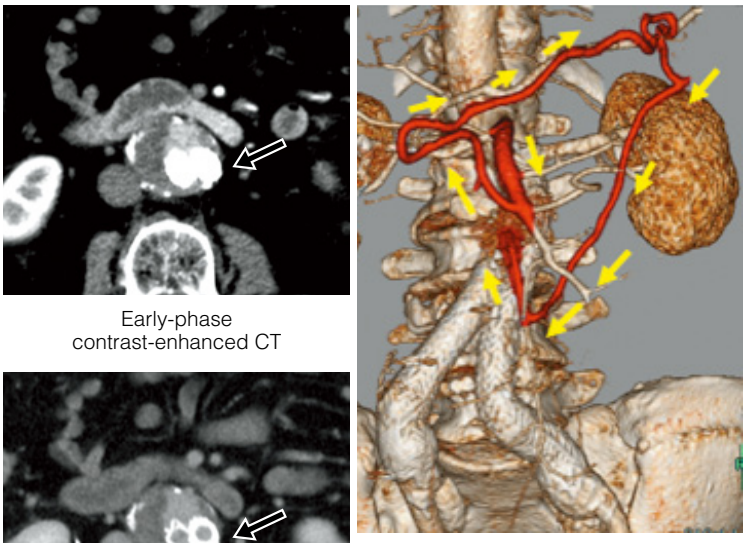
Traumatic aortic aneurysm is caused by blunt trauma and often occurs in the aortic isthmus, which is the junction between the arch and the descending aorta. A thin-walled saccular type aortic aneurysm develops in the aortic isthmus, and hematoma often occurs in its surroundings (**Figure 26**). If complicated by aortic dissection or intramural hematoma, traumatic aortic aneurysm presents with findings similar to those of acute aortic dissection; however, its range is often localized.

iv. Aorto-Enteric Fistula

Aortic gastrointestinal fistula is a pathological condition in which a fistula is formed in the aorta and digestive tract. In the thoracic aorta, it occurs predominantly in the descending aorta (78%), followed by the arch (16%) and thoracoabdominal aorta (6%).[126–129] In the abdominal aorta, it occurs commonly in the duodenum, especially the horizontal limb. It is found in aortic aneurysms with hematemesis or melena, and its CT examination shows air patterns inside and outside the aortic wall and leakage of the contrast medium into the intestinal tract[130] (**Figure 27**).

v. Aortic Aneurysm-Inferior Vena Caval Fistula

Aortic aneurysm-inferior vena caval fistula is a pathological condition in which an aortic or iliac artery aneurysm ruptures/perforates into the inferior vena cava. It may perforate into the iliac vein. Its features include comparable absorption values in the inferior vena cava and the aorta in the early-phase contrast-enhanced imaging, dilatation of the inferior vena cava, and fistula formation between the artery and vein.

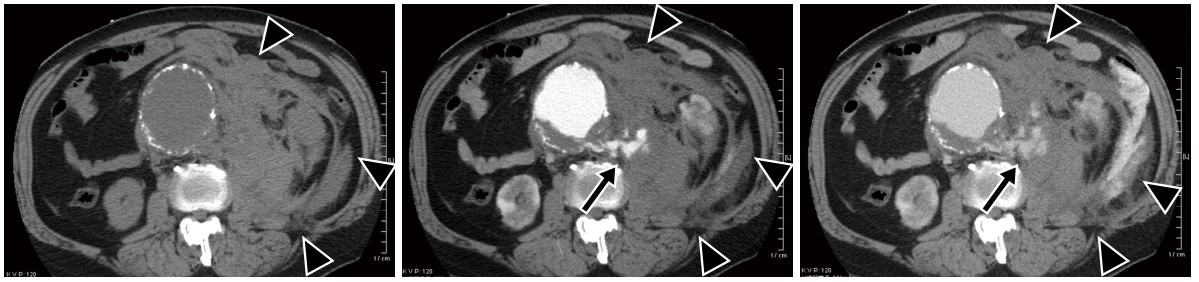


Early-phase contrast-enhanced CT

Delayed-phase contrast-enhanced CT

Contrast-enhanced CT, VR image

Figure 28. Type II endoleak after TEVAR/EVAR. Retrograde blood flow from the superior mesenteric artery to the inferior mesenteric artery via the Riolan artery arch (type II endoleak).



A: Unenhanced CT

B: Early-phase contrast-enhanced CT

C: Delayed-phase contrast-enhanced CT

Figure 29. Frank (open) rupture of aortic aneurysm. (**A**) Hematoma spreads to the left of an aortic aneurysm (▲). (**B**,**C**) Continuous extravasation of contrast medium from the left posterior wall of an aortic aneurysm is observed (↑).

e. Evaluation Before and After Stent-Graft Deployment

CT examination is the most useful for the indication of TEVAR/EVAR and deployment plans. Although the instructions for use (IFU) differ depending on the type of stent graft, the following should be evaluated before surgery: (1) location of the aneurysm as well as central and peripheral aortic diameters and properties (presence or absence and degree of curvature/tortuousness, calcification, and parietal thrombosis), (2) positional relationship and distance between the aneurysm and major branches (distance to the arch branches in TAA and distance to the lower renal artery in AAA), and (3) blood vessel diameter and properties of the iliac artery-common femoral artery, which is the access route (presence or absence and degree of curvature/tortuousness, calcification, and parietal thrombosis).

On the other hand, the change in aneurysm diameter, endoleak, patency, migration, and breakage are evaluated after TEVAR/EVAR. Evaluation of endoleak, including its delayed-phase contrast-enhanced CT, is recommended to differentiate type II endoleaks (regurgitation from the aortic branches) (**Figure 28**). Differentiation of the types of endoleak is important for determining the subsequent treatment strategy; however, it is often difficult.

f. CT images of Rupture/Impending Rupture

When rupture of an aortic aneurysm is suspected, CT examination is useful if sufficient time is allowed based on

the patient's condition. It not only makes a definitive diagnosis of the presence and rupture of an aneurysm but also clarifies the extent of hematoma and the relationship with the surrounding organs. Ruptures and impending ruptures can be classified into frank (open) rupture, in which the arterial wall is completely ruptured, contained (sealed) rupture, in which the arterial wall is completely disrupted, but is contained by hematoma and surrounding organs, and impending rupture, in which the aneurysm is at risk of rupture, but has not ruptured. In frank rupture, hematoma spreads into the mediastinum, thoracic cavity, and heart chamber in TAA and into retroperitoneal space and abdominal cavity in AAA (**Figure 29**). However, caution is needed as hematoma may not be observed if the esophagus, bronchi, intestinal tract, or inferior vena cava is perforated. In addition, the site of rupture may be identified as extravasation of the contrast medium (**Figure 29**).

"Draped aorta sign" is the finding that the posterior wall of the aorta is obscured due to hematoma around the aneurysm while the aneurysm agglomerated with hematoma covers the vertebral body, and it is suggestive of a contained rupture[131] (**Figure 30**). In such a case, the shape of the aneurysm is irregular, and erosion is often seen in the vertebral body in contact with the aneurysm because an inflammatory reaction occurs at the edge of the aneurysm. In addition, the high absorption area found around AAA on unenhanced CT images is called the "high-attenuating crescent (HAC) sign," and it is frequently found during rupture or impending rupture[114] (**Figure 31**). It is believed to indicate acute hematoma within the aneurysm wall or parietal thrombosis, and although its positive predictive value is not high at 53%, it is a notable finding when clinically impending rupture is suspected due to abdominal pain. In terms of the aneurysm diameter, the average enlargement rate of AAA is approximately 2.8 mm/year,[115] and rapid enlargement of 5 mm or greater within a period of 6 months or a sudden morphological change on follow-up CT examinations is considered to be a sign of the risk of rupture.[132]

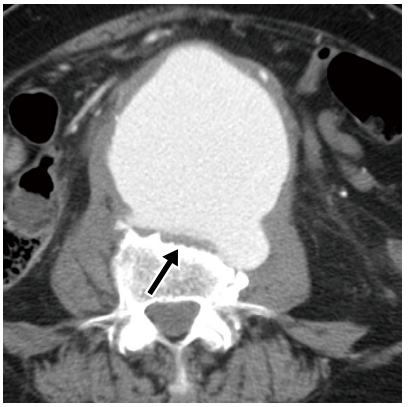


Figure 30. Draped aorta sign of aortic aneurysm (contrast-enhanced CT). An irregularly shaped aortic aneurysm is present, covering the vertebral body. Erosion is observed in the vertebral body in contact with the aneurysm (↑).

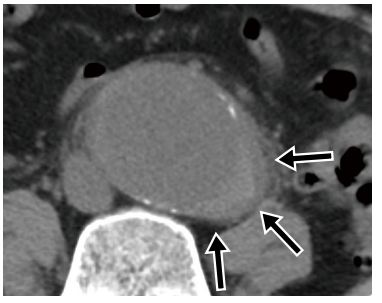


Figure 31. High-attenuating crescent sign (HAC sign) of abdominal aortic aneurysm. The unenhanced CT image shows a crescent-shaped high absorption area on the margin of an aortic aneurysm, suggesting a high-attenuating crescent sign (↑).

PQ 3.
How Should the Size of an Aortic Aneurysm Be Measured?

Recommendation

The diameter of an aortic aneurysm is determined by measuring its major and minor axes in a cross-sectional image perpendicular to the long axis of the aorta.

Background: The use of the maximum minor axis in an axial cross-sectional CT image has been recommended for the measurement of the aortic aneurysm diameter. This is because the major axis does not reflect the aneurysm diameter in the axial cross-sectional image of the tortuous site. However, aortic aneurysms do not always dilatate into a perfect circle. Eccentric dilatation is a common finding not only in saccular type aortic aneurysms, but also in fusiform type aortic aneurysms, and eccentric dilatation on the false lumen side is often seen, especially in chronic aortic dissection. In the distal arch and tortuous areas on the diaphragm, craniocaudal eccentric dilatation cannot be evaluated in axial cross-sectional images. Thus, evaluation of the maximum minor axis alone in axial cross-sectional images may lead to oversight of saccular type aneurysms and underestimation of the risk of rupture.

Summary of Systematic Reviews: The methods for evaluating the maximum diameter in CT imaging have been examined for AAA, and those for TAA have not been investigated. The diameter of AAA can be accurately determined by echographic examination that can create arbitrary cross-sectional images. When it is difficult to create an accurate cross-sectional image perpendicular to the long axis of the aorta, the use of the anterior-posterior diameter leads to less variation.[133] Also, it has been pointed out that the evaluation of the maximum minor axis of AAA in axial cross-sectional CT images may underestimate the diameter of aneurysms with eccentric enlargement,[116] and it is underestimated compared to the evaluation using the anterior-posterior diameter in axial cross-sectional images. In addition, in the evaluation of cross-sectional images perpendicular to the long axis of the aorta, an automated analysis using the center line method leads to lesser variation than the manual image construction using multi-planar reconstruction (MPR).[134]

Other Factors to Be Considered: Software that edits DICOM images of CT examination and constructs arbitrary MPR images by the center line method is widely used in medical

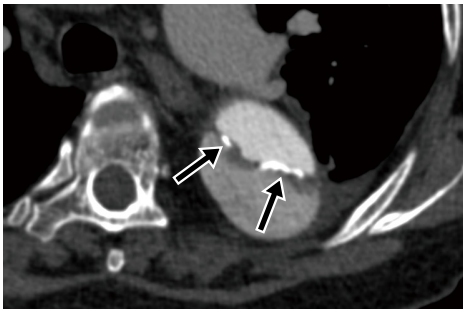


Figure 32. Image of aortic dissection and deviation of the calcified intima. The contrast-enhanced CT image shows inward deviation of the calcification of the aortic intima due to dissection (↑).

facilities in Japan; however, its adoption at the clinic level is insufficient. It is considered difficult for primary physicians at clinics, who regularly follow up patients, to reconstruct the images that were not reconstructed at the facility where images, such as CT, were taken. The criteria for treatment intervention for eccentrically enlarged aortic aneurysms have not been established.

Discussion in the Guidelines Committee: At the facility where the diagnostic imaging of CT/MRI examination is requested, it is desirable to construct at least MPR images of tortuous sites, such as the distal part of the aortic arch and epiphrenic region, to prevent oversight of saccular type aneurysms and accurately identify eccentric dilatation. In facilities without such equipment, the maximum minor axis in axial cross-sectional images is used as an index; however, caution is needed not to overlook the craniocaudal dilatation from the number and width of slices in which the aneurysm is visualized. Estimating the rupture risk of an eccentrically dilatated aortic aneurysm from the minor axis alone is thought to lead to its underestimation. Further accumulation of evidence is awaited to determine whether the intervention criteria should be the major axis or the average diameter.

Summary: The diameter of an aortic aneurysm is determined by measuring its major and minor axes in a cross-sectional image perpendicular to the long axis of the aorta. In areas where ultrasound measurement is possible, such as the abdominal aorta, it is important to create an accurate cross-sectional image perpendicular to the long axis of the aorta at the time of measurement. If it is difficult, the anterior-posterior diameter is used as an index in abdominal echography. In CT and MRI examinations, craniocaudal enlargement at tortuous sites of the aorta is evaluated using MPR images created at the facilities that perform the examinations. In facilities without such equipment, the maximum minor axis is used as an index; however, caution is needed not to overlook the craniocaudal dilatation from the number and width of slices in which the aneurysm is visualized.

3.2.3 CT images of Aortic Dissection

CT examination is essential for diagnosing aortic dissection because of its high reliability, non-invasiveness, ability to evaluate the entire aorta, and ability to examine in a short time in response to an emergency. Aortic dissections are classified according to (1) range of extension (Stanford and DeBakey Classifications), (2) blood flow status of the false lumen (dissections with patent false lumen, ULP type dissections, and dissections with thrombosed false lumen), and (3) disease stage (acute, subacute, and chronic phases), and the type and condition of the disease are expressed by incorporating these three elements. In CT examination, it is important to diagnose complications (such as rupture, cardiac tamponade, and malperfusion), in addition to the classification of disease types in existence diagnosis (range of extension, blood flow status of the false lumen, and identification of entry/re-entry).

Basically, aortic dissections are imaged with unenhanced CT and early-phase and delayed-phase contrast-enhanced CT. It has recently become possible to image the entire aorta with a short breath-holding time by MDCT, and it is necessary to understand the performance of equipment at each facility before performing CT examination. Aortic dissection can be sufficiently diagnosed on transected images; however, multi-planar reconstruction (MPR) images are useful for understanding the extension of the false lumen and ULP in the craniocaudal direction and into the aortic branches. Since unenhanced CT examination can also evaluate calcification and hematoma, the luminal deviation of aortic intimal calcification is an important point in diagnosing aortic dissection (**Figure 32**). In the acute phase of aortic dissection with thrombosed false lumen, the false lumen filled with crassamentum or hematoma extends over a wide area along the aortic wall in the longitudinal direction, and it is observed as a crescent-shaped highly-concentrated area.[135] The early-phase contrast-enhanced imaging captures the entire aorta during the first pass of the contrast medium. It can demonstrate the presence of contrast-enhanced two-cavity structure in dissections with patent false lumen, non-contrast-enhanced false lumen in dissections with thrombosed false lumen, and ULP in ULP type dissections, allowing for diagnosis confirmation.

a. Aortic Dissection With Patent False Lumen

True and false lumina of aortic dissection with patent false lumen (**Figure 33**) are distinguished according to the following criteria:

- The false lumen is enlarged, while the true lumen is often narrowed
- The true lumen exhibits wall calcification (Exception: In chronic dissection, calcification may occur on the wall of the false lumen)
- The false lumen exhibits parietal thrombosis (Exception: In true aortic aneurysm complicated with dissection, parietal thrombosis may be present in the true lumen)
- The true lumen is contrast-enhanced first in the dynamic study, while the false lumen is contrast-enhanced with a delay
- The false lumen exhibits the aortic cobweb (an incompletely detached cord-like structure, which is part of the media)[136] (**Figure 34**)

In addition, if the blood flow of the false lumen is significantly delayed, the false lumen may not be contrast-enhanced in early-phase contrast-enhanced images, and the influx of contrast medium may be observed in the delayed-phase. Thus, it is necessary to image up to the delayed phase (**Figure 33**).

The entry is observed as a tear of the intimal flap on

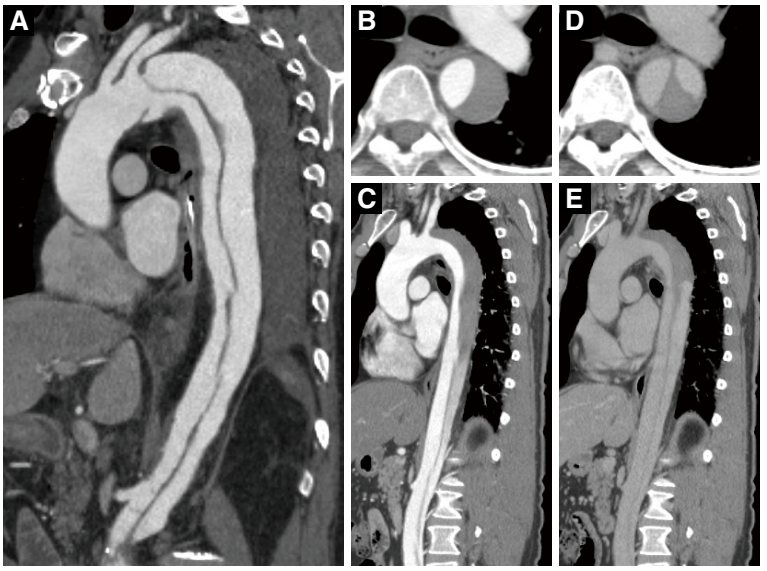


Figure 33. Aortic dissection with patent false lumen. (**A**) Typical aortic dissection with patent false lumen with blood flow throughout the false lumen on an early-phase contrast-enhanced image. (**B**–**E**) A part of the false lumen is not contrast-enhanced in early-phase contrast-enhanced imaging, and is contrast-enhanced with a delay in delayed-phase contrast-enhanced imaging.

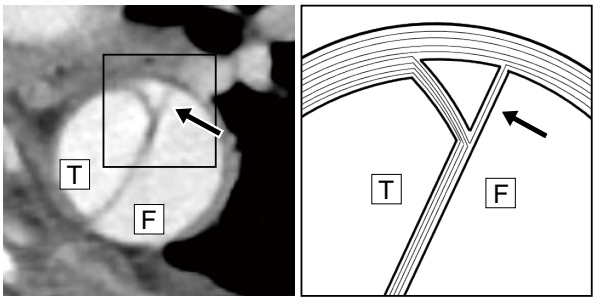


Figure 34. Aortic cobweb (contrast-enhanced CT). A cord-like structure is observed in the false lumen, suggesting the presence of aortic cobweb (↑).

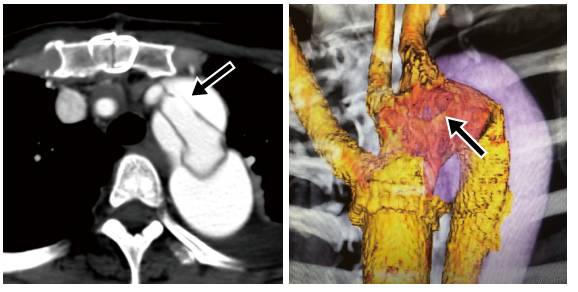


Figure 35. Images of aortic dissection and intimal defect of the entry. A defect in the aortic intima is present (↑).

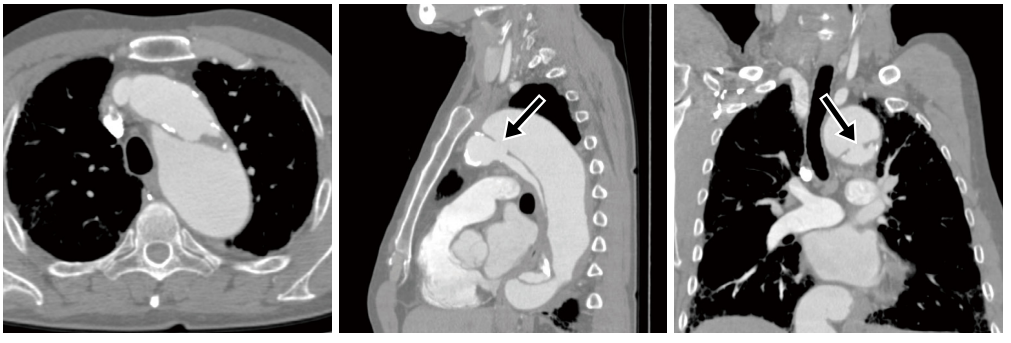
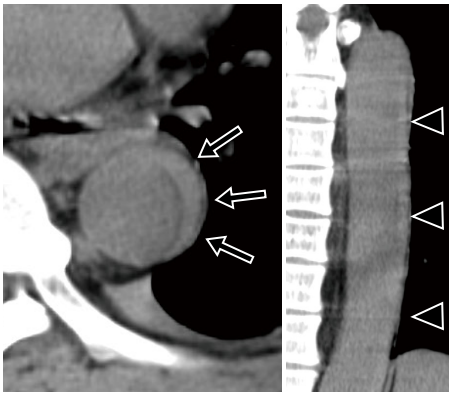


Figure 36. Images of aortic dissection and intimal defect of the entry (MPR image).



A: Unenhanced CT, transected image **B:** Unenhanced CT, MPR image

Figure 37. Acute aortic dissection with thrombosed false lumen. (**A**) A crescent-shaped high absorption area (↑) is observed on the aortic margin, suggesting acute aortic dissection with thrombosed false lumen. (**B**) High absorption area is continuous craniocaudally (▲).

images (**Figure 35**). In the ascending aorta, the intimal flap is perpendicular to the imaging surface, making it easier to capture the entry, and it was reported to be identified by CT in 93% of the cases.[137] On the other hand, in the arch aorta, the imaging surface is parallel to the intimal flap, making it difficult to be identified, and evaluation using MPR images is useful (**Figure 36**). For the closure of the entry by TEVAR, the position of the entry needs to be accurately identified; however, the identification of the entry is difficult using CT with a thickness of 5 mm. The entry can often be identified by carefully interpreting the images taken with a thin slice thickness of 1 mm or less. In addition, electrocardiogram gated imaging is effective for acute aortic dissections with vigorous flap movement in the ascending aorta.

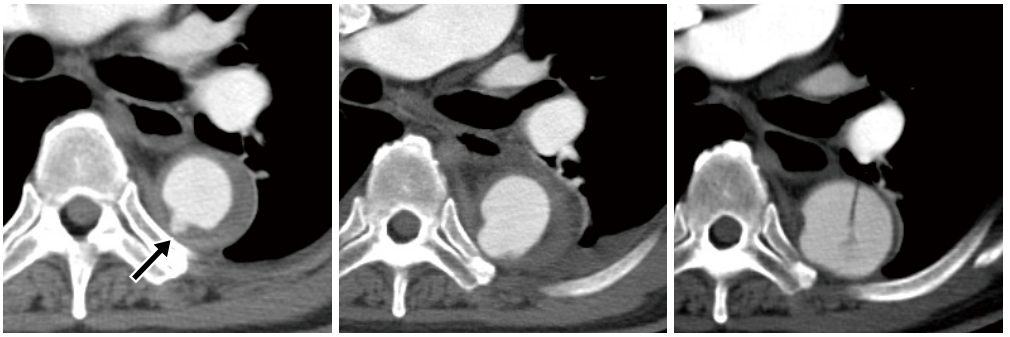
b. Aortic Dissection With Thrombosed False Lumen

In unenhanced CT images of aortic dissection with thrombosed false lumen, the false lumen filled with crassamentum or hematoma is seen as a continuous crescent-shaped or ring-shaped highly-concentrated area in the longitudinal direction of the aorta (**Figure 37**). As this cannot be easily seen in contrast-enhanced CT images, unenhanced CT examination is necessary. In addition, this finding is similar to the high-attenuating crescent sign found in rupture/impending rupture of aortic aneurysm (See **Figure 31**). However, as a differentiation point, while rupture/impending rupture exhibits a highly-concentrated area in localized sites on images, dissection often exhibits a relatively extensive lesion continuous in the longitudinal direction of the aorta. In contrast-enhanced CT images, the interior of the false lumen with thrombosis occlusion shows no contrast-enhancement until the delayed phase. Although differentiation between occluded false lumen and parietal thrombosis of the aorta is a problem, the luminal surface in dissection is often regular, while that of the parietal thrombosis, which is an atherosclerotic change, is irregular, allowing for their differentiation.

c. ULP Type Aortic Dissection

In contrast-enhanced CT images, ULP is observed as an ulcerative lesion into the false lumen (**Figure 38**). Multiple ULP type dissections may be present, and it may occur during follow-up. Also, some may enlarge over time and change to aortic dissection with patent false lumen or may cause rupture. It requires careful follow-up, especially if it is found in the ascending aorta, immediately after the branch of the left subclavian artery, or in the descending aorta near the diaphragm.[138]

In the recent years, the small contrast-enhanced area in the thrombosed false lumen that has continuity with branch blood vessels (such as the intercostal, bronchial, and lumbar arteries), despite unclear continuity with the aortic lumen, has been treated as an intramural blood pool (IBP) in some cases, differentiating it from ULP.[139] Imaging findings of IBP are similar to those of ULP; however, ULP is an unstable condition, whereas IBP less than 15 mm regresses spontaneously with a favorable prognosis.[139] The imaging features of IBP include its appearance as an insular contrast-enhanced area in the thrombosis within the false lumen, its isolated formation on the adventitial side of the



A: Day of onset **B:** 12 days after onset **C:** 38 days after onset

Figure 38. ULP (ulcer-like projection) type aortic dissection. (**A**) An ulcer-like projection protruding into the occluded false lumen is observed, suggesting ULP (↑). (**B**,**C**) The ULP extends over time and eventually transitions to aortic dissection with patent false lumen.

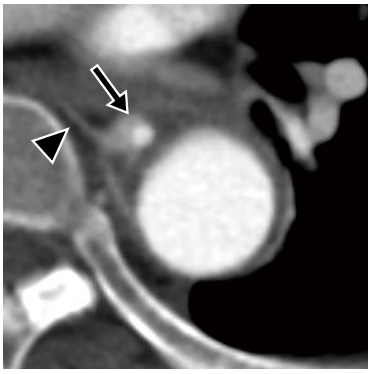
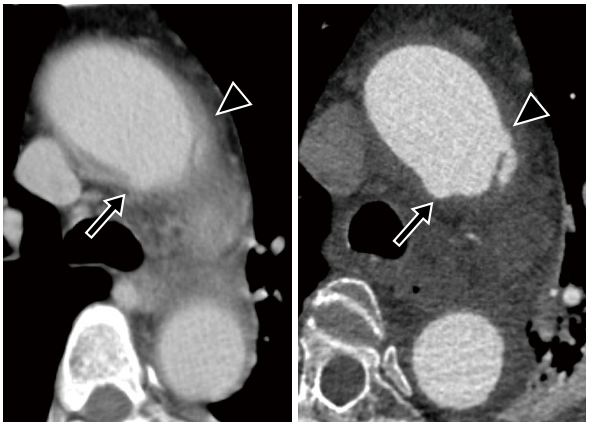


Figure 39. Intramural blood pool in ULP (ulcer-like projection) type aortic dissection (contrast-enhanced CT). A small insular contrast-enhanced area with unclear continuity with the true lumen is observed on the lateral side of the thrombosed false lumen (⇑). It is continuous with the intercostal artery (▲), suggesting intramural blood pool (IBP).



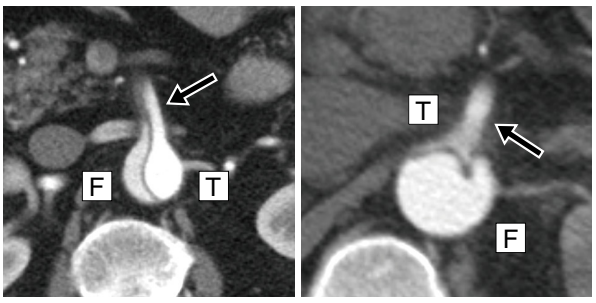
Non-electrocardiogram gated image | Electrocardiogram gated image

Figure 40. Reduction of artifacts in aortic dissection by electrocardiogram gated imaging. The ULP (⇑) and small dissection lumen (▲) of the ascending aorta, which are unclear in non-electrocardiogram gated imaging, are clearly visualized in electrocardiogram gated imaging.

false lumen, and its continuity with branch blood vessels (**Figure 39**). However, a strict distinction between ULP and IBP cannot be made in some cases due to the spatial resolution of CT images.

d. Diagnosis of Complications

Several complications (sequelae) of aortic dissection are serious, including rupture, cardiac tamponade, and malperfusion of organs and limbs. Although hemorrhagic pericardial effusion shows high absorption on unenhanced CT images, caution is needed as high absorption may not be observed if the amount is small. In addition, the evaluation of the aortic root and the ascending aorta by CT examination may be difficult due to motion artifacts by heartbeat. However, the dissection flap, entry, and ULP can be identified by taking electrocardiogram gated images, and the range of extension of dissection can be accurately evaluated (**Figure 40**). The extension of dissection into the carotid, coronary, and superior mesenteric arteries likely causes serious complications, such as cerebral infarction, myocardial infarction, and intestinal ischemia, which require an urgent response. Malperfusion is caused by two mechanisms: stenosis/occlusion due to the extension of dissection into the branch itself (static obstruction) and exclusion/occlusion of the true lumen due to increased pressure in the false lumen without the extension of dissection into the branch itself (dynamic obstruction)[140] (**Figure 41**).



A: Static obstruction | **B:** Dynamic obstruction

Figure 41. Mechanism of organ ischemia due to aortic dissection (contrast-enhanced CT). (**A**) Dissection has spread to the superior mesenteric artery, resulting in the narrowing of the true lumen of the superior mesenteric artery (⇑). F: False lumen, T: True lumen. (**B**) The true lumen is highly excluded by the false lumen, resulting in reduced blood flow in the superior mesenteric artery branching from the true lumen (⇑).

e. Atypical Aortic Dissection

Atypical forms of dissection include three-channeled dissection, localized abdominal dissection, and complication of aortic aneurysm and dissection. Also, relatively rare conditions that complicate special diseases include dissection secondary to coarctation of the aorta and dissection complicating pregnancy. Three-channeled dissection and the complications of aortic aneurysm and dissection are described below.

i. Three-Channeled Dissection

Three-channeled dissection is a special form of aortic dissection with patent false lumen, which presents three lumina as a result of the re-dissection of chronic dissection (**Figure 42**). It often complicates Marfan syndrome and occurs in the descending aorta after prosthetic graft replacement of the ascending-arch aorta. Many of the second false lumina in three-channeled dissection are devoid of re-entry, dead-ended, and confined to the descending aorta. However, if it has a re-entry, the dissection tends to extend over a wide area from the descending aorta to the abdominal aorta.

ii. Complication of Aortic Aneurysm and Dissection

It is a complication of an existing atherosclerotic aortic aneurysm by aortic dissection. Conventionally, atherosclerosis was not considered as a direct cause of dissection, and the relationship between aneurysm and dissection was not investigated. However, such a complication is not rare,

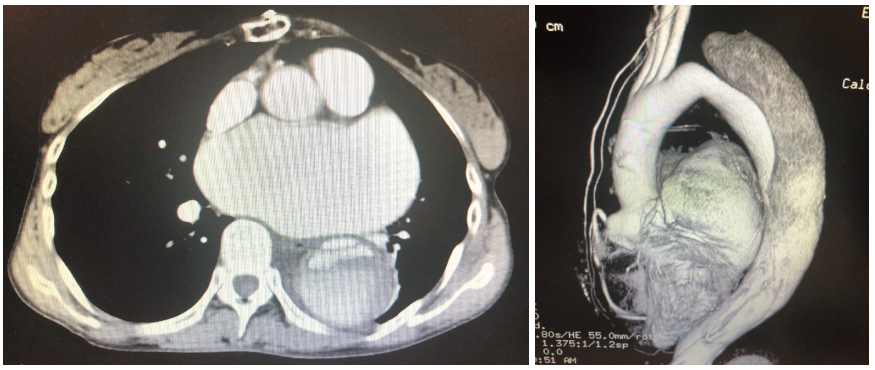


Figure 42. Aortic three-channeled dissection complicating Marfan syndrome.

according to recent reports.[141,142] The relationship between an existing aneurysm and newly developed dissection varies, and while some dissections originate from the aneurysm, others stop their extension at the site of the aneurysm. Although extremely rare, the dissection may extend in the longitudinal direction beyond the aortic aneurysm.

3.3 MRI Examination

3.3.1 Indications

For several aortic diseases, the accuracy of MRA examination is comparable to that of CTA examination.[143,144] The advantage of MRI examination is that it can obtain qualitative information that cannot be collected by other modalities, such as the evaluation of vascular wall/thrombosis using black-blood MRI, dynamic evaluation of aortic valve and intimal flap using cine MRI, and flow dynamics analysis using phase contrast MRI, in addition to the absence of X-ray exposure. On the other hand, MRI examination is not suitable for the acute phase, during which the general condition is unstable, due to the long imaging time, difficulty in monitoring the general condition, and difficulty in emergency response.[144] In addition, the situations where MRA examination is performed are limited, since contrast-enhanced CT is performed in many cases for diagnostic imaging of aortic diseases in the acute phase.

Examinations of aortic diseases for which MRI is indicated are as follows:

- Follow-up of aortic diseases in women capable of pregnancy and children
- Screening for patients at genetic risk of aortic diseases[145]
- Non-contrast-enhanced MRA in patients with severe renal dysfunction and asthma
- Evaluation of endoleak after TEVAR/EVAR
- Qualitative diagnosis and inflammation evaluation of the vascular wall
- Dynamic evaluation of valve diseases and intimal flap complicating aortic diseases
- Evaluation of abnormal blood flow induced by aortic diseases

On the other hand, cases and examinations for which MRI is not indicated include the following:

- Cases with a poor general condition, requiring careful monitoring
- Claustrophobia
- Evaluation of TEVAR/EVAR and its vicinity where a high degree of artifacts is expected on CT images
- Patients who have a device contraindicated for MRI in the body (Devices are classified into different types, such as those that are compatible to MRI examination and those that can be imaged depending on the condition.[147] Although these need to be confirmed by the package insert, they can also be verified online using the "MR compatibility search system for medical devices" [MEDIE Co. Ltd.])

In addition, when performing MRA examination as an alternative to CTA examination or when comparing CTA and MRA images, attention must be paid to the following:

- MRA shows poor contrast of wall structure and soft tissue structure around the wall, while it shows high contrast of the lumen[148]
- MRA cannot visualize calcified lesions
- The spatial resolution of MRA is approximately 1–2 mm, which is inferior to that of CT
- MRI-specific artifacts[149]

3.3.2 Imaging

a. Contrast-Enhanced MRA Examination

Dynamic MRA imaging is performed while intravenously injecting a gadolinium contrast medium.[150] In recent years, time-resolved MRA imaging, which captures serial multiphase contrast-enhanced MRA with a time resolution of approximately 2–10 s, has become the mainstream due to the improvements in imaging technology.[151] It has become possible to visualize the flow dynamics from the true to the false lumen of aortic dissection and the gentle flow of endoleak after TEVAR/EVAR, and its visualization ability is said to be superior to that of CTA.[152]

b. Non-Contrast-Enhanced MRA Examination

Mainly, there are two imaging methods of non-contrast-enhanced MRA.[150] One method, called fresh blood imaging, uses electrocardiography and visualizes the arterial blood by utilizing the difference in the signals of arterial blood flow between systole and diastole.[153] However, it is not suitable for the visualization of blood flow with slow velocity. The other method, which is identical to the one used in coronary artery MRA, is based on steady-state free precession (SSFP) sequencing that can acquire images at high speed while maintaining the blood structure at a high signal.[154] However, it may have difficulty in distinguishing between thrombosis and lumen due to specific artifacts or similarity between thrombosis signal and blood signal.[149]

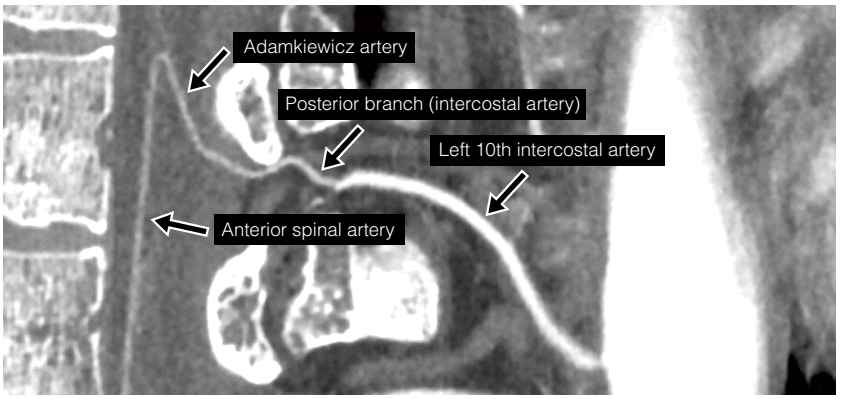


Figure 43. Identification of the Adamkiewicz artery. The Adamkiewicz artery, which branches from the left 10th intercostal artery, exhibits a characteristic hairpin turn at the site where it joins the anterior spinal artery in the spinal canal (↑).

c. MRI Examination of the Vascular Wall

2D imaging requires approximately 1–2 min, while 3D imaging requires approximately 5–10 min. The use of both T1-weighted and T2-weighted images captures the time phase of the aortic aneurysm wall and the development and change of thrombosis in the false lumen of aortic dissection.[155,156] In addition, inflammation of the vascular wall in large-vessel vasculitis, such as Takayasu arteritis, can be visualized by fat-suppressed T2-weighted images and T1-weighted images after the administration of contrast medium.[157] In 3D imaging, an evaluation that combines morphological and qualitative diagnoses can be easily performed by capturing the continuity of vascular wall structure and thrombosis structure.[156] However, the blood flow lumen shows a high signal when there is reflux, disturbance, or delay in the blood flow, resulting in a risk of insufficient separation between the lumen and the vascular wall. In addition, the use of diffusion-weighted images is expected to allow for the qualitative evaluation of aortic tumors.[158]

d. Cine MRI Examination

Cine MRI imaging is commonly used in cardiac function analysis, and it uses SSFP sequencing, which can collect signals at a high speed by maintaining the endovascular lumen at a high signal. It can collect data by dividing one heartbeat into approximately 20–30 fragments.[149,150] The obtained data can be used to evaluate the dynamics of the aortic valve and intimal flap. Because of the disturbance associated with jet blood flow at the entry of dissection and the decreased signal in SSFP images,[159] cine MRI can capture the jet blood flow/abnormal blood flow indirectly.

e. Phase Contrast MRI Examination

Phase contrast MRI imaging can quantify the blood flow velocity and take a cross-sectional image in approximately 10 s to 1 min using the 2D method.[160] It collects data by dividing one heartbeat into approximately 20–30 fragments and quantifies the velocity of the blood flow perpendicular to the cross-section, allowing us to capture abnormal blood flow, such as reflux and pulse wave velocity.[161] 4D flow MRI, which is a three-dimensional extension of 2D phase contrast MRI, has been realized in recent years.[162] It has visualized complex blood flow dynamics, and it is expected to allow for the measurement of new evaluation indices, such as wall shear stress applied to the vascular wall.[163,164]

3.4 Identification of the Adamkiewicz Artery

One of the most serious complications of thoracic descending/thoracoabdominal aortic surgery is paraplegia caused by spinal cord ischemia. To avoid spinal cord ischemia, efforts to identify the Adamkiewicz artery, which nourishes the spinal cord, have been made preoperatively using CT/MRI examination. Its usefulness was confirmed in a large-scale clinical study conducted in Japan (Japanese Study of Spinal Cord Protection in Descending and Thoracoabdominal Aortic Repair [JASPAR] Registry).[165]

3.4.1 CT Examination

MDCT with 16 or more rows, which allows extensive imaging with thin slices, is used to visualize the Adamkiewicz artery.[119,166–168] The slice thickness is approximately 0.5–1 mm. The contrast medium yields a higher visualization rate when a high-concentration preparation is injected rapidly.[168] An image processing device is used for the visualization of the Adamkiewicz artery, and the interior of the spinal canal is observed with oblique coronal sections by multi-planar reconstruction. The Adamkiewicz artery exhibits a characteristic hairpin turn at the site where it joins the anterior spinal artery, which is used as a marker for its identification. However, its differentiation from veins (anterior radicular medullary vein) poses a problem because the anterior radicular medullary vein also exhibits a morphology similar to a hairpin turn. The most reliable way to differentiate between the two is to demonstrate the continuity between the Adamkiewicz artery and the intercostal (lumbar) artery that branches from it. The continuity is demonstrated by visualizing the route from the aorta to the intercostal (lumbar) artery, its posterior branch, the root medullary artery, the Adamkiewicz artery, and the anterior spinal artery as a single blood vessel, like a single stroke of the brush, using curved planar reconstruction (CPR)[119,166–168] (**Figure 43**). The diagnostic ability of the Adamkiewicz artery by MDCT has been reported to be 80–90% when the visualization of the hairpin turn is used as the basis for diagnosis and 29–60% when the proof of continuity is used as the basis for diagnosis.[119,166–168] However, due to the advances in the MDCT devices in

recent years, a high visualization rate of approximately 90% has begun to be reported, even when the proof of continuity is used as the basis for diagnosis.[169–171]

3.4.2 MRI Examination

The Adamkiewicz artery is imaged with contrast-enhanced MRA using a 1.5 or 3 T device, and time-resolved MRA is generally used. This method repeatedly captures a specific site by high-speed imaging with an imaging time of approximately 10 s each while rapidly injecting the contrast medium intravenously at a rate of approximately 3–4 mL/s. With this method, the state of the first pass of the contrast medium can be observed over time, allowing for arteries and veins to be distinguished. Its diagnostic ability of the Adamkiewicz artery has been reported to be 69–84%.[172,173] The advantages of MRA examination include the absence of radiation exposure and influence of bone structure; however, it requires imaging skill and experience compared to CT examination.

3.4.3 Characteristics of CT and MRI Examinations

Each of CT and MRI examinations has its advantages and disadvantages; however, upon focusing on aortic surgery, the main points in diagnosing the Adamkiewicz artery are described below.

a. Collateral Flow

The occlusion of the intercostal (lumbar) artery that branches off the Adamkiewicz artery due to atherosclerosis induces the formation of collateral flow in some cases. Such cases are not rare and are found in 22–24% of aortic aneurysm cases.[167,170,174] It has been reported that 85% of the arteries distributed around the spine, such as the muscular branches and posterior vertebral body branches of the intercostal artery, and 15% of the arteries running on the chest wall, such as the thoracodorsal artery, are the routes of the collateral flow.[174] Since CT images the entire trunk, it has no problem in visualizing these blood vessels. However, MRI cannot visualize the collateral flow running through the chest wall because its imaging range is limited to around the spine.

b. Selective Use of CT and MRI

Although CT and MRI imaging have comparable diagnostic abilities of the Adamkiewicz artery, it is generally easier to perform CT imaging, and CT does not interfere with the visualization of collateral flow. Thus, CT should be the first choice of diagnosis method, and MRI can be added if the diagnosis is difficult with CT alone.[175] Since the visualization of the Adamkiewicz artery is greatly affected by the performance of the devices in both CT and MRI, it is important to understand the characteristics of the devices used in each facility before selecting the examination method.

3.5 Angiography

Due to the development of non-invasive diagnostic methods, such as CT and MRI examinations, there have been fewer opportunities for angiography to be used in diagnosing aortic diseases. However, angiography is used when sufficient information cannot be obtained by CT/MRI examinations. In some cases, angiography is useful in diagnosing an endoleak after TEVAR/EVAR. In addition, angiography may be needed for understanding the relationship between the coronary arteries and dissection and diagnosing malperfusion in aortic dissection. With the improvement in the accuracy of digital subtraction angiography (DSA), intra-arterial DSA using a small-diameter catheter has been performed. A catheter, which is usually a 4–5 Fr pigtail or similar type, is percutaneously inserted through the brachial or femoral artery, and contrast-enhanced imaging is performed by placing the tip of the catheter in the ascending aorta or the descending-abdominal aorta. Basically, images of the thoracic region are taken in two directions of left anterior oblique position at 50–60° and right anterior oblique position at 20–30°, while the front-view images are taken for the abdominal region.

3.6 Echographic Examination

Radiation diagnostic imaging, such as CT examination and angiography, is mainly used for the evaluation and treatment of aortic diseases. However, echographic examinations have some advantages over radiation diagnostic imaging, including the absence of radiation exposure, lack of need for the transportation of the patient, real-time acquisition of information, and the ability to evaluate the properties of tissues and the process of thrombosis formation. Furthermore, blood flow information can be obtained by the Doppler method without using a contrast medium, and recent 3D echography can be used to obtain tomographic and stereoscopic images of various scanning planes similar to those of CT/MRI examinations. Also, the cost of echography is lower than that of other diagnostic imaging. On the other hand, the disadvantages of echographic examinations include the interference of visualization by air and bones and the possible direct impact of the technical skills of the examiner on the accuracy of diagnosis.

Echographic examinations include semi-invasive transesophageal echocardiography (TEE), invasive intravascular echography, intravascular ultrasound (IVUS), and intracardiac echocardiography (ICE), in addition to the ordinary echographic method that scans on the body surface (body surface echography). In the recent years, pocket-sized portable echography (pocket echography) has also been developed, and echography is becoming part of the basic physical examination methods.[176–178]

3.6.1 Body Surface Echographic Examination in ER and ICU

Critically ill patients undergo echographic examinations that mainly evaluate aortic diseases judged to be clinically important, rather than evaluating systematically, which include point of care ultrasound (POCUS) and focused cardiac ultrasound (FOCUS). To obtain information on the aorta, an acoustic window is found by using body surface echography, avoiding the bones, lungs, and intestinal tract. The thoracic aorta is visualized by scanning the parasternal region, epigastric region, cardiac apex, and suprasternal region, while the abdominal aorta is visualized through the parenchyma organs, avoiding the intestinal tract. Also, the arch branches are visualized from the cervical region, while the femoral artery is visualized from the inguinal region (**Figure 44**).[178] Furthermore, the visualization of the descending aorta by paravertebral scanning[179] and abdominal aorta by retrocolic scanning[178] can also be acoustic windows.

Several studies have reported the usefulness of echographic examinations in the diagnosis of the acute aortic

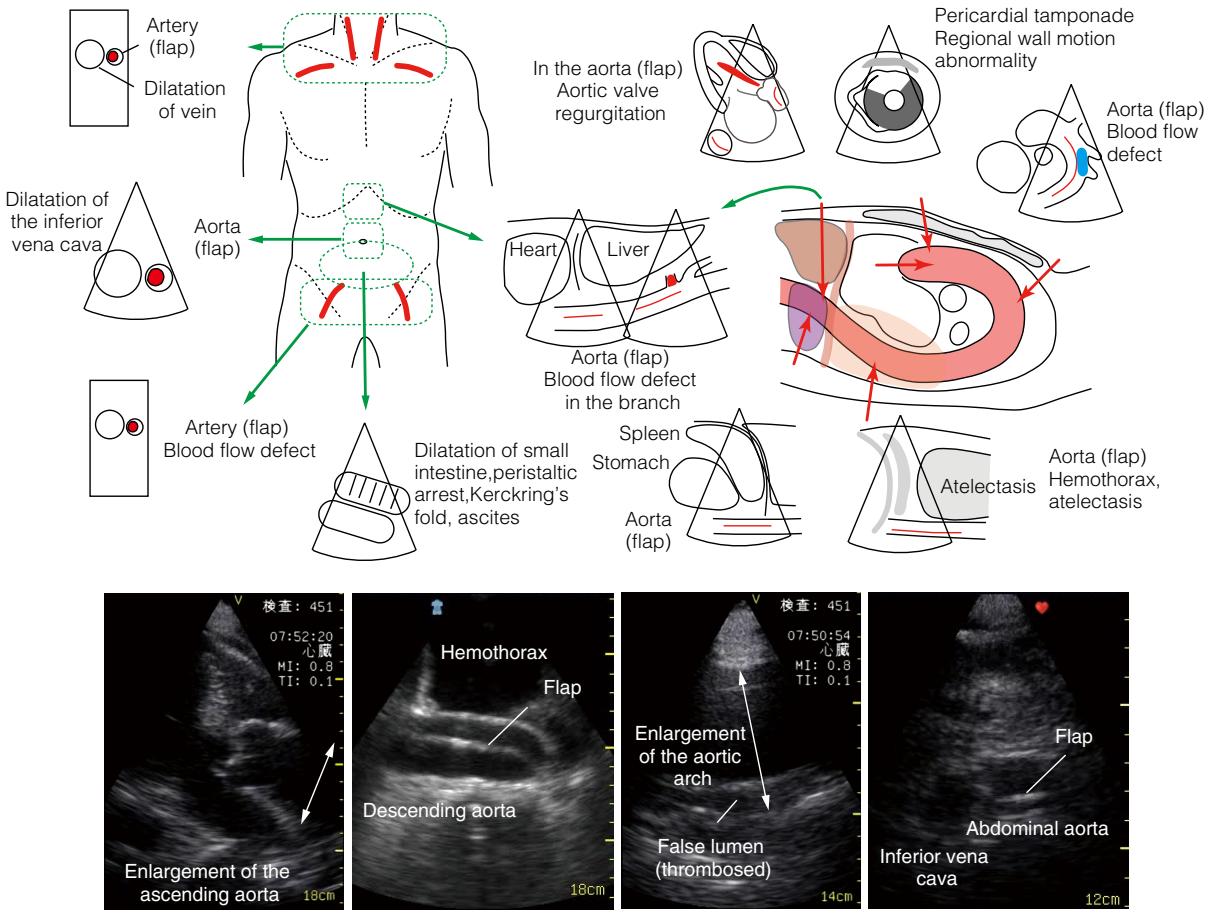


Figure 44. Echographic examination of aortic dissection. (Adapted from Orihashi K. 2015.[178])

syndrome (AAS).[180–185] Echographic examinations need to be utilized as various symptoms presented by patients with acute dissection make its initial diagnosis difficult, affecting the treatment results.[186] In addition, PCI may be performed after acute myocardial infarction is suspected based on the symptoms and electrocardiographic findings.[187] Additionally, lifesaving may become difficult due to fibrinolytic therapy,[188] and the administration of an anticoagulant or antiplatelet agent may increase the long-term mortality rate.[189] The appropriate use of POCUS and FOCUS can reduce the misdiagnosis rate, time till diagnosis, and mortality rate.[190]

For stroke, fibrinolytic therapy at the early stage of onset has a favorable treatment effect, and the administration of t-PA before transport is widely carried out. However, it is fatal in patients with aortic dissection presenting with cranial nerve symptoms. Since such deaths have not been rare in Japan, the National Cerebral and Cardiovascular Center has issued a statement,[191] recommending D-dimer measurement and carotid artery echography. The carotid artery, which is located only a few centimeters from the body surface, can be evaluated by pocket echography.[192]

The gold standard for AAS diagnosis is contrast-enhanced CT examination; however, it is not uncommon for only unenhanced CT examination to be performed in consideration of allergy to contrast media and renal dysfunction, even when AAS is suspected in the initial examination (especially in community medicine). Even if contrast-enhanced imaging is performed, contrast-enhancement may be poor or false positives may occur due to bloom artifacts.[193] Considering that 90% of the patients survive if they reach invasive treatment (open surgery and SG deployment), it is desirable to avoid misdiagnosis and resulting delays in transportation by performing a quick and simple echographic examination. However, although the diagnostic ability of TEE is comparable to that of CT,[194] it may induce rupture due to the stimulation of insertion,[195,196] and it is not considered optimal for initial diagnosis.

3.6.2 Intraoperative Echographic Examination

In the treatment of AAS, it is not uncommon for surgery to be performed with an insufficient preoperative evaluation and for rupture or new malperfusion to occur intraoperatively, at which TEE is useful for deciding and changing the policy.[197–199] TEE provides real-time information at the level from the aortic root to the renal artery without interrupting surgical operations.[200–203] However, attention must be paid to the influence of the skill level of the examiner on the evaluation, as well as esophageal injury. In

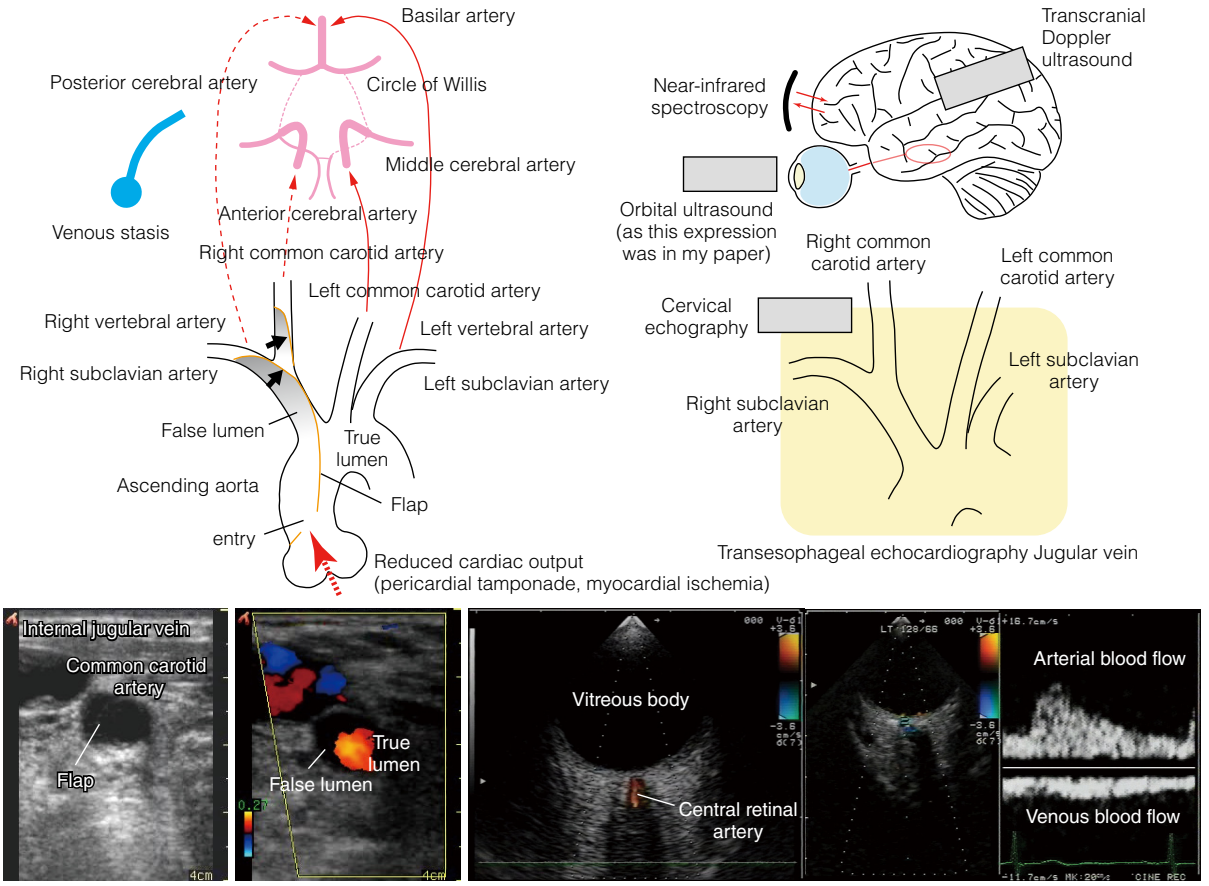


Figure 45. Cerebral malperfusion associated with aortic dissection. (Adapted from Orihashi K. 2016,[192] 2019.[206]) © 2016 Springer Japan https://link.springer.com/journal/595. Modified and reprinted with permission of Nankodo Co., Ltd.

addition, information on the aortic root-aortic arch can be obtained by performing direct echo (epiaortic echo) from the operative field.

a. Diagnosis of Rupture

AAS can cause a rupture in the pericardial sac and intrathoracic hemorrhage; however, TEE allows for rapid diagnosis and real-time evaluation of hemorrhage volume, making appropriate responses possible. If the site of rupture in the hemothorax is unknown, the echo-free space in the mediastinal hematoma may be helpful for the identification of the rupture site.[204]

b. Malperfusion (Branch Malperfusion)

Malperfusion is evaluated by the blood flow in the branch arteries and organ parenchyma and movement of the heart and intestinal tract.[205] While the dynamic/static obstruction in radiation diagnosis is evaluated within the range where the contrast medium reaches in a short time, echography evaluates aortic type (occlusion of the branch entrance by flap in the aorta) and branch type (occlusion of the true lumen in the branch) based on the size and blood flow of each of the true and false lumina in the aorta and branch arteries.

i. Brain

Body surface echography provides information on the blood flow of the common carotid, ocular, and middle cerebral arteries, while TEE provides information on the blood flow in the arch branches (**Figure 45**).[192,200,206] With the transcranial Doppler method, it is difficult to capture blood flow if the cerebral perfusion pressure is low, such as during extracorporeal circulation. Although orbital ultrasound, which evaluates the blood flow in the central retinal artery, is also used,[207] it is performed in a short time to avoid cornea damage. The common carotid artery can be visualized in the cervical region; however, the finding of true lumen occlusion is not always consistent with cerebral malperfusion. The true lumen occlusion of the brachiocephalic artery may not recover even with true lumen perfusion, and TEE is useful for its evaluation.[208]

ii. Myocardium

The myocardium is evaluated by coronary artery blood flow and left ventricular wall motion. In the left coronary artery, true lumen stenosis easily occurs due to the extension of dissection into the left main trunk,[209] and in the right coronary artery, the intima is drawn out at the entry, causing perfusion from the false lumen or ischemia. Intraoperative diagnosis is performed by direct echo or TEE because events, such as failure of the collapsed true lumen to

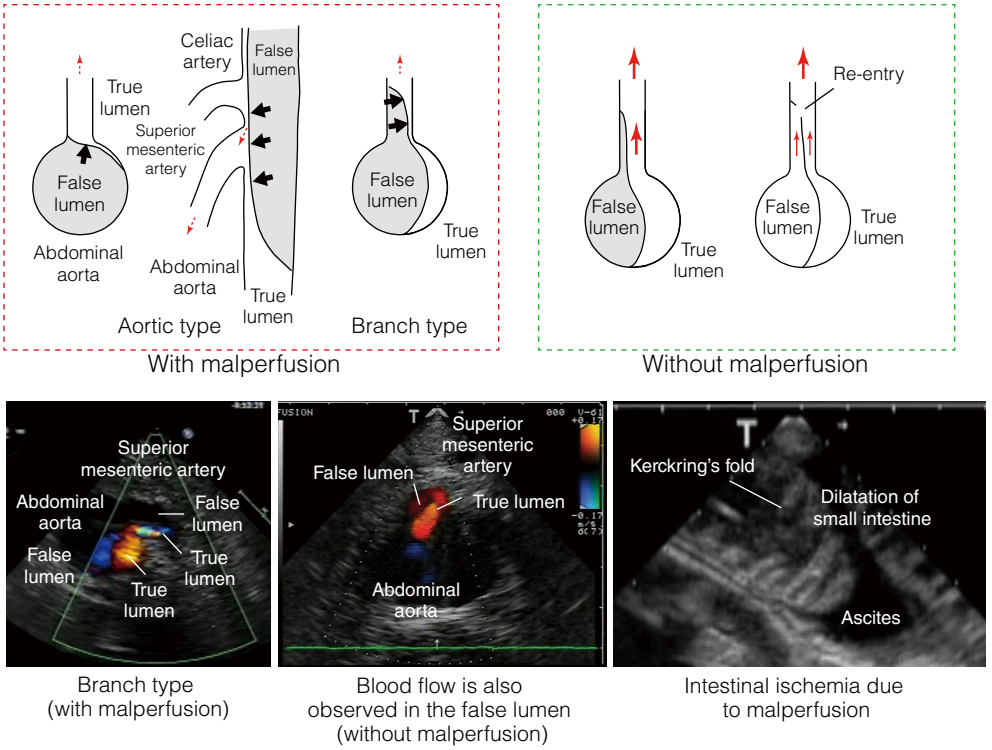


Figure 46. Visceral malperfusion associated with aortic dissection. (Adapted from Orihashi K. 2016.[213]) © 2015 Springer Japan. https://link.springer.com/journal/595.

recover even with the supply of blood to the true lumen,[210] development of new myocardial ischemia caused by the supply of blood to the false lumen,[211] and coronary artery occlusion after aortic reconstruction,[212] may occur.

iii. Intestinal Tract

The intestinal tract is evaluated by blood flow of the superior mesenteric artery and visceral peristalsis (**Figure 46**).[213] The possibility of intestinal ischemia is considered if body surface echography shows dilatation and peristaltic arrest of the intestinal tract. The celiac and superior mesenteric arteries can also be visualized by pocket echography.[213] With TEE, the aortic type and branch type are evaluated.[214,215] Even if the dissection has extended to the branches, the possibility of malperfusion is low in cases with a large true lumen or blood flow in the false lumen. Real-time evaluation is necessary because the true lumen may not recover even if blood is supplied to the true lumen.[210]

iv. Lower Extremity

There is a report that states that malperfusion of the lower extremity led to the diagnosis of aortic dissection.[216] In the femoral artery, the blood flow of the true lumen may not recover even after stump formation due to thrombosis in the false lumen; however, real-time evaluation of the blood flow can be done by body surface echography.[205]

c. Evaluation of Aortic Valve Regurgitation

Aortic valve regurgitation is caused by the lateral deviation of the commissure due to the enlargement of the ascending aorta, valve leaflet deviation due to commissure detachment, and incarceration of flap.[217,218] A flap may circumferentially detach, causing intussusception and deviation to the left ventricle.[219,220] Conversely, the regurgitation orifice may be covered with a flap, leading to the underestimation of regurgitation.

d. Troubles Related to Systemic Perfusion and Intraoperative Dissection

When inserting a perfusion cannula directly into the aorta, its placement in the true lumen is confirmed by TEE.[221,222] In the femoral artery perfusion, predominant perfusion to the false lumen is likely to occur in cases of retrograde extension of DeBakey type III dissection, which should be monitored at the time of initiating systemic perfusion.[211] If intraoperative dissection is suspected in the operative field, evaluation by epiaortic echo,[223] TEE,[224] or both is recommended.[225] However, monitoring with TEE at the start of blood transmission is desirable since the dissection may not be noticed in hemodynamics or the operative field.[226,227] Retrograde dissection may occur from the blocked site after aortic replacement, and TEE is useful for its diagnosis.[228,229]

3.6.3 Hybrid Surgery

When elephant trunk (ET) is deployed for the purpose of staged treatment, TEE can determine whether it is bent in the aorta.[230] When using ET for landing or anastomosis, visualization by TEE may be helpful as a guide.[231,232] In frozen elephant trunk (FET), the TEE guide is used during insertion to avoid paraplegia and wall damage,[233,234] and TEE

that can visualize both the aortic wall and the graft is also useful for diagnosing displacement after deployment.[235,236] In TEVAR for Type B dissection, navigation by TEE is used when advancing the guide wire into the true lumen.[237,238] Furthermore, the TEE guide is also used in the cheese-wire technique for guiding the guide wire to the false lumen,[239] guiding in fenestration,[240] and deploying stent to the re-entry.[241] Since TEE can repeatedly evaluate leaks without using a contrast medium, it may help reduce the use of contrast media in examinations, such as the evaluation of touch-ups.[232,242] Contrast echography[243] and endovascular echography are used to evaluate leaks after EVAR.[244]

3.6.4 Traumatic Aortic Injury

Traumatic aortic injury is a pathological condition of polytrauma, and although CT examination is the first choice for its diagnosis, bedside TEE is useful when hemodynamics is unstable.[245,246] It also has the advantage of simultaneously evaluating concomitant pathological conditions, such as injury to the right ventricle, right atrium, and tricuspid valve and thrombosis in the inferior vena cava.[247,248] However, esophageal injury may occur due to trauma, and it should be kept in mind when using TEE.[249]

3.6.5 Screening for Abdominal Aortic Aneurysm

For AAA, which is often detected incidentally, echographic screening has been performed on the general population, which was reported to significantly reduce aneurysm-related deaths.[250–252] However, its accuracy is inferior to that of CT examination, and there is a concern of overlooking the diagnosis.[253] However, those missed during screening are small aneurysms, and some suggest that the risk does not increase even if they cannot be detected.[254,255] The number of persons to be screened to avoid one death caused by aneurysm rupture (cost-effectiveness) has been controversial.[256–258] To increase the efficiency, there have also been efforts to target population groups by age, gender, and smoking status.[259,260] Some recommend screening for those whose sibling has had AAA or patients with cardiovascular diseases.[261,262]

In addition, AAA may be detected during the evaluation of the abdominal aorta by echocardiography. The patients for whom echocardiography is requested are more likely to have some cardiovascular diseases, and have a higher prevalence rate of AAA than the general population.[263] It was also reported that AAA was detected more frequently in those with aortic root dilatation.[264]

IV. Selection of Treatment

1. Medical Treatment

1.1 Medical Treatment Goals

The treatment goals for aortic diseases differ depending on the stage of the disease. While some diseases require medical treatment at the first stage, invasive treatment is needed once the disease progresses. Despite an invasive treatment, lifelong surveillance and continuation of high-quality medical treatment are still required after diagnosis. The main goal before surgical indication is to prevent the enlargement of the aneurysm/dissection and the progression of comorbidities. To protect patients from aortic disease-related deaths, the timing of invasive treatment should not be missed with regular follow-up using image examinations and appropriate surgical procedure should be selected after consultation with a specialized team.

Lifelong surveillance and comorbidity management are essential even after surgery, and the "quality" of diagnosis/treatment of comorbidities, especially other vascular diseases, and medical treatment for their onset risk factors strongly affects the life prognosis and course of patients with aortic diseases.

1.2 Abdominal Aortic Aneurysm (AAA)

The diagnosis and treatment cascade for abdominal aortic aneurysm (AAA) is shown in **Figure 47**.

AAA is, in principle, asymptomatic and often diagnosed incidentally during medical check-ups or close examinations for other diseases. In clinical practice, symptoms such as feeling of fullness, constipation, and nonspecific lumbar pain rarely lead to the diagnosis of AAA, and since more than 80% of the patients who have suffered its rupture cannot be saved,[265,266] how patients can be screened while they are asymptomatic is an important issue. Palpation for a pulsatile mass is a useful screening method that can be easily performed in the examination room. In addition, abdominal echographic screening should be actively considered for men over the age of 65 years, women smokers over the age of 65 years,[267] and those with a family history of AAA in first-degree relatives,[268,269] who are at a higher risk of developing an aortic aneurysm.

CT examination is performed for the diagnosis of AAA, and its diagnosis is made with a maximum minor axis of 30 mm or greater.[270] Maximum minor axes of 55 mm or greater in men and 50 mm or greater in women are recommended as indications for invasive treatment. However, even if the diameter of the aneurysm is smaller than the indicated values, invasive treatment may be considered depending on the age, physical constitution, and sex of the patient, as well as the morphology/enlargement rate of the aortic aneurysm. With respect to AAAs that do not meet the indications of invasive treatment, newly detected AAAs are re-examined 6 months after their detection to determine whether they exhibit a rapid enlargement of 5 mm or greater. Those detected previously are followed up regularly by CT examination according to the diameter of each aneurysm.

Smoking is a serious risk factor for the enlargement and rupture of AAA and thorough guidance for smoking cessation is given.[271–273] Although there is no evidence that drug therapy suppresses the enlargement of aneurysms, it is important to strictly implement the management of atherosclerotic risk factors aimed at reducing the risk of developing cardiovascular diseases, including blood pressure management, as well as screening for atherosclerotic diseases.

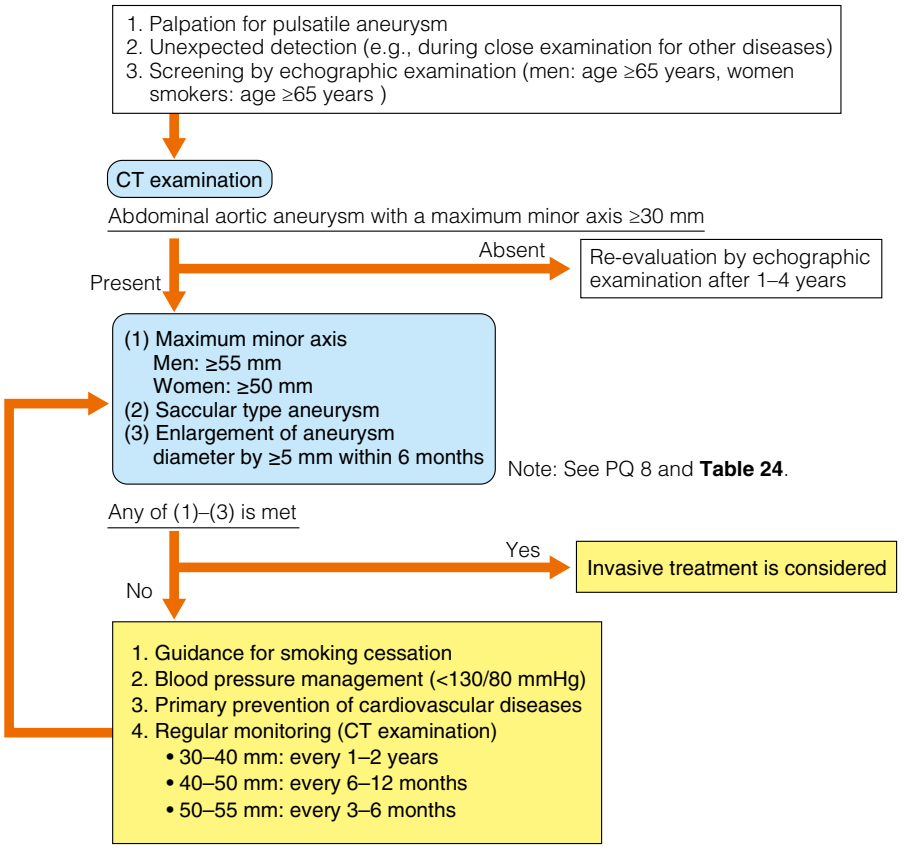


Figure 47. Diagnosis and treatment cascade for abdominal aortic aneurysm.

1.3 Thoracic Aortic Aneurysm (TAA)

The diagnosis and treatment cascade for TAA is shown in **Figure 48**. As with AAA, several TAAs are asymptomatic, and are often detected incidentally during medical check-ups or close examinations for other diseases. The subjective symptoms of TAA include hoarseness, dysphagia, chest pain, and back pain. CT examination is useful for the diagnosis of TAA, and it is performed every year if the maximum minor axis of TAA is less than 45 mm, or every 3–6 months if it is 45 mm or greater and less than 55 mm.

If the maximum minor axis of TAA is found to be 55 mm or greater in the initial CT examination, invasive treatment is considered while examining the surgical risks. In patients with hereditary connective tissue disorders, such as Marfan syndrome, invasive treatment is considered if the maximum minor axis of TAA is 45 mm or greater (See **Table 49** for details). Generally, the enlargement rate of the aneurysm diameter is 1.0–4.2 mm/year.[118,274] However, the rate is slow in TAA with a small diameter, and it increases as the aneurysm diameter enlarges. Thus, the observation interval is determined according to the diameter of the aneurysm. The aneurysms whose diameter increases by 5 mm or greater in 6 months are at high risk of rupture and are a target for invasive treatment. Saccular type TAAs have a high risk of rupture even if their diameter is not large, and invasive treatment is considered for these aneurysms while paying attention to their morphology.

1.4 Acute Aortic Dissection

The diagnosis and treatment cascade for acute aortic dissection is shown in **Figure 49**. When acute aortic dissection is suspected, the physical findings and vital signs are promptly examined, and diagnostic imaging is performed immediately if the hemodynamics of the patient is stable. With regard to the physical findings, pulse palpation of the limbs and examination of heart murmur and abdominal vascular bruits lead to the early detection of complications (sequelae). The presence or absence of myocardial ischemia is evaluated by electrocardiography, while the presence or absence of a dissection flap in the aorta, aortic valve regurgitation, and pericardial effusion is evaluated by echocardiography. CT examination is subsequently performed to achieve a definitive diagnosis. If the patient has high blood pressure and is in great pain, attempts to lower the blood pressure and relieve pain should be carried out.[275] It is also important to evaluate the inflammatory findings by blood tests, D-dimer levels, and the presence or absence of lactic acidosis, which suggests organ ischemia due to blood gas abnormalities.

Unenhanced and early/delayed contrast-enhanced CT images are used to accurately diagnose the morphology, extension, and range of dissection, as well as identifying the entry and the presence or absence of malperfusion. In aortic dissection complicated by malperfusion, vascular echographic examination is also useful when static and

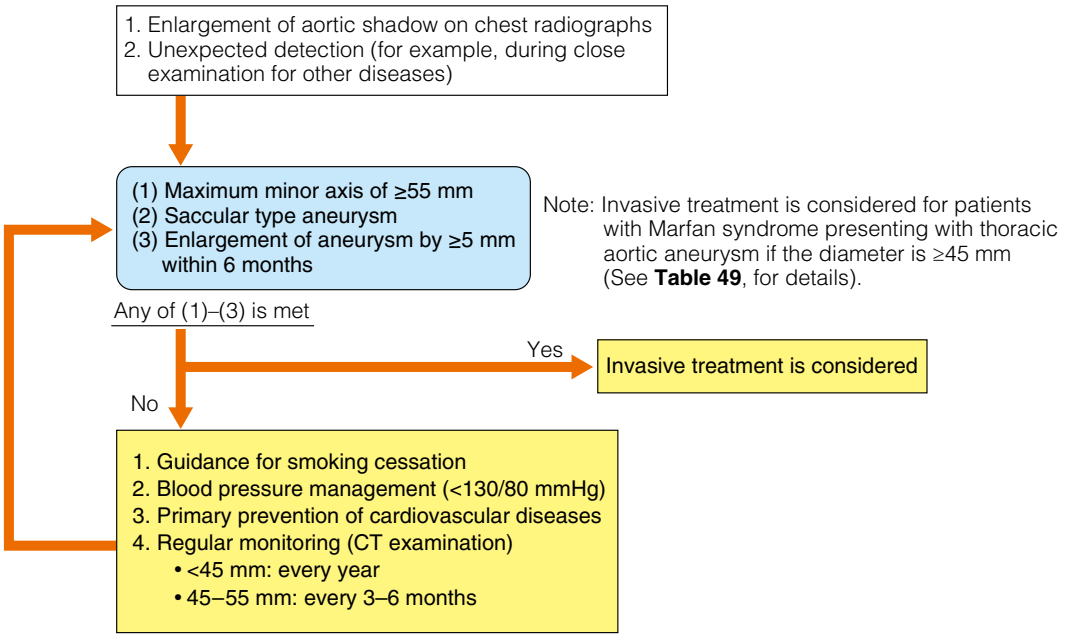


Figure 48. Diagnosis and treatment cascade for thoracic aortic aneurysm.

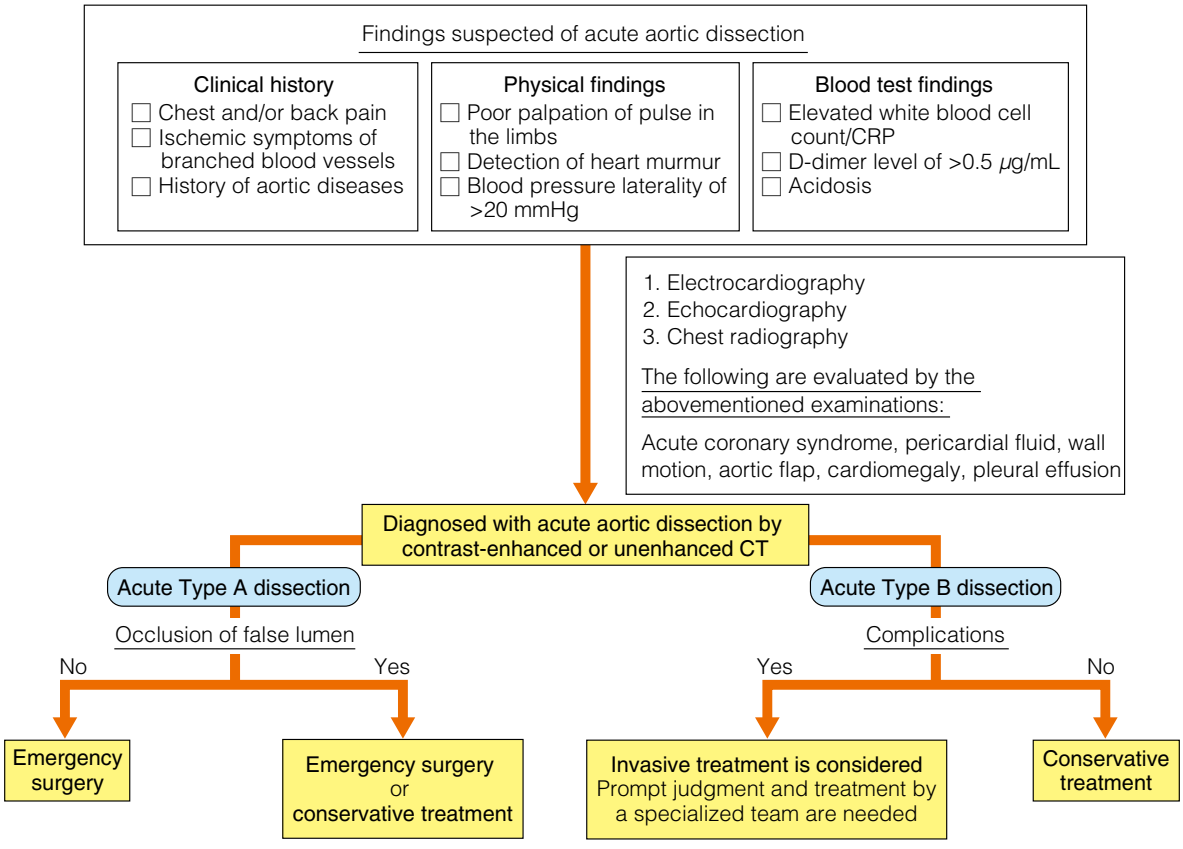
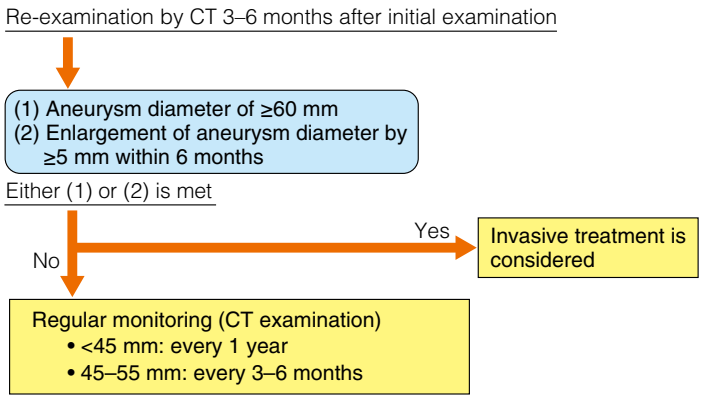


Figure 49. Diagnosis and treatment cascade for acute aortic dissection.



*If the aneurysm diameter is 55 mm or greater and less than 60 mm, invasive treatment is discussed by a specialized team based on the general condition, anatomical conditions, and expected surgical risk.

Figure 50. Diagnosis and treatment cascade for chronic aortic dissection.

dynamic obstructions cannot easily be distinguished. Urgent/semi-urgent surgery is considered in patients diagnosed with acute Type A dissection. Invasive treatment is indicated if a patient diagnosed with acute Type B dissection has complications (complicated dissection). Such a case requires prompt judgment and treatment by a specialized team of cardiologists, cardiovascular surgeons, and radiologists, and treatment in facilities capable of performing multimodal therapy is desired. On the other hand, conservative treatment is selected for uncomplicated dissection. However, complications may occur during the course, and cooperation with a facility capable of performing multimodal therapy is desired in such a case.

1.5 Chronic Aortic Dissection

The diagnosis and treatment cascade for chronic aortic dissection is shown in **Figure 50**. The majority of cases of chronic aortic dissection are followed up after being diagnosed at the onset of acute aortic dissection; however, asymptomatic aortic dissection may be detected incidentally during CT and MRI examinations. It is important to make a definitive diagnosis that the incidentally detected aortic dissection is not in its acute phase. Comprehensive judgment is made based on the inflammatory response by blood tests, the presence and brightness of pericardial effusion by echocardiography, electrocardiographic findings, CT value of the false lumen thrombosis, thickness of the septal wall of the false lumen by unenhanced CT examination, and the shape of the true lumen by contrast-enhanced CT examination, in addition to medical interviews regarding the time of symptom appearances, such as chest/back pain.

If the aortic dissection is determined to be in its chronic stage, the enlargement rate of the aneurysmal site needs to be determined, and the diameter of the aneurysm is measured by unenhanced CT imaging 3–6 months after an initial examination. For chronic aortic dissections with a known time of onset (follow-up cases of acute aortic dissection), CT imaging is performed 1, 3, 6, and 12 months after the onset, which mainly examines the absolute value of the aneurysm diameter and the enlargement rate. If ULP is detected in the initial diagnosis, its morphological changes are also examined by contrast-enhanced CT imaging. Since ULP may newly develop in the chronic stage, it is recommended to perform unenhanced/contrast-enhanced CT imaging at least once within 6 months of onset.

Annual CT examinations are sufficient for chronic aortic dissection if its diameter is below 45 mm. If the aneurysm diameter is between 45 mm and 55 mm, CT examination is performed continuously once every 3–6 months. For chronic aortic dissection (dissecting TAA), invasive treatment is indicated if it enlarges by at least 5 mm/6 months or its diameter is 60 mm or larger. If the diameter is between 55 mm and 60 mm, invasive treatment is discussed by a multimodal clinical team mentioned above based on the general and anatomical conditions of the patient and expected surgical invasiveness.

Several cardiovascular events, such as cerebral infarction and heart failure, occur during the follow-up of chronic aortic dissection. The risk factors for atherosclerotic diseases, such as valvular diseases and arrhythmia, are screened by non-invasive examinations during outpatient follow-up, and they should be appropriately managed.

1.6 Medical Treatment for Comorbidities

The medical approaches to comorbid risk factors and comorbidities are important in managing aortic diseases. The following is an overview of hypertension, dyslipidemia, diabetes mellitus, smoking, heart failure, coronary artery disease, and carotid artery disease.

1.6.1 Hypertension

In patients with aortic diseases, strict blood pressure management is desired with a target of below 130/80 mmHg.[96] β blockers improve the prognosis by reducing the incidence of post-dissection events in chronic aortic dissection[276] and reducing the enlargement rate of aneurysms in Marfan syndrome.[277] On the other hand, no antihypertensive drugs, including β blockers, suppress the enlargement of AAA.[278,279] Therefore, antihypertensive drugs for aortic diseases should be selected in consideration of the short-term/long-term prognosis and drug compliance, including a balance with comorbidities. For hypertension without comorbidities, an antihypertensive drug is selected from Ca

Table 7. Indications of Antihypertensive Drugs for Comorbidities of Aortic Diseases

	Ca blockers	ARB/ACE inhibitors	Thiazide diuretics	β-blockers
Left ventricular hypertrophy	○	○		
Heart failure with reduced LVEF		○	○	○
Tachycardia	○*			○
Angina	○			○
After myocardial infarction		○		○
Chronic kidney disease with proteinuria/ microalbuminuria		○		

*Non-dihydropyridines. ARB, angiotensin II receptor blockers; LVEF, left ventricular ejection fraction.

blockers, renin-angiotensin system inhibitors (ARB/ACE inhibitors), and diuretics.[280] The selection of antihypertensive drugs by risk factor for aortic diseases or comorbidity is described below (**Table 7**).

a. Older Adults

ACE inhibitors are recommended for older adults with repeated aspiration pneumonia, while thiazide diuretics are recommended for older adults at a high risk of fracture.[281] Ca blockers, ARB/ACE inhibitors, and thiazide diuretics are recommended for other aged individuals. The administration of β blockers is considered for heart failure patients with reduced left ventricular function after myocardial infarction, as well as patients with other heart diseases, such as arrhythmia.[280]

b. Cerebral Infarction

The combined use of an ACE inhibitor and a diuretic was reported to suppress the recurrence of cerebrovascular diseases and dementia.[282] The additional administration of a Ca blocker is considered as needed. β blockers are said to be less effective in preventing the recurrence of cerebrovascular diseases than other antihypertensive drugs; however, their administration is considered based on a balance with comorbid heart diseases.

c. Coronary Artery Disease

For angina, Ca blockers and β blockers without intrinsic sympathomimetic activity are the first-line drugs.[283] However, caution is needed as short-acting Ca blockers may induce myocardial ischemia due to rapid hypotension/ reflex tachycardia. On the other hand, in post-myocardial infarction cases, β blockers without intrinsic sympathomimetic activity suppress the recurrence of myocardial infarction and sudden death,[284] and ACE inhibitors improve life prognosis by suppressing left ventricular remodeling and cardiac events, such as heart failure and sudden death.[285,286] Therefore, the combined use of a renin-angiotensin system inhibitor (ACE inhibitors are preferred over ARB) and a β blocker is the first choice in post-myocardial infarction cases.[280]

d. Heart Failure

Blood pressure is often normal or low in heart failure patients with LVEF below 40%. ARB/ACE inhibitors, β blockers, and diuretics are used as standard antihypertensive drugs. Renin-angiotensin system inhibitors (ACE inhibitors are preferred over ARB) and β blockers improve the long-term prognosis, including the prevention of readmission due to heart failure. Diuretics are effective for the treatment and prevention of organ congestion.[287] Mineralocorticoid receptor blockers improve the prognosis of heart failure patients with low LVEF receiving standard treatment.[288] On the other hand, no drugs improve the prognosis of heart failure caused by left ventricular diastolic dysfunction in patients with LVEF of above 50%. Antihypertensive drugs are selected according to the pathological condition of each patient.

e. Atrial Fibrillation

Antihypertensive drugs, mainly ARB/ACE inhibitors, are selected. ARB/ACE inhibitors are highly effective in suppressing atrial fibrillation in patients complicated by heart failure or ventricular hypertrophy.[289] On the other hand, there is no clear evidence that they reduce the seizure frequency or prevent the recurrence and chronicity.

f. Chronic Kidney Disease (CKD)

ARB/ACE inhibitors are recommended for chronic renal failure patients with proteinuria. Any of ARB/ACE inhibitors, Ca blockers, and thiazide diuretics are recommended for patients without diabetes mellitus and proteinuria.[280]

g. Diabetes Mellitus

The selection of antihypertensive drugs in patients with diabetes mellitus varies depending on the presence or absence of microalbuminuria. ARB/ACE inhibitors are used if microalbuminuria is present, while an antihypertensive drug is selected from ARB/ACE inhibitors, Ca blockers, and thiazide diuretics if microalbuminuria is absent.[280]

PQ 4.

What Is the Blood Pressure Management Target for Patients With Aortic Aneurysm or Chronic Aortic Dissection?

Recommendation

The blood pressure management targeting below 130/80 mmHg is desirable.

The target for patients with TAA was set to a systolic blood pressure of 105–120 mmHg in the 2011 edition of the guideline; however, it has not been supported by solid evidence. In principle, the blood pressure management targeting below 130/80 mmHg is desired after comprehensively evaluating the comorbidities, age, and frailty of the patient.[96]

With regard to antihypertensive drugs, an RCT for propranolol showed that the administration of β blockers to patients with AAA did not reduce the enlargement rate of AAA and decreased their QOL.[290] However, the use of β blockers is useful for some comorbidities, such as chronic heart failure and coronary artery disease, and needs to be examined for each case. Regarding other diseases, the use of β blockers was reported to result in a decrease in the incidence of post-dissection events in chronic aortic dissection[276] and improvement of aneurysm enlargement and prognosis in Marfan syndrome.[277]

In addition, no reports have shown that the enlargement of AAA is similarly suppressed by antihypertensive drugs other than β blockers.[278,279] Antihypertensive drugs should be selected for each aortic disease in consideration of short-term/long-term prognosis and drug compliance, with comorbidities in mind. For hypertension patients without any comorbidities other than aortic diseases, an antihypertensive drug is selected from Ca blockers, ARB/ACE inhibitors, and diuretics.[280]

1.6.2 Dyslipidemia

In general, the onset of atherosclerotic diseases and related deaths in the Japanese population can be predicted by their LDL-C levels.[291] In addition, LDL-C levels were shown to correlate positively with cerebral infarction and negatively with hemorrhagic stroke;[292] nevertheless, its evidence in the Japanese population is not sufficient. According to the 2018 AHA/ACC atherosclerosis guidelines, complications of aortic aneurysm fall under atherosclerotic cardiovascular disease (ASCVD), but under high-risk conditions. The lipid management target for patients with aortic aneurysm differs after the age of 75 years. For patients over 75 years of age, it is considered appropriate to reduce the LDL-C levels by an average of 30–49% with moderate-intensity statins or by an average of over 50% with high-intensity statins (Class IIa). On the other hand, for patients under 75 years of age, the target is to reduce the LDL-C levels by over 50% with high-intensity statins (Class I), and the addition of ezetimibe is recommended if the LDL-C level is 70 mg/dL or higher, even with the maximum tolerance dose of statins (Class IIb).[293]

In Japan, although the "Guidelines for Prevention of Atherosclerotic Diseases 2017" did not set the lipid management targets for patients with aortic diseases,[294] there has been a large amount of evidence for coronary artery disease. Since aortic diseases have a high complication rate of coronary artery disease, it is recommended to use the above guidelines as a reference. In patients with a history of coronary artery disease (secondary prevention), if familial hypercholesterolemia, acute coronary syndrome, or diabetes mellitus is complicated by other high-risk pathological conditions, it is recommended to set a highly strict target below 70 mg/dL, as with pathological conditions that require stricter management.

Based on these, if the patient is complicated by familial hypercholesterolemia, a history of acute coronary syndrome, and diabetes mellitus, which are the pathological conditions that require stricter lipid management, in addition to aortic diseases, the target LDL-C level is set to below 70 mg/dL. Additionally, the target is set to below 100 mg/dL if the patient has aortic aneurysm complicated by coronary artery disease, and it is set to below 120 mg/dL if the patient has aortic aneurysm alone.[294]

PQ 5.
What Is the Lipid Management Target for Patients With Aortic Diseases?

Recommendation

The administration of statins is considered for patients with aortic diseases. The target level of LDL cholesterol depends on the comorbidities of each patient.

In Japan, lipid management targets have been proposed in the "Guidelines for Prevention of Atherosclerotic Diseases 2017";[294] however, no clear target specific to aortic diseases has been presented. On the other hand, clear LDL-C target levels have been set because the involvement of lipid plaques has been pointed out in the onset/exacerbation of atheromatous arterial diseases, such as coronary artery disease (CAD) and peripheral artery disease (PAD), and the management of LDL-C levels was reported to lead to the regression and stabilization of the plaques. However, the direct involvement of lipid plaques in the development of aortic aneurysm/dissection has not been demonstrated, and it is unclear whether they should be treated as atherosclerosis like CAD and PAD. Aortic diseases fall under atherosclerosis in the 2018 AHA/ACC secondary prevention guidelines;[295] however, there is no evidence of the direct involvement of dyslipidemia in the enlargement and rupture of aortic aneurysm/dissection. They are regarded as a confounding factor of CAD and PAD.

It was shown that the administration of statins may suppress the enlargement of AAA[296] and improve life prognosis after the surgery of aortic aneurysm,[297,298] and it has been pointed out that the anti-inflammatory effect of statins on the vascular wall may improve the prognosis. In addition, it was shown that the administration of statins may improve the life prognosis of aortic aneurysm/dissection complicated by CAD that requires revascularization.[299] On the other hand, the effectiveness of statins for hereditary aortic diseases is unknown. Animal studies have indicated that the administration of statins may suppress the enlargement of the aortic diameter in Marfan syndrome;[300,301] however, it has not been supported by clinical evidence.

Although no large-scale observational studies or RCT have shown the association between treatment with non-statin drugs (ezetimibe and fibrates) and aortic diseases or their prognosis, the combined use of a statin and ezetimibe was reported to reduce the inflammatory markers in AAA.[302] With regard to lipid-lowering therapies other than statins based on the evidence of dyslipidemia management for atherosclerotic diseases, the administration of ezetimibe in addition to statins or the administration of PCSK-9 inhibitors is considered if an LDL-C target cannot be reached.

Based on these, in Japan, the target value of LDL-C levels is currently set to below 70 mg/dL if the patient has any of familial hypercholesterolemia, a history of acute

coronary syndrome, and diabetes mellitus, which require stricter lipid management, in addition to aortic diseases. If the patient has only aortic diseases and CAD, lipid management with a target LDL-C level below 100 mg/dL is desirable. Additionally, lipid management with a target LDL-C level of below 120 mg/dL is desirable if the patient has aortic aneurysm alone. Considering other comorbidities, lipid-lowering drugs such as ezetimibe and PCSK-9 inhibitors may be administered if a target LDL-C level is not reached or if the patient is statin-intolerant. However, since aortic diseases including hereditary aortic diseases have a wide range of pathological conditions, evidence to support strict lipid management is insufficient, and lipid management is not strongly recommended for all aortic diseases.

1.6.3 Diabetes Mellitus

Diabetes mellitus is a major risk factor in the prognosis of cardiovascular diseases; however, its negative correlation with the prognosis of AAA has been shown in epidemiological and observational studies.[303] The enlargement of aneurysm is slower in AAA patients complicated by diabetes mellitus than in those without the complication, and diabetes mellitus acts protectively against the enlargement, rupture, and life prognosis of aneurysms and retreatment after stent-graft deployment (EVAR). These tendencies in patients with AAA are also observed in those with TAA, and a meta-analysis showed that diabetes mellitus is negatively correlated with the incidence of ascending/thoracoabdominal/descending aortic aneurysm. In contrast, complication with diabetes mellitus was reported to increase the incidence of complications after open surgery for AAA (prosthetic graft replacement), such as myocardial infarction, infection, and pancreatitis, and procedure complications after EVAR.[303]

Although no treatment targets have been set for diabetes mellitus complicating aortic diseases, the "Diabetes Mellitus Treatment Guide 2018–2019" states that a glycemic control target needs to be set according to the condition of each patient, in consideration of age, disease duration, organ damage, risk of hypoglycemia, support system, and severity of dementia.[304]

1.6.4 Smoking

Smoking is the most important risk factor for the enlargement and rupture of aneurysm in both TAA and AAA.[305–311] The incidence of aortic aneurysm increases dependently on the amount of smoking.[307] Therefore, guidance for smoking cessation is of significance from the viewpoint of suppressing the enlargement of aneurysm, even if the diameter of the aortic aneurysm is small.[311,312] In particular, there is a highly strong relationship between smoking and the onset of AAA in men, and the prevalence rate of AAA in men aged 65–75 years with a history of smoking is 6–7%, while that in those without a history of smoking is 2%. In women of the same age, the prevalence rate of AAA is below 0.6% in non-smokers, while it is 0.8% and 2% in those with a history of smoking and active smokers, respectively. Therefore, screening for AAA by echographic and CT examinations is recommended for men aged 65 years and older with a history of smoking.[313] Furthermore, in open surgery for AAA, preoperative smoking cessation for at least 8 weeks reduces perioperative pulmonary complications compared to patients with active smoking habits.[314] The SVS guidelines recommend at least 2 weeks of preoperative smoking cessation.[315]

1.6.5 Heart Failure

There is no definite epidemiology of heart failure in chronic aortic dissection, TAA, and AAA. However, heart disease is the main factor for long-term mortality in AAA,[316] and most of the perioperative complications of invasive treatment (open surgery and EVAR) are heart failure.[317,318] Preoperative chronic heart failure is a risk factor for postoperative pulmonary and renal complications, and a history of chronic heart failure is a risk factor for postoperative cardiac complications.[319,320] Therefore, if an unstable heart disease (unstable angina, severe valvular disease, lethal arrhythmia, or chronic heart failure) is diagnosed preoperatively, the evaluation of left ventricular dysfunction and valvular disease with echocardiographic examination by a cardiac specialist and evaluation of myocardial ischemia with stress testing are required prior to invasive treatment of aortic diseases, and medical management, including drug therapy, is performed according to the pathological condition. However, even if the patient is not preoperatively diagnosed with heart disease, screening should be performed for elective invasive treatment, and daily activity assessment and resting 12-lead electrocardiogram are recommended as screening methods.[315,321] If dyspnea of unknown cause or exacerbated dyspnea is presented, a detailed examination by transthoracic echography should be performed.[315] Prior to the surgery of AAA, patients with less than 4 METs of daily activity and risk factors, such as cerebrovascular diseases, diabetes mellitus, and chronic renal failure, are indicated for non-invasive detailed examination of heart diseases by a cardiac specialist.[315,321]

If a patient with surgical indications for aortic diseases is complicated by NYHA III (movement is limited due to heart failure symptoms) or IV (symptoms are present even at rest) chronic heart failure, the strict management of heart failure by drug therapy (β blockers, antihypertensive drugs, and diuretics) is required, and invasive treatment is postponed.[321–324] The risks and benefits of each case should be assessed by an expert. In addition, aortic valve stenosis is the heart disease that most significantly increases the perioperative risk in the invasive treatment for AAA, and in patients with severe valvular stenosis (average pressure difference of 40 mmHg or more, valve area of less than 1 cm^2, and aortic valve maximum blood flow velocity of 4.0 m/s or more), invasive treatment for aortic valve stenosis is prioritized prior to the surgery of aortic aneurysm.[322,323,325,326]

1.6.6 Coronary Artery Disease

It is estimated that cardiac complications are associated with more than 40% of perioperative deaths after non-cardiac surgery;[327] additionally, the evaluation of the risk of heart diseases is highly important.[328] The detection of left ventricular dysfunction and cardiac valve abnormalities and non-invasive evaluation of myocardial ischemia with stress testing should be performed preoperatively; however, routine catheter coronary angiography is not recommended.[323] This is based on the fact that two RCTs demonstrated the benefits of preventive coronary artery revascularization before aortic surgery only in unstable CAD, even in patients with a lesion in the left main coronary artery trunk or a triple-vessel lesion and patients with

an LVEF below 35%.[326] In the guidelines in Europe and the United States, the indications for preventive coronary artery revascularization are highly limited;[323,326,329] however, it has become actively performed in Japan in consideration of the peculiarities of aortic diseases and surgical invasiveness.

1.6.7 Carotid Artery Disease

The prevalence rate of carotid artery stenosis is high in patients with aortic aneurysm as it shares common risk factors with aortic aneurysm. In the SMART trial, 8.8% of patients with AAA had at least 70% of asymptomatic carotid artery stenosis.[330] It has been pointed out that untreated significant carotid artery stenosis adversely affects the long-term prognosis after the treatment of AAA.[331] Therefore, drug therapy before and after invasive treatment of aortic aneurysm, especially after surgery, is beneficial in patients with carotid artery stenosis. However, the benefits of carotid artery screening before the surgery of aortic aneurysm have not been demonstrated;[332] additionally, routine preoperative screening is not recommended. The ESVS guidelines recommend selective screening for asymptomatic carotid artery stenosis in patients with multiple vascular risk factors, which aims to reduce the long-term mortality and complications due to cardiovascular diseases with drug therapy, rather than searching for cases indicated for invasive carotid artery intervention.[333] The benefits of preventive carotid endarterectomy or stent deployment before aortic aneurysm surgery have not been demonstrated in patients with asymptomatic carotid artery stenosis, even if it is severe.[333]

1.6.8 Aortic Diseases and Antimicrobial Therapy

With regard to antimicrobial therapy, the administration of doxycycline and roxithromycin, which are effective for chlamydia pneumonia associated with the enlargement of AAA due to secondary infection, was reported to suppress the enlargement of aortic aneurysm after 12 months. However, its validation by two RCTs showed no significant benefits in the suppression of the enlargement.[334,335] On the other hand, animal studies have reported that the use of fluoroquinolone antimicrobial drugs promotes the expression of matrix metalloproteinases on the vascular wall and affects the connective tissue. Observational studies have reported that patients taking fluoroquinolone antimicrobial drugs have a higher risk of developing aortic aneurysm and dissection, compared to patients taking penicillin antimicrobial drugs.[336–338] In a notification published in December 2018, the US FDA recommended that patients with aortic diseases and those at high risk of aortic diseases refrain from taking fluoroquinolone antimicrobial drugs.

2. Endovascular Treatment (Table 8, Table 9)

2.1 TEVAR

2.1.1 Indications

TEVAR is indicated for thoracic descending aortic lesions: thoracic descending aortic aneurysm, PAU, blunt traumatic aortic injury (BTAI), Type B dissection and is presently a standard treatment in this field. Particularly, for descending aortic aneurysm including ruptured aneurysm, PAU, BTAI, and acute/subacute complicated Type B dissection that fulfills the anatomical requirements for TEVAR, TEVAR is recommended with priority over open surgery.[341,349–365,384–387] In TAA, PAU, and BTAI, the basic objective of TEVAR is treatment or prevention of rupture by aneurysm exclusion using a stent-graft and decompression of aneurysm. In aortic dissection, it is to reduce the false lumen blood flow and increase the true lumen blood flow by occlusion of the entry and, prevent enlargement and rupture of the false lumen by inducing its thrombosation.

In TEVAR for aortic arch or thoracoabdominal aortic lesions, branch reconstruction for arch branches or major abdominal branches is necessary. But as this requires TEVAR using fenestrated/branched devices, hybrid TEVAR concomitantly using bypasses to branches, and TEVAR combined with a palliative branch reconstruction procedure, such as the chimney or snorkel technique, TEVAR has not attained the position of standard treatment and is still indicated restrictively to cases with high risk or difficulty for open surgery.[374–383] In the ascending aorta, TEVAR is performed only in very limited cases.[388,389]

TEVAR can be recommended for uncomplicated Type B aortic dissection because RCTs and systematic reviews

Table 8. COR and LOE of Endovascular Treatments (TEVAR/EVAR) for Aortic Aneurysm/Dissection

	COR	LOE
It is recommended to evaluate indications of TEVAR/EVAR comprehensively in consideration primarily of anatomical factors: anatomical requirements for TEVAR/EVAR, but also of other factors including the etiology, comorbidities, and life expectancy and by comparison with other treatments: open surgery, conservative therapy	I	C
It is necessary to secure a healthy landing zone of 20 mm or more for TEVAR and 10–15 mm or more for EVAR on both the proximal and distal sides. Also, it is recommended to perform the procedure in each landing zone using an oversized stent-graft 10–30% larger than the aortic diameter	I	C
It is recommended to perform TEVAR/EVAR by a facility and a treatment team skilled in each endovascular treatment of the aorta with a backup system by a surgical team	I	C
After TEVAR/EVAR, it is recommended to continue periodic follow-up using specified imaging modalities for a lifetime: after 1, 6, and 12 months and every 1 year thereafter. If abnormalities are noted, it is recommended to perform follow-up at shorter intervals[339,340]	I	C
If endoleak is detected after TEVAR/EVAR, additional treatment should be given as promptly as possible for type I and III, and when there is aneurysm enlargement for type II and V[341–348]	I	C
TEVAR/EVAR is not recommended at facilities that are not skilled in endovascular treatment of the aorta and have no backup by a surgical team	III	C

COR, class of recommendation; EVAR, endovascular aortic repair; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

Table 9. COR and LOE of TEVAR for Aortic Aneurysm/Dissection		
	COR	LOE
It is recommended to perform TEVAR for ruptured descending aortic aneurysms that fulfill the anatomical requirements[349–353] (See **Table 21**)	I	C
It is recommended to perform TEVAR for traumatic aortic injuries that need invasive treatment and fulfill the anatomical requirements[354–359] (See **Table 33** and **Table 56**)	I	C
It is recommended to perform TEVAR for descending aortic aneurysms that fulfill the anatomical requirements (≥60 mm)[341,358,360–365] (See **Table 17**)	I	C
TEVAR should be considered for descending aortic aneurysms that fulfill the anatomical requirements (55–59 mm)[341,358,360–365]	IIa	C
Cerebrospinal fluid drainage should be considered in TEVAR for thoracoabdominal aortic aneurysms/dissections at a high risk for spinal cord ischemia: stent-graft length ≥200 mm, or after surgery for AAA[366–371]	IIa	C
In TEVAR with proximal Zone 2 landing, left subclavian artery reconstruction should be considered for preventing central nervous system damage[372,373]	IIa	C
In patients with aortic arch aneurysm or thoracoabdominal aortic aneurysm that is a poor indication for open surgery, TEVAR with branch reconstruction (hybrid treatment) should be considered[374–383]	IIa	C
TEVAR may be considered for descending aortic aneurysms ≥60 mm that do not fulfill the anatomical requirements[341,360–365,384]	IIb	C

AAA, abdominal aortic aneurysm; COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

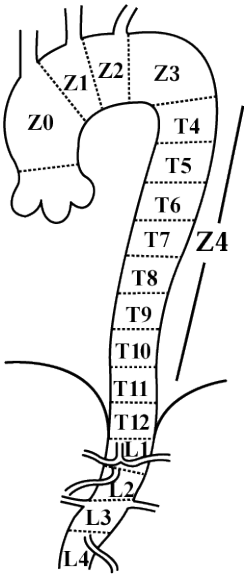


Figure 51. Zoning for aortic stent graft landing and graft placement areas. The proximal/distal landing zones and stent graft deployment areas are described using this zoning scheme.

have reported that TEVAR performed in the subacute to early chronic phase (within 1 year after the onset) aimed to prevent enlargement of the false lumen (preemptive TEVAR) improved the results regarding the outcome, aortic events, and aortic remodeling compared with conservative treatment.[390–395] However, as the risk due to TEVAR in the acute phase of treatment cannot be disregarded, TEVAR is unlikely to apply to all cases of uncomplicated Type B dissection, and selection of cases by prediction of enlargement is expected to become important in the future.[396–401] On the other hand, for chronic Type B dissection with enlargement/aneurysmal dilatation of the false lumen, TEVAR is clearly inferior to open surgery in the therapeutic effect and the outcome in the chronic phase and cannot be recommended even in consideration of the advantages in the acute phase of treatment.[391,402–405]

For infected aneurysms, aorto-esophageal fistula (AEF) including invasion of esophageal cancer, and bronchial fistula including pulmonary fistula and invasion of lung cancer, TEVAR is indicated for patients with hemodynamic instability and those in whom open surgery is difficult to perform. In these patients, it may be necessary to perform additional open surgery after TEVAR with stabilization of the hemodynamics depending on the degree of infection.[406]

2.1.2 Devices Used for Treatment

Stent-grafts (SG) for TEVAR are basically straight (I type) and are made of a self-expanding skeleton consisting of stainless steel and nitinol and fabric consisting of polyester threads or expanded polytetrafluoroethylene. They vary in diameter and length within certain ranges in each manufacturer. Since the aortic diameter often differs between the proximal and distal portions, there are also types of SG tapering from 4–10 mm. SGs are often housed in a 16–24 Fr size sheath in ID and navigated into the aorta except the devices of Gore Medical, which are wrapped in a special wrapping sheet, fixed at the tip of a catheter, and inserted in this state into the aorta. Thoracic devices characteristically have no hook for active fixation in the bare parts at their ends unlike abdominal devices, probably for avoiding aortic injuries, such as retrograde Type A dissection, and because of the difference in shear stress applied to the proximal landing part after SG placement.

2.1.3 Standard Treatment Procedures

Treatment begins with "preoperative planning" based on detailed image information obtained by modalities including thoracoabdominal contrast-enhanced CT. A precondition for treatment is the presence of a healthy and linear part in the aortic wall of at least 20 mm long (healthy landing area) on the proximal and distal sides of the target lesion: aneurysm or entry. However, in aortic dissection, it is often necessary to use the true lumen of the dissected aortic wall

as the landing area, particularly, on the distal side. The landing area is standardized by the zoning scheme of Ishimaru et al. (**Figure 51**). Also, as the diameter of the SG must be 10–30% larger than that of the aorta on which it lands, the diameter of the aorta to which the SG is attached must be ≤42 mm, in principle.

In TEVAR of proximal descending aortic aneurysm or Type B aortic dissection, the SG is often placed to cover the left subclavian artery for securing an adequate proximal landing area: zone 2 landing. In this case, whether the left subclavian artery should be closed simply or revascularization should be reconstructed, such as a bypass, must be determined in consideration of the condition of the collateral flow, the possibility of the appearance of symptom, and the physical condition (presence or absence of complications) in the patient, but reconstruction (e.g., left common carotid-left subclavian artery bypass) is recommended from the viewpoint of brain/spinal cord nerve complications.[372,373] In TAAA, there are times when the celiac artery is covered, and landing is obtained distally to it, but, in this case, revascularization by simple closure or bypassing should be considered after checking the collaterals (from the superior mesenteric artery). Also, in TEVAR of a long segment ≥200 mm, cerebrospinal fluid drainage has often been reported to be effective for reducing spinal cord nerve complications.[366–371]

In TEVAR, the site of sheath insertion which is often the femoral artery but occasionally the common iliac artery or abdominal aorta must be selected carefully, because the sheath diameter is extremely large up to 24 Fr in internal diameter and 27 Fr in external diameter. Also, a very stiff guide wire is needed for insertion of this extremely large sheath, and the sheath and device are inserted to the intended site using this wire. A pull-through wire (through-and-through wire) is not recommended for implementation of simple TEVAR from the viewpoint of brain and vascular complications.[407] Moreover, in SG deployment, a reduction of the cardiac output is the most effective for placing it at the exact position. Rapid pacing is recommended rather than reducing the blood pressure using drugs.[389,408,409]

2.1.4 Results and Complications

Of the 5,246 patients who underwent TEVAR in the acute phase in Japan in 2016 (NCD-JACSM follow-up study), hospital deaths were observed in 4.8%, stroke in 4.0%, and spinal cord injury (SCI) in 2.7%. Although no marked difference was observed between dissected and non-dissected lesions, there was a wide difference in the incidence of stroke between the lesions in Zone 0–2 in the landing area on the proximal side (arch) and those in Zone 3 or more distal areas (descending) (7.6% vs. 1.6%).[410] The mid-term results after elective TEVAR in Japan were stable with 1-, 3-, and 5-year survival rates of 80.7%, 66.9%, and 56.9%, and with 1-, 3-, and 5-year aneurysm-related event free survivals of 97.8%, 95.9%, and 94.2%, respectively.

Postoperative complications included (1) acute aortic syndrome represented by retrograde Type A aortic dissection, (2) endoleak (type I–V, **Figure 52**), re-entry flow,[346] (3) stroke, (4) SCI, (5) access trouble, and (6) localized DIC (consumption coagulopathy).[372,411–415] Concerning (1), (3), and (4), which directly affect the outcome and QOL, preoperative selection of high-risk cases and intraoperative/postoperative preventive measures are necessary.[341,363,366–369,378,407,414,416–422]

The history of TEVAR for thoracic aortic diseases is still short, and further innovations may occur in indications and methods by comparison with open surgery and conservative treatments. For global comparison of TEVAR, data including those of indications (classification), methods, and follow-up in implementation of TEVAR should be recorded using an established format reporting standard.[339]

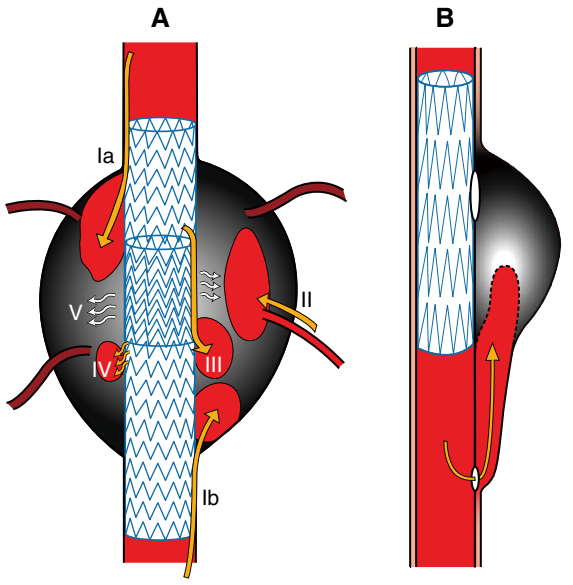


Figure 52. Classification of endoleak after TEVAR/EVAR.

A

I: Perigraft blood flow from the attachment between the arterial wall and stent-graft (SG)
- a: From the proximal side
- b: From the distal side

II: Blood flow into the aneurysm due to backflow through a side branch of the aortic aneurysm (intercostal artery, lumbar artery, inferior mesenteric artery, median sacral artery)

IIIa: Blood flow into the aneurysm from the junction between SGs

IIIb: Blood flow into the aneurysm due to breakage of the SG-fabric

IV: Leakage of blood due to porosity of SG (small holes in the base textile of synthetic blood vessel): endoleak that usually disappears with discontinuation of anticoagulant administration

V: Aneurysm that shows enlargement despite the absence of blood flow in the aneurysm

B

Re-entry flow after closure of the entry by TEVAR

2.2 EVAR (Table 10)

2.2.1 Indications

EVAR has become a standard treatment for infrarenal AAA. The selection of open surgery or EVAR for infrarenal AAA that fulfills the anatomical requirements for EVAR still remains controversial. EVAR has been shown to be superior in acute phase results: mortality and adverse events by several RCTs,[423–428] but in the late results over 10 years, in reverse the superiority of open surgery has been demonstrated.[317,429–436] Therefore, in patients who tolerate both open surgery and EVAR, EVAR is selected for those with more benefits in the near future, but open surgery is

Table 10. COR and LOE of EVAR for Aortic Aneurysm/Dissection		
	COR	LOE
It is recommended to perform EVAR for AAA that fulfills the anatomical requirements with the expectation of improving life expectancy and QOL in the early postoperative period[423–428]	I	A
It is recommended to perform open surgery for AAA with moderate or milder surgical risk that does not fulfill the anatomical requirements for EVAR	I	C
Open surgery may be considered in preference to EVAR for patients with AAA who are expecting 10 years or longer life expectancy[316,317,429–436]	IIb	B
EVAR may be considered for patients with asymptomatic AAA who do not tolerate open surgery[437–439] (See **Table 27**)	IIb	B
EVAR is not recommended for AAA with a milder or moderate surgical risk and who do not meet the anatomical requirements for the proximal neck[440–445]	III	C

AAA, abdominal aortic aneurysm; COR, class of recommendation; EVAR, endovascular aortic repair; LOE, level of evidence; QOL, quality of life.

selected for those expected to have a 10-year or longer survival. In patients with high risk for, or do not tolerate, open surgery, EVAR takes priority, but medical treatment should also be considered depending on age or anatomical conditions.[437–439] Also, while EVAR cannot be recommended for infrarenal AAA that does not fulfill the anatomical requirements set for each device; instructions for use (IFU), there are reports that no difference was observed compared with the results of EVAR not in compliance with IFU, and indications for EVAR should be evaluated individually by comparison with open surgery and surveillance with medical treatment.[440,441,446–450]

Pararenal AAA and suprarenal AAA have limited indications for EVAR. In patients with severe renal dysfunction requiring hemodialysis, EVAR is indicated for those in whom the proximal landing zone can be secured just distal to the superior mesenteric artery. However, in patients in whom the renal artery cannot be sacrificed, comparison with open surgery is required considering the reconstruction method: use of fenestrated/branched devices, use of bypasses, or use of the chimney technique, and the patient's physical condition, e.g., age, presence or absence of complications. [315,318,343,451–458]

If the bilateral iliac arteries show aneurysmal change, the following approaches are available: (1) reconstruction using an iliac bifurcated device,[315,459–466] (2) reconstruction using an external-to-internal iliac artery bypass,[315,463,467] and (3) occlusion of the bilateral internal iliac arteries and use of the external iliac artery as the landing zone. However, without reconstruction of the internal iliac arteries, it has been reported that buttock claudication occurs in a maximum of 63% of the patients with unilateral internal iliac occlusion, and that intestinal complications such as ischemic colitis or ischemic intestinal necrosis occur in a maximum of 9% of the patients with bilateral occlusions.[460,461,468] So, unilateral internal iliac artery reconstruction is strongly recommended.

For the indications of EVAR for inflammatory AAA, AEF (frequently aorto-duodenal), and ruptured cases, refer to the individual sections.

2.2.2 Devices

A stent-graft (SG) for EVAR is made of a self-expanding stent consisting of stainless steel or nitinol, and fabric consisting of polyester or expanded polytetrafluoroethylene. SG is mostly bifurcated style, some are hanging types that are hung from the proximal anchoring site, and others are designed to settle at the aortic bifurcation. Many of the hanging types have suprarenal stents or hooks attached at the proximal anchoring site for active fixation.

2.2.3 Procedure

In most patients, EVAR is performed by obtaining access via the bilateral femoral arteries, implanting a bifurcated style SG from the abdominal aorta to the bilateral iliac arteries, and excluding the aneurysm from the systemic blood pressure. Similarly to the thoracic region, "preoperative planning" is made based on detailed imaging examinations by modalities including thoracoabdominal contrast-enhanced CT, and the proximal/distal landing zones are determined. An undilated straight healthy neck with a length of ≥10–15 mm (≤32 mm) is needed on the proximal side, and an undilated straight landing zone with a length of ≥10 mm (<23 mm) is needed on the distal side. To connect the proximal and distal parts, a 10–30% oversized SG is needed. Besides the setting of these landing areas, there are instructions for use (IFU) concerning the angle of the aorta including the neck and aneurysm, the angle between the neck and suprarenal aorta, and diameter of the access route, but IFU concerning the neck on the proximal side is important because of its direct effect on the outcome.[440–445]

2.2.4 Results and Complications

In 2016, the outcomes of 9,872 cases of EVAR in the acute phase in Japan (NCD-JACSM follow-up study) were hospital death in 1.6%, aneurysm rupture in 0.18%, stroke in 0.4%, renal dysfunction in 3.2%, infarction in 0.9%, and access complications in 1.1%.

Complications after EVAR include (1) aortic/iliac artery injury (rupture/dissection), (2) embolism/thrombosis, (3) endoleak (type I–V, **Figure 52**), (4) renal dysfunction, (5) access trouble, (6) leg embolism, and (7) aneurysm enlargement/rupture.[469]

(1) **Aortic/iliac artery injury (rupture/dissection):** The timing of treatment and methods for additional treatments (surgical conversion) must be evaluated according to the situation

(2) **Embolism/thrombosis:** Large emboli induce disorders such as intestinal necrosis, ischemic colitis, renal infarction, and necrotizing cholecystitis. Cholesterol crystal embolism causes characteristic symptoms such as renal dysfunction accompanied by proteinuria and anorexia in 1–4 weeks, rather than immediately after the operation

(3) **Endoleak (type I–V):** Type I and type III endoleaks

require prompt additional treatment.[343–347] If prolonged (6 months or longer), type II endoleak requires intervention depending on the enlargement of the aneurysm or the decrease in the junction area[348]

(4) **Renal dysfunction:** Renal dysfunction may be caused by obstruction of the renal artery by the SG, use of a contrast agent, and the above-mentioned embolism
(5) **Access troubles:** Access troubles are likely to occur in small women and patients with iliac artery calcification
(6) **Leg embolism:** Leg embolism is likely to be caused by bending in the iliac artery or landing in the narrow external iliac artery
(7) **Enlargement/rupture of aneurysm:** Endoleak (of all types) may be accompanied by aneurysm enlargement. If type I or III endoleak is detected, prompt additional treatment or surgical conversion is necessary, but there is currently no established treatment for type II endoleak since it poorly responds to additional treatment and does not immediately lead to rupture[470–474]

Concerning the prognosis in the chronic phase after EVAR in Japan, refer to the reports of the JACSM follow-up study until 2015.[440] Since the aneurysm is not removed by EVAR, serious events, such as rupture and aneurysm-related death, are likely to occur in the chronic phase. Also, the incidence of such serious events does not reach a plateau with time after EVAR, and continuous follow-up according to an established format is extremely important.[340]

2.3 Other Endovascular Treatments

Endovascular treatments for aortic aneurysm/dissection other than TEVAR/EVAR include endovascular fenestration for true lumen stenosis or malperfusion and bare metal stent placement in the true lumen.[475–481] For recommendations and details, see "**3. Stanford Type B Aortic Dissection**" in **Chapter VI**.

PQ 6.
TEVAR/EVAR Appropriate for Renal Dysfunction/Renal Failure Patients?

Recommendation
TEVAR/EVAR for patients with chronic kidney disease has the risk of exacerbation of renal function, but this disadvantage does not negate the advantage of its low invasiveness. However, it is important to prevent the occurrence of acute kidney injury and contrast medium-induced nephropathy.

Surgical Results: In invasive treatment for aortic aneurysm in chronic kidney disease (CKD) patients, the mortality rate and postoperative complications increase with progression of CKD regardless of whether the procedure is EVAR, TEVAR, or open surgery.[482–485] The results of both EVAR and open surgery were poorer in patients with stage 4 or more advanced CKD (eGFR: ≤29 mL/min/1.73 m^2) than in those with stage 3 or less advanced CKD, but no difference was noted between the two procedures. However, in stage 3 (eGFR: 30–59 mL/min/1.73 m^2) the mortality rate and incidence of cardiovascular events and acute kidney injury (AKI) were significantly higher after open surgery,[482] and EVAR is more advantageous than open surgery in moderate CKD.

The use of Contrast Agents and the Occurrence of AKI: In TEVAR/EVAR, contrast medium-induced nephropathy (CIN) must always be kept in mind as a major cause of postoperative AKI. Risk factors for CIN include CKD, old age, anemia, diabetes, chronic heart failure, dehydration, and the use of nephrotoxic drugs,[486] and the risk of the occurrence of CIN is proportionate to the amount of the contrast agent used.[487] In addition to CIN, perioperative hemodynamic changes and microembolism associated with intraoperative manipulations are also important factors for AKI.[488] Devices with a suprarenal stent have been reported to have no effect on renal function,[489–491] but caution is needed in their placement for suprarenal thrombosis.[487] AKI is an important prognostic factor after TEVAR/EVAR,[492,493] and attention to careful intraoperative catheter manipulation, appropriate device selection, amount of the contrast agent used, and perioperative management is necessary. Although the incidence of postoperative AKI including CIN tends to be higher in CKD patients,[483] there is no sufficient evidence concerning its incidence, relationship with invasive treatments, or the upper limit of the amount of the contrast agent used.

Prevention of CIN: Generally, CIN is defined as an increase in the serum creatinine level of ≥0.5 mg/dL or ≥25% within 72 h after the administration of iodine-based contrast material compared with the pre-administration level.[494] Besides a reduction in the use of the contrast agent, the administration of physiological saline before and after the procedure has been reported to be useful for the prevention of CIN,[495] but further evaluation is necessary about the appropriateness and amount of fluid infusion because a recent RCT has reported no difference in the incidence of CIN and adverse events associated with fluid infusion in CKD patients.[496] In addition, CO_2 angiography may be performed in CKD patients,[497] but as conventional contrast agents are superior in resolution, and as CO_2 is associated with the risk of embolism, its indications are limited.

Postoperative Renal Function: Regardless of the occurrence of AKI/CIN or whether the patient has CKD, there have been no reports that referred to the long-term effects of TEVAR/EVAR on renal function. It has been reported that the early occurrence of AKI was observed less frequently, but the decline in renal function was more notable, in the EVAR group than in the open surgery group.[498,499] One reason is the frequent implementation of contrast-enhanced CT for postoperative follow-up.[499] In CKD patients, it is recommended to reduce contrast-enhanced CT to the minimum necessary level and to evaluate non-contrast-enhanced modalities such as abdominal ultrasonography, unenhanced CT, and MRI.

3. Open Surgery

3.1 Prosthetic Graft Replacement

The major goal of open surgery for aortic aneurysm and dissection is to prevent the crisis of life due to the failure of the aortic wall. Other goals include the release of contiguous organ compression caused by aortic aneurysm,[500] improvement of malperfusion, and prevention of embolism.[501] The basis of open surgery is the replacement with a prosthetic graft. In recent years, SG deployment (TEVAR/EVAR) has been performed in cases where prosthetic graft replacement is difficult; however, prosthetic graft and SG

are used in combination as a hybrid treatment (treatment combining open surgery and TEVAR/EVAR) in some cases.

Prosthetic grafts are roughly classified into those made of polypropylene and those made of ePTFE (expanded polytetrafluoroethylene). Prosthetic grafts designed according to the anatomy from the aortic root to the abdominal aorta are available for use. Homografts, which have been used since before the advent of prosthetic grafts, are used particularly for infectious lesions.[502] There have recently been reports of the replacement with a conduit made of a heterologous pericardium for infectious lesions; however, its long-term results are unknown.[503–505]

Surgery of forming the aortic wall to reduce the aortic diameter and surgery of covering the aorta with felt or prosthetic graft (wrapping) may also be performed.[506–509] The surgery of wrapping the aortic root (external aortic root support) has also been reported in the recent years.[510] However, caution is needed as there was a report that it causes necrosis of tissue.[511] With the increase in TEVAR/EVAR, prosthetic graft replacement after SG deployment (open conversion) is increasing, and some have reported difficulty in terms of procedures.[448,512–514] When removal of all SG is difficult, part of the cut SG must be left; however, its long-term effect is unknown. An extra-anatomical bypass is also performed as needed.

In principle, anticoagulation therapy after prosthetic graft replacement is not necessary. A pseudoaneurysm is known to develop at the anastomotic site long after surgery, and a follow-up by regular diagnostic imaging with CT or MRI is desirable, which also confirms the presence or absence of new lesions.

3.2 Extracorporeal Circulation and Organ Protection

Extracorporeal circulation is, in principle, essential for aortic surgery from the aortic root to the ascending/arch region. Additionally, a cardioplegic method according to cardiac surgery is essential. Extracorporeal circulation is also used for aortic surgery of the descending to thoracoabdominal regions. Extracorporeal circulation is not required for the surgery of infrarenal AAA. During replacement, the lesion is resected after aortic cross-clamping, followed by reconstruction with a prosthetic graft. When aortic cross-clamping is difficult, extracorporeal circulation is used, and hypothermic therapy is performed in combination for circulatory arrest, after which the aorta is opened (open aortic technique) for the resection or anastomosis of the lesion. Organ damage is of the greatest concern when performing the circulatory arrest method or extensive aortic replacement, and selective extracorporeal circulation with perfusion to each organ is used as needed.

3.3 In-Hospital Mortality Rate

According to the report of the Japanese Association for Thoracic Surgery,[43] the in-hospital mortality rates of aortic dissection surgery in 2016 were 11.3% for acute Type A dissection, 10.0% for acute Type B dissection, 4.3% for chronic Type A dissection, and 3.8% for chronic Type B dissection. In addition, the in-hospital mortality rates of non-dissecting aortic surgery in non-ruptured cases were 3.0% for the ascending region, 4.1% for the root region, 6.2% for the arch region, 5.5% for the descending region, and 9.6% for the thoracoabdominal region. The mortality rates in ruptured cases were 17.0% for the ascending region, 19.2% for the root region, 16.9% for the arch region, 29.7% for the descending region, and 28.6% for the thoracoabdominal region.

According to the report of the Japanese Society for Vascular Surgery,[515] AAA surgery was performed in 19,216 cases in 2014, and the in-hospital mortality rates were 3.2% for all cases, 1.2% for non-ruptured cases, and 19.7% for ruptured cases.

V. Treatment for Aortic Aneurysm

1. Thoracic Aortic Aneurysm (TAA)

1.1 Medical Treatment and Indications for Invasive Treatment (Table 11)

1.1.1 Epidemiology and Position of Medical Treatment

In Sweden, the frequency of TAA was 489 per 100,000 autopsies in men and 437 per 100,000 autopsies in women.[517,518] Several cases of TAA are asymptomatic, and it is detected incidentally during medical check-ups or close examinations for other diseases. However, reports on the medical treatment of TAA have been few since invasive treatment is generally selected at the time of its detection, and most reports are related to its difficult surgical cases, the natural history of its rejected surgical cases, or retrospective investigation of its ruptured cases. The medical treatment of TAA aims to minimize the shear stress and impact force on the aortic wall, suppressing further enlargement of the aneurysm. In addition, regardless of surgical and non-surgical cases, patients with TAA often have atherosclerotic risk factors, such as hypertension, dyslipidemia (especially hypercholesterolemia), diabetes mellitus, hyperuricemia, obesity, and smoking. Therefore,

Table 11. COR and LOE for the Medical Treatment of Thoracic Aortic Aneurysm

	COR	LOE
It is recommended to perform blood pressure management with a target blood pressure below 130/80 mmHg[10]	I	C
It is recommended to give guidance for smoking cessation[516]	I	C
Surveillance using imaging examinations (CT or MRI) should be considered (once a year if the aneurysm shows no enlargement of its diameter, or once every 3–6 months if the aneurysm shows an enlargement of its diameter)[95,516]	IIa	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence; MRI, magnetic resonance imaging.

for a better life prognosis, it is highly important to fully instruct patients about these risk factors and improve their lifestyle, including smoking cessation.[95,516,519,520]

1.1.2 Blood Pressure Control

Blood pressure control is of utmost importance, and decompression can suppress stress on the aortic wall. The desired hypotensive target for TAA patients is a systolic blood pressure of 105–120 mmHg;[10] however, in reality, blood pressure below 130/80 mmHg is considered an appropriate target, considering the risk of developing hypotension. Antihypertensive therapy with β-blockers is the first treatment choice for TAA patients.[10,95,521] However, if their blood pressure cannot be sufficiently lowered even with the maximum dose of β-blockers, other antihypertensive drugs are additionally administered as appropriate to reduce their blood pressure to the target level. Nevertheless, several recommendations are based on the clinical studies of non-surgical TAA patients with Marfan syndrome, and it is unclear whether they can be applied to non-Marfan syndrome patients, such as those with atherosclerotic TAA.

a. β-Blockers

β-blockers are the first-line drugs for TAA patients, as their negative inotropic effect suppresses left ventricular contraction and shear stress, reducing the impact force applied to the aortic wall.[522] In an RCT of non-surgical TAA patients with Marfan syndrome, a β-blocker (propranolol) was able to suppress the enlargement rate of the aneurysm by 73%, significantly reducing the incidence of aortic events and mortality rate.[277] Although it is unclear whether TAA patients without Marfan syndrome exhibit similar results, the administration of β-blockers is considered as appropriate.

b. ACE inhibitors and ARBs

The role of the renin-angiotensin pathway in the formation of an arterial aneurysm has been elucidated in animal studies.[523–525] ACE inhibitors may suppress the enlargement of aneurysms by modulating inflammatory mediators and reducing apoptosis in vascular smooth muscle.[526] ARBs may suppress the enlargement of arterial aneurysms by regulating TGF-β in arterial aneurysm patients with Marfan syndrome.[527,528] In a non-randomized trial of young patients with Marfan syndrome exhibiting the enlargement of the aortic root, ARBs significantly reduced the enlargement rate of aortic diameter.[527] Moreover, a study using the mouse model showed the superiority of ARBs over ACE inhibitors in suppressing the enlargement of aortic diameter.

c. Statins

While most studies on statins focus on AAA, statins may effectively suppress the enlargement of aneurysms by suppressing matrix metalloproteinases and plasminogen activators.[529] Moreover, patients taking statins were reported to have a lower mortality rate and a lower incidence of complications than those not taking statins, improving their surgery-avoidance rate.[529]

1.1.3 Exercise Restriction and Lifestyle Guidance

Guidance to avoid smoking, overeating/overdrinking, overwork, lack of sleep, and psychological stress is provided to patients with TAA. In addition, sudden isotonic exercises that cause a rapid increase in blood pressure, such as lifting and pulling heavy objects, should be avoided because the shear stress of the aortic aneurysmal wall can change significantly during such exercises due to alteration in hemodynamics.[530] Non-surgical TAA patients may be complicated by aortic dissection, and although it is thought to develop at normal exercise intensity regardless of exertion or rest in most cases, a small number of patients develop aortic dissection during isotonic exercise.[531] Additionally, guidance to pay attention to straining during defecation and persistent coughing is given to patients with TAA as it causes a sudden increase in blood pressure. Aerobic exercises, such as mild running and use of the exercise bike, are acceptable if the systolic blood pressure is confirmed not to exceed 180 mmHg during exercise stress, such as the treadmill, while taking a sufficient amount of antihypertensive drugs.[10]

1.1.4 Determining the Limit of Medical Treatment

It is difficult to predict the time of rupture of TAA and the enlargement rate of the aneurysm diameter. The risk factors for its rupture include descending/abdominal aortic diameter, advanced age, pain, and COPD. In addition, the yearly incidences of cardiovascular events are 6.5% for TAA with a diameter of 50–60 mm and 15.6% for TAA with a diameter of 60 mm or larger.[118] The enlargement rate of aneurysm diameter in TAA patients without Marfan syndrome or other aortitis is 4 mm/year.[118] Therefore, after the medical treatment mentioned above is given, changes in the aneurysm diameter (maximum minor axis) and shape are regularly evaluated by CT/MRI examination, and invasive treatment intervention is considered if the risk of rupture or mortality rate is determined to outweigh the risk of invasive treatment intervention.

1.1.5 Imaging Follow-up

In principle, CT/MRI examination of TAA is again performed 6 months after the initial imaging taken at the time of its detection, and if it shows no significant change in the aneurysm diameter, the patient is followed up with yearly imaging examinations.[532] A follow-up of every 3–6 months is desired for TAA exhibiting rapid enlargement. Patients exhibiting enlargement of the aortic root or ascending aorta require an examination of the presence of aortic valve regurgitation and bicuspid valve by echocardiography.[533] Follow-up intervals should be modified depending on the size of the aortic aneurysm, and the following are recommended:[95]

(1) Patients with an aortic root/ascending aortic aneurysm: Every 6–12 months for an aneurysm of diameter between 35 and 45 mm, and every 3–6 months for an aneurysm of diameter between 45 and 55 mm
(2) Patients with an aortic root/ascending aortic aneurysm suspected of having heritable connective tissue disorder: Every 6–12 months for an aneurysm of the diameter of 35–40 mm, and every 3–6 months for an aneurysm of the diameter of 40–50 mm
(3) Patients with a thoracic arch/descending aortic aneurysm: Every 12 months for an aneurysm of size smaller than 45 mm, and every 3–6 months for an aneurysm of the size of 45–55 mm

1.1.6 Indications for Invasive Treatment

The probability of facing a fatal situation within 1 year is 15.6% for aneurysms with a diameter of at least 60 mm and 6.5–11.8% for aneurysms with a diameter of 50–60 mm.[118] Thus, invasive treatment (open surgery or TEVAR) is

considered for rapidly enlarging aneurysms, which generally have a thoracic maximum minor axis of at least 55 mm or enlarge by at least 5 mm in 6 months.

For patients with heritable connective tissue disorders, such as Marfan syndrome, congenital bicuspid valve, and coarctation of the aorta, invasive treatment is considered if the diameter of their aneurysm exceeds 45 mm. Attention must be paid to the shape of saccular aortic aneurysms as they have a high risk of rupture even if their diameter is not large.

1.1.7 Evaluation of Heritable/Familial TAA

Heritable or familial aortic diseases are evaluated if the patient has TAA, especially early-onset TAA, or if the enlargement and dissection of the aorta are found within the first degree of the patients who have been diagnosed with an aortic aneurysm. Moreover, relatives of TAA patients within the first degree develop TAA at a probability of 20%.[534]

PQ 7.

At What Size (Millimeters in Diameter) Is a TAA Indicated for Invasive Treatment?

Recommendation

In the aortic root/ascending aorta, the indication criteria for invasive treatment (surgery or TEVAR) are set to an aortic diameter of ≥55 mm for TAA without hereditary aortic diseases, ≥55 mm for TAA with congenital bicuspid aortic valve (without the risk factors of aortic dissection or combined open heart surgery), ≥45–50 mm for TAA with Marfan syndrome, and ≥40 mm for TAA with Loeys-Dietz syndrome. In the aortic arch or lower, the indicative criteria are set to an aortic diameter of ≥55 mm for TAA in the arch region (without hereditary aortic diseases) and ≥60 mm for TAA in the descending/thoracoabdominal region. However, treatment at a smaller diameter may be desired depending on the background of the patient (**Table 12**, **Table 49**, and **Table 52**).

Indications for invasive treatment are determined by the balance between the risk of rupture and the risk of treatment.

The risk of aneurysm rupture is influenced mainly by the aortic diameter and the presence of hereditary aortic diseases, as well as the shape and enlargement rate of the aneurysm. In addition, dissection is more likely to occur as the aorta enlarges. The occurrence rate of rupture or dissection is 7.1% for the aorta with a diameter below 40 mm, 8.5% for 40–50 mm, 12.8% for 50–60 mm, and 45.2% for 60 mm or larger.[535] The probability of the occurrence of complications, such as dissection and rupture, was found to increase sharply when the diameter exceeds 60 mm in ascending aortic aneurysms and 70 mm in descending aortic aneurysms (**Figure 53**).[535] The coefficient obtained by dividing the aortic diameter or cross-sectional area by height (≥4.35 cm/m, ≥10 cm^2/m) represents a risk factor of aortic events in patients with ascending aortic aneurysm/enlargement.[535a,535b] Moreover, because the coefficient was suggested to be involved in poor results in females, early intervention is considered for patients with short stature.

Hereditary aortic diseases include Marfan syndrome, Loeys-Dietz syndrome, Ehlers-Danlos syndrome, familial thoracic aortic diseases, and congenital bicuspid aortic valve, and patients with higher tissue fragility have a smaller aortic diameter, which is an indication for treatment. With regard to shape, saccular aneurysms have a higher probability of rupture than fusiform aneurysms. Thus, the shape of an aneurysm is examined by diagnostic imaging, such as CT examination, and it is used as a reference for indication decisions and follow-up. In contrast, TAA has an aneurysm diameter enlargement rate of less than 5 mm/

Table 12. COR and LOE of Open Surgery for Unruptured Aneurysms of the Aortic Root/Ascending Aorta

	COR	LOE
Open surgery is recommended for asymptomatic non-dissecting aneurysm, IMH, PAU, infected aneurysm, or pseudoaneurysm with ≥55 mm in maximum diameter or even those <55 mm if the enlargement rate is ≥5 mm/6 months[384]	I	C
Marfan syndrome (See **Table 49**)		
Open surgery is recommended when the maximum diameter is ≥50 mm[536]	I	C
Open surgery should be considered when the maximum diameter is ≥45 mm and there are risk factors for aortic dissection* [536]	IIa	C
Prophylactic open surgery should be considered in women expecting pregnancy if the maximum diameter is ≥40 mm[537]	IIa	C
Open surgery may be considered if the maximum diameter is 40–45 mm and there are risk factors for aortic dissection* [536]	IIb	C
Aortic aneurysm associated with bicuspid aortic valve (See **Table 52**)		
Open surgery is recommended when the maximum diameter is ≥55 mm[538–542]	I	C
Open surgery should be considered when the maximum diameter is ≥50 mm if it is performed at an experienced facility for patients with a familial history of aortic dissection, an enlargement rate of ≥5 mm/6 months, and low surgical risk[538,539,543]	IIa	C
In performing aortic valve surgery in patients with severe aortic valve stenosis or insufficiency, simultaneous replacement of the aortic root/ascending aorta should be considered when the maximum diameter is ≥45 mm[544–548]	IIa	C

*Familial history of aortic dissection, an enlargement rate of the aorta ≥5 mm/6 months, severe aortic valve insufficiency, expecting pregnancy. COR, class of recommendation; IMH, intramural hematoma; LOE, level of evidence; PAU, penetrating atherosclerotic ulcer.

year, which increases as the aneurysm diameter enlarges. The aneurysms that enlarge by 5 mm or more in half a year are likely to rupture, and it should be used as a reference when setting the follow-up period. For example, an aneurysm with a diameter of smaller than 50 mm is re-examined by CT 6 months after its initial imaging and should be followed up annually if it then shows no enlargement. However, aneurysms may rupture even if the above criteria are not met. The factors involved in such rupture include strenuous exercise, psychological stress, seasons and time zones, circadian variation of hypertension, and sleep disorders. In addition, the enlargement rate of TAA is increased by the presence of sleep apnea. Since the indication criteria may become inadequate due to the effects of these factors, we must make efforts to treat factors that can be treated during follow-up and to avoid "avoidable events" through patient education and other approaches if enlightenment is effective.

With the improvement in treatment results, even aneurysms with a smaller diameter are now indicated for invasive treatment. According to the 2016 annual report of the Japanese Association for Thoracic Surgery,[43] the in-hospital mortality rate in surgical cases of non-dissecting aortic aneurysm is 2.9–6.9% (including the ascending-thoracoabdominal aorta and TEVAR), and the aneurysms whose rupture risk is greater than this value are generally indicated for treatment. However, this is merely statistical information, and the surgical risk should be determined for each case. As nearly 100% of cases have been registered in the database in recent years, we can now calculate the surgical risks from background factors. With the aging of patients, the surgical risks can be increased by medical and medication histories and frailty, and thus, other considerations, such as selecting a less invasive treatment while the aorta is still small, are also needed.

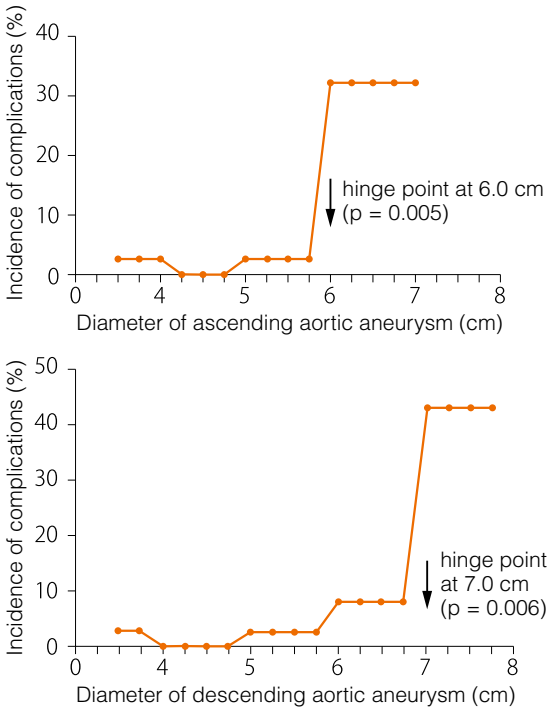


Figure 53. Diameter of thoracic aortic aneurysms and the incidence of complications, such as dissection and rupture. (Adapted from Coady MA, et al. 1997.[535]) Copyright (1997) Mosby-YearBook, Inc., with permission from Elsevier. https://www.sciencedirect.com/journal/the-journal-of-thoracic-and-cardiovascular-surgery.

1.2 Unruptured Thoracic Aortic Aneurysm

1.2.1 Aneurysms of the Aortic Root/Ascending Aorta (Table 12)

a. Standard Surgical Procedure

The surgical procedure is determined in consideration of factors including the extent of aneurysmal changes (enlargement), severity of the aortic valve disease, the diameter of the sinus of Valsalva, and etiology/pathology of the aneurysm (inherited connective tissue disorder, inflammatory diseases, or dissection). Surgery of the aortic root is divided into several procedures basically consisting of replacement by a composite graft with a mechanical or biological valve (Bentall procedure), allograft (homograft), xenogeneic aortic valve, pulmonary autograft (Ross procedure) and valve-sparing aortic root replacement (VSRR).

The modified Bentall procedure, by which the coronary artery is reconstructed using a Carrel patch button technique,[549] is considered the standard procedure, but biological materials, such as allograft (homograft), stentless valve, and autologous pulmonary artery, are selected for conditions, such as endocarditis accompanied by annulus abscess.[550] An RCT that compared allograft (homograft) replacement and Ross procedure reported in 2010 concluded that the long-term results were slightly inferior in the homograft group (Class Ib) but that both procedures were durable.[551]

If there are no abnormal aortic pathologies, such as aneurysmal change, dissection, inflammation, or infection in the aortic root, ascending aortic replacement alone is indicated. While valve replacement may be performed simultaneously depending on the degree of the aortic valve disease, in aortic valve insufficiency associated with dilatation of the sino-tubular junction (junction between the sinus of Valsalva and ascending aorta) (type Ia according to the classification reported by Boodhwani, El Khoury, et al.[552]), aortic regurgitation can be controlled by sino-tubular junction plication.[553] The aortic valve commissural resuspension for acute aortic regurgitation due to dissection is discussed in the section on aortic dissection ("**2. Stanford Type A Aortic Dissection**" in **Chapter VI**). Although wrapping of the ascending aorta is an option, primarily, for high-risk patients, long-term results are scarce, and the procedure is not a common choice at the moment.[506,507]

Concerning distal anastomosis, open distal anastomosis without aortic cross-clamping is often performed in aortic dissection,[554] but it is usually performed with aortic cross-clamping for a true aneurysm. However, if aortic cross-clamping at the proximal level of the brachiocephalic artery is risky or impossible, or if the aorta is enlarged at the clamping site, open distal anastomosis is selected. Although there are no established criteria for the indication for the latter procedure, open distal anastomosis is often indicated in patients with inherited connective tissue disorders, such as Marfan syndrome, to resect the aortic cannulation site or clamping site of the aorta, where dissection may develop in the future. However, an additional

brain protection method is required in open distal anastomosis, and indication must be carefully evaluated by considering the risk of perioperative cerebral complications.

b. Coronary Artery Reconstruction Methods

The following are major coronary artery reconstruction methods.

(1) Original Bentall procedure of anastomosing the ostia of the coronary artery directly to the prosthetic graft using inclusion technique[555]
(2) Button Bentall (modified Bentall) procedure of suturing the coronary button to the prosthetic graft with a Carrel patch[549]
(3) Cabrol procedure of reconstructing by interposing the bilateral coronary arteries using a single small-diameter prosthetic graft[556]
(4) Piehler procedure of utilizing a short interposed graft between coronary ostia and composite graft[557]
(5) For the left coronary artery reconstruction, Svensson's technique utilizing a short interposed graft between the left coronary ostia and composite graft, which is placed posterior side of the prosthetic graft[558]

The original Bentall technique is a devised procedure to control bleeding by wrapping the composite graft using the residual aortic wall. As pseudoaneurysms often develop at the coronary anastomosis site, the procedure is not used today. The Cabrol procedure has the risk of prosthetic graft occlusion,[559] and, recently, the button Bentall technique is widely performed.[549] In patients in whom the coronary artery is difficult to be mobilized due to reoperation, and inflammation, the Piehler procedure or Svensson procedure, by which a prosthetic graft is interposed, is effective.[557,558] Refer to the Guidelines for the Treatment of Valvular Disease[560] by the Japanese Circulation Society for the selection of prosthetic valves for aortic valve replacement in aortic root replacement and ascending aortic replacement.

c. Valve-Sparing Root Replacement (VSRR)

VSRR is divided into Yacoub's remodeling[561,562] and David's reimplantation method.[563] Each has its advantages and disadvantages, but the latter is more widely adopted, because reliable annular fixation is possible, aortic regurgitation is easier to be controlled, and volume of bleeding is less. In the 2000s, the importance of the function of the sinus of Valsalva was proposed with respect to the durability of the native aortic valve, and there have been major advances, such as the development of specially designed prosthetic grafts imitating the sinus Valsalva[564] and modification of the surgical procedure[565–567] and advanced approaches to acute Type A dissection accompanied by severe root dissection.[568–571] The advantages of VSRR compared with the Bentall procedure which is regarded as the standard procedure, including no need for anticoagulant therapy and fewer hemorrhagic complications, the absence of synthetic valve-related complications, and larger valve orifice area under the physiologic condition. Concerns include that it requires a high level of surgical skill, that the surgical risk increases with the duration of aortic clamping time, and that the long-term durability of native aortic valves is unknown.

Recently, high-precision comparison of the Bentall procedure and VSRR has been performed. In a meta-analysis of patients with Marfan syndrome, the incidences of thromboembolism, bleeding, and infective endocarditis were lower, and the survival rate was higher, in the VSRR group.[572] Also, while mechanical valve Bentall procedure is the gold standard by propensity score-matched comparison, the bioprosthetic valve Bentall procedure and VSRR have been reported to be useful for avoiding anticoagulant therapy.[573] According to comparison of mechanical valve Bentall procedure, bioprosthetic valve Bentall procedure, and VSRR by David et al., the survival rate and valve-related event-free rate were significantly higher by VSRR than by the Bentall procedure, the aortic valve reoperation rate after VSRR was significantly lower than that after bioprosthetic Bentall procedure and did not differ compared with the mechanical valve Bentall procedure.[574] Furthermore, in a study that compared postoperative QOL using SF-36, better QOL was obtained by VSRR regarding mental and physical health and valve related murmur.[575] To summarize, the Bentall procedure remains the standard procedure of aortic root replacement, but VSRR by an experienced surgeon in young patients with root enlargement is recommended with class I recommendation and level C evidence.[576]

1.2.2 Aortic Arch Aneurysm

a. Open Surgery (Table 13)

Open surgery is indicated for patients with an aneurysm diameter of 55 mm or larger,[535] patients with symptoms, such as pain, and patients with symptoms due to compression of surrounding organs (such as dysphagia and

Table 13. COR and LOE for Open Surgery for Unruptured Aortic Arch Aneurysm

	COR	LOE
It is recommended to take measures to prevent stroke and higher brain dysfunction[577–585]	I	B
Open surgery should be considered if the maximum diameter is ≥55 mm[535]	IIa	C
Total aortic arch replacement, with combined use of ET method as appropriate, should be considered for aortic aneurysms covering the entire aortic arch, chronic dissecting aortic arch aneurysms, and distal aortic arch aneurysms, including proximal descending aortic aneurysms[586–589]	IIa	B
The concomitant operation of CABG should be considered for patients with a coronary artery lesion of significant stenosis[95]	IIa	C
ASCP/SCP or RCP, in addition to hypothermic circulatory arrest, should be considered to minimize cerebral disorders[577–585]	IIa	B

ASCP/SCP, anterograde selective cerebral perfusion; CABG, coronary artery bypass grafting; COR, class of recommendation; ET, elephant trunk; LOE, level of evidence; RCP, retrograde cerebral perfusion.

hoarseness). Even if their diameter is smaller than 55 mm, aneurysms are indicated for open surgery when the adjacent ascending or descending aorta requires surgery[96] or when they are of the saccular type. Aortic arch replacement has been established as a standard treatment for aortic arch aneurysms because of its favorable treatment results,[590] together with the development of surgical techniques and the cerebral protection method, as well as the standardization of treatment strategies associated with such development.[95] Coronary artery bypass grafting (CABG) is performed concomitantly in patients with significant coronary artery lesions.[95]

Most surgeries of an arch/distal aortic arch aneurysm are performed with median sternotomy because of its advantages, including the ease to establish extracorporeal circulation, reliable protection of the brain and heart, capability of performing cardiac surgery simultaneously, and avoidance of lung compression maneuvers, while left thoracotomy is performed in cases of, for example, distal aortic arch aneurysm that extends to the peripheral side.[591] If necessary, an extensive replacement can be performed in one stage using median sternotomy + separate left thoracotomy, median sternotomy+partial transverse sternal incision + left thoracotomy (door open), or bilateral thoracotomy + sternal transverse incision. However, because of the high invasiveness of the procedures involving left thoracotomy, staged surgery is often selected recently. In the first stage of the surgery, focusing only on the proximal aorta replacement that can be approached by median sternotomy, a prosthetic graft is inserted into the aneurysm remaining on the peripheral side using the ET method.[586–589] In the second stage, descending replacement using ET or TEVAR is performed to reduce the treatment risk.

The open stent graft (frozen elephant trunk, FET) method has also become widely used in the recent years, in which a stent graft is inserted into the peripheral aorta, instead of ET of a prosthetic graft, during circulatory arrest.[592] Since this can replace the anastomosis distal to the aortic aneurysm with a stent graft, it is a useful procedure with the advantages of the ability to treat an extensive aortic arch aneurysm in one stage without a left thoracotomy and the ability to achieve peripheral anastomosis at a shallower position than the conventional method. On the other hand, its high SCI complication rate has been pointed out.[593] Deep insertion up to the level of the 9th thoracic vertebrae and beyond and perioperative hypotension are the risk factors of SCI,[594] against which preventive measures must be taken.

Preventive measures for stroke and higher brain dysfunction are highly important in the surgery of the aortic arch, and treatment results have been improved by minimizing cerebral disorders.[577–585] Thus, anterograde cerebral perfusion (SCP)[596,597] or retrograde cerebral perfusion (RCP) is added[598,599] to hypothermic circulatory arrest[595] during arch reconstruction,

Depending on the range of aortic reconstruction, the procedure can be divided into hemiarch replacement, partial arch replacement, which partially replaces the arch branches, and total arch replacement, which replaces all the arch branches. In hemiarch replacement, due to its limited circulatory arrest time, anastomosis is performed from the peripheral side under cerebral protection, mainly using hypothermic circulatory arrest or RCP (SCP may also be used). The partial arch replacement that replaces only the brachiocephalic artery is useful for ascending aortic aneurysms, including the proximal aortic arch. In total arch replacement, the stepwise method[600] allows a reliable peripheral anastomosis with a clear field of view. Although aortic arch replacement using the island technique had been performed, recently aortic wall and origins of supra-aortic vessels, which often have poor properties, are resected and individually reconstructed using a branched prosthetic graft designed for surgical procedures involving the aortic arch in consideration of ease of hemostasis.[597]

With regard to the order of anastomosis under SCP, the distal aorta is first anastomosed to resume circulation of the body, followed by proximal aortic anastomosis and reconstruction of the arch branches. However, when anastomosis of the left subclavian artery is difficult, it is often performed prior to the proximal aortic anastomosis. A branched graft may also be anastomosed to the left axillary artery exposed by another skin incision without reconstructing the left subclavian artery in the thoracic cavity. In RCP, due to its limited cerebral protection time, the arch first technique is used, in which the arch branch is first reconstructed, followed by distal and proximal aortic anastomosis.[601,602] Deep hypothermia (below 20°C) was the indicator of core body temperature (bladder or rectal temperature) during distal anastomosis (lower body circulatory arrest); however, moderate hypothermia at approximately 25–28°C has become widely referred to the recent years.[603]

b. Endovascular Treatment (Table 14)

i. Hybrid TEVAR

In many patients, aortic arch aneurysms cannot be treated by usual TEVAR alone because of the concern over postoperative endoleak due to graft placement in a curved area and the necessity to secure the blood flow of cervical branches. The first-line treatment for aortic arch aneurysms is total arch replacement, and TEVAR is considered only in elderly patients or patients in whom the risk of open surgery is high-risk. TEVAR is performed by inserting a stent graft (SG) after revascularization of the cervical branch to be occluded by bypass grafting via a non-anatomical approach to secure a landing zone. This procedure is generally called hybrid TEVAR (**Figure 54**).[379,605,612–619]

Hybrid TEVAR is divided into total debranching TEVAR and partial debranching TEVAR. In total debranching TEVAR, all 3 arch branches are reconstructed

Table 14. COR and LOE of Endovascular Treatment for Unruptured Aortic Arch Aneurysms

	COR	LOE
For patients at high risk for open surgery, TEVAR using fenestrated stent grafts,[604] TEVAR with branch reconstruction (hybrid TEVAR),[379,605,606] or TEVAR using in situ fenestration[607–609] is recommended*	IIa	C
For patients at high risk of open surgery, TEVAR using the chimney technique may be considered[610,611]	IIb	C
For patients at low risk for open surgery, hybrid TEVAR is not recommended[612,613]	III	B

*In situ fenestration TEVAR should be performed only in high-risk surgical patients at facilities and by surgeons skilled in TEVAR and catheterization of aortic branches. COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

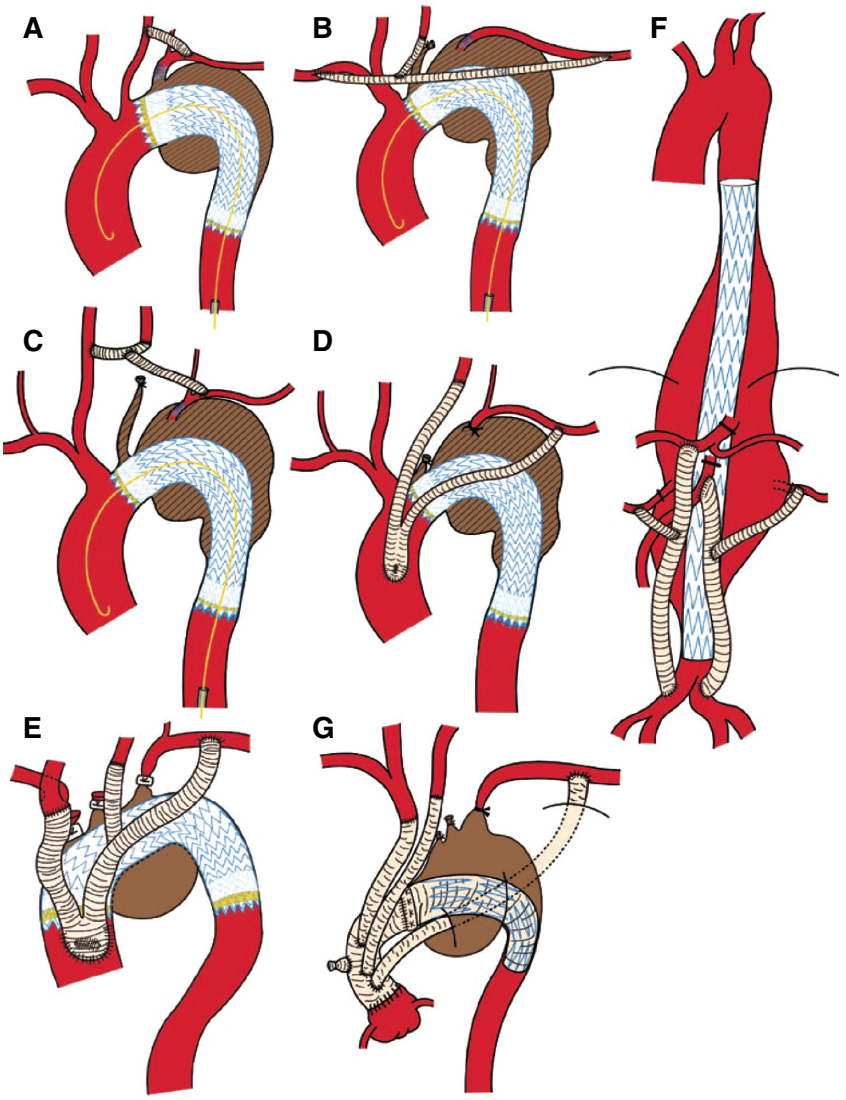


Figure 54. Hybrid TEVAR for abdominal aortic aneurysm. (**A**) Left common carotid to left subclavian artery bypass + TEVAR (1 debranch + TEVAR). (**B**) Right axillary to left common carotid/left axillary artery bypass + TEVAR (2 debranch + TEVAR). Blood is sent from the femoral artery and right axillary artery, left subclavian artery, and left common carotid artery, and the aortic arch is thoracotomized between the brachiocephalic artery and left common carotid artery. (**C**) Right common carotid to left common carotid/left subclavian artery bypass + TEVAR (2 debranch + TEVAR). (**D**) Ascending aorta to left common carotid/left axillary artery bypass + TEVAR (2 debranch + TEVAR). (**E**) Ascending aorta to brachiocephalic/left common carotid/left axillary artery bypass + TEVAR (3 debranch + TEVAR). (**F**) Iliac to celiac/superior mesenteric/bilateral renal artery bypass + TEVAR. (**G**) Open stent graft technique (involves surgery of the ascending and arch parts). The ascending aorta and arch branches are reconstructed using a quadruple-branched synthetic graft. In the descending aorta, a stent graft with a stent fixed on the distal side alone is inserted, and the synthetic graft inserted in the ascending aorta is sutured to the stent graft inserted in the descending aorta in the aortic arch.

by a median sternotomy, and the aneurysm is excluded with SG. The ascending aorta is often used as the major inflow channel, but replacement of the ascending aorta may be performed first if its condition is poor. In partial debranching TEVAR, thoracotomy is often unnecessary, and the aneurysm is excluded with SG after reconstruction of the cervical branches other than the brachiocephalic artery (e.g., carotid artery-carotid artery-left subclavian artery bypass). In debranching of the cervical branches, there is the possibility of induction of cerebral infarction by partial clamping of the ascending aorta, clamping of the carotid artery, manipulations associated with landing or embolism of atherosclerosed vessels.[379,407,620] For this reason, the incidences of perioperative cerebral infarction and retrograde Type A aortic dissection are higher than in distal aortic arch aneurysms, which can be treated by covering the subclavian artery alone.[620]

In comparison with total arch replacement, the duration

of stay in the ICU and the duration of hospitalization are significantly shorter, but the retreatment rate due to endoleak is higher, by hybrid TEVAR.[606,621] However, while hybrid TEVAR was performed more often in high-risk and elderly patients, the mortality rate and incidences of perioperative complications including cerebral infarction were comparable to those after total arch replacement in low-risk patients.[606,621]

In partial debranching TEVAR, the incidence of endoleak is higher because of the shorter proximal landing zone, but the invasiveness was lower, compared with total debranching TEVAR.[622] Also, partial debranching TEVAR, by which aortic aneurysms can be treated without extra-corporeal circulation, is less invasive, and as it contributes to improvements in QOL including shortening of the durations of ICU treatment and hospitalization, it can be the first-line treatment for patients at a higher risk.

ii. Totally Endovascular TEVAR

Recently, attention is being paid to totally endovascular TEVAR, in which the main device of TEVAR is placed in the ascending aorta with mild atheroma, and the brachiocephalic artery and left common carotid artery is reconstructed using covered stents. Procedures of totally endovascular TEVAR include the chimney technique, fenestrated SG, in situ fenestration, and company-made branched SG.

(1) **Chimney technique:** This is a procedure to secure the blood flow of cervical branches by placing covered stents from the cervical branches to the ascending aorta in parallel with usual SG.[623,624] However, gutter leak may occur from the gap in SG. Gutter leak is equivalent to type I endoleak, and there are reports that type I endoleak occurs in about 11% of the cases including those with gutter leak.[610,611] Also, while the mortality rate is relatively low at 4%, the incidence of cerebral infarction is 11%, retreatment rate after the chimney technique is high at 10–25%, and additional surgery is required in not a few patients.[610,625] Therefore, the chimney technique is unlikely to be the first choice among totally endovascular TEVAR procedures. However, it has the advantages that it can be performed using conventional devices and plays some role, for example, in high-risk emergency cases

(2) **Fenestrated SG:** The only SG that can be landed in Zone 0, which was developed in Japan and is covered by health insurance, corresponds to this type. Since it is semi-custom-made, the number of fenestrated areas can be adjusted. Its disadvantage is that it cannot be applied to emergency surgery since about 3 weeks is needed for its preparation. The bird's beak on the lesser curvature side in usual SG placement is considered an important factor for the occurrence of endoleak, but this fenestrated SG also fits the lesser curvature side, and saccular aneurysms on the lesser curvature side of the aortic arch are a good indication for this technique.[413] Also, as it has an internal skeleton unlike other thoracic SGs, aortic dissection that does not require strong fixation force is also a good indication. The initial success rate is reported to be 91%, the aneurysm-related death avoidance rate after 3 years to be 97%, and the re-treatment avoidance rate to be 84%.[604] Since the device is covered by health insurance when it is used in compliance with IFU (instructions for use), it is the first choice for aortic arch aneurysms in high-risk patients who fulfill the anatomical requirements

(3) **In situ fenestration:** This is a technique to secure the blood flow of the cervical branches by making fenestration in SG retrogradely from the subclavian artery or carotid artery using laser or a puncture needle (retrograde in-situ branched stent grafting, RIBS) and placing a covered stent after covering the cervical branches using SG. In this procedure, the use of SG is not covered by health insurance, but the patency rate of the reconstructed cervical branches is high at 100%, the postoperative occurrence of type I or type III endoleak is rare, and favorable results have been reported[607–609]

As observed above, totally endovascular TEVAR is a useful procedure for high-risk patients. Concerning the device selection, while fenestrated SG, which is covered by health insurance, is the first choice, not many aortic arch aneurysms fulfill the anatomical requirements. Therefore, regarding aortic arch aneurysms that are not indications for fenestrated SG, the short-term results are satisfactory by in situ fenestration in consideration of the incidence of postoperative endoleak. However, the long-term results remain unclear, and future reports are awaited.

1.2.3 Descending/Thoracoabdominal Aortic Aneurysm

a. Open Surgery of Descending Aortic Aneurysm (Table 15)

i. Aneurysm Diameter and Surgical Indications

Aortic aneurysms reaching a diameter of 60 mm have a yearly rupture risk of 10%, and they are judged to be indicated for surgery. On the other hand, intervention for aortic aneurysms with a diameter of smaller than 55 mm may not provide survival benefits. However, aortic aneurysms with a diameter of 50–55 mm or larger in women or patients with connective tissue disorders are indicated for surgery.[384] In addition, if the diameter of an aneurysm is found to be 55 mm or larger by the initial CT examination, its surgical indications are discussed while considering its surgical risks.

For follow-up, a CT re-examination is performed half a year after the initial examination, and the interval of subsequent examinations is determined according to the enlargement rate of aortic diameter. The enlargement rate of TAA diameter is 1–4 mm/year.[535,634,635] However, the observation period is determined by the diameter of the aneurysm because aneurysms with a small diameter have a slow enlargement rate, which increases as the aneurysm diameter enlarges. Aneurysms that enlarge by 5 mm or more in half a year have a high risk of rupture and are directed toward surgery. Attention must be paid to the morphology of aneurysms as saccular-type aneurysms have a high risk of rupture, even if their diameter is not large.

ii. Open Surgery

TEVAR can be easily performed on the descending aorta since it runs linearly, and it is unlikely to lead to problems, such as endoleaks and shear of an SG. Thus, TEVAR has great advantages in the region. The advancement of devices has led to stable results, and TEVAR is now becoming the first-line treatment. Therefore, open surgery for descending aortic aneurysms is performed generally on young patients and patients who are not suitable for TEVAR. The main indications for open surgery are as follows:

- Relatively young patients who are not at high risk of open surgery[384]
- Patients with connective tissue disorders, such as Marfan

Table 15. COR and LOE for Open Surgery for Unruptured Descending Aortic Aneurysm		
	COR	LOE
It is recommended to perform preoperative CTA or MRA examination to clarify the lesion range of an aneurysm and identify potential risks associated with spinal cord ischemia, such as main intercostal arteries[626,627]	I	C
Additional preoperative examinations to clarify the severity of potential heart diseases should be considered for patients with a past medical history of coronary artery disease[628]	IIa	C
Preoperative coronary artery revascularization should be considered for patients complicated by symptomatic or severe asymptomatic coronary artery disease[629]	IIa	C
Assessment of perioperative risks associated with the lung, kidney, and cerebral blood vessels should be considered preoperatively[630–632]	IIa	C
Open surgery should be considered for aneurysms with a diameter of ≥60 mm that are not indicated for TEVAR[384,633]	IIa	C
Open surgery may be considered for aneurysms with a diameter of 55–59 mm that are not indicated for TEVAR[384,633]	IIb	C

COR, class of recommendation; CTA, computed tomography angiography; LOE, level of evidence; MRA, magnetic resonance angiography; TEVAR, thoracic endovascular aortic repair.

syndrome
- Patients without a landing zone in the proximal or distal area
- Patients lacking arteries to access an aortic aneurysm[633] and having a "hostile" abdomen, in which approach to the aorta/iliac artery is difficult (such as after frequent abdominal surgery, after the construction of an artificial anus, and after radiation therapy), or patients with severe atherosclerotic diseases in the aortoiliac artery
- Patients with a history of abdominal aortic surgery, decreased blood circulation in the pelvis, extensive thoracic descending aortic aneurysm with the occluded lumbar artery, and considerably high risk of SCI after TEVAR[626,627,636,637]
- Patients with symptoms caused by compression on adjacent organs, such as the thoracic vertebral body (chronic pain syndrome), trachea or left main bronchus (dyspnea), and esophagus (dysphagia)[638]

The size and position of an aneurysm influences the decision on its surgical strategy from the viewpoints of the position and approach method of ribs for intercostal thoracotomy and the use of intraoperative auxiliary means. Therefore, CT examination, including three-dimensional imaging, is mainly used for the preoperative evaluation of an aneurysm, clarifying the size of aneurysm, the presence or absence of parietal thrombosis, vertical extension, and the relationship with surrounding organs. In patients with an aneurysm in the proximal descending aorta, its positional relationship with the arch branch artery poses a problem during open surgery, and it is important to clarify the extension of the aneurysm to the proximal side. Normally, the descending aortic aneurysm is reached under the 5th–6th intercostal left thoracotomy. The 4th–5th intercostal left thoracotomy may be used for proximal descending aortic aneurysms, while the 7th–8th intercostal left thoracotomy may be used for distal descending aortic aneurysms near the diaphragm.

Preoperative examinations should include CTA or MRA examination of the intercostal artery/lumbar artery and the artery in the pelvis, which play a major role in the spinal blood supply.[119,639] Preoperative evaluation of cardiac function, pulmonary function, renal function, and occlusive disease of the carotid and peripheral arteries is essential for minimizing the mortality rate and risk of complications related to surgery of a thoracic descending aortic aneurysm. Patients with a clinical history of coronary artery disease (CAD) or cardiac valvular disease usually require echocardiographic and cardiac catheter examinations, and additional examinations, such as Holter electrocardiogram, may be judged necessary in some cases. In patients with a descending aortic aneurysm complicated by symptomatic CAD, surgery of the aortic aneurysm should be preceded by the treatment of CAD. The treatment of patients complicated by asymptomatic CAD is controversial, given a recent study suggesting non-affirmative treatment.[629] In such cases, a preoperatively planned replacement range by open surgery and severity of CAD is important in determining preoperative strategies.[628]

In addition, the pulmonary function test and arterial blood gas analysis are important since a smoking history and the presence of COPD increases the risk of postoperative respiratory failure.[630]

The risk of postoperative renal failure is higher in patients with renal dysfunction, which can be reduced by ensuring preoperative hydration and proper intraoperative/postoperative renal perfusion.[631]

The risks of spinal cord ischemia, mesenteric ischemia, and renal ischemia are associated with aortic cross-clamping time.[631,632,640,641] The auxiliary means for aortic cross-clamping include partial extracorporeal circulation, left heart bypass, and hypothermic circulatory arrest. The hypothermic circulatory arrest is useful for ruptured cases and cases in which central aortic cross-clamping is difficult.[642] However, a retrospective analysis of 387 consecutive cases of descending aortic aneurysms showed that the application of left heart bypass did not significantly reduce the risk of paraplegia[640] (**Chapter VII**, "**2.3 Spinal Cord Protection Method**" for the prevention of spinal cord ischemia).

The results of elective open surgery for descending aortic aneurysms have improved in high-volume centers with numerous cases over the last 25 years.[640,643,644] However, the accepted results are not supported by data from the National Inpatient Sample (NIS), a large-scale database in the United States, and they reflect the results achieved at high-volume centers with many cases. The mortality rates in patients who had undergone elective and urgent surgeries were 10% and 45%, respectively. Furthermore, spinal cord ischemia has also been reported in the range of 11–15%.[645]

Table 16. COR and LOE for Open Surgery for Unruptured Thoracoabdominal Aortic Aneurysm		
	COR	LOE
It is recommended to evaluate the heart, lung, and renal functions preoperatively to estimate the surgical risks and to start treatment to improve preoperative condition[646–648]	I	C
Open surgery should be considered for atherosclerotic thoracoabdominal aortic aneurysm patients with low-moderate surgical risks showing an aneurysm diameter of ≥60 mm, rapid enlargement of an arterial aneurysm (≥5 mm/6 months), or aneurysm-related symptoms[635]	IIa	C
Extracorporeal circulation to perfuse the lower body and abdominal organs should be considered for patients with an extensive thoracoabdominal aortic aneurysm (Crawford type I, type II, and type III), especially if they require long-term aortic cross-clamping, to reduce complications due to ischemia[649,650]	IIa	C
Cerebrospinal fluid drainage should be considered for patients with an extensive thoracoabdominal aortic aneurysm (Crawford type I, type II, and type III) to reduce the risk of ischemic spinal cord injury[651–653]	IIa	B
The optimization of mean blood pressure and pressure on the distal aorta, moderate hypothermia, monitoring of electrophysiological spinal cord function, and reconstruction of the intercostal artery should be considered for intraoperative spinal cord protection[654]	IIa	C
Centralization to high-volume centers may be considered[655,656]	IIb	C

COR, class of recommendation; LOE, level of evidence.

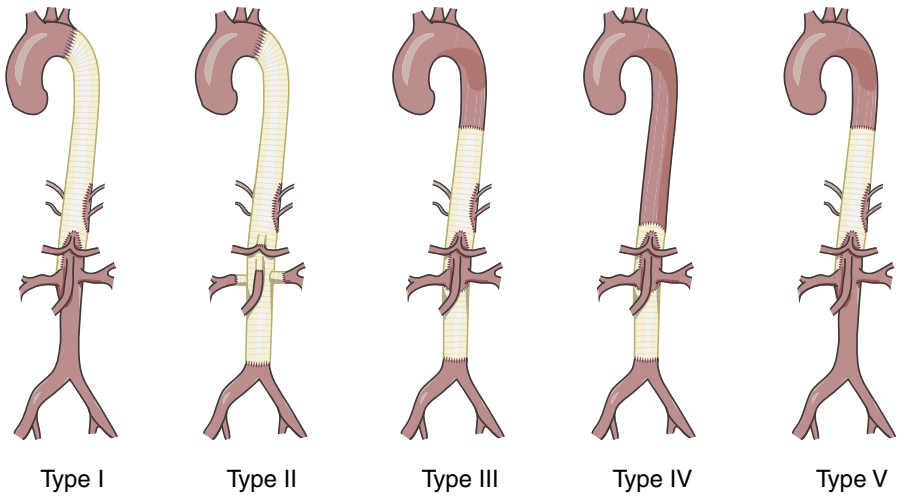


Figure 55. Modified Crawford classification by the range of prosthetic graft replacement for thoracoabdominal aortic aneurysm.

b. Open Surgery for Thoracoabdominal Aortic Aneurysm (Table 16)

i. Crawford Classification

Currently, the classification of TAAA reported by Crawford is generally accepted.[657] This classification is based on the range of continuous prosthetic graft replacement in the surgery of TAAA, and it consisted of four types from type I to type IV at the time of his reporting (**Figure 5**[658]).

Type I: Type I includes the replacement of most of or the entire thoracic descending aorta and the suprarenal abdominal aorta. Therefore, it typically extends from the area immediately distal to the left subclavian artery until the suprarenal area.

Type II: Type II includes the replacement of most of or the entire thoracic descending aorta, as well as the suprarenal and subrenal segments of the abdominal aorta. It generally starts at the area immediately distal to the left subclavian artery and extends to the aortic bifurcation.

Type III: Type III includes the replacement of the distal half of the thoracic descending aorta (below the 6th rib) and varying degrees of the abdominal aorta. In most cases, it begins in the middle descending area of the thoracic aorta and extends to the aortic bifurcation. However, it ends in the suprarenal aorta in some cases.

Type IV: Type IV begins near the diaphragmatic tear and often includes the entire abdominal aorta.

A modification of the Crawford classification has been proposed by Safi et al.[659] (**Figure 55**). The added type V begins in the distal half of the thoracic descending aorta (below the 6th rib) and ends above the renal artery, preserving the subrenal aorta. The original Crawford classification classified this type V as either type I (in terms of preserving the subrenal aorta) or type III (in terms of preserving the proximal thoracic descending aorta). The risk

of spinal complications after type V replacement is low.[657]

The Crawford classification serves several important functions. The risks associated with the surgery of TAAA depend on the site and replacement range of the replaced aorta. Thus, this classification can help in the proper evaluation of risks, planning of surgical approaches according to the extent of the expected treatment of aortic replacement, and development of a framework for selecting specific treatment methods. There has been international consensus on the use of this classification to explain the extent of aortic aneurysm disease. In both open surgery and TEVAR, this classification provides indices of the extent of the treatment, technical challenges associated with surgery, and potential postoperative risks. Furthermore, each of the five types is associated with different organ complications, such as paraplegia, renal failure, and abdominal organ ischemia.

ii. Indications

TAAA is subject to open surgery if it has an aneurysm exceeding 60 mm in diameter (excluding connective tissue disorders), shows a rapid enlargement of aneurysm diameter (≥5 mm/6 months), presents with symptoms, or has low-to-moderate surgical risks.[649,660]

Assessment of the risk of TAAA rupture due to surgical intervention is highly important, and in particular, the preoperative risk analysis of extensive TAAA in patients with comorbidities is also essential in determining the surgical procedures.

iii. Standard Procedure

The spiral incision is performed from the 5th–6th intercostal thoracotomy to the abdomen. The diaphragm is isolated in an arc to preserve the phrenic nerve, and the abdominal aorta is approached retroperitoneally or transperitoneally. Although lateral thoracotomy after incision of the latissimus dorsi and serratus anterior muscles was commonly used in the past, an approach of preserving the latissimus dorsi and serratus anterior muscles has been reported recently, which aims to preserve the blood flow by collateral flow to the spinal cord.[661] Aortic reconstruction is usually performed from the central side using the segmental clamping to shorten the spinal cord ischemia time,[663] although reconstruction from the peripheral side has also been reported.[662] In Japan, the intercostal and abdominal branch arteries are generally reconstructed individually using a prosthetic graft with a small diameter of 8 mm or 10 mm. The intercostal arteries are reconstructed individually or collectively using prosthetic grafts; however, they may be individually reconstructed directly without using a prosthetic graft or reconstructed collectively in an insular manner.[664] In patients with Marfan syndrome, an aneurysm often forms in the arterial wall of the insular reconstruction site of the intercostal artery in the late stage, and in principle, individual reconstruction is performed.[665]

iv. Auxiliary Means

Proximal descending aortic cross-clamping increases preload/afterload on the heart, and conversely, it leads to the loss of circulation in the distal clamping site, resulting in ischemic complications in the spinal cord, abdominal organs, kidneys, and lower extremities. Although reconstruction can be performed under simple clamping, distal aortic perfusion is generally performed with the following extracorporeal circulation to reduce ischemic complications of organs. Organ ischemia can be prevented by (1) femoral vein (right atrium) blood removal and femoral artery blood supply bypass (partial extracorporeal circulation) or (2) left atrial blood removal and femoral artery blood supply bypass (left heart bypass).[649,666] In Japan, (1) is frequently performed in cases of unexpected massive hemorrhage and hypoxemia. The difference between the two lies in the presence or absence of oxygenator use, although there are exceptions, thereby leading to different usages of heparin. Although some surgeons prefer (2) in this aspect, heparin-coating or X-coating circuits have been developed for the former, and in theory, closed circuits require the same amount of heparin. Aortic open vascular anastomosis by hypothermic circulatory arrest under complete extracorporeal circulation, with femoral vein suction blood removal or main pulmonary artery blood removal, is used in cases with difficulty in central clamping near the arch, cases with difficulty in detachment by reoperation, and cases of aortic dissection.[667,668]

v. Protection of Abdominal Organs

Ischemia of internal organs is reduced by blood perfusion in the celiac and superior mesenteric arteries and injection of cooled crystalloid transfusion (such as lactated Ringer's solution) or blood perfusion in both renal arteries.[650] Selective continuous perfusion of each abdominal branch artery is performed using a cannula with a balloon from the lateral branch of the partial extracorporeal circulation or the left heart bypass circuit. Although there is no established theory, a flow rate of 150–200 mL/min per branch is used as a guide. Attention must be paid to the induction of an inflammatory response as mucosal damage may occur despite anterograde perfusion of the superior mesenteric artery.[669]

vi. Methods of Spinal Cord Protection (Chapter VII, "2. Spinal Cord Protection")

The risk factors for developing ischemic SCI include prolonged aortic cross-clamping, extensive aortic aneurysm, aortic dissection, urgent surgery, non-reconstruction of the internal iliac artery, and a history of abdominal aortic surgery. The methods to prevent SCI include distal aortic perfusion, reconstruction of the intercostal artery,[651] intercostal artery perfusion, cerebrospinal fluid drainage (CSFD),[651–653] spinal cooling,[670] and perioperative evaluation of spinal cord function.[671] All the available strategies for the prevention of SCI are summarized in two recent reviews.[651,653]

In Japan, preoperative non-invasive angiography, such as MR and CT examinations, is generally used, if possible, to identify the Adamkiewicz artery and the intercostal/lumbar artery connecting to the Adamkiewicz artery or collateral flow, which serves as a clue for intraoperative reconstruction and preservation of the intercostal artery.[672] A CSFD tube is inserted the day before or on the day of surgery and continuously used for 3 days after surgery.[653] During surgery, spinal cord ischemia is monitored by exertional spinal evoked potentials and somatosensory potentials.[654,673,674] The responsible intercostal/lumbar artery is reconstructed, if necessary, with reference to preoperative identification tests and intraoperative spinal cord ischemia monitoring. A variety of approaches, including CSFD, maintenance of adequate blood pressure, use of distal aortic perfusion, and revascularization of the intercostal artery are effective in reducing the risk of spinal cord ischemia.[675]

vii. Results

The majority of results of TAAA open surgery are from a series of cases performed in highly specialized high-volume centers.[646,660,671] These experienced facilities have reported

a postoperative mortality rate of 5–15%. Additionally, the main complications were respiratory failure (up to 60%), neurological disorders (3–18%), and renal failure (3–15%). Excluding the highly specialized facilities, the mortality rate and incidence of complications are nearly twice as high as these values. In the California-wide database in the United States, the 30-day and 1-year mortality rates after open surgery of TAAA were 19% and 31%, respectively.[675] These results indicate that complex surgery, such as the open surgery of TAAA, should be performed in specialized facilities, and in fact, sufficient support by staff, the size of the hospital, and the number of surgeons were shown to have a significant impact on the postoperative survival rate. Lesser surgical experience has been correlated with an increase in the postoperative mortality rate.[655] This study on 1,542 patients who had undergone surgery of TAAA showed a significant difference ($P<0.001$) in the mortality rate between hospitals with few cases (27.4%) and hospitals with many cases (15%). In addition, hospitals with fewer surgeons (25.6%) had a significantly higher mortality rate ($P<0.001$) than hospitals with many surgeons (11.0%). Such a relationship between the number of cases and the outcome (volume-outcome relationship) has been summarized in a systematic review.[656]

c. Endovascular Treatment of Descending Aortic Aneurysm (Table 17)

Although the evidence from RCTs comparing open surgery and TEVAR for descending aortic aneurysms is not yet available, published studies have shown that the early mortality rate, the incidence of complications, and length of hospital stay after TEVAR are superior to those after open surgery.[360–365,676,677] Open surgery and TEVAR showed no difference in the long-term mortality rates up to 5 years,[362] and TEVAR in the straight area of the descending aorta resulted in little endoleaks (3.9–15.0%). Thus, TEVAR is recommended for descending aortic aneurysms that meet anatomical requirements, except for patients with heritable connective tissue disorders, such as Marfan syndrome.[678] In addition, TEVAR has a lower incidence of SCI than open surgery (2.8–21.0%),[363,676,678–680] and it is characterized by late SCI, with more frequent paresis and relatively rapid recovery. The anatomical risk factors of SCI include the SG coverage area of 200 mm or greater, coverage of the T8-T12 level, AAA replacement, internal iliac artery occlusion, and left subclavian artery occlusion. Chronic renal dysfunction and perioperative hypotension (average of <70 mmHg) also lead to the development of SCI.[678,679,681,682] In such cases, cerebrospinal fluid drainage is performed to prevent SCI. With its current devices, TEVAR is not indicated for cases with the inner aortic diameter of ≥40 mm in the landing area and the landing zone length of ≤15 mm.[365,683] In addition, TEVAR is not indicated for those presenting with compression symptoms caused by an aneurysm (such as the compression of the esophagus and heart) and those with aortic gastrointestinal fistula or infected aneurysm with traffic to the esophagus.[684–686] Since the results of open surgery for bronchial fistula and pulmonary fistula with hemoptysis are poor, TEVAR is often used for these, although they are not considered as good indications.[684,685,687]

During TEVAR for descending aortic aneurysm, 10–50% of the cases require coverage of the left subclavian artery to secure a sufficient landing zone, which increases the incidence of encephalomyelopathy and upper limb ischemia.

Table 17. COR and LOE for Endovascular Treatment of Unruptured Descending Aortic Aneurysm

	COR	LOE
It is recommended to perform TEVAR if anatomical requirements are met[360–365,676–678] (See **Table 9**)	I	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

Revascularization to the left subclavian artery is recommended, at least for cases with the patent left internal thoracic artery connected to a coronary artery or cases in which the left vertebral artery is dominant.[370,371,636,688–692] The safe coverage of the celiac artery to secure a sufficient landing zone is effective,[683] for which grasping the anatomy with a contrast-enhanced CT is important. When covering the celiac artery, angiography should be performed prior or intraoperatively to confirm the traffic between the celiac artery and superior mesenteric artery.[693] Celiac artery occlusion is contraindicated in cases with insufficient collateral flow, poor blood flow in the portal vein, or celiac superior mesenteric artery. In such cases, the scalloped device or techniques called snorkel and chimney methods are used; however, data supporting their safety and usefulness have been scarce.[532]

d. Endovascular Treatment of Thoracoabdominal Aortic Aneurysm

Due to the problems of open surgery, such as cardiopulmonary circulation disorder, kidney injury, and nerve injuries including paraplegia, two alternative methods are now becoming widely used.

One is hybrid treatment, in which the abdominal branch is bypassed by an extra-anatomical bypass, followed by SG deployment. Whether the bypass and SG deployment should be performed simultaneously or in separate stages is controversial. When they are performed simultaneously, the mortality rate and incidence of kidney injury are high. On the other hand, when they are performed in separate stages, there is a risk of rupture between the stages.[694,695] Thus, the waiting period must be determined depending on the diameter of the aneurysm, and the bypass and SG deployment should be performed within a few days, if the aneurysm diameter exceeds 60 mm.[696] As this is performed in high-risk patients, hybrid treatment has a relatively favorable mortality rate and incidence of SCI,[697–699] and its long-term patency rate of abdominal branch bypass is also favorable.[700,701] However, this method is not so minimally invasive. The complete endovascular treatment described below has become widely used overseas, and hybrid treatment is an option only in urgent cases in which the device cannot be obtained in time.[532] On the other hand, due to the lack of approved branched SG in Japan, hybrid treatment has been an important option for aged individuals and COPD patients who are not indicated for open surgery.

The other alternative method is complete endovascular treatment using a branched SG. Because fenestrated devices have achieved favorable results in the treatment of pararenal artery AAA,[702] this method has been developed with the advent of the hybrid surgery room and improvements in imaging technology. There have been no RCTs of this method, and endovascular treatment is administered to

Table 18. COR and LOE for Treatment of Aortic Aneurysm Rupture in the Aortic Root and Ascending/Aortic Arch		
	COR	LOE
It is recommended to perform urgent surgery if there are treatment indications[96]	I	C
It is recommended to perform unenhanced or contrast-enhanced CT examination of the whole body (including the cervical to inguinal regions) for patients suspected of aneurysm rupture[96]	I	C
It is recommended to select TEVAR over open surgery for patients meeting anatomical requirements if it is performed in a facility capable of providing specialized techniques[96,708]	I	C
A combined use of the frozen elephant trunk method may be considered in the total arch replacement for distal aortic arch aneurysm rupture[709,710]	IIb	C
Prediction of surgical risks using the Japan SCORE may be considered[711] Note: Some items are not included in the risk prediction model, such as organ protection methods (e.g., hypothermic circulatory arrest and cerebral perfusion), or frailty	IIb	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

Table 19. Results of Open Surgery for the Rupture of Non-Dissecting Aortic Root-Aortic Arch Aneurysm			
Replacement range	Number of cases	Number of operative deaths	Operative mortality rate (%)
Root	95	19	20.0
Ascending	116	21	18.1
Root-arch	10	5	50.0
Arch	214	43	20.1
Total	435	88	20.2

Based on the data of JCVSD from January 2015 to December 2016. (Excerpted from Shimizu H. et al. 2019[711])

patients at higher risk. Therefore, no significant difference in the 30-day mortality rate and incidence of SCI has been found between this procedure and open surgery.[703–707] In Japan, no device has been approved for this procedure, and it is performed only in a limited number of facilities.

1.3 Rupture of Thoracic Aortic Aneurysm

1.3.1 Aortic Root and Ascending/Aortic Arch Aneurysm (Table 18)

a. Background and Epidemiology

There are no epidemiological statistics on the rupture of non-dissecting TAA in Japan. According to the report of JCVSD on thoracic aortic surgery performed in 2015 and 2016,[711] of the 35,427 patients undergoing thoracic aortic surgery (including thoracoabdominal aortic surgery), 1,399 patients had rupture of a non-dissecting aortic aneurysm, of whom 435 patients had open surgery from the root to the arch (**Table 19**). Reports from overseas include a two-point observation survey in Stockholm, Sweden in the 1980s.[712] It is estimated that the incidence of TAA rupture is 5 per 100,000 population. The rupture of TAA occurred in 82 patients in 1980 and 76 patients in 1989, and of the total of 158 patients, 2 patients underwent surgery. Of the 158 patients, 64 (41%) patients survived and were transported to the emergency outpatient department, 11 (7%) patients died in welfare facilities for the elderly, and 83 (53%) patients died outside a hospital. Their rupture sites were the ascending aorta in 81 patients, the aortic arch in 23 patients, the descending aorta in 45 patients, and unknown in 9 patients. In addition, 54% and 22% of the patients died within 6 h and 7–24 h of the onset of symptoms, respectively, and 24% died thereafter.

b. Risk Factors for Rupture

Predictors for the rupture of TAA include the aneurysm diameter, which has been used as a classic index. The probability of rupture increases when the aneurysm diameter exceeds 60 mm.[535,635] For the aortic arch, an enlargement rate of 5.5 mm or more per year has been extracted as a predicting factor for rupture, and aneurysm diameter of 65 mm or larger and hyperlipidemia influences the increase in enlargement rate.[713] However, several of these factors were examined in retrospective studies, and large-scale studies have been few, resulting in a low level of evidence at present.[714]

c. Diagnosis

Ruptures into the pericardial sac, mediastinum and thoracic cavity are fatal, and patients die at the onset site before communicating with the rescuer. The survival cases present with sudden chest/back pain and consciousness disturbance as the main symptoms. In addition, hemoptysis or hematemesis occurs when a fistula is formed in the trachea or esophagus. Respiratory failure may also result from hemorrhage into the thoracic cavity. It is important to suspect rupture as there are generally no symptoms specific to rupture. Unenhanced and contrast-enhanced CT examinations are essential when rupture is suspected. In deciding the treatment policy, it is important to extend the imaging range of CT examination not only to the thoracic region, but also to the iliac region.[96] If the patient exhibits consciousness disturbance, the head is imaged simultaneously.

d. Treatment

Urgent surgery for lifesaving purposes is essential. Although TEVAR/EVAR has now been established, open surgery is still the standard treatment for rupture from the root to the arch. It is desirable to replace the entire aneurysmal aorta, including the rupture site, with a prosthetic graft. However, since the highest priority lies in lifesaving, the range of replacement should be considered based on the preoperative hemodynamics and respiratory condition, the presence or absence of comorbidity, age, and intraoperative findings, and there is no need to adhere

to the preventive expansion of the replacement range.

There have been reports of TEVAR[708,715] and hybrid surgery combining open surgery and TEVAR[709,710] for TAA rupture; however, the blood flow to the cervical branch needs to be maintained when performing TEVAR from the ascending aorta to the aortic arch. In addition, if an endoleak occurs, the possibility of hemorrhage from the rupture should also be considered. If preoperative hemodynamics is disrupted or worsening, immediate initiation of percutaneous extracorporeal circulation or manual compression of the rupture site by immediate thoracotomy is required.[716] Moreover, there has recently been a report on a method that leads to thoracotomy after performing hemorrhagic control by TEVAR (using bridge).[717] It is needless to say that the initial response according to the pathological conditions of each patient is vital.

e. Surgical Procedure by Site

i. Aortic Root

Rupture of the aortic root is mainly caused by congenital Valsalva sinus arterial aneurysm or annuloaortic ectasia. Arterial aneurysms of congenital Valsalva sinus often rupture into the cardiac cavity, and reports of its rupture into the pericardial sac have been considerably few.[718] It most frequently occurs in the right coronary sinus (approximately 60–80%), followed by the noncoronary sinus (approximately 20%) and the left coronary sinus, which is rare (approximately 1–10%).[719,720] The right cardiac system is the most common destination of its rupture, and heart failure develops by forming a left-to-right shunt. However, the degree of symptoms varies depending on the amount of shunt and disease duration.

The treatment of the aortic root is, in principle, open surgery. An approach is selected based on the location of the ruptured sinus, size of rupture, shunt destination, abnormalities in the aortic valve leaflet, the presence of aortic valve regurgitation, and the presence or absence of congenital interventricular septum deficiency. A direct or patch closure of the rupture is performed by making an incision in one or two sites in the aorta, right atrium, right ventricle, or pulmonary artery. Although rupture can be repaired with the incision of only the aorta or right atrium in some cases, it is generally approached from two directions.[719,720] If the patient has abnormalities in the aortic valve leaflet or aortic valve insufficiency, methods such as aortic root replacement, aortic valve replacement with the closure of the rupture, and VSRR are selected. When closing the rupture, attention needs to be paid to the recurrence of the aneurysm, the occurrence of aortic valve insufficiency, and disorder of the stimulus conducting system. The early and late surgical results are both relatively favorable; however, caution is needed as the late recurrence of aortic valve insufficiency,[721] recurrence and rupture of aneurysm,[722] and atrioventricular block have been reported.

In recent years, transcatheter closure of the rupture site using an occluder for interventricular septum and ductus arteriosus closure has been reported, and with its relatively stable results, it can be a beneficial option for critically ill patients.[723] On the other hand, it was found to be ineffective in some cases of rupture with a size of 10 mm or larger, and the long-term effects of the stress exerted by a rigid occluder on the Valsalva sinus are unclear. Thus, in principle, its use is considered safe if it is limited to patients who should avoid surgery with extracorporeal circulation.[724]

Annuloaortic ectasia is often found in patients with connective tissue disorders, such as Marfan syndrome. Rupture from a non-dissecting state is less likely compared to the rupture after the onset of dissection.[725] Aortic root replacement or VSRR is selected regardless of the presence of aortic valve insufficiency. For details of the procedures, see "**1.2.1 Aneurysms of the Aortic Root/Ascending Aorta**" in this chapter.

ii. Ascending Aorta

Ascending aorta replacement is the first treatment choice. If a rupture is close to the root, replacement under aortic cross-clamping may be performed after the establishment of extracorporeal circulation. If a rupture is present on the arch side, the replacement of the peripheral aorta, including the rupture, may precede under profound hypothermic circulatory arrest by cooling the rupture site while it is manually closed, after establishing extracorporeal circulation.

iii. Aortic Arch

Total arch or partial arch replacement is the basic procedure. Hemorrhage may occur in the pericardial sac, mediastinum, or thoracic cavity depending on the rupture site; however, the rupture site may not be easily visible. Peripheral aortic anastomosis is difficult with median incision alone if the patient has severe calcification around the distal arch or extensive aneurysmal lesions in the descending aorta. In such cases, total arch or partial arch replacement may be performed by median incision with left thoracotomy (such as trapdoor thoracotomy and door open method), left thoracotomy, or left thoracotomy with trans-sternal incision and right thoracotomy (clamshell method).

However, these approaches require time to reach thoracotomy, which poses a problem in ruptured cases that require a prompt response. Thus, a method of opening the ascending aorta and ascending/proximal aortic arch on the central side of the rupture site by median incision alone and deploying a SG in the aneurysmal site, including peripheral rupture site (open SG method or FET method) has also been applied in ruptured cases, which has demonstrated its relatively favorable results.[726]

In addition, although there have been reports on TEVAR after bypass to the cervical branch under thoracotomy or non-thoracotomy, fenestrated SG, and the chimney method,[715] the ESC guidelines for aortic arch aneurysms state that TEVAR should be applied when "anatomy is favorable and the expertise available".[96] In this case, the high complication incidence of retrograde Type A dissection poses a problem.[727]

f. Results of Open Surgery

A report based on JCVSD in 2015 and 2016 showed that the early mortality rate (30-day mortality and in-hospital mortality) for open surgery of non-dissecting TAA rupture was 20.0% in the root region, 18.1% in the ascending region, 50.0% in the root-arch region, and 20.1% in the arch region (**Table 19**).[711] There are no reports investigating the long-term results of surgical cases for non-dissecting TAA rupture in the region from the root to the arch. Furthermore, there are currently no reports analyzing the risk factors associated with early mortality.

1.3.2 Aortic Arch Aneurysm (Table 20)

In a report that compared TEVAR and open surgery (prosthetic graft replacement) for ruptured descending artery aneurysm, more satisfactory results were obtained

Table 20. COR and LOE of Endovascular Treatment for Ruptured Aortic Arch Aneurysms

	COR	LOE
Hybrid TEVAR should be considered for ruptured aortic arch aneurysms[710,715]	IIa	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

Table 21. COR and LOE for Endovascular Treatment of the Rupture of Descending Aortic Aneurysm

	COR	LOE
It is recommended to perform TEVAR as the first treatment choice if the anatomical requirements are met[349] (See **Table 9**)	I	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

by TEVAR, with the 30-day mortality rate being 17% in the TEVAR group and 24% in the open surgery group, and the 4-year survival rate being 75% and 64%, respectively.[349] Therefore, TEVAR is also recommended for ruptured descending artery aneurysms.[352,728,729]

On the other hand, aortic arch aneurysms cannot be managed by TEVAR alone because of the concern over postoperative endoleak due to stent placement in the curved area and from the viewpoint of securing blood flow of the cervical branches. For this reason, the first choice for aortic arch aneurysms is open surgery, and TEVAR should be considered for elderly patients or patients in whom the risk of open surgery is high.

The results of TEVAR in high-risk patients have been reported to be satisfactory.[710,730] In performing TEVAR for aortic arch aneurysm, hybrid TEVAR, in which the stent graft is inserted after bypass revascularization of the cervical branches via a non-anatomical route to secure landing zone, or a total endovascular procedure, such as in situ fenestration, in which fenestration is made by inserting a stent graft, is selected (See "**1.2.2.b Endovascular Treatment**" in this chapter).

Since hybrid TEVAR and total endovascular aortic aneurysm repair do not require thoracotomy, it is less invasive, comparable to open surgery in both the success rate and mortality, and can be an option for patients with ruptured aortic arch aneurysm.[715,731] However, the papers that reported the results of TEVAR for ruptured aortic arch aneurysms are presently those about small-scale evaluations and case reports alone.

1.3.3 Descending/Thoracoabdominal Aortic Aneurysm

a. Open Surgery of Descending Aortic Aneurysm

Rupture of a descending aortic aneurysm has a high mortality rate. The rupture of a descending aortic aneurysm can be treated only with invasive treatment; however, several patients die of hemorrhage before receiving treatment or do not survive even after receiving treatment. In addition, even if they tolerate the surgery, there are risks of multiple organ failure and cerebral/spinal cord injury. In a meta-analysis of 224 cases of descending aortic aneurysm rupture, the 30-day mortality rate after open surgery (prosthetic graft replacement) was 33%,[352] and myocardial infarction, stroke, and paraplegia, which are the main complications, were found in 11.1%, 10.2%, and 5.5% of the cases, respectively. The author of this report also showed that the combined rate of mortality, stroke, and paraplegia in a retrospective multicenter study of 69 cases of descending aortic aneurysm rupture was 36.2%.[349] In addition, a large study using the large-scale database NIS in the United States showed that the mortality rate of 559 cases of descending aortic aneurysm rupture was 28.6%.[351] These data suggest that open surgery in the treatment of the rupture of descending aortic aneurysms is associated with a high mortality rate and a high morbidity.

In ruptured cases of thoracic descending aortic aneurysm, it often requires time to reach aortic cross-clamping due to adhesion to the lung, during which the circulation fails. Therefore, immediately after the patient is transported to the surgery room, extracorporeal circulation is established via the femoral artery and vein before left thoracotomy. Unlike AAA, clamping with a balloon is difficult in thoracic descending aortic aneurysms depending on the rupture site. Thus, the time of circulation failure cannot be predicted even with stable circulation, and aortic cross-clamping is needed as early as possible. If the rupture site can be identified by CT examination, the pleura can be resected to expose the aorta distant from the rupture site for clamping.

On the other hand, as described below, TEVAR has been performed as an alternative procedure to open surgery for descending aortic lesions, including rupture, in the recent years. Additionally, it was suggested that TEVAR has led to reduced mortality rate and incidence of complications.[349,351,352] However, a study using inpatient sample data in the United States showed a contrasting result, in which there was no significant difference in the mortality rate between TEVAR and open surgery (23.4% vs. 28.9%, P=0.064).[351] In addition, the effectiveness of TEVAR for the rupture of descending aortic aneurysms caused by infiltration of the descending aorta of esophageal cancer or lung cancer has been reported,[732–734] and TEVAR has become one of the treatment options.

b. Open Surgery for Thoracoabdominal Aortic Aneurysm

The rupture of TAAA also has a high mortality rate. Definite studies on open surgery have been few, and there were no mentions of open surgery for the rupture of TAAA in the 2016 ESVS guidelines. In the 1990s, its operative mortality rate in the United States was reported to be 53.8%;[735] however, it has recently improved to 14% by omitting cerebrospinal fluid drainage, intercostal artery reconstruction, and concomitant surgery to simplify the procedure even in ruptured cases.[736] As in the rupture of descending aortic aneurysms, the number of facilities treating ruptured TAAA cases with TEVAR is increasing; however, it is not as easy as the one for descending aortic aneurysms. A study analyzed 206 cases of TAAA rupture (144 cases of open surgery and 62 cases of TEVAR) using the database of the National Surgical Quality Improvement Program (NSQIP), and it reported that TEVAR was superior to open surgery in postoperative renal failure (32% vs. 13%, P=0.004) and respiratory failure (58% vs. 37%, P=0.007) despite no significant difference in the mortality rate between the two (38% vs. 26%, P=0.09).[737]

c. Endovascular Treatment of Descending/Thoracoabdominal Aortic Aneurysm (Table 21)

Although no RCTs have compared TEVAR and open surgery for descending/thoracoabdominal aortic aneurysms,

the treatment rate with TEVAR has clearly increased in recent years.[349,738–740] In meta-analysis and retrospective studies, TEVAR was shown to have a lower mortality rate and incidence of complications,[349,352] and TEVAR is the first treatment choice for the rupture of thoracic descending aortic aneurysms if the anatomical requirements are met. However, TEVAR has a high incidence of long-term aorta-related events, including death, and has not shown superiority in long-term prognosis over open surgery.[352,738]

In 38% of urgent cases of rupture, occlusion of the origin of the left subclavian artery associated with SG deployment is needed to ensure a sufficient central landing zone; however, reconstruction of the subclavian artery has not been performed in most cases.[352] There have been no data indicating that reconstruction of the left subclavian artery is unnecessary, and its reconstruction is recommended at least if the patented left internal thoracic artery was anastomosed to the coronary artery or if the left vertebral artery clearly showed left dominance. Otherwise, coverage of the origin of the left subclavian artery associated with SG deployment is acceptable in urgent cases.[689,729] Similarly, coverage of the origin of the celiac artery (CA) with a SG is acceptable in urgent cases. As in elective TEVAR, collateral circulation after balloon occlusion of CA should be confirmed by contrast examination of the superior mesenteric artery. However, ischemic complications in the CA region were reported to occur after the occlusion of the origin of the CA by a SG, even when collateral blood flow from the superior mesenteric artery to the CA region had been confirmed.[532] If possible, the blood flow in the CA should be secured by the parallel or periscope technique using a SG with a small diameter[741] or hand-made fenestrated SG.

Fenestrated SG or branched SG is used in the complete endovascular treatment of TAAA rupture that requires reconstruction of the abdominal branch. The latter is used if there is a possibility of urgent response (off-the-shelf), and treatment of TAAA rupture using branched SG has shown relatively favorable results, with a 30-day mortality rate of 6% and SCI of 6%.[742] However, it will take some time for the technique to be widely used worldwide. In addition, the sandwich method, which combines an existing SG and a long covered stent with a small diameter, has achieved highly favorable results for the rupture of TAAA.[743] Covered stents with a small diameter have been approved in Japan; however, their use is not indicated for aortic aneurysms yet.

Therefore, hybrid treatment is an option, in which a SG is inserted after opening the abdomen and bypassing the abdominal branch from a more distal artery (abdominal debranching). However, the abdominal debranching itself is highly invasive, and its superiority over open surgery is not clear even in elective cases.[744] Since abdominal debranching requires time in the treatment of rupture, its results have been poor in cases of rupture presenting with extravascular hematoma in CT examination, although it may be used for patients with impending rupture presenting with only pain,[745] and it is not indicated for cases with shock.

1.4 Extensive Thoracic Aortic Aneurysm

1.4.1 Open Surgery

Although the definition of extensive TAA has not been established, this section defines it to be non-dissecting TAA from the aortic arch to the descending aorta or abdominal aorta, and its surgical indications and procedures are described.

a. Approach

Due to its anatomical limitations, the region from the arch to the distal aortic arch is a general surgical range of median sternotomy. In addition, by using TEVAR in combination, surgical intervention in the descending aorta can be made through median sternotomy. On the other hand, the surgical range of left thoracotomy can include the thoracoabdominal aortic region by adding the distal arch-descending aortic approach and the retroperitoneal approach. Surgery of extensive TAA is planned by combining median sternotomy and left thoracotomy approach, and one-stage or staged surgery is planned, taking anatomical limitations and surgical tolerance of each patient into consideration.

b. One-Stage Surgery

An approach in one-stage surgery is selected from median sternotomy, median sternotomy + left thoracotomy, or left thoracotomy. In median sternotomy, normal heart-lung machine operation and hypothermia can be applied, but peripheral anastomosis to the descending aorta requires sophisticated surgical techniques, and various anastomotic methods have been reported.[600]

The procedure that combines arch surgery by median sternotomy and open SG allows surgical intervention in the descending aorta and reduces surgical invasion; however, it was reported to increase the incidences of SCI and cerebral infarction.[380,746,747] The 2015–2016 annual report of JCVSD showed that the incidences of SCI in non-dissecting aortic aneurysm surgery were 5.4% (n=958) in hybrid surgery and 2.0% (n=2938) in arch replacement, and attention must always be paid to SCI when using an open SG.[711] In 1996, Kato et al. reported the clinical results of the open SG method,[749] which is also called the "frozen elephant trunk (FET) method"[592,746] as the procedure fixes the elephant trunk (ET) with a stent.[750] Commercial open SGs have been available in Japan since 2014.

The sternotomy + left thoracotomy approach enables reliable surgical operation and typical heart-lung machine operation as it exposes the entire length of the descending aorta from the arch. However, the addition of left thoracotomy increases the surgical invasion, resulting in an increased incidence of respiratory complications.[751] The following approaches have been used: (1) Median sternotomy + left thoracotomy: Peripheral anastomosis of the descending aorta is performed by adding left thoracotomy to median sternotomy. It includes the pull-through method, which runs a prosthetic graft in the descending aorta,[752] and a procedure that excludes the descending aorta.[753] (2) Partial sternal incision + left anterior lateral thoracotomy: This uses the L-shaped thoracotomy (door open) method, which combines upper partial sternal incision and left anterior lateral incision,[754,755] the antero-lateral partial sternotomy (ALPS) method, which combines lower partial sternal incision and left anterior lateral incision,[756] and the clamshell method, which combines left anterior lateral incision with trans-sternal incision.[757]

Operation for the aortic arch is possible even in the left thoracotomy approach by expanding the thoracotomy range to the cranial side. Descending/thoracoabdominal aortic replacement from the arch by left posterior lateral thoracotomy was reported.[758]

c. Staged Surgery

Staged surgery is considered useful in reducing the surgical risks and invasiveness of each procedure; however, there is always concern about the risk of aortic events while awaiting a second-stage surgery. Basically, the initial surgery is aortic arch replacement by median sternotomy, during which ET or FET is commonly used to prepare for the second-stage surgery. Descending aorta replacement by left thoracotomy and thoracoabdominal aortic replacement are performed in the second-stage surgery; however, TEVAR to the descending aorta can be performed to complete the procedure in several cases. In addition, since arch replacement + FET leads to an increased risk of SCI,[746] some have performed arch replacement + ET as the initial surgery and completed the second-stage surgery with TEVAR.

d. Hybrid Surgery

A procedure that combines conventional prosthetic graft replacement and TEVAR has been accepted as hybrid surgery. Bavaria et al.[605] classified hybrid surgery into type 1, which performs TEVAR on the aortic arch by bypassing three arch branches from the central side of the ascending aorta, type 2, which performs TEVAR on the aortic arch by reconstructing three arch branches from the prosthetic graft replacing the ascending aorta, and type 3, which performs TEVAR with aortic arch replacement + ET. Type 1 hybrid surgery can be performed without the use of a heart-lung machine; however, it was reported to have an increased risk of cerebral infarction.[759]

e. Surgical Indications and Procedure Selection Considering Risks

Surgical indications and procedure selection for extensive TAA need to be always examined in consideration of the surgical risks and the incidence of complications.

According to the 2014 annual report of the Japanese Association for Thoracic Surgery, the operative mortality rate of extensive TAA varies depending on the surgical range. The in-hospital mortality rate for non-dissecting aortic aneurysms is 3.5%, if the surgical range is limited to the ascending/arch region, whereas it is 10.2% if the surgical range is the aortic arch+descending aorta, indicating that surgical risks increase with wider surgical range. Furthermore, extensive TAA was reported to have high incidences of cerebral infarction and SCI due to intense atherosclerotic lesions and poor vascular conditions.[760] The surgical indications for extensive TAA require careful consideration since they are determined by the balance between the risk of aortic rupture and surgical risks.

1.4.2 Endovascular Treatment

If extensive TAA requires surgical operation on the arch involved in cerebral circulation and on TAAA surrounding the diaphragm, a SG may be used partially or entirely to minimize the invasiveness. In such a case, the prosthetic graft replacement or SG deployment (TEVAR) is identical to the procedure performed individually, and surgical strategy is determined by balancing between acceptable surgical invasiveness and anatomical requirements required for TEVAR.

It is theoretically possible to treat any aorta by TEVAR if a landing zone can be set in the ascending aorta and iliac artery. However, if the diameter of the ascending aortic has enlarged to 40 mm or larger, banding of the aorta or replacement of the ascending aorta is considered. If the enlargement of the ascending aorta is continuous with the enlargement of the arch, ET or open SG is deployed by ascending arch replacement, and it is used as the central landing zone of TEVAR for the descending or thoracoabdominal aorta. In this case, the aneurysm of the ascending aorta or aortic arch itself may not have reached the surgically indicated diameter (55 mm or larger); however, indications need to be determined by considering the balance of different factors, such as performing ascending replacement to avoid arch replacement that requires cerebral protection and performing arch replacement by a median sternotomy in consideration of high invasiveness of arch surgery by left thoracotomy.

When selecting hybrid surgery for extensive TAA, an emphasis is placed on TEVAR for the descending aorta. If it is extended to the thoracoabdominal aorta, complete endovascular treatment may be performed using a branched SG, although its device has not been approved in Japan. TEVAR may be performed in combination with bypass surgery for the abdominal branch.

In addition to cerebral infarction caused by surgical operation for the aortic arch and SCI caused by surgical operation for the thoracoabdominal aorta, various complications related to each surgery are considered, and extensive surgical operation increases their risks as a whole.

2. Abdominal Aortic Aneurysm

2.1 Medical Treatment and Indications for Invasive Treatment (Table 22)

Non-dissecting AAA is, in principle, asymptomatic, and it is often diagnosed incidentally during medical check-ups. Moreover, it may be detected due to an abdominal pulsatile mass. The treatment policy for AAA needs to be determined according to its maximum diameter. Aortic aneurysms tend to continue to enlarge once they occur, and it is important to diagnose/treat asymptomatic patients since more than 80% of ruptured cases cannot be saved even if patients are transported to a hospital by emergency services.[265,266]

Medical treatment for AAA aims to prevent the enlargement/rupture of the aneurysm and reduce the risk of cardiovascular events associated with atherosclerosis. To date, there is no evidence showing that the enlargement of aortic aneurysms is suppressed by drug therapy. On the other hand, smoking is a serious risk factor for the enlargement/rupture of AAA, and guidance for smoking cessation is an important part of its medical treatment. Furthermore, AAA patients are at a high risk of cardiovascular events, and the major cause of late death after open surgery for AAA is heart disease, followed by lung cancer, and pulmonary disease.[768] A survey on the long-term prognosis of open surgery cases of AAA reported that approximately 40% of deaths were related to cardiovascular disease and that 22% were myocardial infarction.[317] A study examined coronary angiography performed before elective open surgery in patients with infrarenal AAA, and more than half were shown to have CAD.[769] A study evaluating the presence of coronary artery ischemia by stress myocardial SPECT reported that 37% of AAA patients had myocardial ischemia and that its occurrence was higher in patients complicated by peripheral artery disease (77%).[770] Based on these, atherosclerotic risk factors in AAA patients must be strictly managed, and it is

Table 22. COR and LOE for the Medical Treatment and Follow-up of Abdominal Aortic Aneurysm

	COR	LOE
It is recommended to give guidance for smoking cessation[271–273,311,761–764]	I	A
It is recommended to follow up aneurysms with a small diameter (<40 mm) using abdominal echography[765]	I	B
It is recommended to perform strict blood pressure management with a target systolic blood pressure below 130/80 mmHg[763,766]	I	C
It is recommended to follow up aneurysms with CT or abdominal echography as follows[765,767]: Every 3–6 months for aneurysms with a maximum minor axis of 50–55 mm Every 6–12 months for aneurysms with a maximum minor axis of 40–50 mm Every 1–2 years for aneurysms with a maximum minor axis of 30–40 mm (See **Table 68**)	I	B
Invasive treatment should be considered if the enlargement rate of the aneurysm diameter is ≥5 mm/6 months at the time of follow-up[765,767]	IIa	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence.

important to screen for atherosclerotic diseases, aiming to reduce the risk of cardiovascular disease, which they are at a high risk of developing.

2.1.1 Blood Pressure Target

There is no blood pressure target for AAA patients that is supported by evidence; however, as in TAA, a blood pressure below 130/80 mmHg is desirable.

2.1.2 Drug Therapy

a. β Blockers

An RCT on propranolol reported that the drug did not decrease the enlargement rate of AAA and decreased the QOL of patients.[290] However, β blockers may be useful in patients with AAA depending on their comorbidities, such as chronic heart failure and CAD, and their use needs to be examined for each case.

b. ACE Inhibitors and ARBs

A large-scale case control study on the general population suggested the benefits of ACE inhibitors in preventing rupture (odds ratio 0.82, 95% CI 0.74–0.90).[771] However, two recently reported studies showed conflicting results. The UK Small Aneurysm Trial indicated that the use of ACE inhibitors was associated with the enlargement of AAA,[772] while the Chichester study suggested that ARBs and aldosterone blockers suppress the enlargement rate.[773] An RCT of AAA patients showed no significant difference between ACE inhibitors and Ca blockers in the effects on the enlargement of arterial aneurysms, indicating no superiority of ACE inhibitors.[774] Based on these, ARBs/ACE inhibitors are not clearly effective in suppressing the enlargement of AAA, and their use needs to be examined for each case based on its comorbidity.

c. Other Antihypertensive Drugs

There is no sufficient evidence showing that the enlargement of aortic aneurysms is suppressed by antihypertensive drugs, such as antihypertensive diuretics, Ca blockers, and mineralocorticoid receptor blockers. A report showed that Ca blockers tended to suppress the enlargement of aortic aneurysms, although the effect was not statistically significant.[305]

d. Statins

No RCT has clearly shown the preventive effect of statins on the enlargement/rupture of AAA, and the association was not observed in retrospective studies.[772,774] However, a recent large-scale meta-analysis suggested that statins may be a factor in suppressing the enlargement/rupture of AAA and reducing the perioperative risk of surgery for AAA, and their effect of suppressing the onset of cardiovascular events in patients with atherosclerosis has also been reported.[766] Thus, their administration to patients with AAA is recommended.

e. Antiplatelet Agents

The administration of antiplatelet agents was reported to improve the 5-year survival rate in AAA patients. Thus, the administration of antiplatelet agents is considered in patients with AAA complicated by atherosclerotic diseases.

2.1.3 Rest Level, Exercise, and Smoking Cessation

Smoking is said to increase the enlargement rate of aortic aneurysms by 20–25%, and conversely, smoking cessation reduces the risk of its enlargement.[271,272,761,762] It has been found that smokers have a higher rate of AAA rupture and a higher rate of mortality from rupture than nonsmokers or ex-smokers.[763,764] A recent meta-analysis using data from 15,475 cases of AAA with a maximum minor axis exceeding 30 mm showed that ongoing smoking was associated with the aneurysm enlargement rate of 0.35 mm/year, which is twice the enlargement rate in ex-smokers or nonsmokers.[311] Similarly, a study on the general population showed that smoking was the most important predictor of the outcome of aortic aneurysms.[273]

The usefulness of dietary intervention and exercise prescription for the enlargement of AAA has not been demonstrated; however, both provide necessary guidance for AAA patients at high risk of atherosclerotic diseases. In a recent trial of 140 patients with AAA with a maximum minor axis of below 55 mm, 3 years of training at the workplace and home led to no difference in the enlargement rate of aortic aneurysms compared to the conventional treatment; however, it resulted in the improvement of the cardiopulmonary function.[775] However, intense isometric training is not recommended.

2.1.4 Determining the Limit of Medical Treatment

The limit of medical treatment may be considered as the time when the rupture of AAA becomes highly probable. Specifically, the following risks are assessed after adequate

Table 23. Estimated Annual Rupture Rate by Abdominal Aortic Aneurysm Diameter

Maximum minor axis (mm)	Rupture rate (%/year)
<40	0
<40–50	0.5–5
<50–60	3–15
<60–70	10–20
<70–80	20–40
≥80	30–50

(Adapted from Brewster DC, et al. 2003[778] with modifications) Copyright (2003) Society for Vascular Surgery and The American Association for Vascular Surgery, with permission from Elsevier. https://www.sciencedirect.com/journal/journal-of-vascular-surgery

antihypertensive treatment, guidance for smoking cessation, and lipid management. Once the indications for invasive treatment intervention shown in the next section are reached, the treatment policy at a medical institution capable of multimodal therapy intervention needs to be considered.

a. Risk Assessment of Abdominal Aortic Aneurysm

Rupture risk of AAA is assessed by the diameter and enlargement rate of the aortic aneurysm, the shape of the aneurysm, and epidemiological factors.

Aortic aneurysms with a larger maximum minor axis have greater wall tension,[761,776] which leads to a greater likelihood of rupture (**Table 23**).[777,778] The enlargement rate of aneurysm diameter affects the risk of rupture, and aortic aneurysms that enlarge significantly faster have a higher risk of rupture. With regard to the shape of aortic aneurysms, the saccular type has a higher risk of rupture than the fusiform type.[779] In addition, aneurysms exhibiting a protrusion are also likely to rupture.[780,781]

Epidemiological surveys conducted in Europe and the United States showed that the incidence of aortic aneurysm rupture was three times higher in women than in men[763,782,783] and that hypertension, smoking, and complication of COPD increased its incidence.[764,784,785] In particular, with regard to smoking, the risk of death from the rupture of an aortic aneurysm increases 6.5 times for tobacco, 6.7 times for cigars, and 25 times for cigarettes.[19] The risk of rupture is higher in patients with a family history of AAA.[786] In these cases, it is reasonable to set the target of invasive treatment intervention to 55 mm or smaller.

b. Risk of Peripheral Arterial Embolism Due to Aortic Aneurysm

It has been reported that 3–29% of patients with AAA are complicated by peripheral arterial embolism;[787–789] however, it is difficult to predict whether AAA is the peripheral embolic source.

2.1.5 Imaging Follow-up

If AAA is detected by screening, death from its rupture can be reduced by treatment at optimal timing.[765,767] Therefore, regular imaging follow-up is important. Abdominal echographic examinations are thought to underestimate the size of aortic aneurysms compared to CT examination; however, a follow-up with echographic examination is recommended if the aortic aneurysm has a small diameter (below 40 mm).[765] If the maximum minor axis of AAA on CT examination taken during its initial diagnosis indicates invasive treatment (55 mm or larger in men and 50 mm or larger in women), invasive treatment is considered after the general condition of the patient is evaluated.

CT re-evaluation (abdominal echography can be used if the aneurysm is smaller than 40 mm) is performed using the following as a guide: every 3–6 months if the aneurysm is 50–55 mm (or detailed examination for surgery is started), every 6–12 months if it is 40–50 mm, and every 1–2 years if it is 30–40 mm. If the aneurysm enlarges by 5 mm or larger in 6 months, invasive treatment is considered after the general condition of the patient is evaluated. Moreover, follow-up at shorter intervals is considered for women smokers. Imaging follow-up after invasive treatment for AAA is discussed in the section of surveillance (See "**2. Surveillance**" in **Chapter X**).

2.1.6 Indications for Invasive Treatment

A maximum minor axis of 55 mm or larger in men and 50 mm or larger in women are recommended as indications of AAA for invasive treatment. However, invasive treatment may also be considered for AAA with a maximum minor axis of below 40–50 mm, depending on age, physical constitution, and gender of the patient, as well as morphology/shape and enlargement rate of the aortic aneurysm.

PQ 8.

What Size of Abdominal Aortic Aneurysm (Millimeters in Diameter) Is Indicated for Invasive Treatment?

Recommendation

An aneurysm diameter (maximum minor axis) of ≥55 mm is an absolute indication for invasive treatment, and an aneurysm diameter of ≥50 mm is also acceptable as an indication. Moreover, women are at a high risk of rupture, and invasive treatment is considered if the diameter of their aneurysm is ≥45 mm.

Invasive treatment of asymptomatic AAA aims to prevent its rupture. On the other hand, symptomatic AAA indicates that the aneurysm has ruptured or its rupture is impending, and its invasive treatment aims to save the lives of the patients. In addition, saccular-type aneurysms are often judged to have a high risk of rupture due to their shape. Therefore, aneurysm diameter is not an indication criterion for invasive treatment of symptomatic and saccular-type AAA, and the invasive treatment indications for "asymptomatic fusiform AAA," which accounts for the majority of AAA, are discussed in this PQ.

Two studies focusing on AAA with a diameter of 40–55 mm, the UK Small Aneurysm Trial[790] and American Aneurysm Detection and Management,[791] showed that whether prosthetic graft replacement is performed before or after aneurysm diameter reaches 55 mm had no impact on life prognosis after open surgery. Similarly, two studies, the Comparison of Surveillance vs. Aortic Endografting for Small Aneurysm Repair (CAESAR)[792] and the Positive Impact of Endovascular Options for Treating Aneurysm Early (PIVOTAL) Study,[793] showed that it had no impact on life prognosis after EVAR, which is another pivotal treatment. Based on these results, invasive treatment (open surgery and EVAR) for AAA with an aneurysm diameter of ≥55 mm was classified as the class of recommendation 1

and the level of evidence A in the guidelines in Europe and the United States. Therefore, an aneurysm diameter of ≥55 mm is also used as an absolute indication for invasive treatment in Japan.

On the other hand, elective surgery in Japan has shown highly favorable results, and its operative mortality rates in the report from the Japanese Society for Vascular Surgery were 1.0% for open surgery and 0.7% for EVAR,[794] which are more favorable than those in Europe and the United States mentioned above. Therefore, many facilities in Japan have used an aneurysm diameter of ≥50 mm as an indication for invasive treatment, and it has also been acceptable. In addition, the risk of rupture is said to be four times higher in women than in men,[311,763,795] and a meta-analysis showed that the risk of rupture in women with an aneurysm diameter of 45 mm was comparable to the risk of rupture in men with an aneurysm diameter of 55 mm.[795] Thus, considering the favorable surgical results in Japan, an aneurysm diameter of greater than 45 mm may be used as a relative indication in women with smaller physical constitution than men. However, RCTs like the four studies above have not been conducted in Japan, and the level of recommendation for the current indication in Japan is not necessarily high.

2.2 Unruptured Abdominal Aortic Aneurysm

2.2.1 Surgical Indications (Table 24)

Treatment of AAA and iliac artery aneurysm includes open surgery (prosthetic graft replacement) and SG deployment (EVAR); however, there is no difference in their indications.

a. Abdominal Aortic Aneurysm

In the guidelines in Europe and the United States, AAA with a diameter of 55 mm or larger is indicated for invasive treatment. However, many facilities in Japan use a diameter of 50 mm or larger as an indication because of its favorable surgical results. Four RCTs (two by open surgery[790,791] and two by EVAR[797,798]) have been conducted to determine treatment policy for arterial aneurysms with a diameter of smaller than 55 mm. However, they showed no difference between the follow-up group and the early-treatment group in the long-term survival rate, and follow-up is recommended from the viewpoint of cost. Many arterial aneurysms were found to enlarge over time,[796] and the treatment of an aneurysm is determined when its diameter reaches the treatment indication during follow-up. In addition, even with the same aneurysm diameter, the rupture rate in women is four times that in men,[795] and it is reasonable to set the aneurysm diameter for surgical indication in women smaller than that in men. Aneurysms with a maximum minor axis of below 40 mm are not indicated for surgery due to their low risk. However, surgery needs to be considered for saccular-type aneurysms and aneurysms with protrusion regardless of their diameter due to their high risk of rupture. The enlargement rate differs depending on the aneurysm diameter (**Table 23**). Many consider that surgery is performed for aneurysms with an enlargement rate of 5 mm/6 months or more, although it has not been investigated in RCT.[799,800] In any case, symptomatic AAAs have a risk of rupture and indicate surgery.[801–803]

In addition, many AAAs that are an embolic source to the periphery have a small diameter.[788,804] Invasive treatment is considered if embolism is frequently observed. Because infected AAA has a high probability of rupture, open surgery is mainly performed regardless of the diameter of the aneurysm.[805,806] Coagulation disorder related to AAA may be indicated for invasive treatment.[83,806]

Table 24. COR and LOE for Indications for the Invasive Treatment of Unruptured Abdominal Aortic Aneurysm

	COR	LOE
It is recommended to perform invasive treatment if the aneurysm diameter is ≥55 mm[790,791,796–798]	I	A
It is recommended to perform invasive treatment promptly for symptomatic patients	I	C
Invasive treatment should be considered if the aneurysm diameter is ≥50 mm	IIa	C
Invasive treatment should be considered for saccular type aneurysms or aneurysms that show a rapid enlargement (≥5 mm/6 months)	IIa	C

COR, class of recommendation; LOE, level of evidence.

b. Iliac Artery Aneurysm

Historically, several aneurysms with a diameter of 30 mm or larger have been indicated for treatment; however, there were no guidelines. The 2019 ESVS guidelines[321] set the criterion of "treatment may be considered for aneurysms with a diameter of 3.5 cm or larger" for the first time; however, its solid evidence has been scarce. The ESVS guidelines also mentioned that follow-up up to 40 mm is recommended in men with advanced age based on the results of recent retrospective multicenter studies.[807]

2.2.2 Preoperative Evaluation (Table 25)

a. Evaluation of Aortic Aneurysm and Complicating Arterial Aneurysm at Other Sites

Although 95% of AAAs occur below the renal artery bifurcation,[83,808] the aneurysms forming immediately below the renal artery require aortic cross-clamping at the upper part of the renal artery bifurcation. In addition, TAA, which complicates 12% of the cases,[808] the presence of the inferior branch of the renal artery, internal iliac artery aneurysm, which complicates approximately 1/4 of the cases, and peripheral arterial aneurysm, which complicates 3.5% of the cases (femoral artery, popliteal artery),[809,810] are examined by imaging examinations.

b. Evaluation of Surgical Risks

Factors affecting the operative mortality rate of AAA include cardiac function, pulmonary function, renal function, and age of patients, as well as the positional relationship between the renal artery and an aneurysm, the presence or absence of internal iliac artery aneurysm complications, the degree of aortic wall calcification, inflammatory arterial aneurysms, and experience of operator.[810–814] Elective surgery for AAA in specialized facilities that have performed many surgeries has shown favorable results. Its operative mortality rate was reported to be 1–5%, and many have reported that the rate in Japan is 1% or lower. If it is not limited to specialized facilities, the operative mortality rate is high at 4–8%.[812–816] Therefore, the ESVS guidelines recommend its surgical treatment in

Table 25. COR and LOE for the Preoperative Evaluation of Unruptured Abdominal Aortic Aneurysm

	COR	LOE
It is recommended to perform preoperative detailed examination/treatment intervention by cardiologists for patients with low exercise tolerance (below 4 METs) or significant cardiovascular diseases (such as unstable angina, decompensated heart failure, severe valvular disease, and arrhythmia)[322,323]	I	C

COR, class of recommendation; LOE, level of evidence.

Table 26. COR and LOE for Open Surgical Procedure for Unruptured Abdominal Aortic Aneurysm

	COR	LOE
It is recommended to preserve at least one side of the internal iliac artery blood flow[824–826]	I	C
Reconstruction of the inferior mesenteric artery should be considered for patients with a stenosing lesion in the celiac or superior mesenteric artery, dilated collateral flow from the inferior mesenteric artery, a history of colectomy, or the internal iliac artery that cannot be preserved[315,320–323,817]	IIa	C

COR, class of recommendation; LOE, level of evidence.

facilities with 30 or more cases per year.[321,816]

c. Evaluation of CAD

Open surgery for AAA is classified as a high-risk surgery in the ACC/AHA[322] and ECS guidelines;[321,323] however, preoperative invasive detailed examinations, such as coronary angiography, are not recommended for any cases. The clinical severity of patients with stable cardiovascular disease is classified into the low-risk group, intermediate-risk group, and high-risk group by scoring preoperative cardiovascular risk.[315,320,322,323,817] Additional detailed examinations are not essential in the low-risk group. On the other hand, patients with low exercise tolerance (below 4 METs) or patients with symptomatic cardiovascular diseases (such as unstable angina, decompensated heart failure, severe valvular disease, and arrhythmia) require preoperative detailed examination and treatment.

It has been reported that the preoperative initiation of statin administration suppresses the occurrence of cardiovascular events after vascular surgery, and additional administration of statins is recommended.[315,321,818,819] On the other hand, multiple RCTs showed that the new administration of β blockers before surgery worsened cerebrovascular diseases and mortality rate, denying its usefulness.[820–823] If the preoperative administration of β blockers is started to control heart disease, there should be sufficient time before surgery.

Whether to perform preoperative coronary revascularization in patients with coronary artery stenosis is controversial. Preoperative preventive coronary revascularization is not always recommended in patients with stable cardiac symptoms. On the other hand, it was reported that preoperative coronary artery revascularization did not reduce perioperative acute myocardial infarction and long-term mortality in patients with stable coronary artery lesions without the complication of at least 50% degree of stenosis lesion in the left main trunk, left ventricular failure with LVEF of 20% or lower, or severe aortic valve stenosis.[326,823] However, both of these were reported overseas 15 years ago, and there have been slight changes in the situation since then. There has been marked progress in coronary artery catheterization (percutaneous coronary intervention, PCI) and coronary artery bypass surgery under non-extracorporeal circulation (off-pump coronary artery bypass, OPCAB), which are actively performed in Japan, and not only surgery but also EVAR can now be selected for the treatment of AAA. With sufficient consideration of these, the optimal treatment should be selected for each case and for each facility.

2.2.3 Open Surgical Procedure (Table 26)

a. Approach

There are two methods to reach AAA: transperitoneal and retroperitoneal routes. The transperitoneal route can quickly obtain a wide field of view and search for intraperitoneal organs, but it tends to result in the slow recovery of postoperative intestinal motility. The retroperitoneal route enables the operation of displacing the left kidney to the right, and it is considered to be an effective approach in patients with "hostile abdomen" with a history of laparotomy, peritonitis, or radiation exposure of abdominal organs, and patients with a pararenal artery aneurysm or inflammatory arterial aneurysm who require clamping of the upper aorta of the renal artery bifurcation.[315] EVAR has been performed in recent years, which has led to changes in the target of open surgery. Thus, open surgery is now more commonly performed on aneurysm patients who are not anatomically suitable for EVAR, and it is important to select a suitable approach for each case.

b. Aortic Cross-Clamping

The condition of calcification of the wall and atheroma of the aortic cross-clamping site must be evaluated by CT preoperatively. Clamping of the suprarenal aorta, including the upper CA, is required if clamping at the infrarenal aorta is not possible. Suprarenal aortic cross-clamping may reduce the renal function of the patient and increase complications; however, it has also been reported that its operative mortality rate is comparable to that of infrarenal aortic cross-clamping in specialized facilities with a large number of cases.[326,827–829]

c. Selection of Prosthetic Graft

The difference in complications does not depend on the type of prosthetic graft, and it may be selected by the operator's preference. The selection between the straight graft and branched graft is determined by the dilatation of the iliac artery. In addition, rifampicin immersion is used after infected AAA or prosthetic graft infection is detected, with the expectation of its preventive effect on prosthetic graft infection; however, it has not been clearly supported by evidence.[828,830]

d. Maintenance of Pelvic Blood Flow

Surgery of AAA may obstruct blood flow in the inferior mesenteric and internal iliac arteries, resulting in ischemic colitis, buttock claudication, sexual dysfunction, and SCI; nevertheless, their occurrence is influenced by multiple factors.

Table 27. COR and LOE for EVAR for Unruptured Abdominal Aortic Aneurysms

	COR	LOE
It is recommended to perform EVAR with backup by a surgical team[841,842]	I	C
It is recommended to perform life-time follow-up after treatment[317,431,432,768,843,844]	I	A
It is recommended to perform EVAR in patients who fulfill the anatomical requirements and conditions for the proximal landing zone[423,425,426,845–854]	I	A
EVAR should be considered for patients who fulfill the anatomical requirements and have a high risk for open surgery[317,423,425,426,428,431,432,437,768,843,844,854–858] (See **Table 10**)	IIa	A
Simultaneous implementation of coil embolization of the inferior mesenteric artery should be considered at the time of EVAR[859]	IIa	B
Preservation of antegrade blood flow of at least one internal iliac artery should be considered at the time of EVAR[315,461]	IIa	B
EVAR may be considered for patients who fail to fulfill the anatomical requirements other than those for the proximal landing zone[845–853]	IIb	B
EVAR may be considered for pararenal abdominal aortic aneurysms[860,861]	IIb	C

COR, class of recommendation; LOE, level of evidence; EVAR, endovascular aortic repair.

The preventive effect of reconstruction of the inferior mesenteric artery on ischemic colitis remains controversial;[830–834] however, an RCT concluded that it has no preventive effect.[834,835] Reconstruction of the inferior mesenteric artery needs to be considered to prevent ischemic colitis if a stenotic lesion is found in the CA or superior mesenteric artery, if the dilated collateral flow from the inferior mesenteric artery is found, if the patient has a history of colectomy, or if the internal iliac artery cannot be preserved.[315,320–323,817]

Traditionally, it was thought at least one side of the internal iliac artery should be reconstructed to prevent ischemic colitis, buttock claudication, sexual dysfunction, and SCI. It has been reported that colon ischemia occurs in 0.3% of cases when either side of the internal iliac artery is reconstructed and in 2.6% of cases when bilateral reconstruction is not performed.[824–826,835,836] In 48 cases of bilateral internal iliac artery non-reconstruction (32 cases of EVAR and 16 cases of open surgery), buttock claudication and erectile dysfunction were reported to occur in 42% and 14%, respectively, although no severe complications were found.[824,836] It is desirable to ensure blood flow in the internal iliac artery on at least one side, even though it has not been clearly supported by evidence.[824–826]

e. Long-Term Results

As described below ("**2.2.4.b Results of Randomized Controlled Trials**" in the next section), multiple RCTs have reported the long-term total survival rate, aneurysm-related mortality rate, and retreatment rate of patients who are anatomically indicated for both open surgery and EVAR.

The reports from the Vascular Study Group of New England registry are the latest and largest for cases that require clamping of the suprarenal aorta, which are not indicated for normal EVAR. The mortality rate within 30 days after surgery was significantly higher in cases that required suprarenal clamping (443 cases) than in cases of infrarenal clamping (1,432 cases) (3.6% vs. 1.2%, P=0.002); however, there was no difference in the long-term prognosis between the two (postoperative 5-year survival rate of 71%).[837]

It has been reported that the incidence of incisional hernia in the abdominal wound after open surgery for AAA is higher than that after open surgery for other diseases. Although it is thought to be associated with the fragility of connective tissue, it remains unclear.[838] Moreover, its incidence is higher in the transperitoneal route than in the retroperitoneal route, and long-term incisional hernia is found in approximately 10% of cases.[839]

Other long-term complications include the pseudo arterial aneurysm at the anastomotic site. Edwards et al. reported that only 1% of cases had a pseudoaneurysm of the central anastomotic site 8 years after surgery. However, it was observed in 20% of cases 15 years after surgery, and the average period until detection was 12 years.[840]

2.2.4 Endovascular Treatment (Table 27)

EVAR was first reported in 1991 by Parodi and attracted global attention.[862] In Japan, coverage of company-made SG by health insurance was also approved in 2006, and the technique has rapidly become accepted. Recently, it is important to appropriately select its indications with understanding of its advantages and disadvantages.

a. Indications and Devices

The indications are the same as those for open surgery (See "**2.2.1 Surgical Indications**" in this chapter).

i. Stent Graft

At present, 5 kinds of abdominal SGs are available for use in Japan. Because of differences in the anatomical requirements among the SGs, IFU (instructions for use) of each SG should be referred to. In performing EVAR, contrast-enhanced CT is performed first, and whether the lesion is anatomically appropriate for EVAR is evaluated. Although deviation from IFU on the physician's discretion is possible, it should be remembered that it may exacerbate both the short-term and long-term results.[845–852] Particularly, as the indication concerning the proximal landing zone strongly affects the results in the remote period, it should be observed.[849,850,853]

ii. EVAS

Recently, the concept of EVAS (endovascular aneurysm sealing) has been proposed as an alternative for EVAR. It is a method to prevent surgical complications, such as endoleak and migration, by completely sealing the interior of the aneurysm by inflating a polyurethane bag filled with

polymer around a balloon expandable stent covered by PTFE (polytetrafluoroethylene).[863] According to an early Western report, endoleak, migration, and enlargement of the aneurysm occurred more frequently than expected, and the ESVS guidelines also recommend it to be used only in clinical studies approved by the institutional review board until it is appropriately evaluated.[321] Recently, a new device resembling EVAS in which polymer is filled in the proximal neck was also approved in Japan.

b. Results of Randomized Controlled Trials

The usefulness and safety of EVAR were first suggested by the EUROSTAR registry in 2002.[864] Thereafter, RCTs about EVAR and open surgery were conducted in patients who fulfilled the anatomical requirements and were in good general health condition as the EVAR,[425] DREAM,[426] OVER,[854] and ACE trials,[423] and long-term, as well as initial results, have been presented.

i. Short-Term Results

EVAR 1 was the first RCT that compared EVAR and open surgery performed in patients with AAA ≥55 mm in maximum minor-axis diameter who were aged 60 years and above and in good general condition and had anatomical indications for both EVAR and open surgery. The 30-day mortality (1.7% by EVAR, 4.7% by open surgery) and aneurysm-related mortality (3.5% by EVAR, 6.3% by open surgery) were both lower after EVAR, and no significant difference was observed in the overall mortality or aneurysm-related mortality after 6 months between the two groups.[425]

In DREAM, which was conducted under nearly the same conditions, also, the 30-day mortality (1.2% by EVAR, 4.6% by open surgery) and aneurysm-related mortality (4.7% by EVAR, 9.8% by open surgery) were better after EVAR. The two-year survival rate was 89.7% by EVAR and 89.6% by open surgery with no significant difference, but the aneurysm-related mortality was 2.1% by EVAR and 5.7% by open surgery, being significantly lower by EVAR.[426]

In the OVER trial, the 30-day mortality was 0.5% by EVAR and 3% by open surgery and was significantly lower by EVAR,[428,854] and the 2-year overall mortality also tended to be lower by EVAR.

ii. Intermediate-Term/Long-Term Results

In EVAR 1, the aneurysm-related mortality until after 4 years was significantly lower by EVAR than by open surgery but reversed and became significantly higher by EVAR after 8 years. The primary cause of death was rupture of aneurysm. The re-treatment rate was significantly higher after EVAR, and the overall long-term mortality was inferior by EVAR.[317]

In DREAM, the aneurysm-related mortality after 6 years was 68.9% by EVAR and 69.9% by open surgery, and that after 12 years was 38.5% by EVAR and 42.2% by open surgery, and no difference was observed at either point.[431] The re-treatment avoidance rate after 6 year was 70.4% by EVAR and 81.9% by open surgery, and after 12 years was 62.2% by EVAR and 78.9% by open surgery, being significantly better by open surgery.[431]

In OVER, the aneurysm-related mortality after 9 years was significantly higher by EVAR, but the re-treatment rate did not differ significantly.[768] No significant difference was observed in the survival rate, QOL, medical cost, or cost-benefit performance between the two procedures.[844]

In ACE, the survival rate showed no significant difference between open surgery and EVAR during a mean follow-up period of 3 years (82.4% by EVAR, 85.1% by open surgery). The re-treatment rate was significantly higher after EVAR (16% after EVAR, 2.4% after open surgery), and the aneurysm-related mortality tended to be higher after EVAR (4% after EVAR, 0.7% after open surgery).[423]

According to meta-analysis of the above 4 RCTs,[432] the 30-day mortality was lower by EVAR, and the overall mortality was also lower during 0–6 months but did not differ significantly during the subsequent follow-up period. The aneurysm-related mortality showed no difference between EVAR and open surgery from 30 days to 3 years after surgery but was higher in the EVAR group after 3 years. The re-treatment rate was higher in the EVAR group, but the difference between the two groups was not clear when complications associated with laparotomy, such as abdominal wall incisional hernia and ileus, are taken into consideration as in OVER.[428] However, as many of the SGs used were those of the first or second generation, caution is needed in interpreting the above result, and it is also necessary to include the results obtained by the use of new-generation SGs in the evaluation. However, considering the report that the incidence of complications increases 8–10 years after EVAR, leading to loss of its superiority,[856] it is reasonable to recommend open surgery for young patients expected to have long-term survival.

EVAR 2 was an RCT conducted to compare EVAR and observation in frail AAA patients with no indication for open surgery (those with symptomatic heart failure, valvular disease, COPD, or chronic renal failure as a complication).[857] The perioperative mortality (7.3%) and overall mortality (64%) after EVAR were higher than expected. During a 4-year follow-up period, EVAR was not superior in aneurysm-related mortality or overall mortality,[437] but the aneurysm-related mortality was significantly lower in the EVAR group than in the observation group after 15-year follow-up.[858]

c. The Status Quo and Results in Japan

In Japan, SGs self-made at each facility were initially used, but company-made SGs were first approved to be covered by health insurance in 2006, and the number of patients who undergo EVAR has since increased continuously. According to the survey by the Japanese Society for Vascular Surgery, EVAR accounted for only about 2.7% of all surgical procedures in 2006, but the percentage of procedures including hybrid surgery increased to 55.7% in 2014, and SG is used in a majority of operations.[515,865]

In Japan, a follow-up survey using web was made obligatory after the approval of company-made SGs. In December 2006, 11 (currently 10) related academic societies founded the JACSM for safe propagation of EVAR and established the Standards for Implementation of Abdominal Stentgrafting consisting of standards concerning the facility, physician, and instructor (http://stentgraft.jp). Since 2016, a registry in conjunction with NCD (National Clinical Database, http://www.ncd.or.jp/) has been in operation. According to the follow-up survey of 38,003 cases of EVAR registered during the 10 years from 2006 to 2015,[440] the surgical mortality was 0.08%, and the hospital mortality was 1.07%. Among the adverse events, renal dysfunction (2.6%) was the most frequent, and the incidences of endoleak were 6.7% for type I, 16.6% for type II, 0.6% for type III, and 0.6% for type IV. The overall survival rate was 93.5% after 6 months, 88.3% after 1 year, 76.2% after 3 years, 63.7% after 5 years, and 38.8% after 8 years. Also,

EVAR was performed not in compliance with IFU (instructions for use) in 47.6% of the cases, and poor access and marked calcification of the landing zone were strong risk factors for death, re-intervention, and adverse events.

d. Actual Procedure of EVAR

i. Preoperative Evaluation

Since EVAR does not require aortic clamping nor markedly affectc the hemodynamics,[841] the ACC/AHA and ESC/ESA guidelines rates its risk level at low-moderate.[12,866] Detailed examination of the heart is unnecessary if the patient has a physical activity level of ≥4METs and is asymptomatic, but individualized preoperative examinations and perioperative management are recommended if the patient has multiple risk factors such as coronary artery disease, congestive heart failure, diabetes mellitus, renal failure, and cerebrovascular disorder.[866] Contrast-enhanced CT is performed to make judgments about indications for EVAR, and as preoperative planning using CT scans from the carotid artery to the femoral artery is important, it is necessary to check the anatomy including the access route.[867] Usually, the aorta is approached via the femoral artery, but if there is concern over the femoral route due to thrombosis or severe calcification, the iliac artery or other vessels may be selected as an alternative access route.

ii. Preparations and Setting

EVAR is performed in an operation room with a radiographic system capable of digital subtraction angiography (DSA) or an angiography room with a high level of cleanness permitting general anesthesia. Since necessary items vary with the type of the stent graft (SG), the surgeon should be well informed of the IFU of each SG. As the number of surgeons and the size of the facility affects the surgical results,[841,842] the SVS guidelines recommend that EVAR be performed at facilities with the hospital mortality or open conversion rate of ≤2% and 10 or more cases annually.[315]

iii. Anesthesia

EVAR can be performed by any of general anesthesia, epidural anesthesia, and local anesthesia, but the EUROSTAR registry suggests that invasion is milder as anesthesia is lighter,[868] and the operation time, duration of stay in the ICU, and duration of hospitalization were shorter, and the incidence of postoperative complications was lower, by local anesthesia than by general anesthesia. The findings of the ENGAGE registry were similar to those of the EUROSTAR registry, but epidural or local anesthesia is not recommended as the first choice, because there was no difference in the perioperative mortality.

iv. Surgical Techniques

Usually, the femoral artery is surgically exposed to insert the SG, but percutaneous insertion has begun to be selected in the trend for low-profile surgery. The percutaneous approach has been reported to have benefits, such as a shorter operation time and fewer wound complications, compared with the surgical approach.[869] Since the placement method varies with the SG, the characteristics of each SG must be understood. After deployment of the SG, it is affixed using a balloon. Its placement in the optimal position and the absence of endoleak should be confirmed by angiography (**Figure 56**). By the SVS reporting standards, the "initial success" is defined as "placement in the optimal position and the absence of surgical death or open conversion, limb occlusion, and type I/III endoleak".[340]

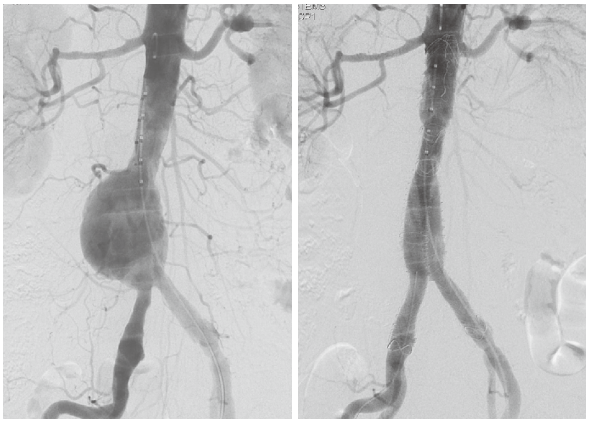


Figure 56. EVAR of abdominal aortic aneurysm.

v. Intraoperative Treatments

The SVS guidelines mention that preoperative therapeutic intervention for renal artery or superior mesenteric artery stenosis is permitted in consideration of the severity and postoperative complications if it is symptomatic but do not recommend it if it is asymptomatic.[315]

e. Complications Specific to EVAR

Since the incidence of remote-period complications and re-intervention rate are higher after EVAR than after open surgery,[435] careful follow-up is necessary. Endoleak is a complication commonly observed in the remote period.

i. Endoleak

Endoleak (See **Figure 52**) is leakage of blood in aortic aneurysms after SG placement,[340] and it may occur immediately after the procedure or with a delay. It is classified into types I–V according to the cause. About half of the endoleaks (primarily type II) are resolved spontaneously,[854] anticoagulant therapy may increase the risk of postoperative endoleak.[870] The risk of rupture of aneurysms due to endoleak is considered to be related to the intra-aneurysmal pressure, and the treatment varies with the type of endoleak.[871,872]

Type I: Leak of blood into aneurysms through a gap in the vascular wall between SG and the landing zone. It is classified into proximal (Ia) and distal (Ib) endoleaks and endoleaks that occur in iliac plug of the aorto-uniiliac SG (Ic). Since high-pressure blood flow enters the aneurysm, rupture is likely to occur,[873] and prompt treatment is necessary. Type I endoleak is treated by either adding SGs and extending the landing zone[874,875] or, if there is no landing zone that can be extended, additional balloon affixation or bare metal stent placement.[875–877] On the proximal side, extension of the landing zone by the snorkel/chimney technique may be effective,[878] but, if it is ineffective, open conversion should be considered.

Type II: Retrograde blood flow from branches (collaterals), which are primarily the lumbar and inferior mesenteric arteries. The ESVS guidelines classify it into the type caused by blood flow from the inferior mesenteric artery (IIa) and the type caused by blood flow from the lumbar artery (IIb).[321] Type II endoleak often disappears spontaneously, and the risk of rupture is low (<1%).[854,879] Type II endoleak

appears in 18% of the patients, persists in 5%, and newly appears during the course in 11%.[879] Predictive factors include age, sex, device, presence or absence of coil embolization of the internal iliac artery, distal extension, intra-aneurysmal thrombus, and anatomical factors such as the number and diameter of the lumbar/inferior mesenteric arteries.[879–882] Indications for treatment have not been established,[472] but embolization is performed by transarterial or direct puncture.[883] Embolization is made using materials, such as NBCA (n-butyl-2-cyanoacrylate) and coils, and its success rate is high using either material, but evidence concerning the timing of intervention or therapeutic effects is scarce.[883–885] Recently, type II endoleak has been reported to be reduced by simultaneous embolization of the inferior mesenteric artery in EVAR.[859]

Type III: Leak of blood through the junction between SGs (IIIa) or due to breakdown of the fabric (IIIb). Similarly to type I, prompt treatment is necessary, but management by SG relining is possible.

Type IV: Leak from SG itself defined as "leak within 30 days after EVAR".[886] It is mostly thrombosed, and retreatment is usually unnecessary.

Type V (endotension): Enlargement of the aneurysm without clear endoleak detected by imaging examinations. Various mechanisms for its occurrence, such as increased graft permeability and direct transmission of pressure through the graft, have been proposed.[887]

ii. Stent Graft Occlusion

Stent graft occlusion is reported to occur at a probability of 1.4–8%,[888–895] and its risk factors include tortuousness and calcification of the iliac artery and oversizing of ≥15%,[888,890,896] but the external iliac artery landing is reported to be the greatest risk factor.[430,888,893]

iii. Enlargement of the Aortic Diameter in the Landing Zone

Enlargement of the aortic diameter in the landing zone is reported to occur at a frequency of 24.6%.[343] Enlargement of the aortic diameter in the proximal landing zone is closely related to SG migration and type I endoleak.[343]

iv. Device Migration

Device migration is defined as "movement of ≥10 mm from the initial position of fixation".[897] A large aneurysm diameter, short landing zone, sharp curving of the landing zone, and SG size have been suggested as risk factors for proximal migration.[884,898,899] Oversizing (>30%), a short landing zone (<20 mm), and the use of a flair rim are risk factors for distal migration.[900–903]

v. Open Conversion

There are acute and late open conversions. Acute open conversion may be caused by access problems, rupture due to a balloon, SG migration, renal artery occlusion, SG thrombosis, and unsuccessful SG placement and was observed in 16% of the patients early after the introduction of EVAR.[904] It decreased markedly due to subsequent improvements in the device, and its incidence was 2.5% in the EVAR 1 trial and 1.8% in the DREAM trial. Late open conversion is often caused by endoleak. Many endoleaks can be managed by endovascular treatment, but open conversion is indicated if the aneurysm continues to enlarge. Initially, SG was completely removed, but the results of this treatment were poor. Recently, the results have been improved[890,894,895] by partial removal of SG.[905,906] Presently, removal of the entire SG is considered unnecessary, and the basic approach is to treat only troubled parts.

vi. Sent Graft Infection

Stent graft infection occurs in 0.6% of the patients[907] and often causes back pain and fever.[908] The diagnosis is made by CT, Ga scintigraphy, or off-label use of FDG-PET.[909] Total extraction of SG is necessary for elimination of the infection focus, and reconstruction is often made by omentum wrapping in addition to anatomical prosthetic graft replacement or non-anatomical synthetic graft bypass,[910] but the hospital mortality remains high.[907] Rifanpicin-bonded synthetic grafts and homografts may be used.[911]

Secondary aortoenteric fistula causes hematemesis or

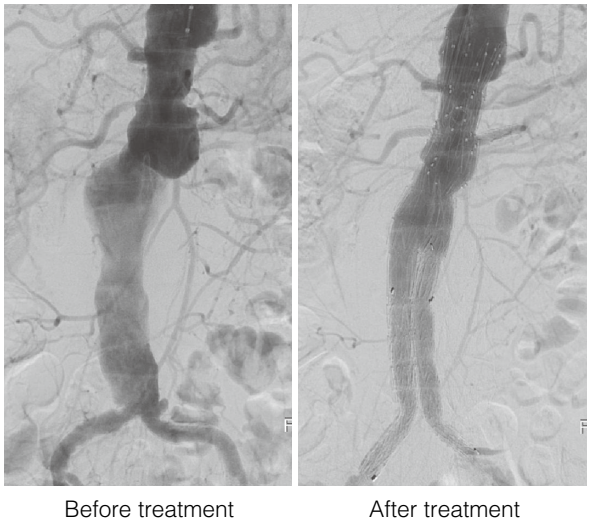


Figure 57. Fenestrated EVAR for pararenal abdominal aortic aneurysm. The celiac artery is preserved, and the superior mesenteric artery and bilateral renal arteries are reconstructed using covered stents.

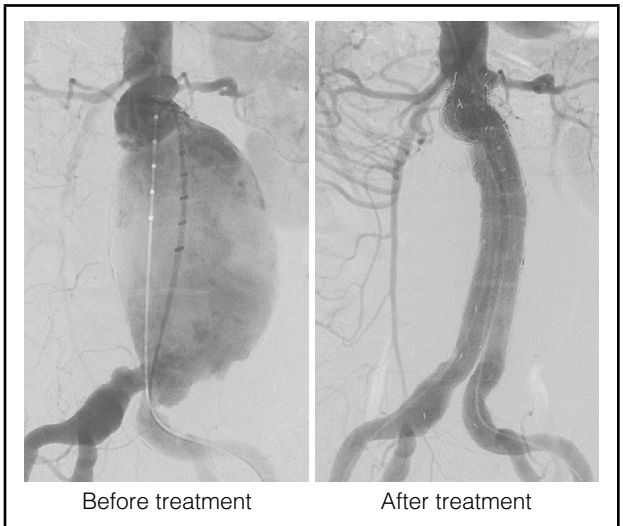


Figure 58. Double snorkel EVAR for pararenal abdominal aortic aneurysm. Reconstruction of the bilateral renal arteries using custom-made stent grafts and bare metal stents.

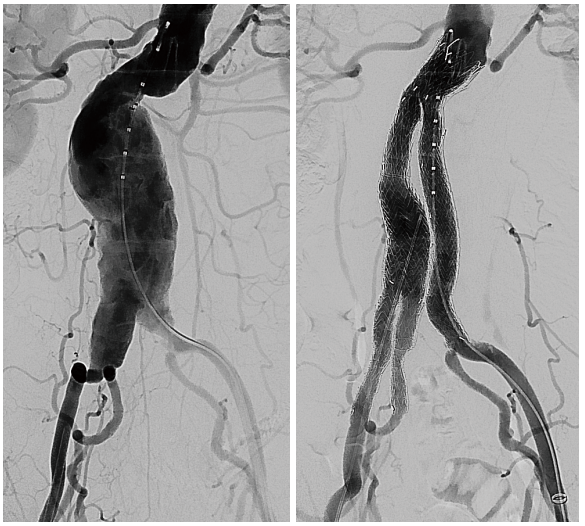


Figure 59. Internal iliac artery preserving device for abdominal aortic aneurysm. Reconstruction of the right internal iliac artery using a company-made internal iliac branch device.

melena. The duodenum is the most frequent site of aortoenteric fistula, accounting for about 80% of all aortoenteric fistulas.[912] For the treatment, complete removal of SG and resection and reconstruction of the digestive tract with fistula (See **Chapter VIII**, "**8.1.4 Treatment**").

f. Postoperative Follow-up

Specific complications and late rupture have been reported as mentioned above, and lifetime follow-up is necessary. The JACSM recommends follow-up imaging examinations shortly after surgery (at discharge), 1 month, (3 months if endoleak is noted after 1 month), 6 months, and 1 year after surgery, and once every year thereafter.

g. Pararenal Abdominal Aortic Aneurysm

Pararenal AAA includes suprarenal and juxtarenal AAA. Aneurysms that involve the superior mesenteric artery are suprarenal AAA, and those that involve celiac artery are distinguished as TAAA (Crawford type IV). It is not an indication for usual EVAR from the anatomical viewpoint. If EVAR is performed, branched EVAR using branched or fenestrated SG (**Figure 57**) or snorkel/chimney EVAR (**Figure 58**) is selected. Branched EVAR can be performed only at limited facilities, and, according to a report that compared branched EVAR and open surgery, the perioperative mortality was comparable by both procedures at 4.1%.[860] Snorkel/chimney EVAR is the procedure of parallel positioning stents or SGs inserted in the main body and an abdominal branch. While it can be accomplished using conventional devices, gutter leak may occur. According to the PERICLES registry, the perioperative mortality was 3.7%.[861] Neither procedure is covered by health insurance in Japan.

h. Iliac Artery Aneurysm

Many iliac artery aneurysms complicate AAA, and solitary iliac artery aneurysms are rare. Although there are no established findings concerning treatment indications, the ESVS guidelines recommend an aneurysm diameter of ≥35 mm as an indication.[321,807,913,914] Recently, favorable results of EVAR for iliac artery aneurysms have been reported.[915,916] EVAR involves embolization of the internal iliac artery, but only the limb is embolized if an appropriate landing zone can be secured, and embolization of the main body is added if not.[917] Embolization of the internal iliac artery causes buttock claudication in 28% of the patients, but it is alleviated in most patients during follow-up.[918] The incidence of buttock claudication is higher after bilateral (38.3%) than unilateral (26.7%) embolization. Impotence was observed in 10% after unilateral embolization and 16% after bilateral embolization with no significant difference, and the incidence of ischemic colitis was also low.[460,918] In addition, as the internal iliac artery serves as a collateral for spinal cord blood flow, attention to the occurrence of paraplegia by subsequent aortic surgery is necessary in patients after embolization of the bilateral internal iliac arteries.[919] The SVS guidelines recommend preservation of at least one internal iliac artery by either EVAR or open surgery.[12,461] Recently, a device that permits preservation of the internal iliac artery (iliac branch device, IBE) has been developed (**Figure 59**), and decreases in buttock claudication have been reported.[920,921] IBE also began to be covered by health insurance in 2016 in Japan.

Table 28. COR and LOE for Treatment of Abdominal Aortic Aneurysm Rupture

	COR	LOE
It is recommended to perform EVAR as the first treatment choice if the anatomical requirements are met[321,922–925]	I	B
It is recommended to measure intravesical pressure after invasive treatment and to perform decompression surgery promptly if abdominal compartment syndrome has occurred[321,922,926–928]	I	B
It is recommended to assess and manage cardiovascular risk after invasive treatment[321,856,929]	I	B
Aortic occlusion balloon should be considered promptly without delay if the circulatory dynamics of the patient is unstable during invasive treatment[321,930]	IIa	B

COR, class of recommendation; LOE, level of evidence; EVAR, endovascular aortic repair.

2.3 Ruptured Abdominal Aortic Aneurysm (Table 28)

The rupture of AAA remains a lethal condition high mortality rate; however, its lifesaving rate has gradually improved due to the advancement of the medical care system and the progress of perioperative management specific to AAA rupture in recent years.[931] In addition it has been accumulated that the results of SG deployment (EVAR) for AAA ruptured AAA are comparable to or better than those of open surgery in recent years, and guidelines around the world, including ours, have significantly changed.[321,922]

2.3.1 Epidemiology

In Japan, approximately 1,600 cases of AAA rupture

reaching invasive treatment were registered annually between the inception of the NCD registration in 2011 and 2014, which accounted for approximately 10% of all AAA surgeries.[515,932–934] On the other hand, the incidence of AAA rupture in Sweden (including autopsy and non-invasive treatment cases) was estimated to be 10.6 per 100,000 person-years in 2000–2004, and men aged 65–94 years were reported to account for at least 70% of the cases.[935]

2.3.2 Diagnosis

Three classic signs of AAA rupture are sudden abdominal/back pain, decreased blood pressure, and abdominal pulsatile mass. However, all three signs are found only in approximately 50% of all cases,[321] and AAA rupture is suspected even if the patient does not exhibit all three signs. Rapid CT examination is recommended in patients with suspected AAA rupture if their circulatory dynamics is stable.[321,922] However, if the patient has unstable hemodynamics and must be transported directly to a surgery room, diagnostic imaging, such as echography, is performed in the surgery room to consider the possibility of EVAR.[321]

2.3.3 Medical Care System

To increase the lifesaving rate, a facility capable of endovascular treatment with a well-established protocol for rupture and well-equipped devices should be selected, and it is important to establish cooperation among hospitals and a patient management protocol for transportation.[922] Hypotension management with restricted transfusion (with a target systolic blood pressure of 70–90 mmHg) is recommended for conscious patients.[321,922]

2.3.4 Anesthesia

When performing EVAR for AAA rupture, the indication of local anesthesia should be considered, as EVAR is advantageous that it can be performed with local anesthesia.[321] In open surgery, since sudden hypotension often occurs during the introduction of general anesthesia, anesthesia should be introduced after surgeons have been scrubbed up and completed sterilization/covering with cloth/draping.[321]

2.3.5 Aortic Occlusion

If the circulatory dynamics of the patient is unstable, the use of an aortic occlusion balloon is recommended not only in EVAR but also in open surgery.[321,930,936]

2.3.6 Selection of Treatment Methods

Although either EVAR or open surgery can be selected, EVAR has been recommended as the first treatment choice if the patient is anatomically suitable for EVAR for the following three reasons.[321,922] Three RCTs, the IMPROVE,[923,924,937] AJAX,[938] and ECAR[939] trials, showed that the results of the EVAR group for AAA rupture were comparable to or better than those of the open surgery group.[925] In addition, the IMPROVE trial showed operative mortality rates of 35.4% in the EVAR group and 37.4% in the open surgery group, indicating no significant difference between the two; however, the EVAR group had a significantly shorter length of hospital stay and a higher home discharge rate.[937] Furthermore, while there was no difference in the survival rate after 1 year, the QOL was significantly higher in the EVAR group.[923] Moreover, the survival rate after 3 years was higher in the EVAR group than in the open surgery group, and EVAR was superior in terms of cost.[924] A large-scale Medicare study showed that the perioperative mortality rates after propensity score matching were 33.8% for EVAR and 47.7% for open surgery ($P<0.001$), showing the superiority of EVAR in early survival.[940] In a meta-analysis, the mortality rates for AAA rupture in patients with unstable circulatory dynamics were 37% for EVAR and 62% for open surgery ($P=0.009$).[941] If the acute-stage and long-term results of EVAR are comparable to or better than those of open surgery, EVAR is prioritized as it is less invasive, and the guidelines in Europe and the United States also recommend EVAR as the first treatment choice.[321,922] As in Europe and the United States, the selection of EVAR for AAA rupture has been increasing year by year in Japan. As of 2014, EVAR was selected for 31% of ruptured AAA cases, and the data collected by the Japanese Society for Vascular Surgery showed that EVAR had contributed to the lifesaving of ruptured AAA patients in clinical practice, leading to the accumulation of its evidence.[515,932–934]

2.3.7 Postoperative Management

Important characteristic complications of AAA rupture in both EVAR and open surgery include abdominal compartment syndrome, ischemic colitis, and multiple organ failure.[321,922] In addition, cardiac complications and respiratory failure are directly linked to life prognosis, and their postoperative management is also important.

a. Abdominal Compartment Syndrome

Abdominal compartment syndrome (ACS) occurs in 7–20% of cases after surgery of AAA rupture.[926,927,942] Increased intraperitoneal pressure leads to multiple organ failure, further leading to increased airway pressure and decreased cardiac output. The 30-day mortality rate in the onset cases with ACS was reported to be approximately twice as high as that in the non-onset cases. Intravesical pressure is measured for the diagnosis of ACS. Early surgical decompression is recommended for patients with intravesical pressure of 30 mmHg or higher and for patients who had organ failure and intravesical pressure of 20 mmHg or higher.[321,922,928,942]

b. Ischemic Colitis

Ischemic colitis occurs in 1/5–1/3 of ruptured AAA cases. Its mortality rate, once it develops, is high (45–67%), and ischemic colitis is the leading cause of death in ruptured AAA cases. The incidences of ischemic colitis were reported to be 23% after EVAR and 42% after open surgery, and early endoscopic examination is necessary in patients suspected of ischemic colitis.[922]

c. Cardiac Complications and Respiratory Failure

Heart diseases, such as CAD (acute coronary syndrome, arrhythmia, heart failure), and COPD complicate AAA at a high rate, and they develop due to rapid fluctuations in circulatory dynamics and blood coagulability, hypoxia, and increased intraperitoneal pressure, in addition to preoperative background. Because they require urgent surgery, preoperative information is scarce, while postoperative management focusing on coronary blood flow, cardiac function, and respiratory function is required. Electrocardiogram recording immediately before and after surgery and evaluation and management of postoperative cardiovascular risks are important.[321]

d. Multiple Organ Failure

Multiple organ failure is caused by unstable circulatory dynamics and ischemia-reperfusion injury. The mortality rate of ruptured AAA cases that have resulted in multiple organ failure is considerably high at 50–70%.[922]

e. Spinal Cord Ischemia and Lower Limb Ischemia

Although rare, spinal cord ischemia is known to occur in ruptured AAA patients. Its occurrence is thought to be associated with prolonged hypotension, in addition to high aortic cross-clamping and long-term blockage of internal iliac artery blood flow.[943] Moreover, complication/exacerbation of lower limb ischemia due to prolonged blockage of blood flow, in addition to atherosclerosis or embolism, is not rare. As this may lead to amputation of the lower limbs or death, it is recommended to examine the blood flow in the lower limbs immediately after the surgery.[321]

f. Incidence of Complications

Table 29 shows the incidences of various postoperative complications of AAA rupture according to the Vascular Quality Initiative (VQI) database in the United States.[944] For these complications, treatment at experienced facilities is desirable from the viewpoint of postoperative management specific to AAA rupture, such as abdominal compartment syndrome, intestinal ischemia, and management/early countermeasures for multiple organ failure.[922]

Table 29. Incidence of Complications After Invasive Treatment for Abdominal Aortic Aneurysm Rupture

	EVAR	Open surgery	P value
Cardiac complications	29%	38%	0.001
Pulmonary complications	28%	46%	<0.0001
Renal failure	24%	38%	<0.0001
Intestinal ischemia	3.9%	10%	<0.0001
Lower limb ischemia	2.7%	8.1%	<0.0001

EVAR, endovascular aortic repair. (Source: Prepared based on Ali MM, et al. 2015.[944])

2.3.8 Short-Term and Long-Term Postoperative Survival Rate

Table 30 shows the mortality rates after treatment for AAA rupture according to several registry databases. With regard to the long-term survival, patients with ruptured AAA who survived 90 days after treatment showed no significant difference in the 5-year survival rate compared to patients with non-ruptured AAA who had undergone elective surgery, and the main cause of death was reported to be cardiovascular events.[856] Management of long-term postoperative cardiovascular risks is important.[321,929]

2.3.9 Rupture of Special Abdominal Aortic Aneurysm

AAA rupturing into the inferior vena cava or iliac vein causes aortocaval fistula, and it is reported to occur in 0.22–6% of AAA patients.[945] Its three signs are abdominal pain, abdominal pulsatile mass, and abdominal vascular bruits; however, it may be detected due to high output heart failure or pulmonary embolism. Its definitive diagnosis can be obtained by double scanning method or CT examination. EVAR and open surgery can be selected for its treatment, but EVAR has a lower risk since open surgery has a risk of massive hemorrhage and pulmonary arterial embolism.[946] Endovascular treatment for the caval side or fistula has been reported in cases in which the arteriovenous fistula could not be closed by EVAR alone.[947,948]

2.4 Aortoenteric Fistula (Table 31)

Aortoenteric fistula is a rare disease, and its diagnosis is difficult without established treatment methods, often leading to fatal outcomes.[912,949] It is classified into primary and secondary aortoenteric fistula according to the cause, and most of them cause a duodenal fistula. The operative mortality rate of all aortoenteric fistulas is 21–40%.[950] Three classic signs of aortoenteric fistula are gastrointestinal tract hemorrhage, abdominal pain, and abdominal pulsatile mass. Gastrointestinal tract hemorrhage, abdominal pain, and abdominal pulsatile mass are found at the rate of 64–94%, 32–48%, and 17–25%, respectively, and all three are found only in 11% of all cases.[951] In addition, patients with an aortoenteric fistula present with back pain, fever, and sepsis. Hb is 8 g/dL or lower in two-thirds of cases, and white blood cell count exceeds 10,000/μL in one-fourth of the cases.[952] Primary and secondary aortoenteric fistulas exhibit precursor hemorrhage called "herald bleed," in which the fistula is temporarily blocked due to angiospasm and thrombus formation, resulting in hemostasis. Several cases require urgent hospitalization at the stage of precursor hemorrhage; however, repeated episodes are also frequently

Table 30. Mortality Rate After Treatment for Abdominal Aortic Aneurysm Rupture

	Vascunet	VQI	NCD
Country	9 European countries	USA	Japan
Survey period	2005–2009	2003–2013	2011–2014
Number of cases	7,040	1,165	6,379
Observation index	Operative mortality rate	In-hospital mortality rate	Operative mortality rate (in-hospital mortality rate)
Total	31.6%	30.0%	17.6% (20.7%)
EVAR	19.7%	25.0%	15.1% (17.9%)
Open surgery	32.6%	33.1%	17.6% (21.0%)

EVAR, endovascular aortic repair; NCD, national clinical database; VQI, vascular quality initiative. (Source: Prepared based on Mani K, et al. 2011,[931] Ali MM, et al. 2015,[944] the Japanese Society for Vascular Surgery[515,932–934])

Table 31. COR and LOE for the Treatment of Aortoenteric Fistula		
	COR	LOE
It is recommended to search aortoenteric fistula if the patient has a history of aortic aneurysm or aortic reconstruction and massive gastrointestinal tract hemorrhage	I	C
It is recommended to perform invasive treatment because the conservative treatment of aortoenteric fistula is fatal	I	C
For patients with massive or persistent hemorrhage, EVAR should be considered as a bridge to hemostasis	IIa	C

COR, class of recommendation; EVAR, endovascular aortic repair; LOE, level of evidence.

exhibited. If untreated despite the initial symptoms, 50% and 29% have a relatively long course of over 24 h and 1 week, respectively, leading to massive hemorrhage.[953]

2.4.1 Difference Between Primary and Secondary Aortoenteric Fistulas

Primary aortoenteric fistula is caused by an aortic aneurysm, infectious disease, malignant tumor, and trauma,[954,955] and its incidence is 0.04–0.07%.[956] Primary aortoenteric fistula complicates 0.69–2.36% of AAA patients, and more than 80% develop a duodenal fistula, resulting in the formation of aortic duodenal fistula.[957]

Secondary aortoenteric fistula causes intestinal tract fistula after open surgery (prosthetic graft replacement) or EVAR. The site that causes the fistula differs depending on the reconstruction site of the graft. However, as with the primary aortoenteric fistula, it is commonly found on the distal side of the duodenum (62%) or proximal side of the jejunum.[912] The incidence of secondary aortoenteric fistula is 0.36–1.6%,[958,959] which is higher than that of primary aortoenteric fistula. The average period from aortic reconstruction to the appearance of symptoms is 4 years (1.5–8.7 years).[912] Secondary aortoenteric fistulas are further divided into those that develop at the anastomotic site of the graft and those that develop at the body of the graft. Those that develop at the anastomotic site of the graft may show massive hemorrhage, whereas those that develop at the body of the graft often show signs of infection in the early stages. Procedural factors, such as infection, pulsatile pressure, and intestinal injury, are thought to be its pathogenic mechanism. The factors associated with both patients and surgery are involved in the cause of the disease, which include frequent vascular open surgery, wound complications, graft infection, urgent surgery, and problems in surgical techniques. In addition, reports of aortoenteric fistula occurring after EVAR have been increasing in recent years.[960] Its pathogenic mechanisms are thought to be aneurysm enlargement with persistent endoleak, effect of frequent coiling during endoleak treatment, endotension, and infection during SG deployment.[961]

2.4.2 Diagnosis

The diagnostic method for aortoenteric fistula differs depending on the circulatory dynamics of the patient. If the patient has massive gastrointestinal tract hemorrhage or has a history of AAA or its treatment (open surgery and EVAR), it is important to always have aortoenteric fistula in mind. If the patient has a massive hemorrhage, a diagnosis may be made by trial laparotomy. If the patient has stable circulatory dynamics, a diagnosis is made by contrast-enhanced CT examination, gastroesophageal endoscopy, or angiography. CT examination is minimally invasive and useful for its initial diagnosis.

a. Contrast-Enhanced CT Examination

Contrast-enhanced CT images may show the disappearance of adipose tissue around the aorta, fluid accumulation around the graft, thickening of soft tissues, ectopic gas patterns, twitching of adjacent thickened bowel loop around the aortic graft, and leakage of contrast medium from the aorta into the entangled intestinal tract.

b. Gastroesophageal Endoscopy

Endoscopic examination is essential for the treatment of acute gastrointestinal tract hemorrhage, and it allows for the ruling out of other hemorrhagic sources even if an aortoenteric fistula cannot be identified. With aortoenteric fistula in mind, skilled endoscopists can detect ulcers and erosions with a prosthetic graft, attached blood clot, or extrinsic pulsatile mass through careful observation. However, the main purpose of the endoscopic examination is also to rule out other pathological conditions as a cause of gastrointestinal tract hemorrhage. An endoscopic examination should be performed only in patients with stable hemodynamics, and it may be performed in the surgery room to respond to massive hemorrhage.

c. Angiography

Identification of an aortoenteric fistula in patients with stable circulatory dynamics is usually difficult, as the fistula is sealed with a thrombus during angiography.

d. Other Examination Methods

MRI examination, echographic examination, and gastrointestinal tract contrast examination do not lead to accurate diagnosis of aortoenteric fistula and have a long procedure time, although they can assist in its diagnosis. Identification of an aortoenteric fistula with MRI or FDG-PET examination is difficult, although they are useful in diagnosing graft infection, and they are not suitable for patients with unstable circulatory dynamics from the viewpoint of examination time.

2.4.3 Treatment

Open surgery is the only lifesaving means for patients with an aortoenteric fistula, as its conservative treatment is always fatal. The important determinants for its effective surgery are involvement of active hemorrhage, identification of whether it is primary or secondary aortoenteric fistula, the presence or absence of sepsis, and anastomosis site of aortic reconstruction. Patients with unstable circulatory dynamics exhibiting active hemorrhage and sepsis patients are indicated for urgent surgery. Evaluation of aortoenteric fistula and planning of surgical procedure are discussed for patients with stable circulatory dynamics exhibiting precursor hemorrhage. Preoperative insertion of a urinary tract stent can reduce the risk of urinary tract injury, even in patients with severe retroperitoneal inflammation. It is strictly monitored and managed, and surgery is performed promptly without delay. Re-hemorrhage occurs in 30% and 50% of patients within 6 and 24 h, respectively.[961]

a. Graft Removal

If the aortic aneurysm is occluded or the graft has occluded it, or if the sufficiently developed collateral flow is seen in preoperative CT examination and angiography, the graft may be removed without its reconstruction.

b. Anatomical Prosthetic Graft Replacement

If the contamination is mild, anatomical revascularization is often performed by local cleaning, cryopreserved blood vessels, and rifampicin-immersed prosthetic graft, although it depends on whether the infection has spread to the aortic side.[962] A retrospective cohort study showed no difference in the operative mortality rate between anatomical and extra-anatomical revascularizations.[963] Efforts to separate the gastrointestinal tract and graft with the retroperitoneum and omentum, as well as long-term administration of antimicrobial drugs, are considered.

c. Anatomical Revascularization Using Autologous Vein

The femoral popliteal vein is used for aortoiliac artery reconstruction with an autologous vein.[964] Attention must be paid to leg compartment syndrome due to venous perfusion failure of the limb on the collection side.

d. Extra-Anatomical Prosthetic Graft Bypass

Extra-anatomical prosthetic graft bypass may be selected if an infection is obvious or if blood circulation in the lower limb and blood flow in the pelvis are expected to require long-term interruption.[965,966] When it is performed in one stage, axillary-bi-femoral artery bypass precedes, and abdominal aortic treatment and reconstruction of the gastrointestinal tract are performed. With the aorta to be dead-end, it is covered with the omentum.

Extra-anatomical bypass infection, which occurs in 15–25%, can be minimized with the administration of appropriate antimicrobial drugs.[967] It is completed in one week if the culture is negative, and the administration of antimicrobial drugs for 4–6 weeks is recommended if the culture is positive.[953]

e. Endovascular Treatment

Recurrence, new infection, and hemorrhage are observed after EVAR, and 29% of the patients die from sepsis. Thus, EVAR should be limited to patients with a poor prognosis or used as a bridge treatment to control infection and stabilize the condition of the patient.[968]

2.5 Inflammatory Aortic Aneurysm (Table 32)

Table 32. COR and LOE for Diagnosis and Treatment of Inflammatory Abdominal Aortic Aneurysm

	COR	LOE
It is recommended to measure the serum IgG4 level when inflammatory abdominal aortic aneurysm is suspected[969,970]	I	C
Anti-inflammatory therapy with steroids should be considered for symptomatic patients[971–975]	IIa	C
EVAR should be considered as the first treatment choice for aneurysms with a diameter exceeding 55 mm in men and 50 mm in women, if the anatomical requirements are met[975,976]	IIa	C

COR, class of recommendation; EVAR, endovascular aortic repair; LOE, level of evidence.

2.5.1 Concept, Pathology, and Pathogenesis

Inflammatory AAA was reported in 1935 as one of the causative diseases of uremia, and its disease concept was first introduced by Walker et al. in 1972.[977] This arterial aneurysm is characterized by an abdominal aortic aneurysm and marked thickening of its wall, extensive fibrosis around the aortic aneurysm and retroperitoneum, and adhesion with surrounding abdominal organs, such as the duodenum and urinary tract. It often occurs under the renal artery; however, it has also been reported to occur in the thoracic aorta, internal iliac artery, and femoral artery.[978,979]

Macroscopically, inflammatory AAA appears as a white, glossy, hard, elevated lesion when observed from the ventral side. Histopathologically, fibrosis accompanied by hyalinization is widely observed in the adventitia and its outer peripheral tissue, and nonspecific chronic inflammatory cells, mainly lymphocytes and macrophages, infiltrate in layers with the formation of lymphoid follicles.[977] As a result, it exhibits a structure in which fibrosis and inflammatory cells are alternately present, and it is a characteristic histological image of this disease. On the other hand, the tissue on the luminal side of the media shows the same changes as normal AAA. Therefore, the media is markedly thinned, and atherosclerosis occurs to cover it. The media may disappear almost completely. The relationship between inflammatory AAA and AAA remains largely unclear, and they cannot be clearly distinguished due to the presence of inflammatory cell infiltration in the adventitia in some AAA cases,[980] the lack of significant difference in the subpopulation of lymphocytes,[981] and similar risk factors between the two. Some suggest that inflammation is more strongly expressed in inflammatory AAA by factors, such as smoking[983] and herpes/cytomegalovirus infection, in addition to the genetic factors.[982,984,985] It was also reported that inflammatory AAA complicates large vessel vasculitis, such as giant cell arteritis and Takayasu arteritis.[986] Furthermore, its complications with IgG4-related diseases have attracted attention in the recent years; however, it was reported that approximately half of inflammatory aortic aneurysms are histopathologically IgG4-positive.[969]

2.5.2 Prevalence Rate

There have been several reports on inflammatory AAA in Europe and the United States, and its prevalence rate is 4–15%.[987–989] According to reports in Japan,[990,991] its prevalence rates are 4.9% in echographic findings and 3% in examination in surgical cases, which are slightly lower than that in Europe and the United States. Its male/female ratio varies in the range of 30:1–6:1, but it occurs more frequently in males. Moreover, its age group is approximately 5–10 years younger than that of atherosclerotic AAA.[985]

2.5.3 Clinical Symptoms

Typical three clinical symptoms of inflammatory AAA are abdominal pain/lumbar pain/abdominal discomfort, weight loss, and increased erythrocyte sedimentation rate/high CRP level, which are thought to be derived from inflammation. With regard to its complications, thickening of the aneurysmal wall may involve the urinary tract[992] and cause hydronephrosis, leading to renal failure, oliguria, and edema. Although rare, it may involve the gastrointestinal tract and cause obstruction or rupture of the gastrointestinal tract.

2.5.4 Diagnosis

Inflammatory AAA is suspected in AAA patients with the clinical symptoms mentioned above. Blood tests often show a high erythrocyte sedimentation rate and high CRP level; however, leukocytosis or culture positivity suggestive of bacterial infection is absent. In addition, measurement of serum IgG4 level is useful for investigating the involvement of IgG4 -related diseases.[969] Imaging findings are important for its diagnosis, for which echographic and CT examinations are useful.

In echographic examination, inflammatory AAA is characterized by thickening around an abdominal aneurysm (mantle sign: low-echo area anterior or anterolateral to the aneurysm). Contrast-enhanced CT examination reveals the area around the aneurysm, which shows low CT values on unenhanced CT, and it can be clearly distinguished from the surrounding area (**Figure 24**). Cases with severe thickening may exhibit involvement of surrounding organs, such as the urinary tract, gastrointestinal tract, inferior vena cava, and renal vein, and the diagnosis of inflammatory AAA is important for the prevention of complications, such as damage to the intestinal tract and urinary tract, during surgery. FDG-PET examination is useful for detecting active inflammation in the aortic wall or its surrounding.[993–995] The site of inflammation is detected as increased accumulation of FDG, and the detection sensitivity and specificity of inflammatory aortic diseases were reported to be 83–100% and 77–100%, respectively.[993]

Inflammatory AAA can be differentiated from infected aortic aneurysm by typical CT findings, negative blood culture, negative tuberculin reaction, and negative syphilis.

2.5.5 Treatment

In addition to the treatment of the aortic aneurysm itself, it is necessary to treat and prevent the obstruction of various organs due to the fibrous thickening around the aneurysm. If the patient who has a small aortic aneurysm that is not indicated for surgery presents with pain, weight loss, or hydronephrosis, administration of steroids is considered to improve inflammation. Their recommended dose and duration have not been determined. Moreover, immunosuppressants and anti-estrogen drugs were reported to be useful in patients who were refractory to steroids.[971–973]

Based on the indications for normal AAA, inflammatory AAA that is 55 mm or larger in males and 50 mm or larger in females is indicated for surgery, but the indication is determined in association with systemic complications, such as cerebrovascular disease, CAD, respiratory disorder, and kidney injury. Inflammation often causes a high degree of adhesion between the aorta and duodenum, and retroperitoneal approach is recommended to avoid duodenal damage when performing open surgery.[996] It has been reported in recent years that treatment with EVAR reduced the aneurysm and improved mantle sign on CT, suggesting its usefulness.[976] However, caution is needed as kinks of the SG legs and stenosis were reported to occur in patients with strong inflammation or adhesion. Moreover, it was reported that exacerbation of fibrosis around the aorta and the enlargement of aneurysm diameter after EVAR tend to occur in IgG4-positive inflammatory AAA.[970] Although obstructions, such as hydronephrosis, often improve after surgery, inflammation remains in many cases, especially after EVAR, and urinary tract catheter deployment and steroid/immunosuppressant administration should also be considered.

2.5.6 Outcome and Prognosis

The natural prognosis of inflammatory aortic aneurysms is unknown. In open surgery, the perioperative complications and mortality rate in patients with an inflammatory aortic aneurysm were reported to be three times higher than those in patients with normal AAA, which was due to extensive adhesions.[974] A review comparing open surgery and EVAR showed that the total mortality rates after 1 year were 14% for open surgery and 2% for EVAR.[975] The thickened adventitia around the aneurysm often alleviates/disappears after open surgery, suggesting that open surgery is more likely to improve hydronephrosis caused by ureteral obstruction than EVAR.

2.6 Infected Aortic Aneurysm

2.6.1 Definition and Epidemiology

All aortic aneurysms caused by infection and preexisting aortic aneurysms with infection are collectively referred to as "infected aortic aneurysm." Infected aortic aneurysm is a relatively rare disease, and it was reported to account for 0.5–1.3% of all aortic aneurysms.[997–999] Although the infection sources may not always be known, they include bacterial translocation from caries or the intestinal tract, spread from urinary tract infection, and exacerbation of atherosclerosis from periodontal disease, and rare iatrogenic cases secondary to catheter operation and surgery also occur. It has also been pointed out that an aging-related increase in risk factors for susceptibility to infection lies in its background. A chronic decline in immune function due to diabetes mellitus, malignant tumor treatment, or collagen disease treatment is also an important risk factor.

With regard to infection sites, infected aortic aneurysms occur in the thoracic aorta in 32%, the abdominal aorta adjacent to the abdominal branch in 26%, and the infrarenal abdominal aorta in 42%, indicating that it frequently occurs in the infrarenal aorta.[1000]

The primary causative organisms were reported to be gram-positive coccus, mainly Staphylococcus, and gram-negative bacillus, mainly Salmonella, in several cases. According to a report from Mayo Clinic,[1000] gram-positive coccus accounted for 50% of the cases (Staphylococcus in 30% and Streptococcus in 20%), and gram-negative bacillus accounted for 35% of the cases (Salmonella in 20% and in 15%). However, a report from National Taiwan University showed that Salmonella accounted for 76% while gram-positive coccus accounted for approximately 10%,[1001] suggesting that there is regionality regarding the primary causative organisms. In addition, some infected aortic aneurysms are caused by acid-fast bacteria and fungus, although it does not occur frequently.

Its mortality rate was reported to be 23.5–37%, which is considerably higher than that of non-infected aortic aneurysm.[1002] Its major causes of death are rupture of an aortic aneurysm, failure of the anastomotic site after surgery, and multiple organ failure due to sepsis.

2.6.2 Diagnosis

Subjective symptoms, such as fever and back pain, develop in several cases of infected aortic aneurysms. Moreover, they exhibit increased inflammatory findings on blood tests; however, they remain to be nonspecific findings. In AAA patients, a pulsatile mass may be palpable. With regard to its diagnostic imaging, the diagnostic accuracy of contrast-enhanced CT examination is particularly high,

but echographic examination is also useful in the abdominal region. Infected aortic aneurysm must always be considered if an aortic aneurysm is found in a patient presenting with signs of infection.

On diagnostic imaging, a localized saccular-type aneurysm occur in several patients with infected arterial aneurysm. However, existing fusiform-type aneurysm may be complicated by infection, and it is difficult to determine the complication of infection from the morphology alone. However, fluid accumulation around the aortic aneurysm indicates edema or abscess formation due to inflammation, and this finding strongly suggests infection. Moreover, aneurysms that enlarge rapidly when observed over time are likely to be infected aortic aneurysms. Preoperative blood culture is an essential examination for the selection of appropriate antimicrobial drugs, and blood should be drawn multiple times based on the diagnosis of infectious endocarditis.

2.6.3 Treatment

a. Antimicrobial Therapy

Intensive antimicrobial therapy is started based on the results of culture test as soon as an infected aortic aneurysm is diagnosed. If the response to antimicrobial therapy is favorable and the signs of infection resolve quickly, antimicrobial drugs are administered for a sufficient period of time, and ideally, surgery is performed after the inflammatory response is shown to be negative, if possible. On the other hand, even if the inflammatory response appears to have subsided, it should be kept in mind that there is always a risk of aortic aneurysm rupture, and it is important to make efforts not to miss the timing of surgery by paying attention to the morphology of the aortic aneurysm and its tendency to enlarge over time. Immediate surgery is considered not only for ruptured cases, but also for cases exhibiting rapid aneurysm enlargement, even if infection control is sufficient. Moreover, early surgery is required in cases showing poor infection control despite the administration of appropriate antimicrobial drugs.

There is no consensus on the need of surgery for cases in which the aortic aneurysm itself is small and not indicated for surgery and the infection has disappeared with antimicrobial therapy.

b. Surgery

i. Procedure

Unlike the surgery of normal aortic aneurysm, infected tissues, including aortic aneurysm, must be removed as much as possible in the surgery of infected aortic aneurysm, aiming to achieve the prevention of rupture and removal of the infection focus simultaneously by resecting the aortic aneurysm. Patients with an esophageal fistula in the thoracic aorta or duodenal fistula in the abdomen often require repair or resection of the gastrointestinal tract. Furthermore, it is important to prevent the spread of infection to the prosthetic graft, its anastomosis site, and aortic stump.

With regard to its reconstruction method, extra-anatomical bypass, which closes the aorta before and after the aortic aneurysm and reconstructs blood circulation in the lower body by axillary artery-femoral artery bypass, was previously the standard procedure for infected infrarenal aortic aneurysms to avoid transplanting prosthetic grafts in the infection focus. However, many have selected in situ prosthetic graft replacement as the first treatment choice in the recent years.[1001–1003] The surgical results of infected infrarenal aortic aneurysms have recently improved, and its early mortality rate was reported to be approximately 10–15%.[1002,1004] Due to its anatomical factors, the surgery and reconstruction of infected suprarenal aortic aneurysm are more complicated than those of infected infrarenal aortic aneurysm, and its prognosis is poor, likely due to a large number of anastomotic sites. While its mortality rate was shown to reach 80%,[1005] some have reported favorable results, with an early mortality rate of approximately 10–16%.[998,1006]

ii. Selection of Graft

Various studies have been conducted on the grafts used in the surgery of infected aortic aneurysms, aiming to prevent the recurrence of infection in transplanted grafts. Among those, cryopreserved allogeneic aortic grafts (homografts) have shown favorable early and long-term results.[1007–1009] Vogt et al. compared the cases of in situ transplantation of cryopreserved allogeneic aortic grafts and the cases using prosthetic grafts as in situ or extra-anatomical bypass for infected aortic aneurysm and prosthetic graft infection, and they reported that homografts were highly effective, especially for infection control.[1007] Lesche et al. reported that occlusion and aneurysm formation were found in 17% of the cases during an average of 3 years of follow-up after homograft transplantation. They also indicated that those cases were not related to infection and that their reoperation was easily performed.[1008] The durable life of a transplanted homograft over 10 years are unknown; however, early infection control is necessary for saving the lives of patients with an infected aortic aneurysm, for which a homograft is considered an excellent material.[1009]

It was previously difficult to obtain homografts in Japan. However, because of the dissemination of tissue donations with the enforcement of the Organ Transplant Law and the activities of tissue banks, homografts are now covered by insurance under certain conditions, and they are expected to be used more widely in the future.

In addition, the use of prosthetic graft immersed in antimicrobial drugs[1010] and autologous femoral vein[1011] has been reported sporadically; however, their superiority over normal prosthetic graft is unknown.

iii. Omentum Wrapping

The omentum, a tissue rich in blood flow and lymph, is considered effective for infection control, and it is often used for the treatment of mediastinitis after open heart surgery.[1012] In the surgery of infected aortic aneurysms, the surrounding of in situ transplanted prosthetic graft is covered with omentum to prevent the spread of infection. Pedunculated omentum that has either the right or left gastroepiploic artery as the vascular pedicle can be used for a wide range of aorta from the thoracic to infrarenal region.[1013]

iv. Postoperative Antimicrobial Therapy

Intensive postoperative antimicrobial therapy is essential. Antimicrobial drugs tailored to the primary causative organisms are administered intravenously, and it is continued for 6 to 8 weeks with the goal of having a negative inflammatory response. While a report stated that the administration of antimicrobial drugs could be subsequently discontinued,[1001] some reported that oral antimicrobial drugs should be administered over a lifetime.[998,1013]

c. Endovascular Treatment

Endovascular treatment using SG for descending TAA

and infrarenal AAA has rapidly become widely used in recent years. Some have reported that infected aortic aneurysms were cured by endovascular treatment in combination with intensive antimicrobial therapy;[1014–1016] however, it often does not lead to lifesaving. Moreover, with this treatment method, focus on infection and prosthetic graft are located adjacent to each other, and the infection focus remains as a closed cavity. Thus, some suggest that this method has a risk of exacerbation of infection and is contraindicated.[1017] However, its significance as a bridge treatment for the prevention of rupture and the subsequent prosthetic graft replacement has been accepted.

2.7 Traumatic Aortic Aneurysm

This section describes rare trauma of the abdominal aorta, and the relatively common trauma of the thoracic aorta is described in a separate section (**Chapter VI**, "**1.4 Traumatic Aortic Injury**").

The trauma of the abdominal aorta is rare, and most of its published studies are case reports and their reviews.[1018–1021] It is roughly divided into penetrating trauma and blunt trauma, and most of the causes of penetrating trauma in Europe and the United States are gunshot wounds.[1019] In stab wounds, there is little damage to the aorta in the deep position, and other organ injuries are common. Most of the causes of blunt trauma are traffic accidents, including injuries caused by seat belts.[1020–1022]

The usefulness of CT examination for its diagnosis, as well as for diagnosis of other traumas, has been established. However, if the hemodynamics of the patient is unstable, a diagnosis must proceed while preparing for open surgery.[1023]

In its treatment, rapid open surgery is prioritized if the hemodynamics of the patient is unstable. The usefulness of endovascular treatment, mainly embolization, has been reported in patients with relatively stable hemodynamics.[1018,1024]

VI. Treatment for Aortic Dissection

1. Overview

1.1 Definition and Classification

For the definition and classification of aortic dissection, see **Chapter I**, "**2.1 Definition**" and "**2.3 Classification**."

Aortic dissection with thrombosed false lumen is considered to have a more favorable prognosis than aortic dissection with patent false lumen. The prognosis of the ulcer-like projection (ULP)-type aortic dissection lies between those of the two, which includes patients with an unstable pathological condition. Therefore, the 2011 edition of the present guideline recommended responses for ULP-type aortic dissection based on those for aortic dissection with patent false lumen.[1] However, the relationship of the location and size of the ULP with the prognosis remains largely unclear, and there is no basis for recommending responses for all cases of ULP-type aortic dissection based on those for aortic dissection with patent false lumen. In addition, the 2011 edition stated that cases showing the false lumen with blood flow despite the thrombosis of most of the false lumen (thrombosed false lumen communicating with true lumen) are classified as aortic dissection with patent false lumen. However, the distinction between this pathological condition (thrombosed false lumen communicating with true lumen) and ULP-type aortic dissection was unclear. Furthermore, in Europe and the United States, the presence of a partially formed thrombus (partial thrombosis) has been reported as a factor for false lumen enlargement in Type B dissection in the recent years;[1025,1026] however, it was pointed out that several cases with partial thrombosis may be ULP-type aortic dissection described in the 2011 edition of the present guideline in Japan.[1027]

Based on the previous guidelines, the present edition of our guideline tentatively defined ULP as those showing an aortic longitudinal extension of less than 15 mm in the contrast-image area of the false lumen. Additionally, it was clearly distinguished from those with patent false lumen extending 15 mm or more (4 or more slices on 5-mm slice thickness CT transected images) in the craniocaudal direction despite the thrombosis of most of the false lumen (classified as aortic dissection with patent false lumen) or partial thrombosis. It would be advantageous to accumulate findings regarding the differences in prognoses between this pathological condition (thrombosis of most of the false lumen with patent false lumen extending 15 mm or more) and ULP-type aortic dissection in the future.

PQ 9.
Management of ULP-Type Aortic Dissection

Recommendation

ULP-type aortic dissection is treated as a type of aortic dissection with patent false lumen, requiring strict follow-up, which includes diagnostic imaging.

Ulcer-like projection (ULP) is an expression of imaging findings, used mainly in the diagnostic imaging of aortic dissection, and it is defined as the "contrast-image area of the thrombosed false lumen with craniocaudal extension of less than 15 mm" in contrast-enhanced CT examination or angiography. ULP-type dissection is distinguished from aortic dissection with thrombosed false lumen by the "presence of ULP," and it is distinguished from aortic dissection with patent false lumen by defining "the major axis of ULP of less than approximately 15 mm."

The difference between the term "intramural hematoma (IMH)" used in Europe and the United States and the term "aortic dissection with thrombosed false lumen" used in Japan has often been controversial. In recent years, the term "IMH" has expanded from its original meaning, now including the presence of concomitant ULP. Like "IMH with ulcer" and "IMH with ULP," used in Europe and the United States and "aortic dissection with thrombosed false lumen and ULP-type aortic dissection" used in Japan has become the concept corresponding to "IMH" (See **Table 4**).

ULP has been suggested to be the primary entry in ULP-type dissection.[1028,1029] Also, its enlargement (transitioning to aortic dissection with patent false lumen or becoming an aneurysm)[1030,1031] and disappearance (reducing in size and transitioning to aortic dissection with thrombosed false lumen)[1032] during the clinical course are important observation points for ULP-type dissection as they are indices of prognosis. The distinction between ULP and penetrating atherosclerotic ulcer (PAU)[33] often poses a problem; however, they have different meanings. It is important to understand that PAU is an "expression of a pathological condition," including the process up to its occurrence, whereas ULP is simply an "expression of morphology on images."

1.2 Intramural Hematoma (IMH)

1.2.1 Concept and Background

Intramural hematoma (IMH) is a pathological condition in which hemorrhage in the aortic media has resulted in the formation of a hematoma. Originally, it was diagnosed pathologically as "a condition without a tear in the dissected intima",[1033,1034] and it was classically considered as a condition caused by the rupture of the vasa vasorum. However, conditions with "no visualized tear, crescent-shaped morphology of the false lumen, and no effect of contrast imaging" on imaging[1035] have been clinically diagnosed as IMH, mainly in Europe and the United States. Therefore, even patients with a tear are diagnosed with IMH if their tear is not visualized by diagnostic imaging and there is no inflow of contrast medium into the false lumen. The rate of progression to classic aortic dissection is high in Europe and the United States, and the results of its medical treatment have been poor, likely because IMH is often diagnosed with a single CT examination without delayed-phase contrast imaging.[60] On the other hand, its medical treatment in Japan and South Korea has shown favorable results due to the high detection rate in mild cases, rigidity of initial diagnosis, and follow-up with CT examination through the course. Due to this ambiguity, the 2011 edition of the guideline recommended the use of the term "aortic dissection with thrombosed false lumen," since "the diagnostic term IMH, which may lead to misunderstanding of its pathological condition, is not used clinically in Japan." Also, the term "ULP-type dissection" for patients with traces of a small tear was used.[1] However, because IMH is widely used in Europe and the United States as a term that includes aortic dissection with thrombosed false lumen and ULP-type dissection used in Japan, the present edition organized the Japanese and English notations (**Table 4**).

1.2.2 Epidemiology

Aortic dissection with thrombosed false lumen accounts for 10–25% of acute aortic syndrome in Europe and the United States and approximately 20–50% of that in Asia. Compared to aortic dissection with patent false lumen, aortic dissection with thrombosed false lumen tends to occur more frequently in elderly men. In Europe and the United States, thrombosed Type A and B dissections occur at the ratios of 30–40% and 60–70%, respectively.[95,96] In Japan, approximately 30–40% of Type A dissection and 40–70% of Type B dissection are aortic dissection with thrombosed false lumen or ULP-type dissection. The dissections rarely extend to the abdominal aorta, and patients presenting with malperfusion are scarce.[1036]

1.2.3 Diagnosis

The process leading to diagnostic imaging in patients with ULP-type aortic dissection is similar to that in patients with normal aortic dissection.

1.2.4 Treatment and Prognosis

In Europe and the United States, Type A aortic dissection with thrombosed false lumen (+ULP-type dissection) is indicated for surgery due to its considerably high re-canalization rate and poor prognosis. However, in Japan and South Korea, conservative treatment under strict management has recently become possible for patients with an ascending aortic diameter of <50 mm and a false lumen thickness of <11 mm based on the accumulated evidence.[1,96] In principle, conservative treatment is selected for Type B aortic dissection with thrombosed false lumen. In addition, endovascular treatment has been actively performed for complicated dissection (malperfusion or rupture) and ULP-type dissection in the recent years.[1036]

1.3 Penetrating Atherosclerotic Ulcer (PAU)

1.3.1 Concept

Penetrating atherosclerotic ulcer (PAU), also referred as penetrating aortic ulcer, is a pathological condition of an atherosclerotic lesion with ulcer formation, in which the ulcer crosses the internal elastic membrane and reaches the media. It may form a hematoma in the media, resulting in the same pathological condition as that of aortic dissection, or it may cross the external elastic membrane, resulting in adventitia failure (=rupture) (**Figure 60**).[33] PAU with dissection extending to a certain length is differentiated from ULP-type dissection by the degree of atherosclerosis; however, their differentiation is often difficult due to overlapping pathological conditions.[1037]

1.3.2 Epidemiology

Classic dissection (double-barrel dissection), IMH, and PAU are collectively referred to as acute aortic syndrome; however, PAU accounts for 5% of cases of acute aortic syndrome in Europe and the United States. Compared to classic dissection, PAU tends to occur more commonly in men with atherosclerotic risk factors; however, it can also occur in young individuals. Also, it is often found to occur in the descending aorta, and occurs at multiple sites in some cases.[96]

1.3.3 Diagnosis

Asymptomatic PAU is detected incidentally by diagnostic imaging. In PAU with acute aortic syndrome, the process leading to diagnostic imaging is similar to that of normal aortic dissection. PAU of the descending aorta can also be diagnosed by transesophageal echography. As mentioned above, localized medial hematoma and ulcerated lumen with blood flow are typically found in a highly atherosclerotic aorta. PAU requires careful judgment as it has carried a high risk of rupture.

1.3.4 Treatment and Prognosis

Patients with persistent symptoms in the acute phase are well indicated for endovascular treatment; however, they

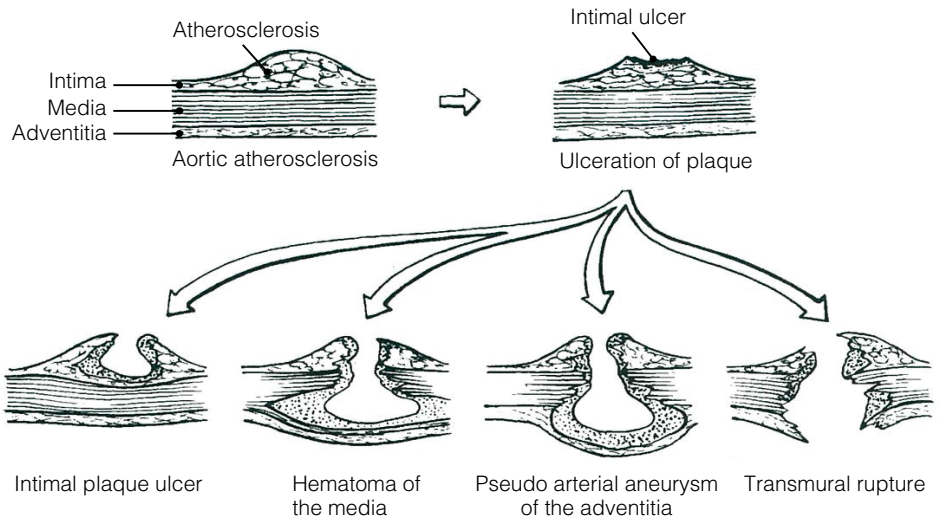


Figure 60. Extension pattern of PAU (penetrating atherosclerotic ulcer). (Adapted from Stanson AW, et al. 1986.[33]) Copyright (1986) Annals of Vascular Surgery, Inc., with permission from Elsevier. https://www.sciencedirect.com/journal/annals-of-vascular-surgery.

often exhibit access problems due to severe atherosclerosis. For other patients, a follow-up is performed under strict management of underlying diseases, and endovascular treatment is considered upon enlargement of diameter or onset of symptoms. Diagnostic imaging every six months is recommended for the first three years. Prosthetic graft replacement is performed if endovascular treatment is anatomically difficult. In any case, the risk of intraoperative embolism is high, and the operative mortality rates of acute PAU were reported to be 7% for endovascular treatment and 16% for prosthetic graft replacement. In addition, the life prognosis for this disease is poor due to systemic atherosclerotic diseases, and its 5-year survival rate in non-surgical cases was reported to be 65%.[1037]

1.4 Traumatic Aortic Injury

1.4.1 Definition and Epidemiology

Blunt traumatic thoracic aortic injury is often caused by a sudden anterior or lateral impact associated with a traffic accident or fall, as well as rapid deceleration of trunk movement. Regional concentration of torsion phenomenon and shear stress in the aorta are likely to occur in the vicinity of ligamentum arteriosum, aortic root, and the vicinity of the diaphragm. Approximately 90% of these traumatic aortic injuries occur in the vicinity of so-called aortic isthmus.[1038] The pathological morphology is divided into intimal cleavage, intramural hematoma, pseudoaneurysm, and rupture, depending on the degree of the injury.

1.4.2 Symptoms and Diagnostic Methods

The mode of onset of traumatic aortic injury is back pain, especially the pain between the scapulae. However, since it is often accompanied by polytrauma, its thoracic symptoms are nonspecific due to the pain caused by other organ injuries in several cases. Its rupture may lead to hypotension or shock. It is diagnosed with high accuracy by contrast-enhanced CT examination. Therefore, contrast-enhanced CT examination may be performed if an enlarged mediastinal shadow or finding of left hemothorax is seen in chest radiography or if physical findings of polytrauma, such as multiple fractures, are observed, in consideration of the complication of traumatic thoracic aortic injury.

1.4.3 Treatment Indications

The timing of treatment intervention for traumatic aortic injury remains controversial. Based on the observation that the aorta often ruptures within 24 h of trauma, urgent surgery was previously considered necessary for all cases of traumatic aortic injury. However, there has been an accumulation of experiences in cases with a certain observation period, such as patients with persistent hemorrhage due to pelvic fracture and patients with prolonged consciousness disturbance due to head trauma. This has led to the recognition of the usefulness of semi-urgent surgery, avoiding urgent surgery, and treatment intervention in the subacute phase, and delayed repair can now be performed relatively safely in certain cases. Large-scale prospective studies and guidelines in the field of trauma surgery have also suggested the usefulness of delayed repair from the viewpoint of reducing the mortality rate and SCI.[1039,1040] However, delayed repair should not be considered for patients who are suspected of having a high risk of aortic rupture based on imaging findings.

1.4.4 Treatment Methods (Table 33)

The treatment of patients with polytrauma requires a medical care team consisting of medical specialists in multiple fields; additionally, consensus formation within the medical care team is useful for determining the treatment priorities for each injury and timing of treatment intervention for aortic injury. Blood pressure management during the course of the treatment is crucial, and it is important that the mean diastolic blood pressure does not exceed

Table 33. COR and LOE for Treatment Selection for Traumatic Aortic Injury

	COR	LOE
It is recommended to perform TEVAR over open surgery in patients requiring invasive treatment if anatomical requirements are met (See **Table 9** and **Table 56**)	I	C
If the general condition is relatively stable, elective surgery may be considered over urgent surgery regardless of the presence of polytrauma	IIb	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

Table 34. COR and LOE for the Treatment of Stanford Type A Aortic Dissection

	COR	LOE
It is recommended to perform urgent open surgery for patients with aortic dissection with patent false lumen[68,1047,1048]	I	B
Urgent open surgery should be considered for patients with aortic dissection with thrombosed false lumen[1049–1053]	IIa	C
Medical treatment should be considered for patients with aortic dissection with thrombosed false lumen[1031,1054–1056]	IIa	C

COR, class of recommendation; LOE, level of evidence.

80 mmHg.[1041,1042] The commonly used and the established invasive treatment is prosthetic graft replacement of the thoracic descending aorta under the right lateral decubitus position, left posterior lateral thoracotomy, and partial extracorporeal circulation. In the recent years, an increasing number of reports have shown less invasiveness and superior treatment results of TEVAR compared to those of open surgery, and TEVAR is recommended as the first treatment choice, if the anatomical requirements of the aorta are met.[1040,1043]

1.5 Iatrogenic Aortic Dissection

Iatrogenic aortic dissection is a pathological condition of the aorta that can develop with treatments, such as coronary artery catheterization, open heart surgery, TEVAR, endovascular treatment for peripheral vascular lesions, and intra-aortic balloon pumping. Although rare, it can also occur during cardiac catheter examination.[1044,1045] In its relatively typical pathological condition, an intimal tear develops in the ascending aorta, especially in the vicinity of the right coronary artery, and the dissection extends to the periphery. Occasionally, it extends proximally, leading to aortic valve regurgitation and cardiac tamponade. Although its diagnosis can be made using the contrast medium retained in the aortic wall, it can be reliably diagnosed by transesophageal echography or CT examination.

The treatment management guidelines for catheter-related aortic dissection have not always been standardized. Generally, conservative treatment is often provided for a dissection localized to the abdominal aorta, peripheral blood vessels, or aortic valve leaflet. However, stent deployment in the coronary artery is required for patients who are observed to develop stenosis at the entry of the coronary artery. If the aortic dissection extends into the ascending aorta for more than a few centimeters, aortic prosthetic graft replacement by urgent surgery may be required; however, it rarely results in rupture.

The most common sites of aortic dissection that develop during open heart surgery are the insertion site of a blood supply tube, injection site of a cardioplegic solution, and aortic cross-clamping site.[1046] It may be diagnosed by the direct visual observation of the change in color of the ascending aorta to dark purple, identification of flaps by intraoperative transesophageal echography, or decreased arterial pressure in peripheral blood vessels. If aortic dissection develops with the blood supply operation, the blood supply route needs to be changed as early as possible. Prosthetic graft replacement of the ascending aorta, as well as the aortic arch, is considered for its treatment.

2. Stanford Type A Aortic Dissection

2.1 Treatment Indications (Table 34)

Type A dissection involving the ascending aorta has a considerably poor prognosis, and its mortality rate was reported to increase by 1–2% per hour after onset.[68] Also, without invasive treatment (open surgery or TEVAR), its mortality rate within 48 h of onset is estimated to be approximately 50%. Its main causes of death include rupture, cardiac tamponade, myocardial ischemia, cerebral ischemia, and intestinal ischemia.[1047,1048] Except for some dissections described in the subsequent sections, the prognosis of medical treatment for Type A dissection is considerably poor, and it is indicated for urgent invasive treatment, especially urgent open surgery. Treatment with stent graft alone (TEVAR or EVAR) has been performed at a small number of hospitals; however, it cannot be considered as a general treatment at present due to its unclear effectiveness.

Consciousness disturbance (coma), shock due to cardiac tamponade, myocardial ischemia, malperfusion, and cerebral ischemia are the important predictors of postoperative mortality when performing urgent surgery. It has been controversial whether surgery improves the prognosis or whether the surgery should be performed, especially for Type A dissection with neurological symptoms or consciousness disturbance.[1057,1058] Patients with the complication of cerebral ischemia generally have a poor prognosis, and surgery is often avoided. However, a favorable neurological prognosis was reported in patients receiving early reperfusion of the brain.[1058] In particular, the effectiveness of active surgery was reported in cases that had taken less than 5 h from the appearance of neurological symptoms to arrival at the surgery room.[1058]

Open surgery for Type A dissection involves ascending aortic replacement with a tear, as well as repair of the annulus, if necessary. Complete occlusion of the distal false lumen occurs in less than 10% of the cases,[1059] and the residual false lumen may develop into an aneurysm in the future. It has been recently reported that the insertion of an open stent graft/FET from the distal arch to the descending aorta can prevent malperfusion and future aneurysm formation.[1060–1062] However, its indications should be carefully considered as it may prolong the surgical time and increase the complications. The details are described in the subsequent sections.

2.2 Acute Stanford Type A Aortic Dissection

2.2.1 Aortic Root/Ascending Aorta/Partial Aortic Arch Replacement

a. General Principle of Urgent Surgery

"Tear-oriented surgery", consisting of resection of the dissected aortic wall involving a tear (entry) and prosthetic graft replacement at the same site, is a fundamental procedure. Briefly, if a tear is present in the ascending aorta, ascending aortic replacement should be performed. If a tear in the aortic arch is present, proximal arch replacement or total arch replacement should be performed. If a tear in the proximal descending aorta is present, total arch replacement + ET insertion into the true lumen[1063,1064] or descending aortic replacement should be performed. Recently, open stent-graft (FET) insertion has been applied for many cases expecting that distal aortic remodeling (false-lumen regression) could be achieved.[1065] There are few patients in whom acute dissection can be treated by direct closure of a tear.

Recently, with the improvement of surgical results, total arch replacement and ET/FET insertion has been performed in patients with a tear in the arch, arch branch, or descending aorta or those with Marfan syndrome. The recent results are favorable.[1066] Each technique is described below.

b. Ascending Aortic Replacement

Median sternotomy is a standard surgical approach. Cardiopulmonary bypass is established by superior/inferior vena cava or right atrial drainage and the femoral artery,[1067] true lumen of the ascending aorta,[1068] axillary artery,[1069] or cardiac apex[1070] are selected as the site of arterial/aortic return. If patients have cerebral or abdominal organ malperfusion, multiple cannulation sites such as the combination of ascending aorta and axillary artery, or ascending aorta and femoral artery are favorable in some cases. If a tear is present in the ascending aorta, ascending aortic replacement can also be performed under aortic cross-clamping. However, the aortic cross-clamping on the fragile dissected aortic wall may lead to aortic injury; strict caution is needed. The current standard organ protection method is deep hypothermic circulatory arrest.[1071] At this time, retrograde cerebral perfusion through the superior vena cava is combined for the brain protection in some cases.

With regard to surgical details the ascending aorta is opened under deep hypothermic circulatory arrest to confirm the site of a tear, which is resected with the surrounding aortic wall. After determining the extent of replacement, prosthetic graft replacement is performed. Aortic cross-clamping is not applied for distal anastomosis, and open distal anastomosis is usually performed under deep hypothermic circulatory arrest. Furthermore, when a tear is present in the distal side of the ascending aorta or proximal side of the aortic arch, hemiarch replacement could be performed: the tear is resected, and an oblique incision is extended on the aortic arch lesser curvature side and the hemiarch replacement completed with an obliquely cut prosthetic graft. Simultaneously, it is important to perform prosthetic graft anastomosis after false-lumen closure with inner and outer reinforced felt strips so that blood may flow in the true lumen alone.

The principle of surgical treatment is to resect the site of a tear and save the patient's life. However, extensive graft replacement is recently selected more to obtain the descending aortic remodeling. Total arch replacement with reconstruction of arch vessels has been selected more rather than ascending aortic/hemiarch replacement in relatively young, low-risk patients[1072] or those with enlargement of the aortic arch or dissection of arch vessels associated with cerebral malperfusion.[1073] Many studies reported that this procedure could be performed without increasing the surgery-related mortality rate or incidence of postoperative complications, but few studies have demonstrated its superiority in the long-term survival rate.

On the other hand, on the proximal side, to minimize residual dissection, the aortic wall is resected just above the sino-tubular junction (junction between the sinus of Valsalva and ascending aorta). When a false lumen remains, it could be closed by infusing a biological glue or surgical adhesive into the false lumen, and reinforced with felt strips for stump-trimming. Subsequently, a prosthetic graft should be sutured. There are three methods: stump-trimming with inner and outer felt strips alone, Teflon felt insertion into a false lumen,[1074] and reinforcement by adventitia inversion technique.[1075]

c. Treatment for Aortic Valve Insufficiency

i. Aortic Valve Resuspension

When aortic dissection at the site of the aortic valve commissure (especially the commissure between the right and noncoronary cusps) causes the prolapse of the aortic valve towards the left ventricle, resulted in valve regurgitation. A technique to resuspend the aortic commissure, close the proximal false lumen with a biological adhesive material, and anastomose the stump with a prosthetic graft on the distal side of the coronary artery (supra-coronary) is available, excluding patients with annuloaortic ectasia, which accompanies with Marfan syndrome, or organic aortic valve lesions.[1076] Several studies indicated that the long-term results of aortic valve resuspension were similar to those of root replacement (Bentall procedure) using a prosthetic graft with a prosthetic valve described below. Considering the postoperative quality of life (QOL), this technique should be initially performed.[1077,1078] For this technique, closure with a biological glue or surgical adhesive is highly useful, but some studies reported intimal necrosis or pseudoaneurysm formation caused by the tissue toxicity of a surgical adhesive.[1079,1080] Much attention must be paid so that the use of its volume may be minimized.

ii. Aortic Root Replacement

Bentall procedure[1081] is indicated for patients with a tear/entry in the sinus of Valsalva or those with annuloaortic ectasia. Currently, button Bentall procedure is used as a standard technique.[549] In addition, recently, VSRR such as Yacoub's remodeling method[562] and David's reimplantation method,[1082] has been attempted. These techniques are indicated for patients without abnormalities of the aortic valve leaflet. They are advantageous in that postoperative anticoagulant therapy is not required, but operations are more demanding than Bentall procedure, requiring skills. However, recently, favorable results have been reported even when patient selection was not conducted[569] in addition to cases in which malperfusion-free patients with stable hemodynamics were selected.[570,571] Favorable long-term results over 20 years were reported from the University of Hanover.[568]

2.2.2 Aortic Arch Replacement

a. Procedure

If an entry is present in the arch, ascending/total arch

replacement is most desirable from the viewpoint of aortic dissection treatment, which is principally the resection of an entry.[1083] Also, total arch replacement is indicated for patients who require repair of the arch due to its complicated dissection, patients with malperfusion of the arch branch, patients with an entry in the arch branch, and patients with an aneurysm in the arch or enlarged arch. Type A dissection in patients with hereditary connective tissue disorders, such as Marfan syndrome and Loeys-Dietz syndrome, is indicated for total arch replacement because enlargement below the aortic arch is often observed in the chronic stage after ascending/hemiarch replacement, even if the entry is present in the ascending aorta.[1084,1085]

For total arch replacement, use of the ET method is recommended, in which prosthetic graft with a diameter of 18–22 mm and a length of approximately 5–10 cm is inserted into the true lumen of the descending aorta like a windsock, aiming to reinforce from the intima side, to prevent leakage of anastomotic site, to close the peripheral false lumen, and to facilitate additional treatment for the enlargement below the descending aorta.[750,1063,1086] In addition, some Type A dissection patients have an entry in the descending aorta,[1087,1088] for which total arch replacement + ET method by a median sternotomy is expected to lead to the closure of the thrombus in the peripheral false lumen, rather than resection of the entry with a left thoracotomy and distal arch/descending aortic replacement.[1089]

With regard to the surgical techniques for total arch replacement, a stump is first formed to close the residual false lumen on the peripheral side (combined use of the ET method), and a 4-branched prosthetic graft for arch reconstruction is sutured. Subsequently, a central aortic anastomosis is performed to sequentially reconstruct the 3-arch branches, or it is preceded by the reconstruction of the 3-arch branches. On the other hand, the surgery of inserting FET into the descending aorta to perform total arch replacement has been observed to increase in the recent years.[1090–1092] The FET method is known to have a slightly higher rate of false lumen occlusion than the conventional ET method; however, it results in SCI and a new entry (stent graft-induced entry flow) in the late stage. The details of FET are described in the next section ("**2.2.3 Frozen Elephant Trunk**").

b. Results

Advances in diagnostic imaging have enabled the early diagnosis of aortic dissection immediately after its onset. Also, its treatment results have been improving due to advances in cerebral protection and improved heart-lung machine, as well as the introduction of various hemostatic materials. In particular, its results in Japan have been favorable, even compared to other countries in the world.[1072,1093,1094] Whether this difference in the results is due to racial differences, surgical techniques, or systems, such as patient transport and speed up to the acceptance of urgent surgery, should be investigated in the future.

According to the academic survey conducted by the Japanese Association for Thoracic Surgery, of the 5,461 cases of acute aortic dissection registered in Japan in 2016, 1,426 cases of total arch replacement without root replacement showed a 30-day mortality rate of 9.0% and an in-hospital mortality rate of 11.3%.[43] According to the report by IRAD, total arch replacement was performed in 334 of the 1,241 enrolled cases, and their in-hospital mortality rate was 17.1%.[1095] Of the 2,137 cases enrolled in the German Registry for Acute Aortic Dissection Type A (GERAADA), total arch replacement was performed in 346 cases, and their 30-day mortality rate was 22.3%.[1096]

Since total arch replacement, which is an extended surgery compared to ascending/hemiarch replacement, is considered more invasive, ascending/hemiarch replacement is considered to be sufficient as a life-saving surgery for acute aortic dissection. However, it is difficult to determine the superiority or inferiority of the two surgical procedures based on the comparison of these results due to the different preconditions of the cases in surgery that principally involve the resection of an entry. In a meta-analysis comparing total arch replacement and hemiarch replacement for acute aortic dissection, Poon et al. showed that there was no significant difference in the results between the two surgical procedures.[1097] However, the data used in the analysis may have been obtained only from facilities with many cases and experienced surgeons. It was also reported that hemiarch replacement accounted for 85% of surgeries for acute aortic dissection performed in a facility.[1098] Therefore, it should also be noted that the replacement range does not need to be unnecessarily expanded as life-saving surgery in acute aortic dissection.

PQ 10.

What Are the Surgical Procedures That Should Be Carried Out for Acute Stanford Type A dissection, Ascending Replacement (Including Hemiarch), or Total Arch Replacement?

Recommendation

Patients with an entry in the arch-proximal descending aorta or supra-aortic vessel, enlarged aortic arch, Marfan syndrome, or young age are considered to be indicated for total arch replacement. However, the indications are judged comprehensively in consideration of the preoperative condition of the patient and the experience of the facility/surgical team.

The primary purpose of surgery for acute Type A dissection is to save the lives of the patients. Therefore, procedure selection requires appropriate judgment in consideration of the anatomical requirements, such as the entry site and the extension range of dissection, as well as the balance with the preoperative condition of the patient, such as the level of consciousness, presence of malperfusion, and age, and surgical invasiveness.

According to the annual report of the Japanese Association for Thoracic Surgery,[43] the numbers of patients undergoing ascending replacement (including hemiarch replacement), root replacement, arch replacement, and root-arch replacement for acute Type A dissection were 2,738, 190, 1,426, and 180, respectively, indicating that the number of patients undergoing ascending replacement was approximately twice that of patients undergoing arch replacement. The in-hospital mortality rates of these procedures were 10.4%, 22.1%, 11.3%, and 17.8%, respectively, showing that the mortality rates greatly differed depending on the use of root replacement. On the other hand, there was no large difference in the mortality rate between patients with and without arch replacement, and the selection criteria for arch replacement in Japan are currently considered valid, at least based on the early results.

The results of the report from JCVSD in 2015 and 2016[711]

also showed no difference between ascending replacement and arch replacement for acute aortic dissection (including Type A and Type B) in mortality rate (without arch replacement: 11.4%, with arch replacement: 11.4%), as well as the complication rates of cerebral infarction (10.8% vs. 11.9%) and paraplegia (3.0% vs. 3.4%), and a significant difference was observed only in renal failure (10.3% vs. 12.0%, P<0.05).

Previously, it was presumed that the procedure should be limited to ascending replacement (including hemiarch replacement) even if an entry is present in the arch, in consideration of the invasiveness of treatment. However, it has been shown that arch replacement has a higher rate of distal false lumen thrombosis in the chronic stage than ascending replacement and that it has low risks of false lumen enlargement and reoperation.[1097,1099,1100] Given its favorable early results, arch replacement based on the principle of entry resection is recommended, at least for patients with an entry in the aortic arch or supra-aortic vessel.

Regarding surgery for false lumen enlargement in the chronic stage, descending replacement by an approach different from the initial surgery (left thoracotomy) or TEVAR can be performed without difficulty after arch replacement. However, patients who have not undergone arch replacement require highly invasive surgery, such as two-stage surgery with prior arch replacement by the same approach as the previous surgery (median incision) and surgery requiring left thoracotomy/circulatory arrest. Thus, performing arch replacement in the initial surgery is also advantageous in this aspect.

In ascending/hemiarch replacement, patients with Marfan syndrome often exhibit enlargement of the aortic arch[1101] and events of the distal aorta[1102] in the chronic stage, even if an entry is present in the ascending aorta and is surely resected. Thus, total arch replacement should be actively considered if dissection is present in the aortic arch.[1063,1064,1066]

Also, if an entry is present in the descending aorta, total arch replacement using the ET method[750] facilitates the formation of peripheral false lumen thrombosis, which is also advantageous for additional treatment.[1088,1094,1103] Although the effectiveness of TEVAR for Type B aortic dissection has been shown in the recent years, evidence of the treatment effect of TEVAR for Type A dissection with an entry in the descending aorta has been scarce, and it is not commonly performed, at least currently. The open stent graft method[749]/FET method[592] enable more reliable entry closure of the proximal descending aorta,[1065] and they were reported to facilitate the formation of false lumen thrombosis and to suppress aneurysm enlargement in the chronic stage, in addition to improving blood flow in true lumen and organ malperfusion in the acute phase.[1060–1062,1104,1105] The ability to perform peripheral anastomosis in a shallower surgical field in comparison to conventional arch replacement has also been a driving force for the dissemination of total arch replacement. If its problems, such as an increase in SCI and stent graft-induced new entry flow can be resolved, the indications of total arch replacement using the FET method may be further expanded in the future.

On the other hand, there is no need to perform arch replacement for all cases of acute Type A dissection, Long-term results of ascending replacement (such as death and reoperation) were reported to be comparable to those of arch replacement if arch replacement is selected based on the indications of the presence of an entry in the arch, an arch aortic diameter of 40 mm or larger, and the presence of malperfusion in the arch branch.[1073] Moreover, it has been pointed out that the proficiency level of the facilities/surgeons and the preoperative condition of the patients should also be taken into consideration for procedure selection since the early results of arch replacement are not comparable to the results of ascending replacement at all facilities.[1097,1099]

Regarding surgery for acute aortic dissection, we should select a procedure that aims to first achieve favorable early results and then improve the long-term results.

2.2.3 Frozen Elephant Trunk (FET)

a. History

In total arch replacement for acute aortic dissection, Kato et al. developed the procedure of inserting a stent-prosthetic graft into the descending aorta on the distal side, aiming for the true lumen enlargement/false lumen closure in the distal aorta.[749] While this was initially called "open stent" or "surgical stent," it is now often called "frozen elephant trunk (FET)"[592] as it uses an elephant trunk (ET)[750] equipped with a stent. The use of FET began with self-build devices in a limited number of facilities,[749,1091,1106–1108] and it rapidly became widely used after the approval of domestic commercial devices in 2014.[1109] While branched FET devices are used overseas, the devices approved in Japan lack arch branches, thus requiring the addition of a branched arch graft for arch replacement.

b. Indications

FET is indicated for both distal arch true aneurysm and aortic dissection (acute and chronic). FET is performed for acute aortic dissection to further promote thrombus closure of the distal false lumen and enlargement of the true lumen, which has been demonstrated by normal ET.[1094,1103] In particular, patients with malperfusion, an entry (tear) in the distal arch or proximal descending aorta, and relatively young age are well indicated for FET.[1110]

c. Sizing and Insertion Location

The sizing of FET is controversial, as it differs between a true aneurysm and aortic dissection. For acute dissection, the aortic diameter of the landing site at the distal end of the FET[1111] or its 90%[1109] has been recommended. However, the use of FET for acute dissection mainly aims to stabilize (fix) the dissected intima, and a smaller FET with a diameter equal to that of the true lumen (resulting in 90% of the aortic diameter or smaller) has often been selected in the recent years due to a concern about a new entry on the distal side caused by FET (stent graft-induced entry, SINE). At the beginning of its dissemination, a short stent (6 cm) was inserted at a shallow (T5-T7) and close position because of a concern about the occurrence of SCI;[1109] however, an increasing number of facilities have been carrying out the insertion of a longer stent into the straight descending aorta to prevent bending of the graft portion (described below) and the occurrence of SINE.

d. Results

The in-hospital mortality rate after total arch replacement with FET for acute aortic dissection was reported to be

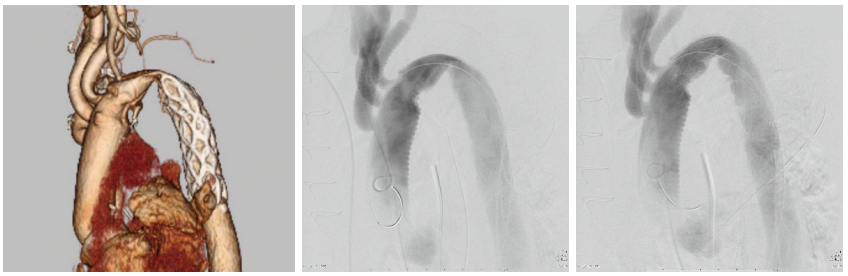


Figure 61. Severe stenosis of a graft in the steep aortic arch and its treatment.

Table 35. COR and LOE for the Diagnosis and Treatment of Coronary Artery Malperfusion in Acute Stanford Type A Aortic Dissection

	COR	LOE
It is recommended to evaluate the presence or absence of myocardial ischemic changes preoperatively by a 12-lead electrocardiogram, and the presence or absence of asynergy is evaluated with echocardiography[1127,1128]	I	C
It is recommended to evaluate the presence or absence of myocardial ischemia occurrence intraoperatively by transesophageal echocardiography[212]	I	C
It is recommended to perform CABG with a venous graft for coronary artery malperfusion that cannot be improved by prosthetic graft replacement alone[1128]	I	C
If dissection is diagnosed during emergency catheterization, coronary artery recanalization with catheter intervention should be considered when the preparation for open surgery is started[1129,1130]	IIa	C
Preoperative coronary artery recanalization by catheter intervention may be considered if the hemodynamics fail due to coronary artery malperfusion and it is difficult to start open surgery promptly[1129,1130]	IIb	C

CABG, coronary artery bypass grafting; COR, class of recommendation; LOE, level of evidence.

5–18.2%.[1106,1109,1111–1114] The remodeling rate of the descending aorta is higher than that of normal ET.[1104] Additionally, compared to ascending replacement, total arch replacement for acute dissection improves the long-term prognosis due to this remodeling effect when FET is deployed in combination.[1061,1105,1115,1116] In addition, FET in the acute phase has a higher remodeling rate of the thoracic descending aorta than FET in the chronic stage (33% vs. 17.5%),[1117] and it has a lower retreatment rate.[1109,1111,1114] Perioperative paraplegia (including transient paraplegia) occurs in 0–22%.[1108,1109,1111–1114,1118–1121] Additionally, its incidence is increased by intraoperative hypotension and the narrowing of the true lumen (cutoff) due to graft bending or residual peripheral dissection.[1107,1122] The incidence of peripheral SINE due to FET is 5% or lower, and half of its cases do not require additional treatment or can be treated with TEVAR.[1123] For the prevention of SINE, it is recommended to deploy the distal end of FET in the straight portion of the descending aorta. It has been reported that the non-stent area results in stenosis with graft bending when a steep arch is present (**Figure 61**), and a device should be inserted such that the stent part is placed at the curved area of the arch.[1124] The early/intermediate results of FET were reported to be relatively favorable even in acute dissection patients with Marfan syndrome.[1125,1126] However, if an entry is located adjacent to the distal end of FET, and for patients with a small true lumen and strong tortuosity as they exhibit a high incidence of complications, the method is not recommended.[1125]

2.2.4 Malperfusion

a. Coronary Artery (Table 35)

Coronary artery malperfusion occurs when aortic dissection reaching the aortic root leads to the occlusion of the coronary ostium with a flap or when dissection spreading to the coronary artery leads to the occlusion of the true lumen by the compression of the false lumen. Coronary artery malperfusion often occurs concurrently with the onset of aortic dissection; however, it occurs with a delay in some cases. Also, it was reported to occur due to increased false lumen pressure at the start of extracorporeal circulation in surgery, and its occurrence was observed after the release of aortic cross-clamping or the completion of surgery due to residual dissection in the Valsalva sinus following supra-coronary prosthetic graft anastomosis.[1131] The incidence of coronary artery malperfusion in patients with acute Type A aortic dissection is 5.7–14.9%; however, it varies depending on whether the report targets only the cases of preoperative ischemia or whether it includes intraoperative and postoperative occurrences.[1127–1129,1132–1140] With regard to its laterality, several studies have reported its more frequent occurrence in the right coronary artery,[1136,1141] which may be because the extension of dissection to the aortic root tends to occur on the greater curvature side. However, no laterality was observed when non-surgical cases were also considered, and some suggested that this is because many patients with left coronary artery ischemia rapidly progress to circulatory collapse and die before surgery.[1140,1141]

Acute Type A aortic dissection with patent false lumen has a low complication rate of atherosclerotic lesions in the coronary artery.[1142] Coronary artery malperfusion complicating aortic dissection suddenly develops at the coronary artery bifurcation in patients with no history of angina, with rapid progression of myocardial necrosis. In complete occlusion, highly advanced myocardial necrosis occurs with recanalization beyond 90 min after the onset.[1143] The treatment results of PCI for acute myocardial infarction due to left main coronary artery trunk occlusion are poor with an early mortality rate of 11–44%.[1144] On the other hand, right coronary artery malperfusion is also complicated by right heart failure associated with right ventricular infarction, making its perioperative management difficult.

Neri et al. classified 24 patients with coronary artery dissection into 3 types according to the occlusion mechanism. Type A has occlusion in which the dissection is located at the ostium, while Type B has occlusion in which the dissection has extended to the coronary artery. Type C has occlusion due to a rupture of the coronary artery intima. Also, they performed the button formation at the origin of the coronary artery in Type A, patch formation by longitudinal incision of the coronary artery in Type B, and root replacement after resecting coronary artery occlusion site and interposing venous graft in type C. The mortality rate of the patients was reported to be 21%.[1127] In Japan, Kawahito et al. performed ascending aortic replacement with the addition of coronary artery bypass surgery on 12 patients with coronary artery malperfusion (9 patients had preoperative ischemia) without performing aortic root replacement, and its mortality rate was 33.3%.[1128] Another report showed the deaths of 45% of patients with left coronary artery malperfusion (11 patients) and 22% of patients with right coronary artery malperfusion (9 patients), indicating that the former has a higher mortality rate.[1135]

Types A and B coronary artery dissections, classified by Neri, do not require coronary artery bypass and aortic root replacement if central repair is performed with the resection of the entry. However, caution is needed for type C dissection, as it can be diagnosed by the leakage of anterograde cardioplegic solution into the false lumen when it is injected from the coronary ostium. In this case, coronary artery bypass and ascending aortic replacement leave an entry in the root dissection cavity. In addition to coronary artery bypass, ascending replacement and ligation of the origin of the coronary artery or root replacement are required.

In 2000, Barabas et al. reported surgical cases for acute Type A aortic dissection after stent deployment in the left main coronary artery trunk.[1145] In Japan, Imoto et al. reported similar cases in 2005.[1146] Subsequently, of 75 patients with dissection spreading to the coronary ostium (48 patients had preoperative ischemia), preoperative coronary artery recanalization with coronary artery stent was performed on 7 patients (right: 4 patients, left: 3 patients), which was shown to prevent postoperative low output syndrome.[1130] In addition, Uchida et al. of the same facility performed coronary artery stent deployment in 14 patients (left: 8 patients, right: 6 patients), 11 (left: 5 cases, right: 6 cases) of whom underwent central repair, and they reported that the lives of the patients were saved in all surgical cases.[1140] There have been similar case reports, most of which focused on patients with left coronary artery malperfusion.[1147–1157]

However, the preoperative deployment of coronary artery stent is not easy in patients with acute Type A dissection. The treatment may be unsuccessful because of an aberrant catheter into the false lumen or restriction of catheter operation due to flap movement. In addition, preoperative coronary artery stent deployment delays central repair, leading to poor results. Whether coronary artery stent deployment should precede in patients complicated by coronary artery malperfusion is determined based on circumstances in each facility. In some cases, urgent coronary angiography has been initiated with the diagnosis of acute myocardial infarction without being aware of the presence of acute Type A dissection. Such cases can be treated promptly and effectively if coronary artery stent deployment is performed on-site concurrently with surgical preparation. A close cooperation between cardiologists and cardiovascular surgeons is essential.

The management of deployed stents also poses a problem. While intraoperative stent removal may cause intimal injury, a stent that is left without being removed leads to a risk of subacute thrombus occlusion of the stent. Since this risk is further increased by insufficient expansion of a stent to the coronary artery diameter, strict antiplatelet therapy is essential.

On the other hand, rapid diagnosis by transesophageal echocardiography is important for coronary artery malperfusion that occurs during central repair.[212,1158] Left ventricular wall motion needs to be evaluated at the start of extracorporeal circulation, as well as at the time of aortic cross-clamping release. Serious myocardial damage can be avoided by early aortic cross-clamping and cardiac arrest with the injection of cardioplegic solution at the start of extracorporeal circulation or by coronary artery bypass with venous graft after the release of aortic cross-clamping.

Table 36. COR and LOE for the Treatment of Acute Stanford Type A Aortic Dissection With Cerebral Malperfusion

	COR	LOE
Central repair for carotid artery malperfusion with acute dissection should be considered to improve carotid artery blood flow in the hyperacute phase[1058,1159–1161]	IIa	C

COR, class of recommendation; LOE, level of evidence.

b. Brain (Table 36)

Cerebral ischemic symptoms associated with acute aortic dissection can be divided into consciousness disturbances, such as coma, and local nerve injury, such as hemiplegia. Its causes are broadly divided into malperfusion due to dissection of the arch branch, thromboembolism on the distal side of the arch branch dissection, hypotension (myocardial ischemia and systemic circulatory failure due to cardiac tamponade or massive hemorrhage), and mechanical compression of the cerebral nerve. Multiple factors, such as decreased blood pressure due to cardiac tamponade, may be involved in stenosis of the true lumen of the arch branch. The rate of dissection spreading to the arch branch due to acute type A dissection is said to be 5–46%.[95] In particular, dissection of the brachiocephalic artery is likely to be associated with acute type A dissection, and in fact, dissection often extends to the right common carotid artery in patients with cerebral ischemic symptoms.

In a study of autopsy cases, 42.2% had dissection in the arch branch.[24] However, dissection spreading to the carotid artery does not always cause clinical cerebral ischemic symptoms, and less than 20% of patients have persistent nerve injury since most cases develop a tear (re-entry) in the periphery of the arch branch.[69,1162,1163]

Whether patients with acute dissection-related cerebral ischemia should receive urgent central repair or medical (conservative) treatment is controversial.[75,96,1164–1166] Central repair using normal extracorporeal circulation may cause cerebral hemorrhage (post-infarction cerebral hemorrhage) and extensive cerebral edema. On the other hand, patients with persistent neurological signs, such as consciousness disturbance and hemiplegia, and highly unstable acute dissection have a considerably high in-hospital mortality rate of 36.2–55.9%.[1167] In particular, malperfusion of the carotid artery is a sign of poor prognosis, and the results of its medical treatment are markedly poor, with a survival rate of 10% or lower.[1168–1170]

However, the usefulness of hyperacute-stage surgery has become clear in the recent years.[1058,1159,1171–1173] It has been reported that 80% of cases achieved neurological improvement when central repair was started within 10 h of onset.[1159] Improvement of neurological signs was seen even in 86% of patients complicated by severe consciousness disturbance, such as coma, when they were transported to the surgery room within 5 h of onset.[1058] Therefore, minimizing the time from onset to surgery is expected to improve the treatment results of central repair even in patients with severe cerebral ischemic symptoms. Furthermore, direct perfusion to the common carotid artery with a relatively little dissection,[1160] as well as extra-anatomical aorta-carotid artery bypass surgery aimed at minimizing the cerebral ischemia time before central repair, was also reported to be useful.[1161] In addition to performing surgery at the earliest timing, it is important that central repair uses the deep-hypothermic therapy in combination with selective cerebral perfusion to appropriately protect the brain and to reliably reconstruct the blood flow in the dissected arch branch. From this viewpoint, some facilities prefer partial arch replacement that requires a shorter time compared to total arch replacement, replacing only the brachiocephalic artery to which dissection is likely to spread.[1170]

c. Abdominal Viscera, Kidneys, and Lower Limbs

i. Incidence, Pathological Condition, and Prognosis

Ischemia of the abdominal viscera, kidneys, and limbs caused by malperfusion is found in 5.8%, 8.7%, and 12.6% of patients with acute type A dissection, respectively, and the odds ratios for early mortality (within 30 days) are high at 3.24 for abdominal visceral ischemia and 1.43 for limb ischemia.[1138] On the other hand, acute Type B dissection has a slightly high incidence of abdominal visceral ischemia of 7.1%, and several patients are complicated by renal or lower limb ischemia, with a high risk of postoperative in-hospital mortality (odds ratio of 4.44).[1174] In particular, intestinal ischemia leads to intestinal necrosis approximately 4 h after the occurrence of ischemia, ultimately progressing to peritonitis and multiple organ failure. In addition, even with reperfusion, lower limb ischemia with an ischemia time exceeding 3–4 h causes myonephropathic metabolic syndrome, adversely affecting the whole body. These indicate the importance of the time until treatment in lifesaving, and rapid transport to a facility capable of providing open surgery and endovascular treatment (including hybrid surgery) with a team of cardiac and vascular surgeons is needed,[1175] for which a prompt diagnosis is desirable.

Dynamic and static obstructions can be evaluated in radiation diagnosis.[1176] In the former, the flap pressed by the high pressure of the false lumen in the aorta blocks the entry of the branch, causing malperfusion; additionally, numerous cases exhibit true lumen stenosis in the central aorta, which reduces the blood flow reaching the branch level. For this type of obstruction, aortic treatment is selected, which includes entry closure with stent graft and a device that dilates the true lumen of the central aorta. On the other hand, dissection in the latter extends to the branch artery, and the thrombosed false lumen occludes the true lumen ("dissecting hematoma" according to a report by Williams et al.[1176]), which is likely to occur in the absence of re-entry in the periphery. This type of obstruction often requires treatment for the branch artery (endovascular treatment or open surgery). Echographic examination, if it can be performed, allows for the real-time evaluation of true lumen blood flow of the aorta and branch artery, as well as the degree of false lumen thrombosis in the branches, which may be helpful in deciding the treatment policy.

ii. Diagnosis of Intestinal Ischemia

Diagnosis of intestinal ischemia is not always easy. While only approximately half of patients with ischemia complain of abdominal pain, it is also complained by approximately 20% of patients without ischemia.[77] Although the pain is likely caused by aortic dissection itself, it is difficult to distinguish the pain based on subjective symptoms alone. Physical examination does not reveal any obvious abnormal findings leading to necrosis, and it cannot be reliably diagnosed by any blood tests at the stage of ischemia.

Contrast-enhanced CT examination is performed as the standard diagnostic imaging method for intestinal ischemia, which can be diagnosed by a clear disruption of blood flow, dilation of the intestinal tract, or ascites. The ratio of the diameter of the superior mesenteric artery (SMA) to that of the superior mesenteric vein was reported to be a finding for suspecting intestinal ischemia before exhibiting irreversible changes;[1177] however, it does not correspond in many cases. Significant intestinal ischemia may occur even with contrast-imaged SMA.[1178] Although it is more reliable to examine the color tone of the intestinal tract directly with a laparotomy or laparoscopy,[1179,1180] aortic surgery may have to be prioritized in patients with unstable hemodynamics. In addition, localized intestinal necrosis may be overlooked under a small laparotomy or laparoscopy.[210] It may not be easily distinguished, even by visual inspection, before reaching complete necrosis; nevertheless, ICG (indocyanine green) contrast examination was shown to be useful.[1181]

Echographic examination, which can be performed quickly and easily, is also considered as an option. SMA can often be visualized by body surface echography, and attenuation of intestinal tract peristalsis is also a reference finding for suspecting intestinal ischemia.[213,1182] On the other hand, transesophageal echocardiography is useful when surgery is started without sufficient preoperative evaluation, when new malperfusion occurs intraoperatively, or when perfusion recovery needs to be confirmed in non-laparotomy cases (See "**3.6 Echographic Examination**" in **Chapter III**). Intestinal ischemia is strongly suspected if the true lumen diameter of SMA is smaller than half the diameter of the entire blood vessel.[214,215]

iii. Treatment of Intestinal Ischemia

Invasive treatments of intestinal ischemia include SMA revascularization using the great saphenous vein under laparotomy,[1183] stent deployment in SMA,[1184] and intimal flap fenestration in the aorta.[1185] In particular, endovascular treatment is becoming mainstream since its results are considered to be comparable to or better than those of conventional open surgery.[1186] The challenges in its invasive treatment are the prioritization of aortic surgery (central repair), SMA revascularization, and resection of the intestinal tract; however, they must be individually determined for each patient. Central repair is preceded if the patient has cardiac tamponade or severe malperfusion of other sites or if intestinal tract ischemia is not severe.[477,1162,1187] Reperfusion of SMA is prioritized if the prognosis is thought to improve by minimizing intestinal necrosis.[477,1136,1188] If both are urgent, central repair may be performed concurrently with temporary selective perfusion of SMA.[1189,1190] The hybrid surgery room is advantageous because central repair and endovascular treatment can be performed quickly in one room.[1175,1191]

iv. Renal Ischemia

The occlusion of bilateral renal arteries is rare, and it is often unilateral occlusion. Branch perfusion is often resumed by performing entry resection and aortic reconstruction with central repair for predominant blood flow in the true lumen (dynamic obstruction), although it does not resume in some cases. Stent deployment is performed for static obstruction of SMA if severe stenosis remains after central repair, including TEVAR.

v. Lower Limb Ischemia

The reported incidence of lower limb ischemia in acute Type B dissection varies in the range of 5.7–30.0%. When acute Type B dissection develops in patients who have received abdominal aortic replacement, lower limb ischemia occurs at a high rate of 75%.[479] Patients complicated by lower limb ischemia have a high in-hospital mortality rate,[1192] which is likely because of frequent complications by intestinal ischemia,[479,1193] resulting in myonephropathic metabolic syndrome. Therefore, early diagnosis of lower limb ischemia is important, although it is not easy in some cases. Many patients undergo thrombectomy with a Fogarty catheter for suspected acute arterial occlusion,[1194] and their lower limb pain is often masked by strong chest and back pain. Thus, dullness of the lower limbs, perceptual disorder, and movement disorder appear in only 15–20% of the patients.[479] Movement disorder of the lower limbs is caused by lower limb ischemia or spinal cord ischemia, and approximately half of the cases are bilateral limb ischemia.

Lower limb ischemia is treated by open surgery or endovascular treatment; however, comorbid malperfusion also needs to be considered. Surgical fenestration, which resects the flap after clamping the aorta above the celiac and renal arteries, is performed for patients complicated by abdominal visceral ischemia or renal ischemia. Also, femoral-femoral artery bypass surgery is performed for patients with unilateral ischemia of the lower limb alone, whereas axillary-bilateral femoral artery bypass surgery is performed for patients with bilateral ischemia. For endovascular treatment, entry closure by TEVAR, stent graft deployment on the peripheral side of the aorta and the iliac artery region, and endovascular fenestration (funnel technique that deploys a balloon only or a stent[1192]) are selected.

While a Doppler blood flow meter is used to evaluate perfusion of the peripheral lower limbs, measurement of regional oxygen saturation (rSO_2) in tissue by near-infrared spectroscopy has also been used.[1195] After the resumption of perfusion, attention must be paid to myonephropathic metabolic syndrome and compartment syndrome. For the former, hemodiafiltration is used as needed to save the lives of patients.[1196] In the latter, muscle edema increases the intrafascial pressure several hours after the onset of malperfusion, which may cause a new blood circulation disorder in the muscle septum and myonecrosis. In addition to palpation, fasciotomy is immediately performed on patients with an intrafascial pressure of 30 mmHg or higher to prevent further exacerbation of compartment syndrome.

2.2.5 Medical Treatment

a. Type A Aortic Dissection With Thrombosed False Lumen

There have been disagreements between Western and Asian countries regarding the treatment strategies for Type A aortic dissection with thrombosed false lumen which is generally known as aortic intramural hematoma (IMH), and opinions on the treatment strategies often differ between surgeons and physicians, even in Japan.

In South Korea, Song et al. reported that aortic dissection with thrombosed false lumen differs from aortic dissection with patent false lumen in several clinical aspects.[1030] With regard to the patient background, aortic dissection with thrombosed false lumen is more common in older adults, and it exhibits fewer complications, such as aortic valve insufficiency and cerebral infarction. In addition, its medical treatment has led to favorable results, and initial medical treatment is recommended for patients without any complications (uncomplicated dissection).[1197] Even in Japan, several hospitals provide initial medical treatment for patients without any complications.[1198–1200] One study reported that initial medical treatment in type A aortic dissection patients with thrombosed false lumen followed by urgent (within 24 h) or semi-urgent surgery (within 2–3 days) for those with increased thrombosed false lumen or those who developed a patent false lumen resulted in a low in-hospital mortality rate of 7% and a favorable long-term prognosis with a 5-year survival rate of 90%.[1031] Several similar results have been reported, mainly in Japan and South Korea.[1030,1054–1056,1197,1201,1202]

On the other hand, numerous studies have strongly suggested urgent surgery for Type A aortic dissection with thrombosed false lumen due to poor results of its medical treatment, mainly in Europe and the United States.[1049–1053,1203–1205] The 2010 thoracic aortic disease clinical practice guidelines prepared by a joint committee in the United States (AHA/ACCF guidelines) classified urgent surgery for Type A aortic dissection with thrombosed false lumen, which is also performed for aortic dissection with the patent false lumen, as Class IIa.[95,1206] In addition, the aortic disease clinical practice guidelines published by the European Society of Cardiology in 2014 (ESC guidelines) also classified the urgent surgery as Class I.[96] In particular, aortic dissection with thrombosed false lumen was reported to have favorable surgical results because of few malperfusion,[1052] which is the basis for recommending urgent surgery.

It should be noted that strict antihypertensive treatment (systolic blood pressure of ≤120 mmHg and heart rate of <60 beats/min are desirable) and follow-up by diagnostic imaging are required if medical treatment is selected in the

early stage. According to reports of medical treatment, approximately 30–40% of patients have shown the progression of dissection, for which surgery have been performed.[1031,1055,1056] On the other hand, patients with an aortic diameter of ≥48 mm,[1207] ≥50 mm,[1056,1208] and ≥55 mm,[1055] or with a thrombosed false lumen diameter of ≥11 mm[1207] and ≥16 mm[1055] have a high rate of dissection progression during medical treatment, and they are regarded as a "high-risk group."

Based on these, the current treatment strategy for Type A aortic dissection with thrombosed false lumen is considered as follows. First, patients complicated by myocardial ischemia, aortic valve insufficiency, or cardiac tamponade are indicated for urgent surgery. Also, early surgery should be considered for patients with obvious blood flow in the false lumen of the ascending aorta, as their dissection is considered to have transitioned to a ULP-type dissection (Note: Such cases with ULP are often regarded as aortic dissection with thrombosed false lumen; however, they were reported to have a poor prognosis.[1035,1209,1210] Thus, it should be noted that the guidelines in Japan regard this pathological condition to be different from the aortic dissection with thrombosed false lumen, defining it as "ULP-type dissection.") Furthermore, patients with an aortic diameter ≥50 mm or a thrombosed false lumen diameter ≥11 mm are regarded as the high-risk group, and early surgery is considered as desirable. However, urgent surgery is not always necessary for patients with stable condition, and they can likely be treated by semi-urgent surgery. An initial medical treatment may be given to patients other than those mentioned above; however, it is important that diagnostic imaging is frequently performed in medical treatment and that its course is followed up. Early surgery is recommended for patients exhibiting an enlarged thrombosed false lumen or blood flow in the false lumen of the ascending aorta during the course. Therefore, the circumstances in which surgery can always be performed are desirable and surgical indications should be examined by the "aortic team," taking the age and surgical risks of each patient into consideration. It is desirable to obtain informed consent for treatment, always taking into consideration the controversy that early surgery is desirable.

b. Retrograde Type A Dissection With a Tear in the Thoracic Descending Aorta

In general, patients with Type A dissection have a tear (entry) in the ascending aorta, from which the dissection often progresses in an anterograde manner. However, some patients lack a tear in the ascending aorta, and dissection progresses in a retrograde manner from a tear in the arch, descending aorta, or abdominal aorta. Among such patients of retrograde dissection, those with completely thrombosed ascending aorta are expected to show regression of thrombosed false lumen, which can be treated with medical treatment. Kaji et al. performed medical treatment on 14 retrograde dissection patients with completely thrombosed false lumen of the ascending aorta and reported a favorable long-term prognosis with a 5-year survival rate of 93%.[1211] In addition, it was reported that medical treatment of 16 retrograde dissection patients with completely thrombosed false lumen of the ascending aorta led to favorable results.[1212] Therefore, patients with completely thrombosed false lumen of the ascending aorta can be medically treated by performing diagnostic imaging frequently and following up the course while paying attention to the enlarged thrombosed false lumen and the presence of new blood flow in the false lumen.

When performing medical treatment, multidetector CT (MD CT) examination or transesophageal echocardiography must confirm that a tear is absent in the ascending aorta of the retrograde dissection and that the false lumen of the ascending aorta is completely thrombosed and occluded without blood flow. Regression of the false lumen cannot be expected if blood flow is found in the false lumen of the ascending aorta, for which medical treatment is not recommended.

2.3 Chronic Stanford Type A Aortic Dissection

2.3.1 Aortic Root and Ascending/Aortic Arch

In patients with chronic aortic dissection, the aortic wall is more rigid than in those with acute dissection, and aortic anastomosis is easier. In addition, false-lumen enlargement/aneurysm formation involving an extensive area is often observed, and the extended aortic replacement may be required. For the establishment of cardiopulmonary bypass, several points must be particularly considered due to chronic dissection, and surgical strategies must be selected in accordance with patients.

a. Establishment of Cardiopulmonary Bypass and Various Techniques

It is important to establish cardiopulmonary bypass safely. However, when retrograde perfusion is selected, organ perfusion is not always maintained. Usually, ascending aortic perfusion through true lumen is impossible in many patients with chronic Type A dissection. As sites for arterial cannulation, the axillary artery,[1213,1214] femoral artery, or cardiac apex[1215] are selected. It is important to carefully determine a site for arterial cannulation in accordance with patients. When dissection involving an aortic arch vessels may affect cerebral perfusion, the carotid artery should be transected at its periphery, and reconstructed with a small prosthetic graft so that cerebral perfusion may be accurately maintained through the true lumen.[1216,1217]

i. Repair of Aortic Valve Insufficiency

In approximately 80% of patients with acute dissection, aortic valve insufficiency is repaired by the aortic valve resuspension (the dissected aortic valve commissure is sutured/refixed with resuspension). Aortic valve plasty (±VSRR) is performed in patients with chronic dissection associated with aortic valve insufficiency, or, aortic valve replacement is selected. When aortic valve insufficiency is caused by advanced degeneration of valve leaflets, plasty/repair are difficult in many cases.

ii. Aortic Root Replacement With a Composite Graft

In patients with annuloaortic ectasia complicated by dissection, VSRR[549] or aortic root replacement using a composite graft (Bentall procedure) should be selected. For reconstruction of the coronary artery, the button technique is generally used, but the Piehler's technique with a small-diameter prosthetic graft interposition[557] is performed in some patients in whom mobilization of the coronary artery is difficult. For this method, short interposition graft should be used to prevent kinking. Concerning left coronary reconstruction, a interposed small graft is placed behind the main tube graft and anastomosed on the right side of the main graft (Svensson's method[558]).

iii. Valve-Sparing Aortic Root Replacement (VSRR)

Among patients requiring aortic root replacement due to enlargement of the Valsalva sinus or dissection involving the aortic root, VSRR with Yacoub's remodeling method[562] or David's reimplantation method[1082] is selected as long as the aortic valve leaflet is normal or repairable. In some patients with chronic dissection, deformity of the entire root and the valve leaflet caused by commissure detachment is observed, VSRR is difficult. Bentall procedure is indicated for the patients. If ascending aortic dissection has been repaired at the supra-coronary level followed by the aortic root enlargement or re-dissection, VSRR is often applicable.

b. Aortic Reconstruction With a Prosthetic Graft

The extent of replacement varies among aortic lesions. Open distal anastomosis under deep hypothermic circulatory arrest, is generally selected for the sufficient resection of fragile aortic wall, preventing mechanical injury by an aortic cross-clamping. For brain protection, selective antegrade cerebral perfusion is safe, but simple deep hypothermic circulatory arrest or retrograde cerebral perfusion is sometimes selected in some cases. In any cases, surgeons must pay meticulous attention for preventing air embolism by increasing venous pressure by the cessation of the venous drainage and head-down position should be maintained when the aorta is opened under circulatory arrest.

i. Ascending Aortic Replacement

Ascending aortic replacement is indicated if an entry (tear) is present in the ascending aorta, with no dilation of the arch (including DeBakey type II dissection). For peripheral anastomosis, open distal anastomosis is usually performed. To avoid additional aortic arch surgery in the remote phase, a prosthetic graft should be anastomosed with the true lumen, but the procedure should be carefully determined in consideration with maintaining brain/distal organ perfusion. There is also a method to prioritize the treatment of the proximal aorta under ascending aortic clamping during cooling (in the presence of moderate or severe aortic valve insufficiency), but the development of distal malperfusion caused by the aortic clamping must be considered, as described for acute-phase surgery. On the other hand, when prioritizing distal anastomosis, antegrade systemic perfusion is resumed through the side branch of a prosthetic graft after the completion of distal anastomosis, and ascending aortic replacement is accomplished by performing proximal anastomosis after false-lumen closure and stump trimming under rewarming. As described for acute-phase surgery, there is also a method to perform the proximal anastomosis with another piece of prosthetic graft, involving the aortic valve treatment, followed by the suture for both proximal and distal prosthetic grafts.

ii. Ascending Aortic/Partial Aortic Arch Replacement

When an entry (tear) is present on the lesser curvature side of the aortic arch, it is possible to obliquely resect the aortic arch involving the tear and replace the ascending aorta and lesser curvature side of the aortic arch (hemiarch replacement). When dissection involves an arch neck vessels, concomitant reconstruction of 1 or 2 branches (partial arch replacement) provides a secure round shaped anastomosis, facilitating the procedure with less postoperative hemorrhage and suture cutting. Even when a tear is present on the greater curvature side of the aortic arch, the condition can be repaired using the partial arch replacement in some cases. For this technique, a distal anastomotic site is located on the more proximal side in comparison with total arch replacement, and the procedure is easier, shortening the operative time.

2.3.2 Aortic Arch

The majority of patients with acute Type A aortic dissection are subject to urgent surgery after being diagnosed. Thus, those who cannot be diagnosed with acute Type A aortic dissection due to the minimal symptoms presented at onset are treated for chronic Type A dissection and are subject to elective surgery. In the present guideline, chronic aortic dissection after ascending replacement for acute Type A dissection is classified as a chronic Type B dissection. Thus, this section covers cases in which the aortic arch is surgically treated due to chronic Type A dissection, in addition to the ascending or aortic root. According to the 2016 annual report published by the Japanese Association for Thoracic Surgery, there were 1,261 surgical cases of chronic Type A dissection. Also, there were 296 cases of arch replacement, 51 cases of root to arch replacement, and 174 cases of FET, 164 cases of which also received total arch replacement. These accounted for 40% of all cases of chronic Type A dissection.[42]

Several chronic Type A dissections are DeBakey type II with a large entry, for which partial arch replacement with the reconstruction of the brachiocephalic and left common carotid arteries is often selected, in addition to ascending aortic replacement. Surgical strategies for extensive aortic dissection are required for patients with a dissection cavity in the arch/descending aorta, in addition to the ascending aorta. As it is difficult to perform one-stage ascending/arch/descending aortic replacement with left thoracotomy, a one-stage ascending arch-descending aortic replacement from bilateral anterior thoracotomy or median sternotomy (+left thoracotomy) is performed for patients who cannot be treated with staged surgery.[1218,1219]

However, aortic arch surgery with median sternotomy is generally performed as the initial surgery, and surgery on the descending aorta is performed in the second stage of staged surgery. Notably, ET or FET that induces blood flow to the true lumen of the descending aorta, in addition to aortic arch replacement, is also performed in the initial surgery.[1220] The patients showing a shrinking tendency of the residual dissection site due to progressed false lumen thrombosis of the descending aorta in the initial surgery can be followed up; however, patients showing an enlarging tendency of residual dissection site are indicated for the addition of TEVAR for the true lumen of the descending aorta or descending/thoracoabdominal aortic replacement by left thoracotomy. A careful follow-up is needed as some patients develop stent graft-induced new entry.[1221]

a. Anastomotic Methods

The aortic anastomosis can be performed more easily in patients with chronic aortic dissection than in those with acute dissection due to their stronger aortic wall. With a thickened adventitia, strong anastomosis can be performed even for the false lumen. Anastomotic methods include the double-barrel method, which anastomoses both the true and false lumina, and the method of anastomosing only the true lumen by angioplasty. The former has no risk of malperfusion; however, it is not expected to lead to false lumen thrombosis. Central anastomosis of chronic Type A dissection targets the true lumen for the entry resection. On the peripheral side, the false lumen is generally closed by angioplasty to induce blood flow to the true lumen of the

descending aorta, and after inserting ET or FET into the true lumen, vascular anastomosis is performed with the inserted graft. A site with small enlargement is selected as the anastomotic site since angioplasty is difficult with an enlarged anastomotic site, and the ascending aorta is selected in some cases. Insertion of ET or FET is difficult in patients with the highly compressed true lumen of the descending aorta. Thus, in some cases, the double-barrel method is used for peripheral anastomosis, or ET is inserted into the false lumen after the resection of the dissection flap. It has been pointed out that the insertion of FET into the true lumen of the descending aorta has the risk of developing stent graft-induced new entry.[1221] Oversizing of the stent graft and deployment at the tortuous arch site were reported to be risk factors.

b. Complications

See the section on chronic Type B dissection ("**3.2.4.f Precautions for the Management of Surgical Cases in the Chronic Stage**" in this chapter).

2.4 Reoperation

2.4.1 Background and Epidemiology

Most patients with acute Type A aortic dissection have an entry (tear) in the ascending aorta. Based on the principle of entry resection, the standard surgical procedure is ascending aortic replacement or ascending/aortic arch replacement. In consideration of the fate of residual dissection on the distal side (aiming for the disappearance of the false lumen below the descending aorta), whether total arch replacement should be performed during initial surgery is still controversial, as the level of recommendation differs depending on the site of entry, the range of dissection, and the experience of the facility and operator.

a. Postoperative Complications in the Late Stage

Aortic valve insufficiency after central repair based on the preservation of autologous aortic valve (supra-coronary repair), mainly aortic valve sling operation (suture and fixation of dissected aortic valve commissure), central/peripheral aortic aneurysm, sutural insufficiency (pseudoaneurysm), and re-dissection/re-canalization can be the causes of reoperation.

b. Aneurysm Formation at the Site of Residual Dissection

DeBakey type I dissection, which accounts for most of acute Type A dissections, remains in the distal aorta even after ascending and arch replacement. Thus, attention must be paid to the long-term extension and enlargement of residual dissection, as well as thrombosis formation in the false lumen. Sustained patency has been found in 46–78% of the residual false lumen on the distal side after the surgery of Type A dissection.[1222–1225] Postoperative survival cases with no enlargement of aneurysm diameter were reported to be 75% at 3 years, 59% at 5 years, and 43% at 8 years.[1226] Reoperation by prosthetic graft replacement or stent-graft deployment (TEVAR/EVAR) needs to be considered for patients exhibiting an enlarged aneurysm.

c. Reoperation Rate

According to the 2016 annual report of the Japanese Association for Thoracic Surgery, which was compiled based on JCVSD, the in-hospital mortality rate of reoperation cases of acute Type A dissection was 7.9%.[43] The causes of reoperation in more than 80% of patients were rupture, re-dissection, and enlargement of an aneurysm.[1227–1229] The freedom rates from reoperation 5, 10, and 15 years after initial surgery were reported to be 94%, 64%, and 35%, respectively,[1229] while the long-term reoperation rate after initial surgery (regardless of the procedure) was reported to be 4–28%.[1230] After ascending aortic replacement for acute Type A dissection (including cases of root replacement that required aortic valve repair), 104 of 592 patients required reoperation, and the time until reoperation was 5.2±5.3 years (0.1–29.3 years), with no relationship between the factors of reoperation and the time until reoperation.[1231] Naturally, the reoperation rate is high in patients who have undergone only ascending aortic replacement in the initial surgery[1232] (initial surgery includes both chronic and acute phases).

For the surgery of residual dissection and aneurysm beyond the distal arch, see "**3. Reoperation**" in **Chapter VII**. The present section outlines the reoperation of the central/peripheral anastomotic sites, including the aortic root.

Table 37. COR and LOE for the Reoperation for Stanford Type A Aortic Dissection

	COR	LOE
It is recommended to perform reoperation for residual aortic rupture or rapid enlargement of aortic diameter (≥5 mm/6 months)[384]	I	C
It is recommended to perform reoperation for the enlargement of residual aortic diameter (≥60 mm)[384,1233]	I	C
CT examinations 1, 3, 6, and 12 months after surgery, as well as every 6 months thereafter, should be considered for patients who underwent only ascending aortic replacement in the initial surgery[1231,1232]	IIa	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence.

2.4.2 Causes of Reoperation and Surgical Indications (Table 37)

The causes of reoperation include central anastomotic enlargement (including aortic root enlargement and aortic valve insufficiency), peripheral false lumen enlargement, and prosthetic graft infection. Basically, the indications for reoperation are the maximum minor axis of ≥55–60 mm and rapid enlargement (≥5 mm/6 months) based on normal true aneurysm, and reoperation is considered based on symptoms in addition to these indications.[384] If the patient has Marfan syndrome or other (hereditary) connective tissue disorders, it is necessary to advance the indications, such as setting the maximum minor axis to ≥45–50 mm.

2.4.3 Procedure and Precautions of Reoperation

Reoperation after the repair of Type A aortic dissection often requires re-thoracotomy (re-median sternotomy). Therefore, it is important to detach and secure the peripheral arteries and veins in advance for a blood supply/removal route, which allows for the instant establishment of extracorporeal circulation upon cardiac/great vessel injury. Several cases utilize unilateral or bilateral arteries and veins in the inguinal region that can be intubated directly and quickly. Although the axillary and subclavian arteries can be used, a blood supply tube with sufficient

thickness cannot be inserted into these in some cases, and a prosthetic graft with a diameter of approximately 8 mm is used as a blood supply route after anastomosis in such cases. Although this is inferior in the immediacy of establishing a blood supply route, it can be used in combination as a blood supply route for selective cerebral perfusion. If a fragile anastomotic pseudoaneurysm adheres to the back of the sternum, it is safe to first start extracorporeal circulation, and sternotomy is performed after cooling to a temperature range that allows for short-term circulatory arrest. If hyperextension of the left ventricle is concerning during cold ventricular fibrillation, it is also effective to reduce the blood supply pressure or to insert a vent directly into the left ventricular cardiac apex from the left 5th intercostal space.

When performing a sternotomy, measures to avoid an injury must be taken if an implanted prosthetic graft or its continuous aneurysmal lesion is close to or adhered to the back of the sternum. It is effective not to easily remove the sternal wire that has been implanted during the previous surgery and to use it as an invasion index of the sternal saw or a protective shield for organs. To avoid organ injury, it is also effective to carry out the guidance of the sternal saw and traction of the sternum itself to the ventral side, as well as to manually separate the adhesion between the back of the sternum and the prosthetic graft or the aneurysmal wall by making a small incision between the parasternal intercostals outside the pleura immediately prior to the sternotomy.

a. Aortic Root Enlargement and Central Anastomotic Pseudoaneurysm

Enlargement of the aortic root, concomitant aortic valve insufficiency with a moderate or higher degree, and anastomotic pseudoaneurysm are indicated for reoperation. The procedure is decided in consideration of age, surgical tolerance, lesions, and comorbidities. The passivity of coronary artery trunk or coronary artery entry point may be difficult after root replacement because of strong adhesion after the reconstruction of the coronary artery. Also, it may be difficult to make a coronary artery button due to tissue degeneration caused by surgical glue. In such a case, the Piehler method, which interposes a small-diameter prosthetic graft, is useful.

The incidence of complications during the reconstruction of the coronary artery in reoperation is high at 25–50%,[1234–1236] and perioperative myocardial infarction and unexpected addition of coronary artery bypass surgery are independent risk factors for early mortality.[1235,1237] In addition, several patients with aortic dissection do not have lesions of the aortic valve itself, and they, mainly those at a young age, may be indicated for VSRR. Furthermore, the procedure of preserving the prosthetic valve and replacing the root with the prosthetic graft is an option for patients who have undergone aortic valve replacement as initial surgery, if the prosthetic valve is a mechanical valve.[1238]

It should be noted that central anastomosis is reinforced with felt in most cases, and the excessive separation/removal causes injury to the right atrium, coronary artery, and pulmonary artery. In addition, some of surgical glues and hemostatics used during the initial surgery remain even after the reoperation, causing embolism, and attention must be paid to their careful removal. Some surgical glues may cause tissue degeneration under heavy use, and the strength of the residual tissue also needs to be considered.

b. Peripheral Anastomotic Pseudoaneurysm and Enlargement Beyond the Anastomotic Site

Total arch replacement is performed based on the procedure for true aneurysms. It should be noted that ascending and partial arch replacement or total arch replacement may be selected in the initial surgery for the DeBakey type III retrograde dissection, while leaving an entry (tear) below the descending aorta. In such cases, the false lumen below the descending aorta enlarges in the late stage. For this, one-stage or staged surgery using ET/FET or TEVAR in combination is considered. In reoperation with distal aortic anastomosis, great care must be taken in both the operation of the true lumen enlargement and the anastomosis, including excessive FET insertion, since the plasticity of dissection flap in the chronic stage is often poor. As with the central side, attention must be paid to the separation/removal of the outer felt and the management of surgical glues.

2.4.4 Procedure of Initial Surgery From the Viewpoint of Reoperation

According to a report by Kazui et al.,[1239] the patent false lumen remained on the distal side in most cases of ascending replacement for acute Type A dissection, and the aorta-related event avoidance rate, including reoperation, was reported to be 70% at 6 years. It was also reported that while the patent false lumen in the thoracic descending aorta was found in 50–70% of patients after ascending/partial arch replacement, it was found only in 30% after total arch replacement.[1091] In 1992, Crawford et al. reported that acute Type A dissection patients, even those with an entry in the ascending aorta, should be treated with ascending/total arch replacement, which can be performed in the same field of view, if they have no surgical risk factors.[1064] In fact, some have reported that the reoperation rate is reduced by performing extended surgery (root replacement or total arch replacement) to the possible extent in the initial surgery of acute Type A dissection.[1091,1231,1240–1242] However, extended surgery with insufficient preoperative information, including examinations before urgent surgery, as well as circulatory failure or organ ischemia due to aortic dissection itself, carries some risks. Thus, its indications need to be carefully determined as they may worsen early results during the initial surgery, which aims to save the lives of patients in several cases. In particular, various urgent surgeries are performed at night, which may be handled by facilities with a small number of cases or inexperienced surgeons, and the policy of giving first priority to lifesaving is important.

Total arch replacement may be an effective option for DeBakey type III retrograde dissection with an entry in the descending aorta because the patients are expected to exhibit an enlarged descending aorta in the late stage. In this procedure, FET is inserted into the descending aorta, or the ET method is performed for a sufficient landing zone, considering the possibility of additional TEVAR.

2.4.5 Results of Reoperation

In a recent report,[1233] the in-hospital mortality rate 30 days after reoperation was 7.0%, and the survival rates 1 year and 5 years after reoperation were 85.9% and 64.9%, respectively. Age and function of major organs, such as the brain, heart, lungs, kidneys, and liver, can affect the approach, procedure, and results. In fact, preoperative cardiac and renal functions were reported to be factors

affecting the in-hospital mortality in reoperation of the aorta with median sternotomy.[1243]

2.5 Endovascular Treatment (Table 38)

The FET method is the most applied stent-graft (SG) deployment for Type A aortic dissection. Normal TEVAR was performed on only 90 of 4,875 patients with acute Type A dissection (1.8%) and 161 of 1,211 patients with chronic Type A dissection (13.3%); however, these may include TEVAR performed after prosthetic graft replacement for DeBakey type III retrograde dissection and acute Type A dissection (data collected by the Japanese Association for Thoracic Surgery in 2015).[42]

In Type A dissection, an entry is most often found in the ascending aorta. Therefore, although open surgery (prosthetic graft replacement) is the first treatment choice, it cannot be easily performed in patients of advanced age, frailty, difficulty in reaching thoracotomy, reoperation, comorbidities such as heart failure and COPD, and refused blood transfusion due to religious reasons, in addition to severe malperfusion, such as dementia, advanced cancer, and cerebral disorders.[1247] Due to the poor prognosis of its medical treatment,[1248] TEVAR for entry closure is currently performed only in limited cases for which open surgery is difficult.

The closure of an entry in the ascending aorta by SG has been studied with a simulation using CT examination;[1249–1251] however, the possibility of its implementation has hardly been established. Branched and short SGs have been developed for the deployment in the aortic arch and ascending aorta, none of which is currently approved in Japan.

TEVAR for the ascending aorta performed immediately after the onset of acute Type A dissection has been reported since 2004.[1252–1254] In addition, there have been medium-scale reports on TEVAR performed not only in the acute phase but also in the subacute and chronic phases and TEVAR for the ascending aorta, including residual dissection and aortic aneurysm after prosthetic graft replacement.[389,1255–1261] However, these reports were based on limited indications using open surgery as the first choice, and their evidence is scarce due to varying disease stages and sites.

In DeBakey type III with an entry in the descending aorta, patients with retrograde Type A dissection extending to the ascending aorta generally have a favorable prognosis, including the cases in which thrombosis has formed in the dissection cavity of the ascending aorta, and it has been reported that they can be treated with medical treatment in the acute phase.[1211,1212,1262] In addition, TEVAR for retrograde Type A dissection has been reported since it was first described by Kato et al. in 2001.[1244–1246] The method is useful for closing the tear of the descending aorta that cannot be easily reached by prosthetic graft replacement with median sternotomy, and it may be considered a minimally invasive treatment for high-risk patients, such as older adults. However, if the dissection involves the enlargement of the ascending aorta or pericardial effusion, prosthetic graft replacement should also be performed. A similar effect is expected with the FET method. However, while TEVAR is minimally invasive, the FET method poses a concern about the recurrence of aortic dissection caused by a new intimal tear due to dissected central landing zone.

Table 38. COR and LOE for TEVAR for Stanford Type A Aortic Dissection

	COR	LOE
TEVAR may be considered for patients with retrograde Type A dissection due to an intimal tear of the descending aorta and who are at high risk of aortic arch replacement[1244–1246]	IIb	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

3. Stanford Type B Aortic Dissection

3.1 Acute and Subacute Dissection

3.1.1 Indications of Treatment: Overview

It is the most important for diagnosis to "suspect" acute aortic dissection based on clinical symptoms and basic laboratory findings.

Clinical symptoms/findings suggestive of acute dissection include sudden severe chest and back pain/precordial anxiety, shock vital, abnormal hypertension, consciousness disorder/paralysis of the lower limbs, abdominal pain, lower back pain, wandering pain, laterality in the blood pressure, blood pressure differences between the upper and lower limbs, and pulse deficit. Laboratory findings suggestive of acute dissection include enlargement of a mediastinal shadow on chest X-ray, pleural effusion, electrocardiographic abnormalities, increases in the leukocyte count and C-reactive protein (CRP) level on hematology, anemia, and an increase in the D-dimer level. In particular, the sensitivity of an increase in the D-dimer level is high, becoming an opportunity to promote further investigation under a tentative diagnosis of dissection.[98] Furthermore, findings, such as pericardial fluid retention on transthoracic echocardiography, aortic valve insufficiency, and enlargement of the Valsalva sinus, suggest acute aortic dissection. If acute dissection is suspected through the above examinations, diagnostic imaging, such as contrast-enhanced CT, should be performed. On imaging, Type A dissection should be differentiated from Type B. If a diagnosis of acute Type B dissection is made, complicated dissection should be differentiated from uncomplicated (See "**3.1.2.a Definition**" in this chapter).

Unlike acute Type A dissection, acute Type B dissection has a low mortality rate of approximately 10% with conservative treatment,[1192,1263–1265] therefore, medical treatment involving heart rate/blood pressure control and resting has been recommended for uncomplicated dissection patients without serious complications (sequelae) such as rupture and malperfusion.[1192,1263–1270] For medical treatment, target heart rate and blood pressure values are established, respectively; heart rate <60/min, 100≤ systolic blood pressure ≤120 mmHg.[1264,1266–1270] The persistence, resolution and recurrence of pain in the acute phase is the most important. If persistent/recurrent pain is present, emergency treatment should be considered under a diagnosis of complicated Type B dissection.[390,1271]

To treat complicated acute Type B dissection, endovascular treatment is recommended as invasive treatment.[386,1272] In the case of rupture, TEVAR should be prioritized unless there is concomitant aneurysm.[1273] In the case of malperfusion, extra-anatomical bypass, which had been routinely

Table 39. Predictive Factors for Chronic-Phase Enlargement in the Acute/Subacute Phases of Stanford Type B Aortic Dissection

Positive predictive factors	Negative predictive factors
Age: <60 years	Heart rate: ≤60/min
Heart rate: ≥60/min	Use of Ca antagonists
Marfan syndrome and genetic aortic disease	Aortic diameter: <40 mm
FDP: ≥20 μg/mL	Round true lumen/oval false lumen
Aortic diameter: ≥40 mm	Complete thrombosis/occlusion of a false lumen
Oval true lumen/round false lumen	A large number of entries/re-entries
False-lumen patency	
A false lumen or entry on the lesser curvature side	
Partial thrombosis/occlusion of a false lumen	
A single entry	
False lumen diameter: ≥22 mm	
large entry: ≥10 mm	

FDP, fibrin degradation product.

conducted in Japan, should not be indicated, excluding patients with static obstruction. Closure of a major entry by TEVAR (±aortic branch stenting)[386,1272,1274,1275] or fenestration (endovascular treatment or open surgery) at the abdominal aortic level should be performed in the patient with malperfusion.[140,477–481,1276–1279]

If complications similar to those in the acute phase appear in the subacute phase (within 3 months after onset) following the acute phase (within 2 weeks after onset), treatment should be performed in accordance with acute-phase strategy.[1280–1286]

On the other hand, in the patient of high-risk uncomplicated who has no serious complication but whose false lumen is expected to enlarge, preemptive thoracic entry closure: preemptive TEVAR within 1 year after onset is recommended.[385,396–400,1287–1292] (See "**3.1.3.a Definition**" in this chapter and **Table 39** for **PQ 11**). Concerning the timing of preemptive TEVAR, there is an opinion that it should be performed in the acute phase (≤14 days after onset),[1293,1294] but there is little evidence. To avoid retrograde Type A dissection, which relatively frequently develops after acute-phase TEVAR,[417] subacute- to early-chronic-phase (≤1 year) TEVAR, with a lower risk of retrograde Type A dissection, may be adequate.[390,1287,1295–1299] In the future, a randomized controlled trial (RCT) should be conducted under patient selection based on the prediction of enlargement.

PQ 11.
When Should We Perform EVAR for Stanford Type B Dissection?

Recommendation

TEVAR should be performed in acute-/subacute complicated cases.

Preemptive TEVAR in the subacute/early chronic phases should be performed in high-risk uncomplicated cases.

In this guideline, the indications for Type B dissection are

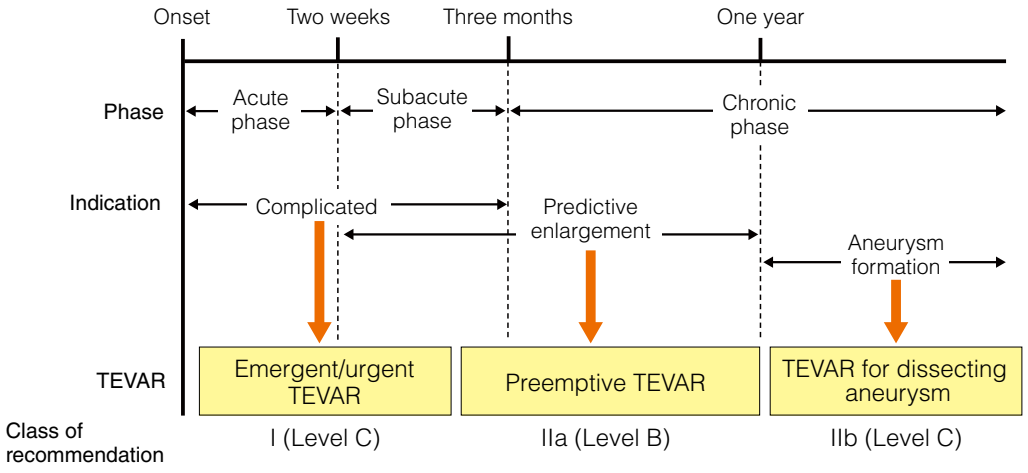


Figure 62. Stage of Stanford Type B aortic dissection and indication of TEVAR.

Table 40. COR and LOE for the Treatment of Complicated Acute/Subacute Stanford Type B Aortic Dissection		
	COR	LOE
As initial treatment in acute-phase, strict heart rate/blood pressure control is recommended; heart rate <60/min, 100 mmHg≤sBP≤120 mmHg[1264,1266–1270]	I	C
Acute-phase patients should be transported to an institution where emergent invasive treatment (endovascular or open surgery) is possible[68]	I	C
TEVAR is recommended for acute/subacute phases patients[384,386,390,399,1271,1272,1274,1275,1280,1288,1308–1311]	I	C
In acute-/subacute-phase patients with malperfusion, endovascular treatment (intravascular fenestration/endovascular stenting) should be considered[140,477–481,1276–1279]	IIa	C
In patients with malperfusion in whom endovascular treatment is difficult, open surgery (surgical fenestration/bypass) should be considered[1133,1278,1312–1315]	IIa	C
In patients with acute-phase rupture, for whom TEVAR is not indicated, prosthetic graft replacement should be considered[386,1272,1308–1310]	IIa	C
In patients for whom endovascular treatment is not indicated, total arch replacement with a frozen elephant trunk may be considered[1316]	IIb	C
In acute-phase patients, open surgery may be considered[1273,1312]	IIb	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

Table 41. COR and LOE for the Treatment of Uncomplicated Acute/Subacute Stanford Type B Aortic Dissection		
	COR	LOE
Medical treatment is recommended for acute-phase patients[1263–1270]	I	C
When the abdominal pain appears or repeats, or visceral branch malperfusion is suggested, repeated contrast-enhanced CT (early and delayed phases) or transabdominal ultrasound should be considered[390,1271,1363]	IIa	C
β-blockers should be considered as a first-choice drug[1264,1266,1267,1269,1270,1364–1367]	IIa	C
Follow-up by CT, contrast enhanced if possible, should be considered within 1 week after initial diagnosis[68,1269]	IIa	C
Transportation to an institution where emergent invasive treatment is possible in the acute phase should be considered[68]	IIa	C
Preemptive TEVAR should be considered in the subacute to early chronic phase for patients whose false lumen is expected to enlarge in the future: high-risk uncomplicated case[385,1287,1289]	IIa	B
Preemptive TEVAR may be considered in the acute phase[1293,1294]	IIb	B
Open surgery is not recommended in the acute phase	III	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

listed separately for acute-/subacute- and chronic-phase, which may cause confusion. Therefore, supplementary information regarding the stage and indications is provided here.

The indication of TEVAR for Type B dissection can be classified into three (**Figure 62**):

(1) Emergent/urgent TEVAR for acute-/subacute-complicated cases
(2) Preemptive TEVAR in the subacute to early chronic phases (≤1 year after onset) for high-risk uncomplicated cases
(3) TEVAR in chronic-phase for dissecting aneurysm cases

The first one represents TEVAR for complications (rupture, malperfusion) in the acute/subacute phases. (Refer to **Table 40** in "**3.1.2 Complicated Dissection**" in this chapter). The second one represents preemptive TEVAR for preventing future aortic events. The third one represents TEVAR for preventing rupture in chronic Type B dissection patients with false-lumen enlargement/aneurysm formation. When reviewing the indication of preemptive TEVAR, comparison with surveillance by medical treatment is necessary. When reviewing the indication of TEVAR in patients with dissecting aneurysm, comparison with surgery is necessary. Concerning the former, there is only evidence based on an RCT.[1287] However, concerning the latter, there is no evidence.

Preemptive TEVAR (TEVAR for preventing false-lumen enlargement) is indicated for chronic Type B dissection patients within 1 year from the onset, based on the results of the INSTEAD trial.[1287] This study involved patients with thoracic false-lumen patency/subacute to early chronic Type B dissection, within 1 year from the onset. A 2-year follow-up survey[1300] showed that the results (prognosis) of medical treatment were better, but the results of TEVAR were more advantageous through 5-year follow-up.[1287] Therefore, it cannot be recommended that

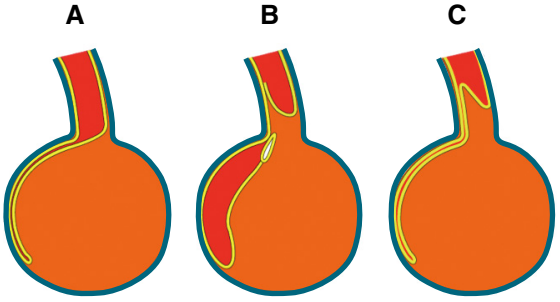


Figure 63. Classification based on the mechanism of malperfusion in aortic dissection. (**A**) Dynamic obstruction: Malperfusion with narrowing of the true lumen of the aorta. (**B**) Static obstruction: Malperfusion with the migration of the dissected intima into a branch orifice. (**C**) Mixed-type obstruction: Malperfusion with a combination of **A** + **B**.

TEVAR should be indicated for all patients with false-lumen-patent Type B dissection. Currently, it is recommended that TEVAR should be indicated for patients in whom it is expected that medical treatment alone will lead to false-lumen enlargement/aneurysm formation after a few years (**Table 39**)[385,399,400,1279,1287–1291] (See **Table 41** "**3.1.3 Uncomplicated Dissection**" in this chapter).

On the other hand, there is little evidence regarding the indication of TEVAR for chronic Type B dissection patients with false-lumen enlargement/aneurysm formation, and this treatment cannot be recommended as an equivalent procedure to open surgery. Several studies reported that, even when only an entry was closed, there was no reduction in the enlarged false lumen, and that further enlargement did not reduce the risk of rupture.[1279,1301,1302] These results are not equivalent to those of open surgery.[402–405,1279] If all entries/re-entries remaining in the thoracoabdominal and abdominal/iliac artery regions can be closed to achieve complete exclusion, similar effects with open surgery may be obtained through a reduction in the false lumen.[1303] If false-lumen intervention, such as the candy plug method,[1304] knickerbocker method,[1305] and false-lumen embolization with a coil or embolic agent,[1306] results in complete exclusion of an enlarged false lumen, therapeutic effects may be obtained.[1307] In any case, TEVAR cannot be strongly recommended unless its results are equally compared with those of open surgery. Currently, TEVAR is recommended only for high-risk patients for open surgery in patients with false-lumen enlargement/aneurysm formation.

3.1.2 Complicated Dissection (Table 40)

a. Definition

"Complicated acute Type B dissection"* is defined as "a life-threatening condition that occurs with the onset of dissection":[1271,1308,1309]

(1) Rupture/impending rupture
(2) Malperfusion (branch malperfusion): Malperfusion of the main visceral branches, lower limbs, and spinal cord
(3) Persistent or recurrent pain
(4) Uncontrollable hypertension
(5) A large aortic diameter, concomitant dissection at a site with a true aneurysm, or rapid enlarging/deteriorating aortic dissection

*The above (1) to (5) criteria for complicated dissection are adopted from the IRAD. However, in the "Reporting standard for Type B aortic dissection" recently reported from the Society for Vascular Surgery (SVS)/Society of Thoracic Surgeons (STS), the above (1) and (2) criteria were classified as complicated dissection, and the (3) to (5) criteria as uncomplicated dissection. In addition, the latter was classified as "high-risk aortic dissection", that is, a condition that may lead to complicated dissection (rupture or aneurysm formation) in the subacute to chronic phases.[1317] The (1) and (2) complications are fatal, whereas the risk of death related to the (3) to (5) complications is low; therefore, the SVS/STS Reporting standard classification may be more useful for equally comparing the results. However, in most references quoted in this section, complicated dissection was evaluated in accordance with the IRAD classification; the (1) to (5) criteria were regarded as "complicated" in this guideline.

Complicated aortic dissection refers to the above 5 items, but all of these can be summarized into (1) and (2). Persistent/recurrent pain (3) means the deterioration of dissection (5) or a strong stretch of the dissected aortic wall, and can also be interpreted as impending rupture (1). Furthermore, a large aortic diameter (5) or rapidly enlarging aortic dissection refers to the concomitant development of dissection in the presence of a true aneurysm or rapid enlargement related to false-lumen stretching, leading to impending rupture (1). Uncontrollable hypertension (4) may mean a malperfusion (2) related increase in upper half body vascular resistance or renovascular/abnormal hypertension related to renal artery stenosis. Complicated acute Type B dissection accounts for approximately 25% (20 to 50%) of all patients with Type B dissection. In the presence of the (1) and (2) items, emergency invasive treatment is necessary. In the presence of the (3) to (5) items, urgent invasive treatment should be considered.[390,399,1271,1308–1310]

Concerning the mechanism of rupture/impending rupture, the blood flow that has entered the false lumen has no place to escape, and rupture occurs when it breaks on the adventitia. For this reason, there is no re-entry in many patients with rupture/impending rupture. Therefore, if arrest of blood flow into a false lumen, that is, entry closure, is considered as basic treatment, the condition may be resolved in majority of cases.

The mechanism of malperfusion is classified into 3 (**Figure 63**): a: dynamic obstruction, b: static obstruction, and c: mixed type obstruction. In type a, there is no place to escape for blood flowing from an entry into a false lumen, and blood retaining in the false lumen may compress the true lumen, inducing malperfusion. In type b, the dissected intima may migrate into a branch, hindering branch blood flow. Type c refers to a combination of types a and b. In type a patient, entry closure by TEVAR should be performed. In type b/c patients, direct treatment of an occluded vessel (bare stent insertion, aortic fenestration, or branch bypass) should be conducted in addition to entry closure.[1274,1318–1322]

Thus, we can understand the reason why primary entry closure by TEVAR is recommended as a first option, considering the pathogenesis of complicated acute Type B dissection.[386,1272] However, in the case of rupture, it is necessary to stop all channels into a false lumen. In

particular, to treat complicated Type B dissection with a true aneurysm, graft replacement by open surgery should be selected if complete exclusion is not achieved on TEVAR. When a catheter cannot be guided into an occluded blood vessel in type b or c obstruction, bypass or branch artery fenestration is recommended.

b. Diagnosis

i. Symptoms, Physical Findings

As symptoms and physical findings, shock vital, abnormal hypertension, anxiety/restlessness, chest and back pain/low back pain, abdominal pain, lower limb pain, lower limb paralysis, acrotism of the upper and lower limbs, a dissociation of limb blood pressure, and a decrease in the urine volume are observed. Persistent or recurrent pain is important for the diagnosis of complicated dissection.

ii. Blood Biochemistry

Malperfusion results in the rapid deterioration of the renal function and increases in the lactic acid or creatine phosphokinase (CPK) levels. However, before these parameters elevate, malperfusion-related organ/tissue damage occurs; the timing of treatment may be too late. Rapidly progressing anemia is helpful for the diagnosis of rupture/impending rupture.

iii. Diagnostic Imaging

In most cases, contrast-enhanced CT is mandatory.[385,399,1281,1301,1323–1327] A diagnosis of rupture can be made based on the presence of aortic dissection and a periaortic hematoma. A diagnosis of impending rupture is made based on the presence of aortic dissection and peripheral bloody pleural effusion leakage, but it is difficult to diagnose pleural effusion based on CT pixel values alone. It is diagnosed in reference to symptoms (persistent thoracic pain) or pleurocentesis (pleural effusion Ht value: ≥50% of the blood Ht value). In patients with an aortic diameter of >50 mm or those with a rapid ≥5 mm increase in the aortic diameter within 2 weeks after onset, the condition should also be regarded as impending rupture. For the diagnosis of main abdominal branch or lower limb malperfusion, transabdominal vascular ultrasound and ankle brachial pressure index testing are also useful. However, even when a diagnosis of malperfusion-related organ/tissue damage is made, contrast-enhanced CT is mandatory to determine therapeutic strategies (such as entry closure by TEVAR); the above two procedures are auxiliary diagnostic methods. Transesophageal ultrasonography facilitates the diagnosis of Type B dissection and assessment of an entry/the degree of true-lumen stenosis. This diagnostic imaging method is useful when contrast-enhanced CT is impossible. When there is a sufficient time in patients with renal hypofunction, magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA) are useful for diagnosis.[1328,1329] There is a limitation that their resolution is lower than that of CT, but the two procedures are useful for determining therapeutic strategies involving entry diagnosis.

c. Endovascular Treatment

i. Indication

As serious complications related to acute Type B dissection, rupture, malperfusion-related organ ischemia, refractory pain, uncontrollable hypertension, and rapid enlargement are observed. Both the urgency and severity in these complicated acute Type B dissection is high, and invasive treatment is needed in accordance with the condition. Prosthetic graft replacement for rupture or aortic enlargement, dissected flap fenestration or visceral/lower limb artery bypass for malperfusion have been performed, but the results of treatment were poor.[1330,1331] However, to date, the efficacy of TEVAR for complicated acute Type B dissection which facilitates entry closure without thoracotomy/laparotomy or cardiopulmonary bypass has been established (Class I, Evidence level: C).[96,1332–1335]

Impending rupture is often associated with refractory pain and is a good indication for TEVAR. Furthermore, patients with sealed or contained rupture, which shows a relatively stable state among various types of rupture are also good indication for TEVAR. Although organ ischemia is not well defined and the indications for endovascular treatment are often difficult to determine, aggressive endovascular treatment is recommended for impaired blood flow in the celiac and superior mesenteric arteries, which are often life-threatening. On the other hand, in the care of unilateral renal or iliac arteries, where there is no symptomatic or abnormal blood test results, although there is impaired blood flow on imaging, there is no certainty about the indication for endovascular treatment.

According to an annual survey conducted by the Japanese Association for Thoracic Surgery in 2016, TEVAR, including hybrid treatment, was performed in 469 (85.3%) of 550 patients who underwent treatment for acute Type B dissection.[43]

ii. Methods

As of 2019, three types of stent graft (SG) have been approved in Japan as therapeutic device for complicated acute Type B dissection. Furthermore, a type of bare stent is available as an auxiliary device, and it is possible to conduct the PETTICOAT method.[1336,1337] The TEVAR procedure for aortic dissection is not so different from that for aortic aneurysms.

(1) **Access:** For TEVAR for aortic dissection, SG deployment into the true lumen is necessary. When inserting a guidewire or device, it is important to sufficiently confirm the site of guidewire or device passage using aortography or intravascular ultrasound imaging

(2) **Landing zone:** Adequate landing zones are necessary for an SG to be adhered/fixed to the aortic wall in the proximal and distal of an entry to be closed, and inadequate adhesion/fixation will result in incomplete entry closure (type I endoleak). For proximal landing, a non-dissected area should be selected wherever possible. This is to avoid stent graft-induced new entry (SINE) on the proximal side, which can easily cause retrograde Type A dissection. In most patients with acute Type B dissection, the distal landing zone comprises a dissected area, and a non-flexed straight portion is selected wherever possible

(3) **SG diameter:** The diameter of SG for aortic dissection should be selected smaller (5 to 9% oversizing) than that for true aortic aneurysm, since TEVAR for aortic dissection is more prone to SINE.[416,1338] The aortic diameter in a non-dissected area is measured as usual, but measurement methods in a dissected area (particularly on the distal side) are controversial. There are three methods: a method in which the circumferential diameter of the intima is measured, and established as the diameter of the true lumen, regarding it as a perfect circle (**Figure 64A**), a method in which the long diameter of the true lumen is regarded as a true lumen diameter (**Figure 64B**), and a method in which the post-dissection

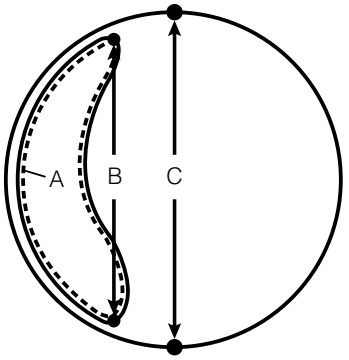


Figure 64. Aortic true lumen diameter-measuring methods for TEVAR. (**A**) A method in which the circumferential diameter of the intima is measured, regarded as a perfect circle, and adopted as a true lumen diameter. (**B**) A method in which the long diameter of the true lumen is regarded as a true lumen diameter. (**C**) A method in which the aortic short axis diameter (only in the acute phase) is regarded as a reference.

aortic diameter (only in the acute phase) is regarded as a reference (**Figure 64C**)

(4) **PETTICOAT method:** In cases of malperfusion, SG is often limited to the minimum length to close the entry to avoid SCI, but PETTICOAT method may be used to expand the true lumen without covering the intercostal/lumbar arteries or abdominal branches by a large diameter bare stent. Its efficacy was reported[1336,1337]

(5) **Re-entry:** In many patients with aortic dissection, several tears are present in addition to a major entry. Even when closing the major entry by TEVAR, blood flow from other tears to a false lumen remains in some cases. False-lumen blood flow may also remain through regurgitation from branches. Residual false-lumen blood flow may make rupture-related hemorrhage control impossible, and may fail improvement of organ ischemia if false lumen enlargement is not obtained

(6) **Additional treatment for malperfusion:** Etiological factors for true lumen blood flow disturbance include the true lumen of a branch dissected from the aorta and false-lumen-related compression. In patients with stenosis related to compression of the true lumen by a patent false lumen (dynamic obstruction), entry closure with an SG may lead to the disappearance of false-lumen blood flow, resulting in true-lumen enlargement. On the other hand, in the case of thrombosed false lumen-related compression or intimal flap packing in aortic branches (static obstruction), compression is not relieved even when closing an entry, requiring additional treatment such as stenting or bypass grafting for those branches[140]

iii. Results

The mortality after TEVAR for complicated acute Type B dissection is not low, but there is a marked decrease in comparison with conventional open surgery. In Europe and the United States, the 30-day mortality rate is reportedly 2.8 to 13.3%.[1308,1311,1334,1339–1345] According to an annual report by the Japanese Association for Thoracic Surgery in 2016, the 30-day mortality rate after TEVAR in 418 patients with acute Type B dissection, excluding those who underwent hybrid treatment, was 6.5%.[43]

On the other hand, the incidence of complications related to TEVAR for complicated acute Type B dissection is reportedly about 3 times higher than that for chronic Type B dissection.[1333] The incidence of cerebral infarction is reportedly 2.8 to 7%, and that of SCI is 3.4 to 13.3%.[1308,1311,1339,1340,1342,1343] However, cardiac complications, respiratory failure, renal failure, gastrointestinal complications, such as intestinal ischemia, hemothorax after rupture, and lower limb ischemia, may also occur. Overall, the incidence of complications is reportedly 20 to 30%.[1308,1343]

Furthermore, dissection in TEVAR for acute aortic dissection, there is a risk of new tears in the dissection flap due to the SG deployment technique and compression of the SG itself.[1346–1348] Retrograde Type A dissection, as the most serious complication, does not occur only in TEVAR cases for acute aortic dissection. Although it occurs infrequently, once it does occur, the mortality rate is high and efforts should be made to avoid it.[1311] Retrograde Type A dissection more frequently develops in patients with aortic dissection than in those with true aortic aneurysms, and in patients with acute dissection than in those with chronic aortic dissection.[417] In addition, Distal SINE occurs distal to the end of the SG, but it also does not occur only in TEVAR cases for acute aortic dissection. However, the incidence of distal SINE after TEVAR for chronic dissection is higher than after TEVAR for acute dissection.[1349] This may be related to differences in the inflexibility of a dissected flap.

iv. Long-Term Outcome

The 1 to 2-year survival rates ≥80% and 5-year survival rates ≥70% after TEVAR for complicated acute Type B dissection are reported.[1341–1346] A previous study indicated that the freedom from major complication at 2 years was 48%,[1346] but recently, many studies reported that the freedom from reintervention at 5 years was approximately 60%.

One of the reasons why the additional treatment rate is relatively high is inability to obtain aortic remodeling in which a false lumen is thrombosed/reduced with true-lumen enlargement. After TEVAR for acute to subacute Type B dissection, remodeling in an SG-inserted area is almost accurately achieved regardless of complicated or uncomplicated dissection, whereas abdominal remodeling is poor, requiring additional treatment in some cases.[1284,1343,1344,1350,1351]

PETTICOAT method is particularly effective in case of malperfusion because it can obtain true lumen enlargement without covering the main abdominal branch or intercostal lumbar artery origins. Some studies indicated that it contributed to early thoracic to abdominal aortic remodeling,[1284,1350] but its long-term effectiveness has not been confirmed.[1284,1318,1337,1352,1353]

d. Open Surgery

First-choice invasive treatment for complicated acute Type B dissection has changed to endovascular treatment including TEVAR. The opportunity of performing open surgery has decreased. However, endovascular treatment is not effective in all patients; its application is difficult in some cases, or endovascular treatment alone is ineffective in other cases, depending on the degree of dissection involving the aortic arch, mode of rupture, or mechanisms of malperfusion. Among various types of complicated acute Type B dissection, conditions for which open surgery may be indicated, and reasons and techniques that may be selected are described with respect to complications.

i. Malperfusion

Williams et al. defined malperfusion that may be resolved through false-lumen decompression as dynamic obstruction and malperfusion that may not be resolved as static obstruction. They indicated that direct revascularization was necessary for the latter.[1176] This was reported as guidelines for endovascular treatment including TEVAR, but the principle can also be applied for open surgery. Briefly, false-lumen decompression can be achieved through entry closure or aortic fenestration, and direct revascularization through bypass or prosthetic graft replacement.[1133]

Dynamic obstruction: In the TEVAR era, open surgery for dynamic obstruction has been indicated only for patients in whom TEVAR is anatomically inappropriate. Accordingly, FET surgery under median sternotomy has been increasingly selected when performing surgical central aortic reconstruction for closing an entry,[1316] and the frequency of aortic repair through a left thoracotomy has decreased. On the other hand, fenestration of the abdominal aorta (combined with infrarenal prosthetic graft replacement in many cases) can be performed under simple aortic cross-clamping, being minimally invasive. As its effects are more consistent than those of endovascular fenestration, this procedure is a useful option.[1315] However, in this technique, double-barrel (classical) aortic dissection is deliberately formed, and this technique is disadvantageous from the viewpoint of long-term false-lumen enlargement. Fenestration is possible under infrarenal aortic cross-clamping, but the distance from an abdominal branch to the site of fenestration becomes longer, making relief of malperfusion insufficient in some cases. Therefore, the dissected intima near the branch orifice is resected (incised) under suprarenal or celiac cross-clamping in some cases. Even in such cases, the clamp placed on the suprarenal or celiac aorta should be moved to the infrarenal aorta after intima resection to minimize the duration of ischemia. There is also a method in which the dissected intima is resected through thoracoabdominal incision, but this method is highly invasive, and false-lumen enlargement/rupture may occur in the long-term.[1278]

Axillo-femoral bypass for aortic-type dynamic obstruction[1354] has been performed in Japan. It is effective for ischemia of the lower limbs alone, but its results are unstable due to an insufficient volume of blood flow when abdominal organ ischemia is present; this procedure cannot be recommended.

Static obstruction: Percutaneous stenting is a treatment of choice. However, open surgery, such as bypass and thrombectomy, may be indicated when the length of branch occlusion is long or when true-lumen thrombus-related occlusion is present. To treat unilateral iliac artery occlusion, femoro-femoral artery bypass is frequently performed.[1313,1314] When endovascular treatment of the superior mesenteric artery is difficult, iliac-superior mesenteric artery bypass is indicated. For celiac/superior mesenteric/renal artery bypass, it is necessary to secure arterial inflow site. When narrowing of the true lumen is observed in the upstream of the inflow artery, infrarenal abdominal aortic replacement for fenestration is simultaneously performed in many cases. When intestinal ischemia is suspected, a laparotomy approach, through which reversibility of intestinal ischemia can be confirmed, is selected in many cases. As bypass conduits, autologous veins or expanded polytetrafluoroethylene (ePTFE) synthetic grafts are often used, but venous conduits are selected in many cases, based on the risk of infection. For superior mesenteric artery bypass, a retrograde technique (inflow: infrarenal abdominal aorta or iliac artery), which provides flexibility of graft design, is primarily used due to the presence of aortic dissection at the bypass inflow site and location of distal anastomosis peripheral to the site of occlusion. If the site of distal anastomosis is too far from the site of occlusion, blood flow may be insufficient.

ii. Rupture/Impending Rupture

Many studies regarding the results of treatment for complicated acute Type B dissection involved patients with malperfusion and those with (impending) rupture, and there are few studies involving those with rupture alone. Even in such a current status, emergency TEVAR is recommended because the results of open surgery are poor.

According to the IRAD findings, the mortality rate after open surgery is 50%,[1312] whereas the 30-day mortality rate after TEVAR for rupture is 17%[1313] according to a survey conducted by the Outcome Committee of the SVS. In addition, it is 16% according to reports from two institutions in France.[1273] However, after TEVAR, postoperative re-rupture occurred in some patients. Hemostasis may be difficult in patients with active hemorrhage. The above SVS survey also showed that the 1-year mortality rate was 42%, and that the interval from TEVAR until death was ≤3 months in most patients.[1313] Several studies in Japan also presented early results after TEVAR: the in-hospital mortality rate varied from 0 to 55%.[1355,1356] Even in a study reporting no in-hospital mortality, the 1-year survival rate was 71%, being similar to that after surgery (86%).[1356] Briefly, concerning rupture, excluding impending rupture, the superiority of TEVAR to open surgery has not been sufficiently established, and open surgery is still an important option.

The most important advantage of surgery in comparison with TEVAR is that the site of adventitial rupture can be directly repaired. Therefore, in many cases, direct surgery under left thoracotomy is selected. A study regarding FET surgery for acute complicated Type B dissection did not also primarily involve patients with rupture.[1316,1357]

Adjuncts for surgery under left thoracotomy include deep hypothermic circulatory arrest and distal aortic perfusion. The former is more likely to be selected when proximal extension of dissection makes proximal aortic cross-clamping distal to Zone 2 difficult/impossible/highly risky. In particular, in the presence of acute dissection, cross-clamping the dissected aorta should be avoided. For open surgery in patients with active hemorrhage, cooling can be continued under manual compression of the site of bleeding if it can be promptly confirmed after thoracotomy through the establishment of cardiopulmonary bypass before thoracotomy. However, active hemorrhage into the right thoracic cavity or posterior mediastinum may occur; caution is needed. According to the IRAD findings, deep hypothermic circulatory arrest is performed in 60% of patients undergoing open surgery for acute Type B dissection.[1312] On the other hand, distal aortic perfusion is selected when surgery under aortic cross-clamping is possible, but it is necessary to promptly cross-clamp the proximal aorta after thoracotomy in patients with active hemorrhage. For this reason, partial cardiopulmonary bypass through femoral cannulation, which is possible before thoracotomy or in parallel with thoracotomy operations, is advantageous. This method is also advantageous in that it facilitates the management of massive

hemorrhage or switching to circulatory arrest. As parietal pleural incision at the site of hematoma may induce active hemorrhage even in patients with contained rupture, dissection and exposure of the aorta should be initiated in the peri-hematoma area to initially secure the site of proximal aortic cross-clamping.

iii. Results of Surgery

According to the findings on 1,529 patients from the JACC Interdisciplinary Expert Consensus in 2013, the early mortality rate, incidence of cerebral infarction, and that of spinal cord infarction were 17.5 (95% confidence interval (CI): 15.6 to 19.6%), 5.9 (95% CI: 4.8 to 7.3%), and 3.3% (95% CI: 2.4 to 4.5%), respectively. In addition, the 5-year survival and 5-year aortic event-free rates were 44 to 64.8% and 58.7 to 68%, respectively.[1358]

e. Medical Treatment

i. Initial Treatment

When examining patients with symptoms suggestive of acute aortic dissection, physical findings and vital signs should be promptly evaluated, and diagnostic imaging must be promptly performed. All of upper and lower limb blood pressures should always be measured for the detection of dissection and malperfusion. In many patients with acute Type B dissection, the blood pressure at the time of onset tends to be higher than in those with Type A dissection.[68,1359–1361] When pain is severe, with a high blood pressure, the echocardiography and enhanced CT should be promptly conducted for diagnosis with intravenous antihypertensive and analgesic agents. Antihypertensive agents must be selected, based on the development of reflex tachycardia. Beta-blockers and non-dihydropyridine Ca antagonists (verapamil, diltiazem) are appropriate.

In the case of complicated acute Type B dissection, emergency TEVAR or prosthetic graft replacement is necessary. Treatment in a special institution where the both procedures are possible is recommended. Furthermore, even in the case of uncomplicated acute Type B dissection, the condition may change into the complicated type during the course of medical treatment. Management should be performed in a similar institution.

ii. Initial Treatment After Diagnosis

After complicated acute Type B dissection is diagnosed, invasive treatment (TEVAR should be prioritized rather than prosthetic graft replacement) should be promptly prepared. When invasive treatment is difficult, or when the patient refuses it, medical (conservative) treatment involving antihypertensive therapy should be continued. In any case, after a definitive diagnosis is made, arterial and peripheral venous lines should be kept while waiting for invasive treatment. Subsequently, a central venous line should be kept to prepare acute deterioration of patient's condition. Sheaths introducer may be inserted into the femoral artery/vein in preparation for percutaneous cardiopulmonary support (PCPS).

According to the results of medical treatment in patients with complicated dissection, excluding serious-status patients, the acute-phase mortality rate is reported 23.2 to 35.6%.[1271,1362]

3.1.3 Uncomplicated Dissection (Table 41)

a. Definition

Patients who are not "complicated acute Type B aortic dissection" as described above should be diagnosed as "uncomplicated". In patients with uncomplicated dissection, medical treatment involving heart rate/blood pressure control is performed in the acute phase.[1263–1270] Recently, RCTs demonstrated that intervention by TEVAR for uncomplicated Type B dissection improved the chronic-phase prognosis (life/aortic false-lumen prognoses).[1287,1289] The selection of patients and timing of intervention are controversial.[385,396–400,1267,1287–1292,1295,1368–1370]

Patients to be selected are those with enlargement of the false-lumen and are at risk of rupture during the chronic phase with conventional medical therapy. The condition is also termed "high-risk uncomplicated dissection".[1317] Chronic-phase false-lumen enlargement may be predicted in the acute/subacute phases after the onset of Type B dissection based on the parameters presented in **Table 39**.[385,396–400,1287–1292] Furthermore, chronic-phase enlargement in patients with uncomplicated Type B dissection can be predicted using a calculator developed by Stanford University.[401]

With respect to the timing of intervention by TEVAR, refer to "Timing of preemptive TEVAR" in the next section and **PQ 11**.

b. Endovascular Treatment

i. Indications of Preemptive TEVAR

An RCT, INSTEAD trial, compared TEVAR for uncomplicated Type B dissection with drug therapy, and concluded that intervention by TEVAR deteriorated the life prognosis 1 and 2 years after assignment.[1287,1300,1371] Therefore, it is not considered that TEVAR should be indicated for all patients with uncomplicated Type B dissection.[392,393,1267,1281,1372] In other words, patient selection may be necessary for TEVAR for uncomplicated Type B dissection. TEVAR should be indicated when false-lumen enlargement in the chronic phase is expected (high-risk uncomplicated dissection).[385,396–400,1287–1292] Chronic-phase enlargement in patients with uncomplicated Type B dissection can be predicted based on acute-/subacute-phase parameters. To date, various predictive factors have been reported.[385,396–400,1287–1292] And, false lumen enlargement and aorta-related events in the chronic phase are reported to occur in up to 40% of uncomplicated Type B dissection cases.[1373]

ii. Timing of Preemptive TEVAR

Although the enrolment period of patients with uncomplicated acute Type B dissection in INSTEAD trial, as the base of recommendation was from 2 to 52 weeks after the onset (subacute to early chronic phases),[1287,1300] TEVAR was performed within 6 months in most patients. Many investigators emphasize that the most appropriate timing of preemptive TEVAR is ≤6 months after onset.[1287,1295,1368–1370,1374,1375] This timing is also consistent with the period when favorable thoracoabdominal remodeling of a false lumen after TEVAR is achieved, supporting the recommendation. On the other hand, an RCT of preemptive TEVAR in the acute phase did not verify its superiority to medical treatment for the prognosis one year after TEVAR, being contrary to the above opinion.[1293,1294] In particular, a high incidence of retrograde Type A dissection after TEVAR for acute Type B dissection makes physicians hesitate to perform preemptive TEVAR in the acute phase.[417] In contrast, comparison between TEVAR and medical treatment for uncomplicated acute Type B dissection indicated the superiority of the former for aortic remodeling after ≥1 year, suggesting the importance of preemptive TEVAR in the early timing after the onset.[1294,1376,1377] This is controversial.

iii. Methods of Preemptive TEVAR

Initially, thoracic entry closure with a stent graft (SG) should be planned based on the information obtained on contrast-enhanced CT. The entry site should be accurately identified, and a ≥20 mm proximal area from the origin of the entry should be established as the proximal end of landing. Furthermore, this proximal landing area should be a non-dissected area with an aortic diameter of ≤37 mm, and the SG diameter should be ≤109% of a landing aortic diameter.[416,417] In addition, for insertion to Zones 2 and 3, the design of insertion must be carefully selected to prevent bird's beak on the lesser curvature side. These cautions regarding proximal landing contribute to success/failure in entry closure and the prevention of retrograde Type A dissection as a fatal complication. The position of distal landing should be established in a straight area of the descending aorta ≥20 mm distal to the end of an entry. The SG diameter on the distal side should be established as 110 to 120% of the true lumen diameter calculated from the circumferential diameter of a true lumen measured on CT. As a result, there may be an approximately 8- to 10-mm difference between the proximal and distal SG diameters, but this should be managed by attaching a taper graft or connecting two SGs. Attention must be paid so that there may be no spring back force over the entire length.

For preemptive TEVAR, it is not necessary to consider main abdominal branch malperfusion related to entry closure. Briefly, in the case of false-lumen perfusion, an entry or re-entry always remains in the same area. For access of the device, a side to which the true lumen may be led should be selected, and the true lumen must be confirmed using intravascular ultrasound. Super- or extra-stiff guidewires should be used, as described for standard TEVAR. Pull-through wires frequently induce vascular complications; therefore, they should not be used if there is no excessive flexion.[407,1378] On SG deployment, rapid pacing should be performed, and an SG should be inserted after reducing the cardiac output.[409] Touch-up ballooning after device insertion should not be conducted.

iv. Follow-up After TEVAR

After TEVAR, whether a target entry is closed, the position of the residual entry, extent of flow from a re-entry, and state of main abdominal branch or lower limb artery perfusion should be evaluated by contrast-enhanced CT and transabdominal vascular ultrasound. The aortic, true-lumen, and false-lumen diameters at specific points (maximum diameter area, SG terminal, diaphragm level, infrarenal abdominal aorta) should be serially checked (after 1, 6, and 12 months, subsequently: every year). In many cases, the proximal end of the re-entry flow tends to enlarge in the chronic phase; therefore, attention must be particularly paid to the aortic diameter of this area.

v. Results of Treatment and Complications

With respect to the early results of acute-/subacute- to early chronic-phase preemptive TEVAR, the timing of treatment varies, and there are no relevant data. However, the results of TEVAR for uncomplicated Type B dissection are not favorable: in-hospital mortality rate, 7.1%; SCI, 3.4%; respiratory complications, 13.2%; and renal dysfunction, 14.7%.[393,1299,1372,1374] These results in acute phase are poorer than those of conservative treatment, but the results regarding rupture, prognosis, and aortic remodeling ≥1 year after treatment are more favorable than those of conservative treatment, and these results are the basis for acute phase treatment. Concerning the chronic-phase survival rate, aorta-associated event-free rate, and aortic remodeling, refer to the INSTEAD and ADSORB trials.[1294,1300,1371] These results (prognosis, aortic remodeling) of preemptive TEVAR in early phase from the onset are significantly more favorable than those of conservative treatment.

As complications related to TEVAR for Type B dissection, the followings have been reported:

(1) **Retrograde Type A dissection:** Its incidence after TEVAR for Type B dissection is 4.0–6.9%, being higher than that after TEVAR for degenerative TAA.[416,417,1379] Furthermore, the results of treatment after this complication are poor (mortality rate: ≥30%). Therefore, great care must be taken to prevent the occurrence of this complication.[416,417,1379] As for the timing of the onset of this complication, it occurred during TEVAR in approximately 20%, within 30 days after TEVAR in approximately 50%, and ≥31 days after TEVAR in approximately 30%. Its development ≥1 year after TEVAR is rare.[416,417,1379] As predictive factors for this complication, intrinsic factors include acute-phase treatment, partial or complete thrombosis in the false lumen, central landing Zone 0, and an aortic diameter of ≥40 mm at proximal landing. Patients who fit these factors should be regarded as "TEVAR unfit: not meeting anatomical requirements".[416,417,1379–1382] Extrinsic factors include SG oversizing (≥10%) and proximal bare stent-installed devices. Planning should be established, paying much attention to these matters[416,417,1379,1380]

(2) **Stroke:** The incidence of cerebral infarction increases in landing more proximally to Zone 2. Left subclavian artery reconstruction is recommended as it has been shown to decrease the incidences of SCI and cerebral infarction[372,373]

(3) **SCI:** In many patients undergoing TEVAR for Type B dissection, an SG is inserted into the proximal descending aorta through the distal arch. It may be rare to directly obstruct the spinal-cord-feeding artery (Adamkiewicz artery). However, central entry closure may lead to intercostal artery occlusion of a false-lumen branch with the time course after TEVAR. This is complicated by delayed SCI in some cases. When a large number of intercostal arteries are false-lumen branches on preoperative contrast-enhanced CT, intra-/postoperative strategies to prevent SCI must be established as high-risk patients for SCI

(4) **Renal dysfunction:** Entry closure may result in malperfusion of the renal artery with false-lumen perfusion. However, if false-lumen perfusion persists, a tear may be present in the same area in the acute phase; complete closure of the tear within 6 months after the onset is extremely rare. Renal blood flow on central entry closure should be confirmed by intraoperative angiography. If renal blood flow insufficiency is suspected, renal artery reconstruction through a tear may be necessary

(5) **Peripheral stent graft-induced new entry (SINE):** For TEVAR in patients with aortic dissection, the peripheral side of an SG is often inserted to the site of dissection, and a new entry develops in the intima of the peripheral region of the SG. This is termed SINE. As the mechanism of development, SG-related ulceration at its end or fatigue related to intimal flap swinging after SG deployment may be involved. The positions of the two types of new entry tear subtly differ, but the

condition is similar; it is not necessary to differentiate them. If this new entry is connected with the original false lumen, a double barrel before initial treatment may be formed, but rarely, new dissection may occur, leading to three-cavity dissection. Its incidence is approximately 7.9%. Factors involved in development include the timing of treatment (acute: 4.3%, chronic: 12.9%), SG oversizing (positive factor), and the use of a restrictive bare stent (PETICOAT stent): negative factor.[1349,1383–1386] When preemptive TEVAR is performed as initial treatment, an intended reduction in a false lumen is not achieved due to a new tear; therefore, early additional treatment (additional TEVAR in most cases) is necessary[1387]

(6) **Endoleak:** TEVAR for types I to IV is similar to that for TAAs. However, in double barrel patients, blood flow may blow up from a re-entry into a false lumen after entry closure with an SG. This should be regarded as re-entry flow (false lumen retrograde flow), and distinguished from endoleak (**Figure 52B**). If there is a tendency for enlargement associated with re-entry flow, additional treatment is necessary[1306]

c. Open Surgery

Medical treatment is generally selected to treat acute uncomplicated Type B dissection, and open surgery is not indicated. Since the results of the INSTEAD XL trial[1287] were reported, (preemptive) TEVAR, as a preemptive attack, has been performed by selecting patients in the subacute phase. However, this is indicated on the premise of minimally invasive TEVAR, and does not correspond to invasive surgery. In some institutions, preemptive total aortic arch replacement + FET surgery is performed in patients with retrograde dissection involving the aortic arch. However, the usefulness of such treatment must be investigated by comparing risks with benefits.

When the process of dissection involves a pre-existing true aortic aneurysm, the risk of rupture increases; this condition should be exceptionally managed even if the dissection itself is uncomplicated.[1388] In this case, it may be regarded as a type of complicated dissection, but there is no evidence to recommend acute-phase treatment. Follow-up must be carefully performed based on symptoms and imaging findings, and invasive treatment should be conducted at an optimal time. Surgery is indicated for some patients based on anatomical circumstances. In patients with aortic arch aneurysms, FET surgery is also selected.

d. Medical Treatment

i. Initial Treatment

As initial treatment for uncomplicated acute Type B dissection, medical treatment has been selected. Because the incidence of life-threatening complications, such as rupture and malperfusion, is low, differing from Type A dissection which may induce cardiac or cerebral complication. Therefore, the necessity of invasive treatment is low, and the results of medical treatment for uncomplicated acute Type B dissection were more favorable than those of surgery.[1389] Despite recent advances in less invasive endovascular treatment, including TEVAR, the acute-phase mortality rate after medical (conservative) treatment for uncomplicated dissection is still reportedly 2.4 to 6.3%, being similar to or slightly lower than that after TEVAR (6.6 to 7.1%);[393,1272,1390] therefore, medical treatment is recommended as standard acute-phase treatment for uncomplicated dissection. However, in the chronic phase (≥1 year after onset), the prognosis of patients treated by acute-phase TEVAR is reportedly better than that of those treated by medical treatment.[393,1390,1391] In the future, an RCT should also be conducted in this field.

(1) **Management of the heart rate and blood pressure:** In the acute phase, rupture or malperfusion-related organ failure, deterioration of dissection, and redissection should be avoided. Therefore blood pressure/heart rate/pain control and resting are important. After diagnosis of acute Type B dissection, heart rate/blood pressure control (dV/dt and dP/dt reduction) should be initially performed. A target heart rate is established as <60 beats/min, and a target systolic blood pressure as 100 to 120 mmHg. Prompt adjustment is recommended.[96,275,532,1270,1288] As hemodynamic monitoring, a monitor electrocardiogram, arterial pressure line, and central venous line should be prepared. Under such monitoring, close adjustment should be conducted so that a target heart rate/blood pressure value may be obtained in a range in which organ blood flow is maintained. A study reported that heart rate control (<60 beats/min) in the acute phase reduced the incidence of aorta-associated events in the chronic phase.[1270] If there is no contraindication, the heart rate should be controlled to <60 beats/min by intravenously injecting a β-blocker in the early phase.[1206,1269,1365–1367] If β-blockers cannot be used, the heart rate should be controlled with non-dihydropyridine Ca antagonists. If a blood pressure of ≤120 mmHg is not achieved after heart rate control, the blood pressure should be controlled by combining the above Ca antagonist with antihypertensive drugs such as other Ca antagonists, ACE inhibitors, and ARBs.

In the hyperacute phase, blood pressure/heart rate control with intravenous agents should be performed because their regulatory property is superior. However, oral or patches b-blockers may be started/combined the day after onset or later. Several studies indicated that the long-term intravenous administration of nicardipine at a massive dose induced tachycardia, concomitant phlebitis, or paralytic ileus.[1392–1394] Combination therapy with oral agents should be started in the early phase

(2) **Pain control:** In addition to antihypertensive therapy, analgesia/sedation for persistent pain should be promptly achieved. Because persistent pain increases in the heart rate/blood pressure. Adequate analgesia with intravenous opioids facilitates heart rate/blood pressure control

(3) **Management of fever/inflammation, hypercytokinemia, and respiratory failure:** With acute aortic dissection, systemic inflammatory response syndrome (SIRS) occurs, and the C-reactive protein (CRP) level increases. Periaortic inflammation-related pleural effusion and bed rest related atelectasis are involved in respiratory failure associated with acute dissection. In some cases, marked inflammatory responses lead to SIRS, being complicated by acute lung disorder This is associated with hypercytokinemia related to aortic dissection. Respiratory complications should be avoided by administering sivelestat in addition to a postural change

(4) **Bed rest level:** Resting is required within 24 h during which the risk of rupture or deterioration of dissection is high.[1395,1396] Concerning subsequent resting/relief,

Table 42. COR and LOE for the Invasive Treatment of Chronic Stanford Type B Aortic Dissection

	COR	LOE
It is recommended to perform invasive treatment for patients with a maximum minor axis of ≥60 mm[1330]	I	C
TEVAR should be considered for ULP-type and DeBakey type IIIa dissection in the chronic stage	IIa	C
Open surgery should be considered for DeBakey type IIIb dissection in the chronic stage[402,1399,1400]	IIa	C
TEVAR should be considered for cases of DeBakey type IIIb dissection in which open surgery is difficult	IIa	C
TEVAR may be considered for DeBakey type IIIb dissection in the chronic stage[1400,1401]	IIb	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair; ULP, ulcer-like projection.

refer to 1. Rehabilitation for aortic dissection in **Chapter IX**. Restlessness or delirium in elderly patients, which are often accompanying, may also be associated with excessive resting or fasting. According to some studies, in low-risk patients for complications, ambulation by early rehabilitation decreased the incidence of delirium. Management in accordance with the severity of dissection is necessary[1395,1397]

ii. Follow-up by Diagnostic Imaging

Follow-up CT should be performed within 1 week after initial diagnosis. In some cases, a rapid increase in the aortic diameter, deterioration of dissection, or redissection-related malperfusion is observed a few days to a few weeks after an initial diagnosis of uncomplicated acute Type B dissection . When the deterioration of the condition is suspected, it is necessary to promptly conduct additional CT. Furthermore, malperfusion-related renal ischemia induces renal dysfunction or refractory hypertension; therefore, blood flow of renal artery assessment by CT and ultrasonography must be considered. A study indicated that intestinal ischemia was the most frequent causes of death as well as aortic rupture.[1192] It is the most important to pay attention to abdominal pain or abdominal swelling, but if regular blood gas analysis show an increase in the lactic acid level in addition to gas detection on abdominal X-ray, CT or vascular ultrasonography should be performed under a tentative diagnosis of abdominal organ ischemia.

In patients with chronic kidney disease (CKD) or those with renal dysfunction after the onset of dissection, frequent contrast-enhanced CT increases the risk of contrast medium-induced nephropathy; therefore, if there is no change in the general condition or finding suggestive of malperfusion, contrast-enhanced CT is not always necessary. In contrast, in patients in whom malperfusion is suspected, especially in those with intestinal ischemia, early therapeutic intervention improves the prognosis. Therefore physicians should not hesitate to perform contrast-enhanced CT. As risk factors for aorta-associated events in the chronic phase, an aortic diameter of ≥40 mm in the acute/subacute phases, a false lumen diameter of ≥22 mm, and imaging findings such as partial thrombosis of a false lumen have been reported.[396,1025,1398] In corresponding or similar patients, follow-up by imaging must be more carefully performed.

iii. Drug Therapy After the Acute Phase

Issues in the acute phase following the hyperacute phase (within 24 h) are blood pressure/heart rate control, the relief of the bed rest level, and management of delirium or respiratory failure. For blood pressure control, a reference range should be established as 100–120 mmHg. However, when renal dysfunction related to a reduction in the perfusion pressure, such as a decrease in the urine volume, occurs, it is sometimes necessary to increase a target blood pressure. In patients with acute dissection in the presence of arteriosclerosis as a background factor, including elderly patients, medical treatment for arteriosclerosis such as lipid-lowering therapy, diabetes control, and smoking cessation, must be considered in addition to blood pressure control to prevent cardiovascular events in the remote phase regardless of treatment methods (surgery, medical treatment). This may contribute to chronic-phase management.

3.2 Chronic Stanford Type B Aortic Dissection

3.2.1 Surgical Indications and Procedure Selection (Table 42)

a. Indications

Various surgeries of chronic Type B dissection beyond the window period of preemptive TEVAR have been performed to prevent rupture after enlargement/aneurysm formation. Therefore, it is considered appropriate that its indication criteria are based on those of non-dissecting aortic aneurysm. In fact, the indications are judged individually in consideration of age, the presence of subjective symptoms, the presence of COPD, physical constitution, enlargement rate, and genetic background. However, attention is needed as aortic dissection is said to have a faster enlargement rate than non-dissecting aortic aneurysm.

According to the guidelines published in the United States in 2010, the surgical indication for thoracic descending aortic aneurysm is a diameter of 55 mm, which is distinguished from a diameter of 60 mm for TAAA; however, they did not distinguish dissection and non-dissection cases.[95] More than half of the surgeries for chronic Type B dissection require highly invasive deep hypothermic circulatory arrest, even with descending aortic replacement, and the early results of arch + descending aortic replacement are comparable to those of thoracoabdominal aortic replacement in Japan. Considering these, it is appropriate that the surgical indications for chronic Type B dissection are based on those for TAAA.

On the other hand, according to the guidelines published in Europe in 2014, the indications for non-dissecting thoracic descending aortic aneurysm are a diameter of 55 mm for TEVAR and 60 mm for open surgery (prosthetic graft replacement).[96] When focusing on chronic Type B

dissection, TEVAR has more favorable early results than open surgery. However, they show no difference in the 5-year survival rate, and the freedom rate from additional treatment is lower in TEVAR.[1358] Therefore, there is little evidence to recommend early intervention with TEVAR over open surgery.

The 2013 European Expert Consensus divided complicated Type B dissection into acute and chronic stages, and it recommended TEVAR (open surgery if anatomically unsuitable) even for the chronic stage (chronic complicated dissection).[1358] Its definition of complicated dissection is the recurrence of symptoms, enlargement/aneurysm formation (>55 mm), and enlargement exceeding 4 mm per year. However, given the considerations described above, careful attention must be paid to invasive treatment (open surgery and TEVAR) interventions for these complications in the chronic stage. In fact, the concept of chronic complicated dissection is followed in the guidelines published in Europe in 2014; however, the treatment intervention criteria were revised to a maximum diameter of 60 mm and an annual enlargement of 10 mm or larger, regardless of TEVAR or open surgery.[96] Taken together, a diameter of 60 mm is considered appropriate as a threshold for invasive treatment intervention for the enlargement/aneurysm formation of chronic Type B dissection.

For preemptive TEVAR for Type B dissection beyond the subacute phase, see "**3.1.3.b Endovascular Treatment**" in this chapter.

b. Procedure

As in non-dissecting aortic aneurysm, TEVAR is expected to have a treatment effect on ULP type and DeBakey type IIIa of enlarged/aneurysmal chronic Type B dissection. On the other hand, in chronic DeBakey type IIIb dissection, the entry closure by TEVAR and flap fixation by stent skeleton are expected to suppress aneurysm enlargement only up to the distal arch-descending aorta, where the effect of retrograde blood flow in the false lumen (re-entry flow) is small.[1286] Therefore, open surgery is the first treatment choice for more extensively dilated lesions, and indications of TEVAR are limited to patients at high risk of open surgery. In TEVAR on such patients, various additional treatments have been performed for retrograde blood flow in the false lumen (See "**3.2.2 Endovascular Treatment**" in the next section).

Prosthetic graft replacement that covers the enlarged part is selected in open surgery, which is a direct surgery with a left thoracotomy in most cases. Since total arch replacement with FET, which can be performed from a median sternotomy incision, often does not replace the enlarged part, its treatment effect is thought to be comparable to that of TEVAR.

Hypothermic total cardiopulmonary bypass, or distal aortic perfusion by partial cardiopulmonary bypass or left heart bypass is selected as circulatory adjuncts for left thoracotomy surgery. More than half of patients with chronic Type B dissection are subject to proximal open aortic anastomosis using total cardiopulmonary bypass/deep hypothermic circulatory arrest due to difficulty in the clamping of the arch or proximal descending aorta. On the other hand, aortic cross-clamping in the aortic arch or its vicinity is mandatory under the latter circulatory adjuncts; however, it poses a concern about aortic injury associated with clamping, such as retrograde Type A dissection. Therefore, careful operation of aortic cross-clamping, such as blood pressure management during clamping, is required.

The replacement range is determined by the aortic diameter; however, staged surgery may be advantageous from the viewpoint of preventing SCI. However, there is a risk of rupture if the dilated part remains, and a careful judgment is made for each patient and lesion. Generally, patients with a distal descending aorta-abdominal aorta of approximately 40 mm or smaller are not subject to replacement, and staged surgery is often selected. Nevertheless, patients with hereditary aortic diseases, such as Marfan syndrome, are often indicated for one-stage thoracoabdominal aortic replacement because of their high enlargement rate and high risk of rupture. In staged surgery, it has been controversial whether the peripheral side should be anastomosed only to the true lumen or to both lumina; notably, the judgment is made based on the lumen where the major abdominal branch originates, the position and size of the tear in its vicinity, and the site and lumen where the spinal feeding artery originates.

If the patient presents with the enlargement of the infrarenal abdominal aorta alone, an intervention is performed based on the indication criterion of AAA (50–55 mm). However, this is based on the premise that a non-enlargement part is present at the renal artery level, and indications for patients showing a series of enlargements are determined based on those of TAAA.

3.2.2 Endovascular Treatment

Traditionally, the chronic stage of aortic dissection was defined to be at least 2 weeks after its onset. Based on this definition, preemptive TEVAR has often been performed in the chronic stage, but with the consideration of the improvement in long-term prognosis, it is now suggested to be performed within 6 months to 1 year of onset. Therefore, concepts, such as subacute and early chronic stages, in addition to the chronic stage, have been proposed. Here, as with open surgery, we discuss TEVAR for the prevention of rupture in chronic Type B dissection that has developed an aneurysm, and preemptive TEVAR performed beyond 2 weeks after the onset according to the conventional definition is discussed in another section (See "**3.1.3.b Endovascular Treatment**" in this chapter).

The procedure of TEVAR for aortic dissection itself is not considerably different from that for aortic aneurysm. A landing zone is required for sufficiently crimping and fixing a stent graft (SG) to the aortic wall around the entry to be closed, and insufficient crimping and fixing result in blood flowing through the gap into the entry (type Ia endoleak). Regarding the proximal landing zone, cTAG® manufactured by W. L. Gore & Associates, Inc. states it to be "at least 20 mm from the major entry to the proximal side," but Zenith® for aortic dissection manufactured by Cook Medical states it to be "at least 20 mm of non-dissected aortic part in the proximal region to the entry." In contrast, the length of the distal landing zone is not specified.

In TEVAR for chronic aortic dissection, the true lumen of the descending aorta is often narrowed, and many cases require an SG with different diameters on the proximal and distal sides. For this, a tapered SG that is 5–10 mm thinner on the peripheral side than the proximal side may be used, or a small-diameter SG may be deployed on the distal side in advance, inside which the central stent graft can be stacked.

Several patients with chronic dissection are observed to

develop a new intimal tear due to SG (stent graft-induced new entry), and the diameter of SG selected for chronic dissection patients should be smaller (approximately 5% larger than the aortic diameter) than that for patients with aortic aneurysm.[416,1402] On the other hand, the length of SG deployment has been controversial. Although its primary purpose is to close an entry, the deployment length may be extended to simultaneously close the entry located at the origin of small branches, such as the intercostal artery. On the other hand, extensive closure of the intercostal artery raises a concern about SCI.

Several patients with aortic dissection have multiple tears in addition to the major entry, and even if their major entry is closed with an SG, blood flow from the residual tear to the false lumen (re-entry flow) may remain. In relation to this, a report showed that patients with partially thrombosed false lumen had a poorer prognosis than those with patent false lumen,[1025] and patients with DeBakey type IIIa dissection, which can often block blood flow in the false lumen by entry closure, was reported to have more favorable prognosis than those with DeBakey type IIIb dissection, in which re-entry remains in the abdominal aorta.[1402a] Changes in the false lumen hemodynamics after entry closure by TEVAR are thought to be related to the time from onset, as well as the location, number, and site of re-entry; however, they are not accurately predicted at present.

If the blood flow in the false lumen remains after TEVAR for chronic Type B dissection and results in enlargement, the procedure may be completely shifted to prosthetic graft replacement, which includes the site where TEVAR has been performed. However, to resect the residual re-entry, the aorta may be cut at the periphery of the SG to close the false lumen, and the area below it may be replaced with a prosthetic graft. In addition, the re-entry at the origin of the abdominal branch may be closed by TEVAR with branched SG based on the procedure for TAAA; however, branched SG has not yet been approved in Japan.

Because the false lumen of the proximal-middle descending aorta often enlarges, there have been efforts to prevent the enlargement of the false lumen of the proximal descending aorta by blocking the blood flow from the abdominal aorta in the false lumen of the distal descending aorta. Coil embolization requires a large number of coils and has not been generally used; however, a method of deploying a short drum-shaped SG in the false lumen of the distal descending aorta immediately above the diaphragm from the re-entry of the iliac artery or abdominal aorta (candy-plug method) has been reported.[416,1402–1404] While dedicated devices are used overseas, they have not been approved in Japan. Thus, a ligature is applied to the central part of the existing short SG to form a small ring by limiting the deployment, and the lumen remaining in the SG is closed by a vascular plug.[1405,1406] Also, there is a method of deploying a large-diameter SG in the true lumen to compress the false lumen with a balloon and expand it until it is occluded (knickerbocker method); however, it has not been generally used.[1305]

In DeBakey type IIIa dissection, entry closure by TEVAR often leads to complete thrombosis of the false lumen, which is well indicated for TEVAR. On the other hand, DeBakey type IIIb dissection poses a concern about the enlarged false lumen due to residual re-entry.

Thoracoabdominal replacement for chronic Type B dissection has relatively favorable results because of the large number of young patients and few atherosclerotic changes; however, TEVAR remains to be advantageous in terms of operative death and the occurrence of complications. However, although there is no RCT showing the long-term results of the two, they have no difference in the life prognosis, and the retreatment rate is clearly higher in the TEVAR group. Therefore, their indications need to be judged according to the patient and lesion.

3.2.3 Open Surgery

a. Arch/Descending Aortic Replacement

Since distal aortic arch is frequently involved in aortic dissection, distal part of aortic arch is frequently included in the ectent of replacement during descending aortic replacement. The intercostal space for thoracotomy is selected from the 4th to 6th depending on the replacement range, and a rib-interruption ribcross is often performed. Normally, the proximal side is anastomosed to the aorta that does not have dissection. When anastomosing the distal side to the dissected area, the graft is anastomosed to two lumina after fenestration in some cases, while anastomosis only to the true lumen is performed with reapproximation of dissection in others. Anastomosis only to the true lumen is performed with the expectation of remodeling of the downstream false lumen; however, the false lumen that has enlarged to some extent is not expected to show significant remodeling in chronic-stage surgery. In addition, attention is needed if the Adamkiewicz artery is derived from the false lumen or if the major abdominal branch, especially the superior mesenteric artery, originates from the false lumen, and it must be kept in mind that the spinal cord[1407] and intestinal tract may become ischemic. Furthermore, open distal anastomosis should be used to avoid creating a tear at the distal clamped site.

The surgery is performed through left thoracotomy under differential lung ventilation. To avoid respiratory failure due to pulmonary hemorrhage, the left lung is left untouched to the extent possible, and no left lung ventilation is performed during heparinization. In surgery under clamping, proximal aortic cross-clamping is often performed between the left common carotid artery and the left subclavian artery. This may lead to severe complications, such as cerebral infarction in patients with atheroma lesions, and clamp injury and retrograde Type A dissection in patients with the fragility of the aortic wall, such as cases with aortic arch enlargement. Therefore, careful attention must be paid to the condition of the aortic arch, and deep hypothermic circulatory arrest is selected for patients with a risk. However, deep hypothermic surgery through left thoracotomy is highly invasive, and its application requires sufficient preparation.

Distal aortic perfusion is used for spinal cord/abdominal organ protection during aortic cross-clamping. Potential malperfusion of the spinal cord or abdominal organs caused by this method can be prevented by temporarily releasing the aortic cross-clamping on the distal side and re-clamping the aorta after resecting and fenestrating the flap. If the replacement range includes the Adamkiewicz artery, a treatment plan based on thoracoabdominal aortic replacement should be applied.

The deep hypothermic circulatory arrest method is used in patients whose dissection has extended to the aortic arch, patients with the dilated aortic arch, and patients for whom central clamping is avoided. Right atrial blood removal via the femoral vein is frequently used for blood

removal; however, it is important to achieve favorable blood removal, for which vacuum-assisted blood removal should be used by deploying a cannula tip with widely placed lateral holes in the superior vena cava. The femoral artery on the side connected to the true lumen is frequently used for blood supply; however, many surgeons prefer the ascending aorta or axillary artery because of a concern about the occurrence of cerebral infarction due to malperfusion or debris.

Arch/descending aortic replacement tends to cause insufficient cerebral and myocardial protection, and various measures have been taken. Since cerebral protection is based on hypothermia, it is cooled to a blood removal temperature of 18°C or lower that reflects the brain temperature (nasopharyngeal or tympanic temperature may also be used). Although there are restrictions on the surgical field, selective cerebral perfusion may be added, and barbiturate or anticonvulsant fosphenytoin may also be administered. Since the ischemia time is approximately 30 min, this level of hypothermia alone is sufficient for myocardial protection. However, if asystole cannot be achieved by hypothermia alone, the administration of a potassium bolus of approximately 20 mEq immediately before circulatory arrest, the administration of anterograde cardioplegic solution via a balloon catheter after circulatory arrest, and the administration of anterograde cardioplegic solution by ascending aortic cross-clamping depending on the surgical field is also performed. Left ventricular venting during ventricular fibrillation is of more importance, and in particular, left ventricular enlargement during rewarming must be avoided.

After transecting the central aorta under opening, the aortic arch is anastomosed with a prosthetic graft. After anastomosis, the air is sufficiently extruded, and upper body perfusion is resumed from the lateral branch of the graft at 1–1.5 L/min. Peripheral anastomosis of the graft is performed during rewarming, and the intercostal artery and left subclavian artery are reconstructed as needed.

b. Thoracoabdominal Aortic Replacement

Thoracoabdominal aortic replacement is indicated for patients with diffuse enlargement from the thoracic descending aorta to the abdominal aorta. It is often indicated for patients with genetic background, such as Marfan syndrome, because of the high rate of dilation of the dissection part in the late stage. It has a high operative mortality rate and incidence of paraplegia, and its results for Crawford type II particularly pose an issue.[1408] However, favorable results with an early mortality rate of 3.6–5.8%, a paraplegia incidence of 2.6–6.0%, and a 5-year survival rate of 65–79% have also been reported in the recent years.[1409,1410] Also, its results are relatively favorable in the disease group with genetic background.[1408] On the other hand, a staged surgery was reported to reduce the incidence of SCI,[1411] and if the downstream enlargement remains moderate, a staged surgery with descending aortic replacement and thoracoabdominal aortic replacement is also considered. In such cases, a careful decision must be made in consideration of the risk of the second-stage surgery, which is a re-thoracotomy, in addition to the risk of rupture while awaiting second-stage surgery.

Spinal cord protection and abdominal organ protection are important in thoracoabdominal aortic replacement, in addition to the considerations given to (arch) descending aortic replacement. For spinal cord ischemia, distal aortic perfusion based on collateral network concept, prevention and perfusion of segmental artery steal, cerebrospinal fluid drainage, and hypertensive management are performed, in addition to the identification of the spinal cord feeding artery, electrophysiological monitoring, and pharmacological protection. Segmental artery reconstruction is preferred as it reduces the risk of late SCI associated with non-reconstruction of the spinal cord feeding artery. For details, see **Chapter VII**, "**2.3 Spinal Cord Protection Method**". In addition, because hypothermia extends the spinal cord ischemic tolerance time, deep hypothermia has also been selected for spinal cord protection, including cases in which segmental artery reconstruction cannot be performed under small segmental clamping, which is expected to maintain collateral blood flow through the epidural arcade.

When reconstructing the major abdominal branch artery, organ protection is performed by selective perfusion for the celiac and superior mesenteric arteries and selective perfusion or perfusion with lactated Ringer's solution at 4°C for the left and right renal arteries.[1412] The effectiveness of perfusion with the Custodiol® solution is also being investigated. Perfusion is not always necessary when using deep hypothermic therapy. In addition, due to the presence of autoregulation in the renal blood flow, single forced perfusion with a pump has a high risk of kidney injury due to high-pressure perfusion, even at a low flow rate (150–200 mL/unilateral). When performing selective perfusion, it is important to provide an escape route together with the celiac artery, superior mesenteric artery, or iliac artery.

c. Frozen Elephant Trunk (FET)

FET may be selected for patients who have insignificant dilation of the distal descending aorta with a dilated aortic arch, or patients with chronic-stage complications other than dilation/aneurysm formation. Total arch replacement is performed in the same manner as normal aortic arch replacement, and FET is inserted into the distal true lumen. Because the extended insertion length leads to a concern about SCI, its insertion is limited from T8 to the central region. However, if the insertion is too short, the distal end hits the tortuous site of the descending aorta, increasing the risk of inducing stent graft-induced new entry (SINE). With regard to the stent graft diameter, it is recommended to select the size with a lower oversize ratio based on the true lumen diameter at the distal end of the deployment part to avoid the distal SINE. The distal aortic anastomotic site is often found in the periphery of the dilated part in patients with enlarged arch; however, it can be found in the central side of the subclavian artery for other indications. The area without a stent requires attention as it may become stenotic due to tortuosity or kinks, if it is excessively long.

d. Abdominal Aortic Replacement

When only the infrarenal abdominal aorta is dilated, surgery based on normal AAA is performed. In such a case, it is necessary to resect/fenestrate the flap of the central anastomosis site and anastomose the graft to both lumina to avoid the induction of malperfusion due to re-entry closure.

3.2.4 Medical Treatment

The primary goal of chronic-stage patient management is to prevent re-dissection and rupture and to decide the

timing and procedure of surgery/reoperation. In addition, it has been reported that patients after surgery for aortic diseases also have a high risk of cardiovascular events, such as myocardial infarction and stroke, than patients before surgery.[299] Thus, regardless of surgery, optimal medical treatment (OMT), which is medical treatment aimed at improving the blood pressure, lipid, and atherosclerotic risk factors, is important.

a. Blood Pressure Management

Blood pressure management is of the utmost importance. Favorable blood pressure control was reported to reduce the occurrence of re-dissection by approximately 1/3.[1413] Its hypotensive target is below 130/80 mmHg. With regard to the selection of antihypertensive drugs, it is important that they achieve a reliable hypotensive effect; however, only the effects of β blockers have been supported by evidence, such as reducing aortic dissection-related events like hospitalization[276] and suppressing the enlargement of the aneurysm diameter.[1414] According to the analysis of IRAD, β blockers were reported to have the highest usage rate in chronic aortic dissection, contributing significantly to the improvement in its survival rate.[1269] It has also been reported that the ARB losartan slows the enlargement of aortic diameter in Marfan syndrome patients.[1415] Regardless of the drugs used, it is important to administer the maximum permissible dose until the target blood pressure is reached and to perform strict blood pressure control.

b. Management of Atherosclerotic Risk Factors

In surgical and medical treatment cases of aortic dissection caused by atherosclerosis, medical treatment, such as control of lipid-lowering therapy and diabetes mellitus and smoking cessation, is important for suppressing cardiovascular events in the late stage, in addition to blood pressure control. As in coronary artery disease, statins were reported to suppress cardiovascular events in aortic diseases,[299] and their active introduction is desired.

c. Rest Level and Exercise

There are a few restrictions on the normal daily life. Although there is little evidence about exercise, it is recommended that patients perform mild to moderate aerobic exercise (equivalent to 3–5 METs), such as walking and light running, which are effective in lowering the systolic blood pressure, for at least 30 min a day and at least 150 min a week.[1416] Weightlifting, which increases the intrathoracic pressure, should be avoided, and exercise should be stopped before feeling a burden with a light load. The exercise intensity should be set for each patient such that the systolic blood pressure does not exceed 180 mmHg, and the exercise intensity should be estimated by a treadmill exercise stress test.

d. Follow-up by Imaging Examinations

Changes in the aortic diameter are observed over time in the outpatient department by performing CT/MRI examinations at regular intervals for 2 years, the period in which aortic dissection-related events often occur. With regard to the follow-up intervals for CT examination, it was reported that CT examination for follow-up should be performed 1, 3, 6 months after the onset, and every 6 months thereafter up to 2 years of the onset, or 1, 3, 6, 9, and 12 months after the onset.[68] The interval between CT examinations may be shortened if the aortic diameter is close to the surgical indication. Also, considering radiation exposure and kidney injury due to the contrast medium, the interval between CT examinations may need to be slightly increased in patients with a small aortic diameter and the thrombosed and occluded false lumen without ULP.

Table 43. COR and LOE for Postoperative Follow-up of Aortic Dissection and Additional Treatment

	COR	LOE
After surgery, regular (after 1, 6, and 12 months and, subsequently, every year) follow-up involving imaging procedures is recommended[1291,1418–1420]	I	C
Additional invasive treatment is recommended for patients with symptoms related to residual false-lumen enlargement	I	C
Additional invasive treatment is recommended for patients with residual false-lumen enlargement (aortic diameter: 55–≥60 mm)	I	C
When false-lumen enlargement or narrowing of the true lumen is predicted in patients after open surgery for acute Type A dissection/with residual false-lumen patency, early TEVAR should be considered in those meeting anatomical requirements[1421,1422]	IIa	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

e. Limitations of Medical Treatment

Whether (re-) surgery is performed or the course is monitored only with hypotensive treatment must be determined based on the results of CT/MRI examination. Aortic dissection is also generally indicated for surgery under the same conditions as a true aneurysm; however, the treatment policy needs to be reexamined if the patient has ULP and significant morphological changes.

f. Precautions for the Management of Surgical Cases in the Chronic Stage

For long-term postoperative complications, a follow-up by CT examination is required to examine the presence or absence of suture failure, anastomotic pseudoaneurysms, and re-dissection.

For aneurysm formation caused by residual dissection, a follow-up by CT examination is required to examine the extension and enlargement of residual dissection, the degree of thrombosis formation, and the state of the false lumen. It has been reported that false lumen patency is found in 46–78% of postoperative Type A dissection patients,[1222–1225] while 75%, 59%, and 43% of patients survived without the enlargement of aneurysm diameter at 3, 5, and 8 years after surgery, respectively.[1226] The addition of open surgery or TEVAR is considered in patients who exhibit enlargement in the late stage.

3.3 Postoperative Follow-up and Additional Treatment (Table 43)

3.3.1 Postoperative Follow-up

In many patients with aortic dissection, residual dissection is present even after open surgery or TEVAR. Strict follow-up is important. In particular, as follow-up with images, CT must be performed 1, 6, and 12 months after initial treatment, and, subsequently, every year. When

renal dysfunction makes contrast enhancement impossible, true/false lumen blood flow should be evaluated by MRI or transesophageal ultrasonography.[1328,1329] In patients with false-lumen patency or genetic predispositions, closer follow-up should be considered.

3.3.2 Indication of Additional Treatment

In some patients, false-lumen enlargement is observed at the site of residual dissection (arch/descending aorta) after surgery for Type A dissection or after invasive treatment (open surgery or TEVAR) for Type B dissection.[342,1079,1085,1421,1423–1431] Furthermore, endoleak involving a stent graft-induced new entry (SINE) after TEVAR for Type B dissection is the most frequent reason for additional invasive treatment.[342,512,1423] Indication criteria for additional invasive treatment for these types of residual dissection are as follows:

(1) Presence of symptoms related to residual dissection false-lumen enlargement or true-lumen stenosis (chest/back pain, hoarse voice, dysphagia)
(2) Residual dissection aortic diameter: ≥55 to 60 mm
(3) Rapid enlargement of a residual dissection aortic diameter (≥5 mm/6 months) or redissection, endoleak after FET surgery or TEVAR, SINE, or retrograde Type A dissection
(4) Patients in whom future false-lumen enlargement is predicted in the presence of residual dissection after surgery for Type A dissection; indication of preemptive TEVAR

3.3.3 Frequency of Additional Treatment

a. Distal Side After Surgery for Type A Dissection

Additional distal treatment is performed in 11.6–22.7% of patients after surgery for acute Type A dissection.[1079,1085,1421,1426,1428–1434] The additional distal treatment rate depends on the contents of initial surgery. Some studies indicated that total arch replacement, including FET surgery, reduced the risk of additional treatment (hazard ratio) to 0.37 in comparison with ascending aorta/hemiarch replacement.[1435–1437] Therefore, FET-combined total arch replacement is recommended as initial surgery when the benefits of avoiding additional treatment outweigh the disadvantage of increased risk of acute surgery. Of course, the additional treatment rate is high in patients with residual distal false-lumen patency. Follow-up by CT is important.[1291,1418,1419]

b. After Surgery for Type B Dissection

Additional treatment after surgery for Type B dissection depends on the timing and methods of initial treatment. When TEVAR for acute complicated dissection was performed as initial treatment, the additional treatment rate after 1 year was 15.4%.[342,1424] On the other hand, the additional treatment rate after TEVAR for chronic dissection was 20.2% (6.0–53.3%), with a mean follow-up of 33.7 months, being significantly higher than after open surgery (11.8%, 0–26%).[342,386,402,404] In addition, the interval until additional treatment was significantly shorter (TEVAR: 15.4±2.3 months, surgery: 65±9 months). When selecting open surgery as initial treatment, the additional treatment rate depends on the timing of initial open surgery. In many cases of acute complicated dissection, the extent of treatment is limited to the thoracic region; therefore, the additional treatment rate after 1 year is 5.5%, being similar to that after TEVAR.[386] On the other hand, thoracoabdominal aortic replacement is selected in approximately 50% of patients with chronic Type B dissection, and the additional treatment rate was 11.8% (0–26%), with a mean follow-up of 27 months, being lower than after TEVAR.[342,386,402,404,405,1438]

3.3.4 Methods and Results

a. Distal Side After Surgery for Type A Dissection

When selecting ascending aorta/hemiarch replacement as initial surgery, a residual dissection entry often remains in the site of distal anastomosis (dissected flap injury) on initial surgery, arch/proximal descending aorta, or arch branches. In open surgery as additional treatment, an enlarged area involving these entries is replaced with a prosthetic graft. In endovascular treatment, entries that remain are closed with a stent graft (SG). When an entry remains in the arch/arch branch, open surgery is primarily selected.[1113,1233,1429,1439–1441] When it remains in the descending aorta, TEVAR is primarily selected. Techniques to perform arch/arch branch treatment by TEVAR or hybrid treatment have been established, and the results of acute-phase treatment are more favorable than those of surgery.[1421,1422] However, TEVAR in patients with dissection may lead to further additional treatment,[1421] and the timing of additional treatment is earlier than that of open surgery in many cases.[1422] This is due to the fact that favorable remodeling of the enlarged false lumen is difficult to achieve by entry closure with a SG alone.

b. After Invasive Treatment for Type B Dissection

Additional treatment methods are comprehensively selected based on the etiology, general condition, expected prognosis, and adherence in addition to a technique of initial treatment (open surgery or endovascular treatment including TEVAR), enlarged area, residual entry/re-entry positions, and state of main branch perfusion: perfusion from true-lumen/false-lumen. A basic concept for surgery consists of resection of an enlarged area and prosthetic graft replacement, and that for TEVAR/EVAR is closure of a residual entry, as described for initial invasive treatment.

When performing additional endovascular treatment in patients treated by TEVAR as initial treatment, a false lumen at target may remain without reduction or further enlargement due to blood flow from re-entry sites.[391] Thus, the achievement of complete exclusion is a shortcut to settling the residual dissection.[1303] Furthermore, intervention to a false lumen should also be considered to achieve complete thrombosis of a target false lumen.[1307,1406]

As an additional treatment method, open surgery is prioritized in patients with false-lumen enlargement, but endovascular treatment is also selected for additional treatment in many patients who underwent endovascular treatment as initial treatment. In those who underwent surgery as initial treatment, surgery is also often selected for additional treatment.[405] However, after initial treatment for aortic dissection/in the presence of residual dissection, the lesion involves the entire aortic region in many cases; treatment with an adequate combination of the two techniques and hybrid treatment may contribute to an improvement in the prognosis. Therefore, this complex dissection treatment should be performed in both open surgery- and endovascular-treatment-skilled institutions.

Concerning additional treatment for Type B dissection, the extent of open surgery or endovascular treatment involves the thoracoabdominal aortic region in many

cases. There were no marked differences in the comparison of prognosis or incidence of SCI between open surgery and endovascular treatment (TEVAR, hybrid treatment, EVAR with fenestration-type/branched devices) involving this thoracoabdominal region.[1442] However, the repeated treatment rate in the chronic phase is markedly higher in patients treated by endovascular treatment; techniques should be selected, based on the patient age, etiology, and adherence.

3.4 Extensive Aortic Dissection

3.4.1 Open Surgery

In chronic Type B dissections, (dissecting) aortic lesions with a large false lumen from the descending aorta to the abdominal aorta are referred to as "extensive aortic dissection." Residual dissection after ascending aorta/hemiarch replacement for acute Type A dissection is also included in this category, and its surgical indications and procedures are described in this section. In addition, patients with Type B dissection are defined as "those without dissection in the ascending aorta." However, patients with an entry in the arch and Type B dissection patients with a false lumen in the arch tend to be classified as those with "non-A non-B dissection".[1443]

a. Approach

In median sternotomy, the treatment range of the general open surgery covers from the arch to the distal aortic arch. The entry of the descending aorta can be closed with a median sternotomy by combining a total arch replacement with the insertion of FET into the true lumen of the descending aorta. On the other hand, with left thoracotomy, the descending aorta and subsequently, the abdominal aorta can be reached from the distal arch. In addition, operation in the pericardial sac and surgical operation on the aortic arch can be performed with left thoracotomy. Patients with non-A non-B dissection require a surgical operation to the ascending/aortic arch, for which staged surgery is performed, with total arch replacement with median sternotomy in the initial stage and surgery on the descending aorta in the second stage. In the initial stage of surgery, ET or FET that induce blood flow in the true lumen or both lumina of the descending aorta is performed, in addition to total arch replacement. In the second stage of the surgery, TEVAR is added for the true lumen of the descending aorta, or open surgery with left thoracotomy (descending aortic replacement or thoracoabdominal aortic replacement) is performed. One-stage surgery is selected for patients who can undergo extended surgery, such as young patients, or patients with a high risk of or difficulty in staged surgery (giant descending aortic aneurysm or impending rupture).[1218,1219]

b. Anastomotic Methods

See the section on chronic Type A dissection ("**2.3.2 Aortic Arch**" in this chapter).

c. Complications

In surgery for extensive chronic Type B dissection from the arch to the thoracoabdominal aorta, attention must be paid to cerebral infarction and SCI.

Normal heart-lung machine operation can be performed in the median sternotomy approach; however, the selection of the blood perfusion site is important because of the presence of the false lumen in the aortic arch. The axillary artery,[1213,1214] femoral artery, and cardiac apex blood supply can be selected for blood perfusion site in addition to the ascending/aortic arch. In this procedure, attention must be paid to organ blood flow failure due to retrograde perfusion via the femoral artery and dispersion of thrombus in the false lumen. Hypothermia is introduced by a heart-lung machine, and selective cerebral perfusion and retrograde cerebral perfusion are used as a cerebral protection method. The establishment of selective cerebral perfusion may be difficult in patients whose dissection has spread to the arch branch, and it is important to maintain reliable cerebral perfusion, such as prior perfusion after suturing a prosthetic graft. In patients with false lumen thrombus in the branch, attention must be paid to cerebral infarction due to thrombus dispersion.

Femoral artery blood perfusion is the first choice in the left thoracotomy approach; however, it has a risk of embolism due to the dispersion of false lumen thrombus caused by retrograde perfusion. The axillary artery, as well as the ascending aorta and cardiac apex,[1215] can also be selected as the anterograde blood perfusion site. Basically, hypothermia is used for cerebral protection. There is a procedure that does not perform aortic arch clamping by using retrograde cerebral circulation with hypothermic circulatory arrest or the Takamoto method,[1444] while another method performs cerebral perfusion by deploying a blood supply tube with a balloon in the aortic arch. Anterograde cerebral perfusion, in which anterograde blood supply is carried out from the axillary artery and the ascending aorta by clamping the aortic arch, has been performed. However, the left thoracotomy approach has a more unstable cerebral/cardiac protection effect than median sternotomy, and particular attention must be paid to cerebral infarction. The Takamoto method, originating in Japan, is a cerebral protection method that performs retrograde cerebral perfusion by clamping the descending aorta to be replaced, carrying out blood perfusion from the femoral artery, and raising the right atrial pressure to 15–25 mmHg in the Trendelenburg position.

SCI is also a serious complication. In median incision surgery, FET is often performed in addition to total arch replacement. Intercostal artery occlusion by FET and intercostal artery occlusion associated with false lumen thrombosis are considered to be the causes of SCI. Late SCI, which occurs after surgery, has also been reported.[1408] The incidence of SCI is high in patients with an extensive surgical range from the descending aorta to the thoracoabdominal aorta.[1445] In the 2015 annual report of JCVSD, the incidences of SCI in chronic aortic dissection surgery were 1.5% for open surgery and 7.1% for hybrid surgery.[711] Several cases of hybrid surgery are performed with FET, and attention must always be paid to SCI associated with FET, even in chronic Type B dissection.

3.4.2 Endovascular Treatment

In patients with chronic Type B dissection requiring surgical operation for the arch and for TAAA across the diaphragm, stent graft (SG) may be used on some or entire area to minimize the invasiveness. The same applies to patients whose dissection remains in the arch after ascending replacement or partial arch replacement for Type A (DeBakey type I) dissection. Total arch replacement is performed when there is leakage at the distal anastomosis site of ascending replacement or partial arch replacement

for Type A dissection, when an entry remains in the arch or arch branch, and when an entry in the proximal descending aorta can be resected by a median sternotomy. If ET or FET is deployed in such a procedure, it can be used in subsequent TEVAR for descending aortic lesions.

On the other hand, an entry in the proximal descending aorta can be closed by TEVAR, and when occluding the arch branch, the hybrid treatment that first performs bypass surgery is generally selected. There have been some reports of TEVAR using branched SG. Therefore, it has recently been recommended to select partial arch replacement in the initial surgery, which replaces only the brachiocephalic artery or the brachiocephalic artery and the left common carotid artery, instead of simple ascending replacement and hemiarch replacement. This procedure does not require total arch replacement for subsequent similar issues, and they can be solved by a hybrid treatment.

If an entry cannot be easily achieved with a median sternotomy, the entry can be closed by simple TEVAR without the need for arch branch bypass. However, since the proximal landing zone is often dissected, it poses a concern about injury to the dissection flap, and the oversizing of SG diameter to a smaller extent is desirable.[416]

Complete endovascular treatment can be performed on patients with TAAA by using branched SG. However, since the device itself has not been approved for insurance coverage in Japan, it is indicated for hybrid treatment in which TEVAR is performed in combination with abdominal branch bypass surgery. Also, when anastomosing prosthetic graft to SG, it is possible to anastomose SG alone; however, the prevention of hemorrhage and stabilization of SG can be achieved by anastomosing with the aortic wall around the SG.[1446] Since an autologous expandable stent is used for SG, it can be expanded again when the clamping by forceps is released.

Although the treatments mentioned above are performed in combination, prosthetic graft replacement for the arch region and TEVAR for descending/thoracoabdominal region are generally performed in stages. Complete endovascular treatment of the arch, descending, and thoracoabdominal regions, as well as hybrid treatment with TEVAR for descending/thoracoabdominal region combined with abdominal branch bypass surgery, can be performed in one stage. However, whether it is performed in one or multiple stages is carefully considered by examining the deployment length of SG, SCI due to deterioration of hemodynamics, such as hemorrhage, and the invasiveness of abdominal branch bypass surgery.

VII. Issues Associated With Aortic Surgery

1. Cerebral Protection

Cerebral protection has to be performed as an auxiliary means when the open distal technique is required for ascending aortic replacement or aortic arch replacement, or when the open proximal technique is required to approach the distal aortic arch under left thoracotomy. Cerebral protection can be performed with profound hypothermic circulatory arrest alone; [595] however, it leads to a time constraint. In particular, as total aortic arch replacement requires long-term cerebral protection, anterograde selective cerebral perfusion (ASCP/SCP)[596] or retrograde cerebral perfusion (RCP)[598] has been added as a safer method, leading to improved results (Class IIb).[1447]

In the general method of SCP, a cannula with a balloon is inserted into the brachiocephalic artery, left common carotid artery, and left subclavian artery under hypothermia at approximately 20–22°C; and the brain is perfused in an anterograde manner using a flow rate of 10 mL/kg/min.[596] Because of its safety, surgery under moderate hypothermia at 25–28°C has also been performed recently (Class IIb).[603,1448] However, even if the minimum body temperature is raised to 28°C, its significant clinical advantages compared to the results at lower temperature settings have not been demonstrated.[1449] In addition, hypothermia is considered essential in RCP, and the brain is perfused in a retrograde manner via the superior vena cava under ultra-hypothermia at approximately 18°C using the central venous pressure of 15–20 mmHg.

In RCP, cerebral protection is thought to have a time constraint of up to 60 min, and the arch first technique (reconstruction of the arch branch is followed by anastomosis of the peripheral and subsequently central regions) is used as a solution to the constraint.[601] In addition, regarding the definition of hypothermia in aortic surgery, an expert consensus was published, which defined "profound," "deep," "moderate," and "mild" nasopharyngeal temperatures as "14°C or lower," "14.1–20°C," "20.1–28°C," and "28.1–34°C," respectively.[1450] These criteria are expected to be used in future academic reports. The usefulness of RCP was not demonstrated in an RCT with profound hypothermic therapy alone (Class Ib),[1451] and an increased incidence of transient cerebral disorders was observed in an RCT with SCP (Class IIa).[1071] In addition, the matched paired analysis of the Japan Cardiovascular Surgery Database showed that RCP extended the length of ICU stay.[585]

Because of these results, SCP with physiological perfusion and less time constraints has become the most widely used cerebral protection method in Japan. On the other hand, the insertion of cannulas into the arch branches during SCP is not required in patients with a limited time of profound hypothermic circulatory arrest, such as ascending replacement using hemiarch replacement or open distal anastomosis, and some facilities use the RCP method, which is simple and capable of reducing the risk of embolism.

Observation of the regional cerebral oxygen saturation (rSO2) over time using near-infrared spectroscopy is useful for intraoperative monitoring, in addition to the observation of temperature (tympanic/nasopharyngeal temperature and bladder/rectal temperature) and perfusion pressure (such as left and right radial arterial pressure, cannula tip pressure, and lower-limb artery pressure). Also, the selection of an aortic return site during extracorporeal circulation, operation of the arch branch during insertion of cannulas for SCP or reconstruction, and prevention of cerebral air embolism during circulatory arrest and extracorporeal

Table 44. COR and LOE for Spinal Cord Protection in the Invasive Treatment of Aortic Aneurysm/Aortic Dissection

	COR	LOE
In open surgery for extensive descending/thoracoabdominal aortic replacement, it is recommended to perform cerebrospinal fluid drainage if it is not contraindicated[652,1452]	I	B
It is recommended to perform cerebrospinal fluid drainage for delayed-onset spinal cord injury[682,1453,1454]	I	C
The preoperative identification of spinal feeding arteries by non-invasive examinations, such as contrast-enhanced MRI and contrast-enhanced CT, should be considered[165,1455]	IIa	C
Preservation or reconstruction of identified feeding arteries should be considered[165,1455]	IIa	C
Intercostal artery reconstruction should be considered for extensive thoracoabdominal aortic replacement[1408,1456]	IIa	C
Distal aortic perfusion should be considered for beating-heart surgery[1457]	IIa	C
Intercostal artery reconstruction utilizing the epidural network by small-range segmental clamping should be considered[1458,1459]	IIa	C
Staged surgery should be considered for patients who do not require one-stage surgery[1411]	IIa	C
Cerebrospinal fluid drainage should be considered in TEVAR for patients at a high risk of spinal cord injury, if it is not contraindicated[1460]	IIa	C
Continuous intravenous administration of naloxone during the perioperative period may be considered[1461]	IIb	C
Electrophysiological monitoring of the spinal cord function may be considered[671,1456]	IIb	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence; MRI, magnetic resonance imaging; TEVAR, thoracic endovascular aortic repair.

circulation resumption are important preventive measures for cerebral complications, and require careful handling.

2. Spinal Cord Protection (Table 44)

The causes of ischemic spinal cord injury (ischemic SCI) during the aortic perioperative period include decreased blood flow associated with temporary/permanent occlusion of the feeding artery and embolism; additionally, there are immediate and delayed-onset ischemic SCI, depending on the time of onset. Spinal cord protection requires a correct understanding of the various pathological conditions of ischemic SCI and approach from various angles.

2.1 Anatomical Characteristics of Spinal Cord Blood Supply

The arterial blood supply to the human spinal cord consists of a longitudinal anterior spinal artery and a pair of posterior spinal arteries (**Figure 65**). The anterior spinal artery, which nourishes most of the gray matter and the ventrolateral funiculus, is important, and communication between the two is poor except for the medullary cone region (terminal region).[1462]

The anterior spinal artery is embryologically a connection between the anterior radicular arteries derived from the segmental arteries.[1463] Since numerous anterior radicular arteries regress during the fusion process, an average of only 6–8 radiculomedullary arteries (anterior radicular arteries that reach the spinal cord) remain.[1462,1463] The anterior spinal artery becomes thinner from the caudal side of the T4 level and becomes thicker from the caudal side of the Adamkiewicz artery junction described subsequently.[1462,1464] Therefore, the thoracic spinal cord level is vulnerable to ischemia (critical zone[1462,1464]), and severe spinal cord ischemia caused by prolonged simple clamping results in paraplegia from around the T4 level.

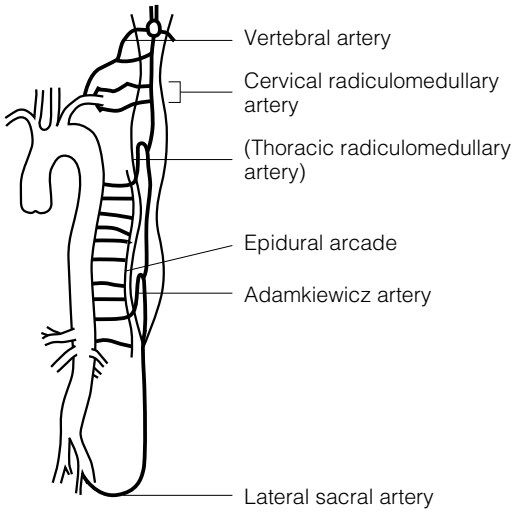


Figure 65. Anatomical characteristics of the spinal cord blood supply.

In the cervical spinal cord/T1-T2 thoracic spinal cord, the anterior radicular artery branches from the subclavian artery system (vertebral artery, costocervical trunk-deep cervical artery/supreme intercostal artery, and thyrocervical trunk-ascending cervical artery), or from the ascending pharyngeal artery of the external carotid artery system in

some cases.[1462–1464] Therefore, perfusion/preservation of the left subclavian artery is important for spinal cord protection.

At the thoracic spinal cord/lumbar spinal cord level, the anterior radicular arteries are derived from the segmental arteries (3rd intercostal–4th lumbar artery), of which 1–2 become radiculomedullary arteries.[1462,1464] Of these, the thickest and most important one at the lower thoracic spinal cord/upper lumbar spinal cord level is called the Adamkiewicz artery. While 3/4 of this originates from T9-T12, 3/4 originates from the left side.[1462] The radiculomedullary artery derived from the segmental arteries exhibits a characteristic hairpin curve. This is because (1) it ascends in the spinal canal due to the difference in growth between the vertebra and spinal cord and (2) the artery takes a continuous morphology to the caudal side since the anterior spinal artery on the cranial side of the radiculomedullary artery junction has a small diameter. Therefore, the blood flow through the Adamkiewicz artery is mainly distributed in the lumbar spinal cord, and its involvement in the blood flow of the lower thoracic spinal cord is considerably small.[1464] The segmental arteries form vertical and horizontal anastomoses inside and outside the spinal canal. Anatomically, anastomosis outside the vertebral body is predominant in the longitudinal direction, whereas anastomosis inside the spinal canal and epidural anastomosis are predominant in the lateral direction.[1463] Due to the presence of this abundant network, the occlusion of one segmental artery that branches off the Adamkiewicz artery does not cause SCI in most patients. This has been known as the alternative pathway since the early 1970s.[1464]

At the sacrum bone level, the segmental arteries are reconstructed into the lateral/median sacral artery, and the 5th lumbar artery branches from the median sacral artery and the iliolumbar artery.[1463] The lateral sacral artery is most important for spinal cord blood flow, and serves as the source of blood flow from the cauda equina to the medullary cone region.[1462,1464] Therefore, internal iliac artery blood flow is important for spinal cord blood flow.

2.2 Pathophysiology of Ischemic Spinal Cord Injury

2.2.1 Immediate and Delayed-Onset Injury

There are immediate and delayed-onset ischemic SCI. An immediate SCI is irreversible injury to the spinal cord due to intraoperative spinal cord ischemia. While it may be caused by permanent ischemia, such as suture closure of the feeding arteries and embolism, transient ischemia may also cause an irreversible injury if the tolerance time is exceeded. Experimentally, ischemic tolerance time is considered to be approximately 5–10 min at normothermia. Clinically, however, there is a difference in the degree of ischemia due to the presence of collateral blood flow, and it is difficult to determine the spinal cord temperature. In addition, due to the presence of collateral blood flow, non-reconstruction of the segmental artery does not mean permanent ischemia.

The factors of the delayed-onset SCI include postoperative feeding-artery occlusion (such as the occlusion of the reconstructed artery and occlusion associated with the progression of false lumen thrombosis in dissection), postoperative increase in the cerebrospinal fluid pressure associated with spinal cord edema,[1465] and decrease in spinal cord perfusion pressure associated with the deterioration of hemodynamics.[1462] In the latter pathological condition, the volume of spinal blood flow, which had decreased to the injury-occurrence borderline dependently on the collateral blood flow due to surgery, is thought to have further decreased to the injury-occurrence level due to the postoperative deterioration of hemodynamics. Experimentally, the blood flow reserve of the collateral flow after total closure of the segmental arteries remains insufficient up to approximately 72 h after surgery,[1466] and it has been shown that it does not meet the increased demand for blood flow after surgery. Clinically, the delayed-onset SCI is often seen in procedures that do not reconstruct the segmental artery[1467] and TEVAR.[679] Additionally, it has been reported that the proportion of delayed-onset SCI of these procedures exceeds 80%.[679,1467] As its countermeasure, it is recommended to maintain high-blood pressure management + cerebrospinal fluid drainage for three days after surgery in patients with non-reconstruction of the segmental artery.[1466,1468,1469] Experimentally, the delayed-onset SCI may be caused by apoptosis due to intraoperative ischemia[1470] and reperfusion injury, and they have been the pharmacological targets for spinal cord protection.

2.2.2 Effectiveness of Collateral Flow

The effectiveness of collateral flow during feeding-artery occlusion depends on the anatomy, modification by lesions and previous surgery, hemodynamics, and surgical strategy. The collateral flow is mediated by the anterior spinal artery, network within the spinal canal (epidural arcade), or network outside the spinal canal. In addition to these, some patients have a developed extrathoracic collateral flow as a result of modification by lesions and previous surgery.

The collateral blood flow mediated by the anterior spinal artery does not easily distribute from the caudal side to the cranial side of the Adamkiewicz artery because the anterior spinal artery narrows on the cranial side of the hairpin-shaped Adamkiewicz artery. This is the reason why distal aortic perfusion cannot always prevent SCI.[1471] On the other hand, approximately 40% of patients have a second radiculomedullary artery on the caudal side of the Adamkiewicz artery (several are derived from the lumbosacral segmental artery).[1472,1473] This second feeding artery often does not have a hairpin shape and joins the anterior spinal artery from the caudal side (without the narrowing on the cranial side from the junction).[1473] In such cases, the blood flowing from the distal radiculomedullary artery to the anterior spinal artery is thought to reach the Adamkiewicz artery region, even if the Adamkiewicz artery is blocked. In fact, it was shown that patients with a second feeding artery could avoid spinal cord ischemia by distal aortic perfusion and prevention of a steal phenomenon.[1473]

The collateral flow mediated by the epidural arcade is always present between the vertical and horizontal adjacent segmental arteries. It is commonly observed that the segmental artery with weak back-bleeding exhibits vigorous back-bleeding during surgery after the closure of the surrounding segmental arteries. Experimentally, it has also been shown that the collateral blood flow mediated by the epidural arcade functions immediately after the occlusion of the Adamkiewicz artery.[1474] Therefore, a strategy that utilizes collateral blood flow mediated by the epidural arcade from the adjacent intercostal artery is advantageous for the reconstruction of the intercostal artery that connects to the Adamkiewicz artery. One of such methods is the

small-range segmental clamping,[1458,1459] which has been developed in Japan.

The collateral blood flow mediated by the network outside the spinal canal does not function immediately after the occlusion of the feeding artery, and it has been experimentally shown that it requires some time for the opening of the channels.[1474] On the other hand, a clinical study measuring the peripheral intercostal arterial pressure after the closure of the intercostal artery showed significantly decreased peripheral intercostal arterial pressure in the transition from pulsatile flow to steady flow.[1475] This suggests that maintaining a favorable pulsatile flow in the distal aorta may improve the volume of the collateral blood flow mediated by the network outside the spinal canal, even in the acute phase. This may be a factor for the low incidence of SCI in TEVAR despite the non-reconstruction of the segmental artery. Therefore, it is suggested that a strategy to maintain pulsatile flow in the distal aorta may be effective even in open surgery.

Since an extrathoracic collateral flow also develops after the occlusion of the segmental arteries, it may take some time before sufficient blood flow is supplied. Yoshioka et al. showed on imaging that the collateral flow derived from the thoracodorsal artery, which had not been present before the surgery, developed postoperatively after occluding the Adamkiewicz artery by TEVAR.[1476] Griepp et al. experimentally showed an increase in the network outside the spinal canal and extrathoracic collateral circulation 5 days after the occlusion of the segmental arteries.[1477] To utilize the extrathoracic collateral circulation, a staged surgery preserving the artery that serves as the source of the extrathoracic collateral circulation is considered advantageous. Etz et al. reported that a staged surgery significantly reduced the incidence of SCI despite its more extensive occlusion of the segmental arteries than one-stage surgery.[1411]

2.2.3 Collateral Network Concept

The collateral network concept proposed by Griepp in 2007[1478] states, "Since the spinal cord has many inflow arteries and abundant collateral flow inside and outside the spinal canal, the blood flow does not depend on a single artery, and it is important to maintain collateral blood flow." This anatomical/hemodynamic fact has been known since the 1970s. In clinical settings, Acher reported in 1990 that the incidence of SCI was 5% even in Crawford type II using the strategy of segmental artery non-reconstruction +cerebrospinal fluid drainage (+naloxone).[1461] Additionally, Borst stated in his textbook in 1996, "The segmental artery should be closed to the earliest extent possible to prevent a steal."

This concept is often expressed by using a model of pouring water from multiple faucets into one water tank. However, this model is applicable to cases in which the anterior spinal artery lacks a narrow area, and even if it is present, it is applicable only to cases with developed collateral flow due to the presence of the second radiculomedullary artery or modification by previous surgery, which are thought to account for approximately 40% of all cases.[1473] A model that connects multiple water tanks by a thin pipe, instead of one water tank, is more suitable for the remaining 60% of cases (**Figure 66**).[1459] The presence of a thin connecting pipe (a narrow area of the anterior spinal artery on the cranial side of the Adamkiewicz artery junction) is one of the major factors for inadequate spinal cord protection with distal aortic perfusion alone,[1471] and it also leads to several cases of delayed-onset SCI in the procedures that do not reconstruct the segmental artery. Therefore, while the collateral network concept shows that the spinal cord blood flow does not depend on a single artery, it does not deny the reconstruction of the segmental artery that serves as the source of collateral blood flow. The interpretation that "reconstruction of the segmental artery is meaningless" is incorrect.

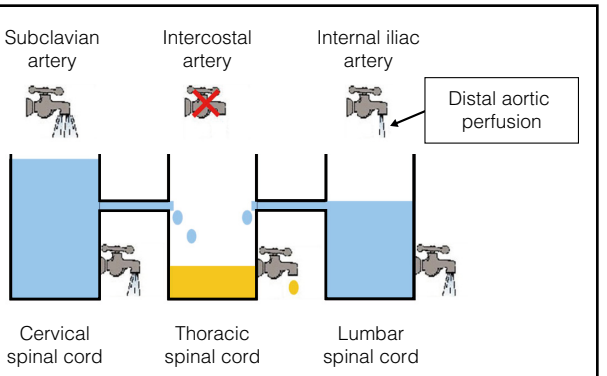


Figure 66. The water tank model of the collateral network concept. (Adapted from Shiiya N, et al. 2019.[1459]) © 2019 The Japanese Association for Thoracic Surgery. https://link.springer.com/journal/11748.

2.2.4 Mechanism of Injury Development by Procedure

The main cause of SCI in open surgery with segmental artery reconstruction is spinal cord ischemia during reconstruction.[1479,1480] Therefore, it is caused by spinal cord ischemia exceeding the tolerance time, even transiently, as a result of a prolonged aortic cross-clamping time due to the time required for reconstruction (the time it takes for pulsatile flow to recover in the collateral flow derived from the distal aorta is prolonged), despite the inability to maintain sufficient collateral blood flow during reconstruction. Therefore, several such cases result in immediate SCI.[1459] Other causes of injury development are thought to include embolism associated with the operation of shaggy aorta[1481] and ischemia associated with occlusion of the reconstructed segmental artery.

The main cause of SCI in the procedures that do not perform segmental artery reconstruction is the perioperative decline in blood flow associated with feeding artery closure. Because this is influenced by the volume of collateral blood flow, it depends on the anatomy, modification by lesions and previous surgery, hemodynamics, and surgical strategy. Ischemia occurs not only intraoperatively, but also postoperatively, and it often takes the form of a delayed-onset injury.

In open surgery without segmental artery reconstruction, it is advantageous to minimize a steal, shorten the aortic cross-clamping time, and sequentially close the segmental arteries from the outside prior to the aneurysm incision, with the expectation of opening the channels of collateral flow to some extent.[1482,1483] In non-reconstruction of the segmental artery, the application of deep hypothermia cannot take full advantage of the extension of ischemic tolerance time. Additionally, it has the disadvantage of a decreased collateral blood flow due to low pressure/steady

flow perfusion during rewarming. Thus, considering its invasiveness, it is not an ideal option in open surgery without segmental artery reconstruction.

TEVAR is intraoperatively more advantageous than open surgery due to the lack of aortic cross-clamping, maintained pulsatile flow in the distal aorta, and the absence of the steal phenomenon. However, sufficient caution is needed for injury caused by embolism.[1481] On the other hand, spinal cord blood flow becomes dependent on the collateral blood flow after surgery since the segmental artery cannot be reconstructed, and it has a risk of delayed-onset SCI for several days. Also, the risk becomes higher with a longer coverage length, because the source of collateral blood flow decreases. In the EUROSTAR registry, the overall risk of paraplegia is 2.5%; however, it has an odds ratio of 3.5 with three or more devices, which cannot be considered advantageous over open surgery.[688] This is particularly prominent when covering the Adamkiewicz artery.[1455]

There are various causes of SCI associated with the FET method. Given that deeper distal deployment[594,1484] and non-perfusion of the left subclavian artery[746] are risk factors, a decrease in the collateral blood flow dependent on the coverage length is also considered a cause, as in TEVAR. However, in the 1990s, even shallower deployment frequently caused injuries, showing its unique causes. Embolism, including air and atheroma, is thought to be involved, given that measures to fill the aorta with distal perfusion during deployment is effective.[594,1484] In addition, in some cases of dissection, SCI is associated with rapid thrombus occlusion of the false lumen.

2.3 Spinal Cord Protection Method

2.3.1 Identification, Preservation, and Reconstruction of the Spinal Cord Feeding Artery

Although selective intercostal/lumbar arteriography was previously used, it did not become widely used because of its low identification rate of 55–89% and SCI that could be caused by the examination itself.[1462] Recently, examinations using minimally invasive multidetector row CT (MDCT) and contrast-enhanced MRI have become widely used, and they have an identification rate of 70–94%.[119,165,166,1460,1485]

With the dissemination of the collateral network concept, the misunderstanding that the identification/reconstruction of such feeding arteries is meaningless has spread. However, this concept essentially indicates that the spinal cord blood flow does not depend on a single artery, and it does not deny the reconstruction of the segmental artery, which is the source of collateral blood flow. Several studies have reported that non-reconstruction of the intercostal artery is a risk factor for the development of SCI in open surgery of extensive TAAA.[1408,1456] A multicenter joint study in Japan also concluded that the preservation/reconstruction of the preoperatively identified Adamkiewicz artery reduces the incidence of SCI.[165] In addition, coverage of the patent Adamkiewicz artery was shown to be a risk factor for the development of SCI, especially if the length of treatment is long, even in TEVAR.[1455]

Intraoperative identification of the spinal cord feeding arteries has been attempted using a combination of segmental aortic cross-clamping and electrophysiological monitoring,[1480,1486] or infusion of a cold crystalloid solution into the clamping segment and the reconstructed artery combined with electrophysiological monitoring[1487] or an epidural temperature sensor. However, the significance of intraoperative monitoring is changing, as the feeding arteries can now be identified preoperatively with minimal invasiveness.

2.3.2 Electrophysiological Monitoring

Clinically, intraoperative monitoring of spinal cord function has been attempted using somatosensory evoked potential[1486] and evoked spinal cord potential[1480,1488] since the 1980s. However, despite its simplicity, the somatosensory evoked potential monitors the sensory nervous system, including the peripheral nerves and brain, because of peripheral nerve stimulation-cortical sensory area derivation, and it has low sensitivity and specificity.[1489] Evoked spinal cord potential, which is spinal cord stimulation-spinal cord derivation by two epidural electrodes, is spinal cord-specific and highly resistant to anesthesia, with a favorable specificity. However, its problems include epidural hematoma and inability of monitoring due to poor electrode position in some cases. In addition, it is disadvantageous that it requires a long time from ischemia to potential change because it reflects the function of the spinal tract rather than the spinal motor neurons.[1488]

Since the latter half of the 1990s, train stimulation has been introduced into transcranial electric stimulation, and motor-evoked potential has also become widely used in the field of aortic surgery.[673] This monitors the motor function of motor cortex stimulation-limb electromyographic derivation, and it is currently used most frequently due to its high sensitivity and rapid response to ischemia.[1488] However, it is easily affected by anesthetic agents, and care must be taken in anesthesia management. Also, it is affected by the brain, peripheral nerves, and neuromuscular junction, and its specificity and stability pose a problem. Therefore, some measures have been taken to improve its stability, such as transesophageal stimulation;[1490,1491] however, it is still in the stage of clinical research.

Electrophysiological monitoring was applied in the 1990s for the identification of the segmental artery to be reconstructed;[1480,1486] however, its significance has changed with the advent of non-invasive preoperative identification of the feeding artery. Therefore, the monitoring of sufficient intraoperative collateral blood flow and proper reconstruction of the segmental artery has become the main objective.[671,1456] For this purpose, oxygen saturation monitoring of the erector spinae muscles using near-infrared spectroscopy has been attracting attention in recent years as monitoring of collateral blood flow mediated by the network outside the spinal canal.[1492,1493]

2.3.3 Distal Aortic Perfusion

Distal aortic perfusion has been used in combination with segmental aortic reconstruction to reduce the total clamping time of the segmental artery by maintaining segmental artery perfusion during proximal aortic anastomosis. However, distal aortic perfusion alone was found to be insufficient as a measure against ischemia during segmental artery reconstruction. In the era of the collateral network concept, the purpose of distal aortic perfusion has changed to the maintenance of a high volume of spinal cord collateral blood flow during aortic cross-clamping, including during segmental artery reconstruction. Therefore, it is recommended to maintain high proximal blood pressure and distal perfusion pressure during aortic cross-clamping/distal aortic perfusion.[1483] This has been the basis of surgical

strategy, along with cerebrospinal fluid drainage + segmental artery steal prevention, when selecting surgery under aortic cross-clamping.[1457,1483] In addition to these, strategies to utilize collateral blood flow mediated by the epidural arcade (such as segmental artery reconstruction by small-range segmental clamping[1458,1459]) and devises to utilize pulsatile flow on the distal side have been implemented in Japan.

2.3.4 Prevention and Perfusion of Segmental Artery Steal

Steal of spinal cord collateral blood flow due to back-bleeding from the segmental artery during reconstruction has been known to be an important factor of SCI since the 1980s.[1494,1495] Therefore, back-bleeding from the segmental artery needs to be controlled promptly, except when using deep hypothermic circulatory arrest with a long ischemic tolerance time. Balloon catheter deployment from the lumen and clamping from the outside are used to control back-bleeding from the artery to be reconstructed. If the artery is not to be reconstructed, its prompt hemostasis is important. The strategy of sequentially clipping from outside the aneurysm prior to aortic cross-clamping is useful not only for opening channels of collateral flow, but also for avoiding a steal.[1483]

On the other hand, intercostal artery perfusion has been performed mainly when monitored spinal cord ischemia is not improved by steal control. Although it is difficult to effectively perfuse the small-diameter intercostal artery, a dedicated cannula is now commercially available, and the optimal perfusion volume was reported to be 30–40 mL/min at a circuit pressure of 150–200 mmHg.[1496]

2.3.5 Cerebrospinal Fluid Drainage

Since the spinal canal is a closed cavity, spinal cord perfusion pressure is defined by the difference between mean arterial pressure and cerebrospinal fluid pressure. It has been reported that the spinal cord blood flow decreases when the perfusion pressure falls below 50 mmHg[1497] and that SCI occurs at the perfusion pressure below 15 mmHg.[1498] Cerebrospinal fluid drainage (CSFD) for increasing spinal cord perfusion pressure was first proposed by Miyamoto et al. in 1960.[1499] Although some facilities have reported its favorable results[1461,1468] it did not become widely used because an RCT conducted by Crawford et al. in 1991 concluded that 50 mL of drainage was ineffective.[1500]

CSFD has gained popularity after Coselli et al. reported its usefulness in 2002 using the pressure-limited drainage method, which is currently used clinically.[652] Around this time, the results of several cohort studies also showed its usefulness in open surgery.[1452] Furthermore, the improvement of delayed-onset SCI by CSFD was reported in patients that had undergone not only open surgery,[1453] but also TEVAR,[682,1454] and CSFD has become a basic strategy in the era of the collateral network concept. However, its severe complication has been reported, including intracranial subdural hematoma, an epidural hematoma, meningitis, tube rupture, and headache.[1452] Intracranial hemorrhage is said to be caused by rupture of the bridging vein, and a high drainage volume is considered a risk factor. Therefore, a drainage pressure of 10–13 cm H_2O or higher[1501] and a drainage rate of <15 mL/h[1452] are recommended.

2.3.6 Hypothermia

Although hypothermia extends the ischemic tolerance time of the spinal cord, Q10 (temperature coefficient) of the spinal cord has not been established since there is no fixed temperature-monitoring site that clinically serves as a surrogate for spinal cord temperature. Experimentally, it has been reported that a temperature drop of 1°C in the range of 34.5–38.5°C extended the ischemic tolerance time by 5.5 min in the rabbit model.[1502]

Mild/moderate systemic hypothermia with perfusion cooling and natural drift has been used in beating-heart surgery. On the other hand, surgery under deep hypothermic circulatory arrest for spinal cord protection has also been performed, mainly in cases in which proximal aortic cross-clamping or segmental aortic cross-clamping is difficult. However, deep hypothermic surgery through a thoracotomy surgical field showed poor results in Europe and the United States in the early 1990s due to limitations in cardiopulmonary protection and high surgical invasiveness.[1503] Its results have improved since Kochoukos et al. reported its highly favorable results in the late 1990s;[667] however, there are only a limited number of facilities that select it as the first treatment choice.

Also, attempts of topical spinal cord cooling have long been made with perfusion cooling of the subarachnoid cavity[1504] and epidural cavity.[1505] Although the latter has been used in Japan, it is still in the stage of clinical research.

2.3.7 Staged Surgery

In 2010, Etz et al. reported that staged surgery reduced the incidence of SCI.[1411] This is likely because staged surgery provided sufficient time for the collateral flow to develop after the occlusion of the segmental arteries by the initial surgery. Aortic pathologies that can be treated by staged surgery are mostly chronic aortic dissection, and it depends on the decision of how much downstream aortic enlargement is allowed to be left. If staged surgery is selected, it is important to assess the risk of second-stage surgery, which requires re-thoracotomy, in addition to the risk of rupture while awaiting second-stage surgery.

2.3.8 Pharmacological Protection

Several drugs have been experimentally demonstrated to have the effect of spinal cord protection; however, no drug is supported by clinical evidence. Naloxone has been widely applied clinically since the report by Acher et al.[1461] However, a comparative examination of its effect of spinal cord protection has not been reported; additionally, there is only supporting evidence that it suppresses the release of neuroexcitatory amino acids in the cerebrospinal fluid.[1506] On the other hand, the vasodilator nitroprusside has been shown to increase cerebrospinal pressure and to be disadvantageous for spinal cord protection.

3. Reoperation

3.1 After Open Surgery (Table 45)

Aortic reoperation in the thoracic and abdominal regions can be broadly classified into two types.[1507,1508] One is the case in which a new lesion extends from the replacement site in the initial surgery or the stent-graft (SG) deployment site to the adjacent non-aneurysmal site, and it can be further divided into proximal and distal lesions depending on the location of the new lesion. The other is caused by repair or healing failure at the site of initial surgery, and it includes anastomotic aneurysm after open surgery

Table 45. COR and LOE for the Preoperative Examination of Aortic Reoperation and Extracorporeal Circulation Before Re-Thoracotomy		
	COR	LOE
Preoperative multi-slice contrast-enhanced CT examination should be considered	IIa	C
If preoperative multi-slice contrast-enhanced CT examination shows that the sternum is adjacent to the heart/ascending aorta/ coronary artery bypass graft, the establishment of extracorporeal circulation via cannulation to the peripheral blood vessels prior to sternum re-incision should be considered	IIa	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence.

(prosthetic graft replacement), pseudoaneurysm on the side of the proximal or distal end, patch aneurysm, prosthetic graft infection, fistula formation in adjacent organs, aneurysm enlargement due to endoleak after TEVAR, the onset of dissection, SG infection, and fistula formation. Their surgical results vary depending on the complexity of the pathological condition; however, according to the annual report of the Japanese Association for Thoracic Surgery, the operative mortality rate at the time of reoperation was 2–5 times higher than that at the time of initial surgery.[42] Technical implementation and modifications of auxiliary means during reoperation are needed. However, TEVAR after open surgery and open surgery after TEVAR have often been selected in recent years, and they have become complementary skill sets.

3.1.1 Aortic Root

Pseudoaneurysm formation at the annulus suture site and coronary artery reconstruction site is characteristic of reoperation after aortic root replacement; additionally, minimally invasive transthoracic echography and transesophageal echography are useful for its diagnosis. It may be difficult to capture structural changes around the prosthetic valve; however, electrocardiogram-gated CT examination is useful in such cases, with a considerably high diagnostic accuracy. Congenital connective tissue disorders, autoimmune disease, and infectious complications often lie in the background of pseudoaneurysm formation.[1509] With the dissemination of VSRR, treatment intervention for valvular lesions due to exacerbation of aortic valve insufficiency has been increasing in the recent years. There have also been some reports that aortic root enlargement lesion after the radical cure of cyanotic heart disease in the field of adult congenital heart disease is indicated for surgery.[1510] Aortic valve insufficiency due to long-term annulus enlargement, which is called pulmonary autograft failure after Ross surgery, is also indicated for reoperation.[1511]

According to a definite report on reoperation for the aortic root or the ascending aorta, the analysis of surgical results of 56–269 cases at each facility showed an early mortality rate of 6.0–16.4%.[1509] Its mortality rate is said to be three times higher than that of the initial surgery in the same field. The large difference in the numerical values is thought to be due to the difference in the background of the disease to be treated by surgery. Risk factors during reoperation include NYHA cardiac functional classification of III or IV, age of 75 years or older, female sex, chronic pulmonary disease, preoperative renal dysfunction, coronary artery disease requiring unplanned bypass surgery, perioperative myocardial infarction, urgent surgery, extension of extracorporeal circulation time, and conditions that require postoperative intra-aortic balloon pumping.[1509]

As a reoperation method, individualized procedure selection in consideration of the pathological condition and the general condition of the patient is needed. Pseudoaneurysm repair is often performed for anastomotic pseudoaneurysm by direct surgery from the same surgical field. However, coil embolism, closure with a plug, or re-TEVAR may also be selected as endovascular treatment if minimally invasive treatment can be selected based on morphological considerations.[1512,1513] Prosthetic graft infection is generally cured by a series of treatments consisting of re-thoracotomy drainage, wound cleaning, re-replacement, omental transfer, and wound closure. However, if the condition of the patient is considerably poor, there is an option to perform vacuum-assisted wound closure (VAC) therapy and omental transfer, avoiding re-replacement with prosthetic graft or allogeneic cryopreserved tissue (homograft).[1514,1515]

There are some points to note when performing the re-median sternotomy that is required for the open surgery described above. Unlike reoperation in valvular disease, coronary artery disease, or congenital heart disease, it is not uncommon for the enlarged aorta itself or prosthetic graft replaced in the previous surgery to adhere firmly to the back of the sternum. Under some anatomical situations, injury to the aorta or prosthetic graft cannot be avoided, despite careful attention in making an incision in the sternum. It has also been reported that the operative mortality rate in patients who developed massive hemorrhage during re-thoracotomy is as high as 47%.[1516] Preoperative contrast-enhanced CT examination is useful for grasping its possibility in advance, and electrocardiogram-gated CT is useful for a highly accurate evaluation.[1509] If it is determined that injury to the aorta or prosthetic graft during re-thoracotomy is inevitable, it is necessary to prepare for massive hemorrhage prior to re-thoracotomy by exposing peripheral blood vessels, such as the femoral arteries and veins, and establishing extracorporeal circulation in advance.[1509] If massive hemorrhage is expected, it is necessary to complete the re-thoracotomy and aortic cross-clamping operation within the tolerance time and resume extracorporeal circulation using deep hypothermic circulatory arrest in combination. If the circulatory arrest time is expected to be prolonged, a method of establishing selective cerebral perfusion by selectively cannulating the bilateral common carotid arteries in advance is also considered useful. Furthermore, given the significance of myocardial infarction as a cause of death in reoperation in the proximal site of the aorta, special attention must be paid to intraoperative cardioplegia.[1517]

3.1.2 Ascending/Aortic Arch

Pathological indications for reoperation after ascending aortic replacement and aortic arch replacement include anastomotic pseudoaneurysm, extension of aneurysmal lesion beyond the replacement site, onset of dissection, and prosthetic graft infection. These pathological conditions can similarly occur after descending aorta/thoracoabdominal aortic replacement. A so-called patch aneurysm after arch/

thoracoabdominal aortic replacement is a pathological condition in which an aneurysm forms in the surrounding of multiple cervical branches, intercostal arteries, and abdominal branch blood vessels that are end-to-side anastomosed to prosthetic grafts in an insular shape. An aneurysm around the intercostal artery may be treated with TEVAR; however, it has a risk of developing ischemic SCI. Reconstruction of individual branches or TEVAR after debranching the branch may be selected for the abdominal branch.

According to a definite report on thoracic descending aortic replacement as reoperation requiring re-left thoracotomy as well as thoracoabdominal aortic replacement,[1507] reoperation accounted for 10.2–30.0% of all cases of thoracic descending/thoracoabdominal aortic prosthetic graft replacement, and its early mortality rate was 8.7–22.9%. Several have reported that this mortality rate does not show a statistically significant difference compared to that of initial surgery,[1507,1518] while some have reported that the mortality rate was significantly higher than that of initial surgery.[1508] In general, the proportion of patients with congenital connective tissue disorders, such as Marfan syndrome, is high in those undergoing reoperation. Because several of these patients belong to a relatively young age group, the risks associated with reoperation may be offset. Therefore, risk assessment during reoperation needs to correctly incorporate the risk factors of each patient. Also, it should be kept in mind that the results mentioned above were reported by facilities with abundant surgical experience in TAAA. Similarly, it has been reported that there is no statistically significant increase in the major complications during reoperation, while some have reported that the postoperative incidences of SCI, kidney injury, and respiratory disorders are increasing. In particular, several cases of re-left thoracotomy cannot avoid injury to the pleura and pulmonary parenchyma that are firmly adhered to the chest wall during the dissection of the left lung from the surrounding tissue, which increases the risk of subsequent pulmonary complications, such as pulmonary hemorrhage and atelectasis.

3.2 After Endovascular Treatment

Migration of the stent graft (SG) into an aneurysm after TEVAR, endoleak, enlargement of aneurysm diameter, rupture, retrograde Type A aortic dissection (RTAD),[417] peripheral stent graft-induced new entry,[1221,1349] infection, and esophageal fistula/bronchial fistula are indicated for reoperation.

Prosthetic graft replacement is the basic treatment for RTAD, infection, and esophageal/bronchial fistula, and prosthetic graft replacement is selected case by case for type I endoleaks, SG shear, SG damage, and false lumen enlargement after TEVAR for aortic dissection.[513,1446,1519,1520]

In principle, in prosthetic graft replacement for infection and esophageal/bronchial fistula, SG is completely removed during surgery. However, part of the aortic wall used as the landing zone of SG is generally thinned/weakened and, it is often difficult to use it for anastomosis after the removal of SG. Therefore, if there is no infection and complete removal of SG is not necessary, SG in the landing is, in principle, cut and left, which is then used for anastomosis together with the aortic wall.[1446,1520,1521]

Prosthetic graft replacement after TEVAR often requires urgent or semi-urgent surgery due to RTAD, infection, and esophageal/bronchial fistula, and treatment results for these have been slightly poor.[1522] On the other hand, stent graft-induced new entry after TEVAR and aneurysm in the vicinity of SG can often be treated by TEVAR.[1349] With regard to the treatment of endoleaks, endovascular treatment (such as the additional deployment of SG, coil, and plug) can often be performed for type III or type I endoleaks that are located distant from the branch artery. However, approach with a catheter to the inflow blood vessels (intercostal artery and bronchial artery) is often difficult in type II endoleak, unlike that in the abdominal region.

In addition, various procedures of endovascular treatment have recently been devised and practiced for the chronic-stage false lumen enlargement after TEVAR for aortic dissection.[1523]

VIII. Other Aortic Diseases

1. Hereditary Aortic Diseases

While the onset-age distribution of aortic aneurysm and dissection peaks at an advanced age, they are known to develop even at a young age. Such cases often involve family history, and heredity has been suggested to be involved. Abnormalities in the *FBN1* gene were first identified in Marfan syndrome, which is well known to be a cause of early-onset aortic diseases. However, some of such patients do not meet the diagnostic criteria for Marfan syndrome, and the concept of so-called "Marfan-related diseases" has been established for those who cannot be diagnosed with Marfan syndrome despite their early-onset aortic diseases. As with Marfan syndrome, Marfan-related diseases are thought to be associated with vascular fragility due to genetic abnormalities, and with the progress of genetic analysis technology, such genetic abnormalities have been elucidated one after another.

As mentioned above, when patients develop aortic diseases at a young age (under 50 years of age), it is important to first consider their heredity. The differential diseases include juvenile hypertension, obstructive sleep apnea, and aortitis, and the possibility of hereditary aortic diseases increases if these can be ruled out. In terms of physical appearances, tall patients with a family history are suspected of having Marfan syndrome. Patients with Marfan syndrome were reported to account for approximately 5% of those patients with acute aortic dissection.[1524] Although Marfan syndrome is the most common hereditary aortic disease, accounting for more than only 50% of cases; and non-Marfan aortic diseases caused by genetic abnormalities were reported to nearly account for the other half.[1525] However, several genetic abnormalities have not yet been elucidated.

While the diagnosis of each genetic abnormality is

discussed in the next section, hereditary aortic diseases are treated based on the following ideas. Genetic abnormalities cannot be denied simply because of the absence of family history. A patient may be a proband (the first patient to have a gene mutation in the family). Marfan syndrome can be clinically diagnosed using its diagnostic criteria (revised Ghent nosology)[1526] without genetic testing. Other hereditary aortic diseases do not have clinical diagnostic criteria, and their definitive diagnosis requires genetic testing.

Genetic abnormalities include syndromic diseases (with some characteristics of physical findings), such as Marfan syndrome, Loeys–Dietz syndrome, vascular Ehlers–Danlos syndrome, and *SMAD3* gene abnormalities, and non-syndromic diseases (genetic abnormalities cannot be estimated based on the physical appearances of patients), such as *ACTA2* gene abnormalities.

Genetic abnormalities may lead to aortic diseases at a young age by causing abnormalities in the media of the aortic wall. The degree of medial lesions, which defines the fragility of the aorta, varies greatly depending on the disease, and it is considered to be one of the determinants of the onset age of aortic diseases. Previously, medial lesions were expressed as "cystic medial necrosis (CMN)." However, other terms, such as cystonecrosis, cystic degeneration, and mucoid degeneration were also used, and the lack of a unified term caused confusion. Thus, the Society for Cardiovascular Pathology in the United States and the Association for European Cardiovascular Pathology have recently recommended the use of "mucoid extracellular matrix accumulation (MEMA)," which has been defined clearly.[1527]

1.1 Definition

"Hereditary aortic diseases" are aortic diseases whose onset is defined by heredity. However, family and relatives of a patient may not have aortic diseases if a new mutation occurs in the patient's generation, if the disease does not develop despite a genetic change due to its low penetration rate, or if the disease does not develop in heterozygotes due to its recessive inheritance form. Several hereditary aortic diseases have autosomal dominant inheritance, and they are broadly divided into "syndromic" diseases, which show characteristic findings outside the aorta, and "non-syndromic" diseases, whose lesions are mostly limited to the aorta. However, some patients may present with minimal changes other than aortic lesions even if the disease is caused by the same etiologic gene.

Histologically, hereditary aortic diseases often exhibit the finding of cystic medial necrosis. Mutation analysis of the causative genes has been emphasized in the diagnoses of Marfan syndrome and vascular Ehlers–Danlos syndrome; however, it does not necessarily identify all gene mutations (See "**1.4 Genetic Diagnosis**" in this chapter). Furthermore, some hereditary aortic diseases are caused by changes in unidentified causative genes. Also, because numerous diseases are caused by new mutations, detailed family history surveys may not reveal the heredity of the disease, and such mutations may not be easily distinguished from benign mutations (polymorphisms), which cannot be etiology even if their genetic changes (mutations) are identified. Thus, genetic analysis (testing) is not useful for all cases. In addition, a bicuspid aortic valve has a high familial incidence, and it is known to be associated with the development of an aortic aneurysm, having a high risk of developing aortic dissection. Also, some cases of bicuspid aortic valve were reported to be associated with mutations in specific genes.

1.2 Syndromic Hereditary Aortic Diseases

1.2.1 Marfan Syndrome

Marfan syndrome is an autosomal dominant inheritance disease named after the pediatrician Marfan publishing its report (1896),[1528] and it is a systemic hypoplastic disease of connective tissue complicated by cardiovascular lesions, musculoskeletal abnormalities, and ocular lesions, which exhibits hereditary onset.[1528,1529] With the elucidation of its cause and pathological conditions, the disease is known to develop due to a mutation in the *FBN1* gene that encodes fibrillin-1, a major component of microfibrils.[1530] Its mutations are known to cause abnormalities in the formation and assembly of elastic fibers, as well as abnormalities in binding to smooth muscle cells.[1531] The pathological condition is also caused by increased TGF-β signaling, which plays a key role in cell differentiation and proliferation, due to the functional change in TGF-β caused by fibrillin-1 mutations.[528,1532]

Notably, 20–30% of Marfan syndrome cases are caused by new mutations, and not all of cardiovascular, bone and joint, and ocular lesions are found in some patients. With regard to its diagnostic criteria, the Berlin nosology was first proposed, followed by the Ghent nosology as its revised version. Furthermore, the revised Ghent nosology (**Table 46**)[1526] was proposed in 2010, highlighting the importance of genetic testing/familial information. Its diagnostic criteria focus on aortic root enlargement and dislocation of the ocular lens (ectopia lentis) and emphasize the laboratory findings of the *FBN1* gene. Patients presenting with both aortic root enlargement and ectopia lentis are diagnosed with Marfan syndrome even if they do not have a family history. Patients presenting with either aortic root enlargement or ectopia lentisare diagnosed with Marfan syndrome if they have an *FBN1* mutation or a physical sign score of 7 points or higher. In patients with a family history, the diagnosis of Marfan syndrome is made based on ectopia lentis, a physical sign score of 7 points or higher, or aortic root enlargement. The physical signs are scored according to the items listed in **Table 46**;[1526] additionally, their evaluation is made by echocardiography (mitral valve prolapse and aortic root enlargement), CT examination (systemic aortic aneurysm and dura mater expansion), bone radiography (scoliosis, kyphosis, and acetabular protrusion), ophthalmological examination (ectopia lentis), and genetic testing. The Z score for aortic root diameter is calculated by correcting for age and height/body weight (body surface area),[1533–1535] and Marfan syndrome is determined by the aortic root diameter with a score of >2 (>3 in children). However, as in other aortic diseases, it is also important to measure the aortic diameter and determine the presence or absence of dissection.

1.2.2 Vascular Ehlers–Danlos Syndrome

Vascular Ehlers–Danlos syndrome (Ehlers–Danlos syndrome type IV) is caused by abnormalities in type III collagen molecules due to dysfunction of the *COL3A1* gene.[1536] It is a rare hereditary disease that causes dysfunction of systemic organs, including various arteries, and it is diagnosed by clinical/imaging findings and identification of a *COL3A1* gene mutation.[1537] Although it is an autosomal dominant

Table 46. Revised Ghent Nosology for the Diagnosis of Marfan Syndrome and Its Related Diseases (2010)

In the absence of family history:

(1) Ao [Note 1)] (Z≥2) AND EL → "Marfan syndrome"*

(2) Ao (Z≥2) AND *FBN1* gene mutation (FBN1) [Note 2)] → "Marfan syndrome"

(3) Ao (Z≥2) AND Syst (≥7 points) → "Marfan syndrome"*

(4) EL AND *FBN1* with known Ao [Note 3)] → "Marfan syndrome"*

- Patients with EL (with or without Syt AND with an *FBN1* not known with Ao or no *FBN1*) are considered to have "ELS".
- Patients with a mild aortic root lesion (Ao; Z<2) AND Syst (≥5 points) without EL are considered to have "myopia, mitral valve prolapse, aortic root dilatation, striae, skeletal findings, aortic aneurysm syndrome (MASS)".
- Patients with MVP AND mild aortic root lesion (Ao; Z<2) AND Syst (<5 points) without EL are considered to have "MVPS".

In the presence of family history: [Note 4)]

(5) EL AND FH of Marfan syndrome (as defined above) → "Marfan syndrome"

(6) Syst (≥7 points) and FH of Marfan syndrome (as defined above) → "Marfan syndrome*

(7) Aortic root lesion (Z≥2 for 20 years old and over, Z≥3 for under 20 years old) AND FH of Marfan syndrome (as defined above) → "Marfan syndrome"*

*The diagnosis of such patients requires discrimination from related diseases, such as Shprintzen–Goldberg syndrome, Loeys–Dietz syndrome, and vascular Ehlers–Danlos syndrome. When these diseases are suggested based on the findings, judgement should be made after various examinations, such as the *TGFBR1/2*, collagen biochemistry, *COL3A1* testing if indicated. In addition, diseases and genes that require discrimination may change in the future.

Note 1) Aortic diameter at the sinuses of Valsalva above indicated Z-score or aortic root dissection

Note 2) *FBN1* gene mutation: Specified elsewhere (details are omitted)

Note 3) *FBN1* with known Ao: *FBN1* gene mutation that has been identified in an individual with aortic aneurysm

Note 4) Family history: those having an individually diagnosed propositus in the family according to (1)–(4) above

Scoring of systemic Features

Maximum total: 20 points. score ≥7 points indicates systemic involvement

• Wrist AND thumb sign	3 points
(Either positive wrist sign or positive thumb sign	1 point)
• Pectus carinatum deformity	2 points
(Pectus excavatum or thorax asymmetry only	1 point)
• Hindfoot deformation	2 points
(Plain pes planus only	1 point)
• Pneumothorax	2 points
• Dural ectasia	2 points
• Portrusio acetabuli	2 points
• Reduced US/LS AND increased arm/height AND no severe scoliosis	1 point
• Scoliosis or thoracolumbar kyphosis	1 point
• Reduced elbow extension	1 point
• Facial features (3 or more out of 5): dolichocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, retrognasia	1 point
• Skin striae	1 point
• Myopia (over –3D)	1 point
• Mitral valve prolapse (all types)	1 point

Ao, aortic diameter; EL, ectopia lentis; ELS, ectopia lentis syndrome; FH, family history; MVP, mitral valve prolaps; MVPS, mitral valve prolapse syndrome; Syst, systemic score; US/LS, upper/lower segment ratio. (Adapted from Loeys BL, et al. 2010.[1526]) Reproduced with permission from BMJ Publishing Group Ltd.

inheritance disease, its pathology is diverse because of the presence of new mutations and the lesions extend not only to the arteries, but also to organs throughout the body. Its characteristic finding is the thin and permeable skin, and patients are hemorrhagic, having a characteristic facial appearance and short life span. Also, sudden death due to the rupture of the intestinal tract or uterus and arterial hemorrhage is not uncommon. With the changes in the vasculature of the whole body, patients may develop dissection in the aorta, branch arteries, and cerebral arteries, and it is thought that there is no association between the arterial diameter and dissection. Non-invasive examinations should be performed to the greatest possible extent.

Vascular Ehlers–Danlos syndrome is diagnosed by characteristic clinical/imaging findings and the identification of pathological changes in the *COL3A1* gene. Regarding its diagnostic criteria, the disease is suspected if a patient meets one of major criteria or multiple minor criteria listed in **Table 47**,[1537] and its diagnosis is made by genetic testing. Its final diagnosis is made based on the identification of the etiologic mutation (variant) of the *COL3A1* gene. If it identifies no mutation, a biochemical analysis of type III

Table 47. Diagnostic Criteria for Vascular Ehlers–Danlos Syndrome (2017)

Diagnosis is suspected with the presence of one of the major criteria or multiple minor criteria (especially in patients under 40 years old)

The following clinical findings are useful in determining the implementation of genetic analysis

A. Major criteria

- Family history of vascular Ehlers–Danlos syndrome with documented causative variant in COL3A1;
- Arterial rupture at a young age;
- Spontaneous sigmoid colon perforation in the absence of known diverticular disease or other bowel pathology;
- Uterus rupture during the third trimester in the absence of previous C-section and/or severe peripartum perineum tears
- CCSF formation in the absence of trauma

B. Minor criteria

- Bruising unrelated to identified trauma and/or in unusual sites such as cheeks and back
- Thin, translucent skin with increased venous visibility
- Characteristic facial appearance
- Spontaneous pneumothorax
- Acrogeria
- Talipes equinovarus (Clubfoot)
- Congenital hip dislocation
- Hypermobility of small joints
- Tendon and muscle rupture
- Keratoconus
- Early onset varicose veins (under age 30 and nulliparous if female)

The diagnosis of vascular Ehlers–Danlos syndrome in the propositus is made based on one of the following:

(1) Causative variants of the *COL3A1* gene are identified as heterozygotes by genetic testing

(2) While no causative variant of the *COL3A1* gene is identified in a patient suspected of having vascular Ehlers–Danlos syndrome, abnormal production or mobility of type III collagen is found by biochemical analysis of type III collagen in cultured fibroblasts

In addition, (1) genetic testing of the *COL3A1* gene is recommended when a clinical diagnosis is suspected, and (2) genetic testing is valuable when there are clinically similar findings or when they are mild

In rare cases, causative variants are identified in both alleles of the *COL3A1* gene

Usually, vascular Ehlers–Danlos syndrome is inherited by autosomal dominant inheritance

CCSF, carotid-cavernous sinus fistula. (Adapted from Malfait F, et al. 2017.[1537])

collagen of cultured fibroblasts is performed, and vascular Ehlers–Danlos syndrome is diagnosed upon the identification of any abnormality.

1.2.3 Loeys–Dietz Syndrome

Patients with Loeys–Dietz syndrome initially present with physical findings similar to those of patients with Marfan syndrome, having a tortuous aorta and systemic aortic aneurysm, widely spaced eyes, and bifid uvula as the three main signs. However, it is an autosomal dominant inheritance disease without ectopia lentis, and its etiology was reported to be a gene mutation in the TGF-β type I/II receptor.[1538]

Patients with this syndrome present with extensive vascular symptoms (aortic aneurysm/dissection, small and medium arterial aneurysm, and congenital cardiac anomaly) and various skeletal symptoms, such as pectus excavatum or pectus carinatum, scoliosis, flaccid joint, congenital clubbed foot, early cranial fusion, and cervical instability at a high rate.[1539] Its clinical features are highly broad, including patients with findings similar to those of Marfan syndrome (including a disease formerly known as type 2 Marfan syndrome),[1540] hemorrhagic patients such as those with vascular Ehlers–Danlos syndrome, highly heteromorphic patients such as those with Shprintzen–Goldberg syndrome, and patients diagnosed with familial aortic aneurysm without non-vascular symptoms.[1541] Subsequently, mutations in genes encoding SMAD3 and TGF-β ligands (*SMAD3*, *TGFB2*, and *TGFB3*), which make up the TGF-β signaling, were reported in patients with aortic aneurysm/dissection exhibiting similar clinical symptoms.[1542–1544] This disease concept is broad, and it differs from Marfan syndrome and other thoracic aortic aneurysms/dissections in terms of the rapid progression of a disease condition.

The differentiation of Loeys–Dietz syndrome from Marfan syndrome and vascular Ehlers–Danlos syndrome is important since some patients with Loeys–Dietz syndrome present with few physical findings. Some patients exhibit the characteristics of this syndrome as a result of the haploinsufficiency of these genes due to chromosome segmental deletion. Such patients show mild findings of aortic aneurysm/dissection itself. The degree and findings of symptoms vary widely regardless of whether patients have the same or different gene mutations; however, they have a similar overall life prognosis. On the other hand, rapidly progressing aortic aneurysm[1545] is one of the characteristics of this syndrome, and particularly, patients with strong craniofacial findings having a mutation in the *TGFBR1* or *TGFBR2* gene develop aortic dissection even with small vascular diameter.

Diseases with these gene mutations are now diagnosed/managed as Loeys–Dietz syndrome, despite a wide variation in the clinical findings among patients. Its diagnosis is made by identifying pathological changes in the genes known to be its etiology (such as *TGFBR1*, *TGFBR2*, *SMAD3*, *TGFB2*, and *TGFB3*) with reference to clinical/imaging findings. Furthermore, it should be noted that there may be unknown etiologic genes. Also, attention should be paid to the widely varying progression of aortic lesions among its patients.

1.2.4 Arterial Tortuosity Syndrome

Arterial tortuosity syndrome is a rare autosomal recessive inheritance disease characterized by tortuous aorta/medium-sized artery and their extension, as well as aneurysm formation.[1546] Patients may present with regional stenosis of the pulmonary artery and aorta. Also, they may exhibit Marfan syndrome-like skeletal characteristics, such as characteristic facial appearances, including a long face, shortened palpebral fissure, palpebral fissure inclination, hooked nose, high-arched palate, and maxilla, and soft and stretchable skin peculiar to connective tissue diseases, tall height, thoracic deformity, arthrochalasis, and arthrogryposis.

Arterial tortuosity syndrome is caused by mutations in the *SLC2A10* gene encoding the sugar transporter GLUT10.[1547] Its diagnosis is made based on vascular

findings (tortuous aorta/medium-sized artery and their extension, as well as aneurysm formation), characteristic facial appearances, skin findings, skeletal findings, and abnormalities in the *SLC2A10* gene; however, it may be caused by changes in unknown genes.

1.2.5 Other Gene Mutation-Related Diseases

Mutations in the *BGN* gene with X chromosome-linked inheritance were reported in aortic disease patients with physical findings similar to those of Loeys–Dietz syndrome patients.[1548] Also, aortic diseases in osteogenesis imperfecta with mutations in the *COL1A1* or *COL1A2* gene,[1549] as well as *FLNA* gene mutations with X chromosome-linked inheritance that are associated with heterotopia disorders in aortic disease patients with Ehlers–Danlos syndrome-like physical findings or mitral valve disease,[1550] have been reported. These gene mutations are thought to be the etiology of aortic diseases. Their diagnoses are made based on clinical findings of each disease and identification of the etiologic gene mutation; however, it is presumed that there are etiologic genes that have not been identified at present.

1.2.6 Turner Syndrome

Turner syndrome is caused by monosomy (deletion) of all or some of X chromosome.[1551] Its patients (females) present with short height, various cardiac structure malformations, aortic diseases, obesity due to changes in the metabolic endocrine system, impaired glucose tolerance, dyslipidemia, and ovarian dysfunction. Hypertension due to coarctation of the aorta, bicuspid aortic valve, and cardiac structure malformations are found in 12%, 30%, and 75% of patients, respectively. The incidence of aortic dissection was found to be 100 times higher in Turner syndrome patients than in control. The etiologic genes for cardiovascular changes have not been elucidated. The diagnosis of Turner syndrome is made based on the characteristic clinical findings described above and chromosomal examination (X chromosome monosomy or partial deletion of X chromosome).

1.3 Non-Syndromic Hereditary Aortic Diseases

1.3.1 Familial Thoracic Aortic Aneurysm/Dissection

Familial thoracic aortic aneurysm/dissection is an autosomal dominant inheritance disease. However, it does not have a high penetration rate, and its hereditary/familial causes may be unclear in some cases, including those caused by new mutations. Its known causes include mutations in genes encoding vascular smooth muscle contraction proteins (*ACTA2*, *MYH11*, and *MYLK*).[1552–1554] Patients with a *ACTA2* gene mutation may present with cerebral arterial malformations similar to coronary artery disease, cerebrovascular disease, or moyamoya disease.[1555] Patients with a *MYH11* gene mutation may have patent ductus arteriosus,[1553] and patients with a *MYLK* gene mutation may develop dissection without the enlargement of arterial diameter. Also, aortic aneurysm/dissection was reported to be caused by a mutation in the *PRKG1* gene, which encodes a cGMP-dependent protein kinase associated with vascular smooth muscle relaxation.[1556] Its diagnosis is made by the confirmation of the mutations in the causative genes described above; however, attention should be paid to new mutations and their low penetration rate.

The *ACTA2* gene encodes vascular smooth muscle α actin, and approximately 15% of non-syndromic familial TAA cases are caused by mutations in this gene.[1552] In an analysis conducted in Japan, mutations in this gene were identified in approximately 20% of juvenile non-syndromic familial TAA patients with onset before the age of 50 years.[1557] In addition, families with *ACTA2* gene mutations often have complications with coronary artery disease and cerebrovascular diseases, such as moyamoya disease. Complications with cerebrovascular diseases, such as moyamoya disease,[1555] are characterized by specific *ACTA2* gene mutations. The penetration rate of aortic lesions is 48%, which is not necessarily higher than that of Marfan syndrome; however, it should be noted that several studies have reported dissection in patients under the age of 20 years and young individuals. The diagnosis in these cases is made based on the analysis of the *ACTA2* gene.

On the other hand, the *MYH11* gene encodes a smooth muscle myosin heavy chain, and its mutations have been reported in patients with TAA.[1553] The characteristic of TAA caused by the mutations in this gene is thought to be the presence of patent ductus arteriosus; however, the mechanism of the disease has not been elucidated due to the small number of reported cases.

1.3.2 Bicuspid Aortic Valve

Bicuspid aortic valve (BAV) is the most common congenital cardiovascular structural abnormality, and it is found in about 1% of all births.[1558] The fusion of the left coronary cusp and the right coronary cusp accounts for at least 70% of its cases. Also, the fusion of the right coronary cusp and the noncoronary cusp accounts for 10–20% of its cases, while the fusion of the left coronary cusp and the noncoronary cusp accounts for less than 10%. The aortic enlargement is more likely to be seen in patients with a bicuspid valve than in those with the normal valve. Enlargement of arterial diameter was reported to occur in the early stage, although epidemiological studies have not been sufficiently conducted. Patients with the fusion of the left coronary cusp and the right coronary cusp are complicated by coarctation of the aorta, and BAV patients with coarctation of the aorta are complicated by aortic aneurysm and dissection at a high rate.

Mutations in the *NOTCH1* gene have been reported in some BAV cases,[1559] in which bicuspid valve with autosomal dominant inheritance is detected in the family of the patient. Also, unidentified causative genes are said to be present for BAV. BAV is detected by echocardiography, and aortic diseases are diagnosed by MRI or CT examination. However, they may be diagnosed by a mutation in the *NOTCH1* gene found in genetic testing.

1.4 Genetic Diagnosis

1.4.1 Clinical Significance

Hereditary aortic diseases with identified causative genes are broadly divided into two types: "syndromic" diseases, in which aortic lesions are observed as symptoms of systemic diseases caused by hereditary connective tissue disorders, such as Marfan syndrome, and "non-syndromic" diseases, which are limited to the lesions of the vascular system. In the former, characteristic symptoms for each causative gene are often observed in the skeleton/eye/skin from an early stage, and their diagnosis is commonly made based on those physical findings. However, the onset of vascular manifestations tends to be delayed compared with that of other syndromic features, and vascular complications are often overlooked. In the latter, several cases are

Table 48. Hereditary Syndromes Complicating Thoracic Aortic Aneurysm/Dissection (Alphabetical Order)			
Group	**Causative gene**	**Mode of inheritance**	**Related clinical disease type**
Group A. Aortic aneurysm/dissection is exhibited as the main symptom			
A1. Genes for syndromic aortic aneurysm/dissection			
Definitive	*COL3A1*	AD	Vascular Ehlers–Danlos syndrome
	FBN1	AD	Marfan syndrome
	TGFB2	AD	Loeys–Dietz syndrome 4
	TGFBR1	AD	Loeys–Dietz syndrome 1
	TGFBR2	AD	Loeys–Dietz syndrome 2
	SMAD3	AD	Loeys–Dietz syndrome 3, AOS
A2. Genes for non-syndromic aortic aneurysm/dissection			
Definitive	*ACTA2*	AD	
	MYH11	AD	
	MYLK	AD	
Strong	*LOX*	AD	
	PRKG1	AD	
Group B. Aortic aneurysm is exhibited as a side symptom; however, the risk of progressing to dissection is low			
Moderate Limited	*EFEMP2*	AR	Cutis laxa syndrome
	ELN	AD	Cutis laxa syndrome
	FBN2	AD	Beals syndrome (congenital contractural arachnodactyly)
	FLNA	XL	Periventricular nodular heterotopia, etc.
	NOTCH1	AD	Bicuspid aortic valve
	SLC2A10	AR	Arterial tortuosity syndrome
	SMAD4	AD	Juvenile polyposis syndrome
	SKI	AD	Shprintzen-Goldberg syndrome
Group C. Occasionally complicated by aortic aneurysm			
Limited	*CBS*	AR	Homocystinuria
	COL4A5	XL	Alport syndrome
	PKD1	AD	Polycystic kidney disease
	PKD2	AD	Polycystic kidney disease
Others. Novel genes whose association with aortic aneurysm/dissection has not been established			
Uncertain	*BGN*	XL	
	FOXE3	AD	
	HCN4	AD	Sick sinus syndrome
	MAT2A	AD	
	MFAP5	AD	
	SMAD2	AD	
	TGFB3	AD	Loeys–Dietz syndrome

AD, autosomal dominant inheritance (dominant inheritance); AR, autosomal recessive inheritance; XL, X chromosome-linked inheritance; AOS, aneurysms-osteoarthritis syndrome.

not diagnosed until the onset of aortic dissection.

Noteworthy, several patients with hereditary aortic diseases develop aortic aneurysm/dissection at an early age; however, dissection can be prevented by early interventions, such as medication with oral beta-blockers and/or preventive aortic root replacement surgery. In April 2016, genetic testing for the diagnosis of several hereditary aortic diseases, such as Marfan syndrome, began to be covered by national health insurance because of its high effectiveness in their early diagnosis. Furthermore, genetic counseling before and after genetic testing, including patient management and family care, is essential, and the genetic counseling regarding the explanation of the results of genetic analysis is also covered by insurance.

1.4.2 Causative Genes for Hereditary Aortic Diseases

Aneurysms/dissections differ in the thoracic and abdominal aortic regions according to the analysis of their factors. Several aortic aneurysms of older adults predominantly develop in the abdominal aorta, and their occurrence is associated with hypertension and atherosclerosis. Also, environmental factors, such as lifestyle, have a large effect on their onset. On the other hand, 10–20% of patients with abdominal aortic aneurysm/dissection have a family history, suggesting the involvement of genetic factors.[1560] However, these are multifactorial diseases that involve both genetic and environmental factors in their onset,[1561] and those caused by mutations in a single gene are highly rare.

On the other hand, some thoracic aortic aneurysms/dissections (TAAD) are caused by a single gene abnormality.

Typical examples are syndromic hereditary connective tissue disorders, such as Marfan syndrome. However, they account for less than 10% of all TAAD patients; additionally, a significant number of cases are of non-syndromic aortic aneurysms with no symptoms other than aortic lesions. However, approximately 20% of non-syndromic TAAD patients have family members with TAAD,[534] and families that develop dissection at a young age without risk factors, such as hypertension/atherosclerosis, may have an abnormality in a single gene. As a result, up to 25% of TAAD are caused by an abnormality in a single gene, and they are called "hereditary TAAD." Because many of them are autosomal dominant inheritance diseases, clarification of their causative genes enables patient management based on the pathological condition, which is expected to lead to an early diagnosis/treatment and family screening.

In 2018, causative genes for hereditary aortic diseases were re-evaluated based on the risks of aortic dissection. As a result, 11 genes were found to have a high risk of developing aortic aneurysm/dissection (Group A), and 8 genes were found to have a risk of progressing to dissection although the risk is not high (Group B). It also revealed 4 genes that may be associated with aortic aneurysm/dissection with unknown risk (Group C) and 23 genes that have no risk of aortic aneurysm/dissection (Group D). The other 7 genes whose risks could not be determined in the evaluation were classified as those requiring further examinations (recent genes)[1562] (**Table 48**). Group A are the genes found to be definitively associated with HTAAD and are clinically actionable. Thus, the patients were found to be complicated by aneurysm and dissection at a high rate, and active clinical intervention is recommended. Group A is further divided into three subgroups – A1 (definitive): causative genes of syndromic aortic aneurysm/dissection, A2 (definitive): causative genes of non-syndromic aortic aneurysm/dissection, and A2 (strong): genes that are judged to have a considerably high risk of aortic aneurysm/dissection based on experimental data despite the small number of cases. Of these, this section discusses the A1 and A2 genes with a relatively high frequency, having great clinical significance.

a. A1: Syndromic Aortic Aneurysm/Dissection

i. *FBN1* Gene (15q21)

The *FBN1* gene is the causative gene of Marfan syndrome, and it encodes a precursor protein for fibrillin-1, which is a major component of the extracellular matrix.[1530] Fibrillin-1 is not only an essential glycoprotein as a constituent of elastic fibers that make up the skin and blood vessels but is also thought to be involved in maintaining homeostasis of the vascular wall by controlling the activity of TGF-β signaling. As approximately 1/3 of pathogenic variants are mutations that inhibit peptide synthesis, such as nonsense and frameshift variants, several symptoms of Marfan syndrome can be explained by haploinsufficiency of the *FBN1* gene.[1563] In addition, patients with such a haploinsufficiency variant are more likely to develop severe vascular complications.[1564] On the other hand, some missense variants have a dominant inhibitory effect due to the mutant protein. Also, several patients complicated by ectopia lentis (lens displacement) have cysteine-related missense variants, and severe cases that are diagnosed in the neonatal period often have missense variants in specific regions or major structural abnormalities.

ii. *TGFBR1* (9q22) and *TGFBR2* (3p24) Genes

The *TGFBR1* and *TGFBR2* genes are the causative genes of Loeys–Dietz syndrome, and they encode type I and type II receptors of TGF-β, respectively.[1538–1540] Since the TGF-β signaling system is widely involved in the maintenance of the homeostasis of the body through the regulation of cell proliferation/differentiation, its abnormal regulation causes symptoms to appear in connective tissues of the whole body, mainly in the bones and blood vessels. Abnormalities in the *TGFBR1*/*TGFBR2* genes generally present with a clinical form of syndromic aortic aneurysm/dissection. However, attention must be paid to patients with little extravascular symptoms because the symptoms vary greatly among patients, even if they have the same gene variant.

iii. *COL3A1* Gene (2q32)

The *COL3A1* gene is the causative gene of vascular Ehlers–Danlos syndrome, and it encodes the precursor protein of type III collagen.[1565] Type III collagen is abundant in the skin, lung, intestinal tract wall, and vascular wall as a major component of the extracellular matrix. Its pathogenesis is mediated by dominant inhibition or haploinsufficiency; however, the latter generally leads to mild pathological conditions.[1566]

iv. *SMAD3* Gene (15q22)

The *SMAD3* gene encodes an intracellular protein that acts on signal transduction as R-Smad (receptor-regulated Smad) downstream of TGF-β ligands. Upon activation by the type I receptor of TGF-β, it is translocated into the nucleus, and it is involved in the expression of various genes. The *SMAD3* gene is classified as one of the causative genes of Loeys–Dietz syndrome; however, it is characterized by the findings of aneurysms-osteoarthritis syndrome with osteoarthritis.[1542]

b. A2: Non-Syndromic Aortic Aneurysm/Dissection

i. *ACTA2* Gene (10q23)

The *ACTA2* gene encodes vascular smooth muscle α actin, and approximately 15% of non-syndromic aortic aneurysms/dissections are caused by mutations in this gene.[1552] Because they show little extravascular symptoms, it is difficult to diagnose them before onset without a family history. However, some gene variants have a syndromic clinical form with characteristic findings in cerebral blood vessels, ductus arteriosus, coronary arteries, iris, and intestinal tract, and patients with these variants require detailed systemic examination.

ii. *MYH11* Gene (16p13)

The *MYH11* gene encodes smooth muscle myosin heavy chain, and mutations in this gene have been reported in TAAD patients,[1553] although the number of cases is small. They are sometimes complicated with patent ductus arteriosus; however, its mechanism has not been elucidated due to the small number of reported cases.

1.4.3 Interpretation of Genetic Test Results

With the recent rapid advancement in genetic analysis technology, genetic testing has become an indispensable examination for diagnosing hereditary diseases. In particular, panel analysis using the next-generation sequencing has become mainstream, enabling the simultaneous analysis of multiple candidate genes, and its testing accuracy/rapidity/cost effectiveness now greatly surpasses those of the conventional Sanger method. As a result, the current diagnosis tends to focus more on genetic testing than on clinical findings. However, it is important to note that the

Table 49. COR and LOE for Open Surgery for Hereditary Aortic Diseases		
	COR	LOE
It is recommended to perform open surgery on patients with Marfan syndrome with an aortic root or ascending aortic diameter of ≥50 mm[536] (See **Table 12**)	I	C
Open surgery should be considered for Marfan syndrome patients with risk factors for aortic dissection* who have an aortic root or ascending aortic diameter of ≥45 mm[1567] (See **Table 12**)	IIa	C
Open surgery should be considered for female patients with Marfan syndrome who desire for pregnancy when the aortic root or ascending aortic diameter is ≥40 mm[1568–1571] (See **Table 12**)	IIa	C
Open surgery should be considered for Loeys–Dietz syndrome patients even if their aortic root or ascending aortic diameter is smaller than that of Marfan syndrome patients[1539]	IIa	C
Open surgery under left thoracotomy should be considered over TEVAR in Marfan syndrome patients with a descending/thoracoabdominal aortic lesion[1572]	IIa	C
Open surgery may be considered for Marfan syndrome patients with an aortic root or ascending aortic diameter of ≥45 mm[1567]	IIb	C
Open surgery may be considered for Marfan syndrome patients with risk factors for aortic dissection* who have an aortic root or ascending aortic diameter of 40–45 mm[1567] (See **Table 12**)	IIb	C

*Such as family history of aortic dissection, aortic enlargement rate of ≥5 mm/6 months, severe aortic valve insufficiency, and desire for pregnancy. COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

presence of a mutation (variant) alone should not be interpreted as a diagnosis. For example, the *FBN1* gene, which is the causative gene of Marfan syndrome, is a giant gene containing 65 exons in the coding region alone, and has many benign variants that are not directly related to the disease. Caution is needed in interpreting whether the individual variants detected are pathogenic or not.

1.5 Open Surgery (Table 49)

1.5.1 Aortic Root Replacement for Marfan Syndrome

A typical hereditary aortic disease is Marfan syndrome. It is characterized by annuloaortic ectasia, in which the Valsalva sinus dilates in a pear shape, and it maintains the relatively normal shape of the autologous aortic valve. It is mainly caused by abnormalities in the *FBN1* gene, and its early-onset is more common than that of atherosclerotic aortic diseases. Thus, long-term prognosis after surgery needs to be considered in patients with Marfan syndrome. Regarding its surgical criteria, a retrospective cohort study of Marfan syndrome patients without a surgical history was conducted in 2012. It showed that the risk of aortic events (sudden death/dissection) in those with an aortic diameter of below 50 mm was 0.05%/year and that the risk was 4 times higher in those with an aortic diameter of 50 mm or larger. Therefore, the study recommended earlier preventive aortic surgery for patients with an aortic diameter of 50 mm or larger than for non-Marfan syndrome patients.[536] In addition, early surgical indications with an aortic diameter of below 50 mm are desirable for patients with a family history of aortic dissection or patients showing a rapid enlargement of aortic diameter (>10 mm/year) or severe aortic valve insufficiency.[1567] Female patients with Marfan syndrome are known to be at high risk of aortic dissection during pregnancy and the puerperal period, and the enlargement rate of Valsalva sinus diameter also increases during pregnancy. Thus, early preventive surgery with Valsalva sinus diameter of at least 40 mm is desirable for women with Marfan syndrome who desire for pregnancy in the future.[1568–1571]

Aortic root replacement using a composite graft with a prosthetic valve became the standard treatment for aortic root disease Marfan syndrome patients after it was first reported by Bentall in 1968.[555] However, because of the problems of the method, such as thromboembolism related to prosthetic valves, the remodeling method[561,562] and reimplantation method[563] have been performed for valve-sparing root replacement (VSRR) since the 1990s. In 2015, David reported a prospective trial of VSRR in 146 Marfan syndrome patients, which examined 121 patients undergoing the reimplantation method and 25 patients undergoing the remodeling method. It showed a postoperative 15-year survival rate of 93%, which was lower than that of the age-gender-matched control. However, their recurrence rate of aortic valve insufficiency was 7.9%, and it was more favorable in patients undergoing the reimplantation method. In addition, 17% of patients developed aortic dissection within 15 years after surgery, and it was the major cause of death.[1573] In 2013, another facility reported that there was no perioperative death in 178 patients with heritable connective tissue disorders (84% had Marfan syndrome) undergoing the reimplantation method, with a postoperative 8-year survival rate of 94% and a postoperative 6-year freedom rate from aortic valve reoperation of 92%. Also, the main causes of their reoperation were infectious endocarditis and failure of valvuloplasty and their postoperative 4-year recurrence rate of a moderate or higher degree of aortic valve insufficiency was 12%.[1574] It was reported in Japan that there was no operative death in 59 patients, including 47 Marfan syndrome patients, who underwent the reimplantation method, with a postoperative 5-year survival rate of 94% and a freedom rate from aortic valve reoperation of 96%, and their recurrence rate of a moderate or higher degree of aortic valve insufficiency was 11%.[1575] In addition, the aortic valve replacement avoidance rate decreased to below 60% at 10 years after VSRR, and the remodeling method was considered to be its factor.[1576]

Several comparative studies of Bentall surgery and VSRR for Marfan syndrome have been reported in the recent years. In a single-center retrospective study, while VSRR had fewer cases of thromboembolism and hemorrhagic complications than the Bentall method, there was no difference in the long-term survival rate and freedom rate from reoperation between the two.[1577,1578] In 2014, a prospective multicenter joint study of 316 Marfan syndrome patients compared 239 patients in the VSRR group and 77

patients in the Bentall group. Despite no difference between the two groups in the postoperative 1-year survival rate at 97–98%, a moderate or higher degree of aortic valve insufficiency occurred in 7% of the VSRR group, and further reports on mid/long-term prognosis are awaited.[1579] In addition, a meta-analysis of 1,385 patients (VSRR group: 413 patients, Bentall group: 972 patients) in 11 studies was conducted in 2011, and it showed that the reoperation rate was higher in the VSRR group than in the Bentall group (1.3% vs. 0.3% annually) and was higher in patients undergoing the remodeling method than in those undergoing the reimplantation method (2.4% vs. 0.7% annually). On the other hand, the incidence of thromboembolism was higher in the Bentall group than in the VSRR group (0.3% vs. 0.7% annually).[1576] A report published in 2017 examined 2,976 patients in 23 studies (VSRR group: 1,352 patients, Bentall group: 1,624 patients), and it showed that the VSRR group had a lower long-term mortality and a lower risk of thromboembolism than the Bentall group, with fewer cases of hemorrhagic complications and infectious endocarditis. On the other hand, there was no significant difference in the freedom rate from reoperation between the two groups.[572] In 2018, VSRR (reimplantation method only) and Bentall surgery were compared using the data of 2,156 patients in 20 studies, and it showed that patients undergoing the reimplantation method had a more favorable mid/long-term survival rate, in-hospital mortality rate, and freedom rate from reoperation than those undergoing Bentall surgery.[1580] Regarding prosthetic valves in Bentall surgery, several patients had valve-related complications and heart-related death. Patients with a bioprosthetic valve showed a high reoperation rate, and patients with a mechanical valve presented a high rate of anticoagulant-related complications.[574]

These reports indicate that in aortic root replacement for hereditary aortic diseases, such as Marfan syndrome, VSRR is well-indicated for young annuloaortic ectasia patients with maintained aortic valve function. Also, the reimplantation method is expected to lead to a more favorable prognosis than the remodeling method from the viewpoint of recurrence of aortic valve insufficiency. However, VSRR requires slightly more complicated surgical techniques than the Bentall method and has an increased surgical risk, such as prolonged cardiopulmonary bypass time and cardiac arrest time. Thus, VSRR should be performed by surgeons and facilities skilled in its surgical techniques, and continuous follow-up by regular echocardiography and CT examination is essential for the prevention and treatment of postoperative cardiac-valve and aorta-related complications.

1.5.2 Acute Aortic Dissection in Marfan Syndrome Patients

Patients with hereditary aortic diseases, such as Marfan syndrome, are likely to develop aortic dissection due to the fragility of their aortic wall, and attention must be paid to their residual aorta even after treatment for aortic dissection. In a study of 6424 patients, including 258 Marfan syndrome patients, the data of IRAD showed no difference in the in-hospital mortality rate for acute Type A dissection between patients with and without Marfan syndrome. However, patients with Marfan syndrome had a 5-year survival rate of 80.1% and a freedom rate from reoperation of 55.3%, and they had a high risk of reoperation.[1581] The results of treatment beyond the arch after aortic root replacement for hereditary aortic diseases showed an operative mortality rate of 2.5% with no complication with paraplegia. With a postoperative 10-year survival rate of 62% and an aortic event avoidance rate of 24%, it was found that aortic dissection, once it develops, requires reoperation at a high rate.[1582]

For acute Type A dissection, various surgical procedures are selected depending on the position of an entry and surgical risk, which include ascending aortic replacement, aortic root replacement, and arch replacement. In a study examining whether to perform ascending aortic replacement or root replacement at the onset of acute Type A dissection in Marfan syndrome patients, the freedom rate from root reoperation after 20 years was lower in patients undergoing ascending replacement alone at 20% than in patients undergoing root replacement at 79%. Thus, Bentall surgery or VSRR is recommended for Marfan syndrome patients at the onset of Type A dissection.[1583] On the other hand, regarding the aortic arch, the reoperation rate for the arch in non-dissection patients is approximately 3% when the arch replacement is not performed concurrently with root replacement. However, the reoperation rate for the arch in patients with acute Type A dissection significantly increases to 33% if total arch replacement is not performed.[1584] However, in reality, lifesaving is the primary goal, and invasiveness greatly increases when root replacement is also performed. Therefore, whether total arch replacement is performed at the onset of acute Type A dissection should be carefully decided in consideration of the experience of the facility and surgeons as well as the surgical risk.

The effectiveness of open stent graft/FET has been demonstrated recently. A study of 106 Marfan syndrome patients undergoing total arch replacement with FET for acute dissection showed an operative mortality rate of 6.6% and an SCI incidence of 0.9%. The long-term mortality rates were reported to be 4% at 5 years, 18% at 8 years, and 25% at 10 years, while the freedom rates from reoperation were reported to be 88.8% at 5 years and 84.2% at 8 years.[1105] In addition, entry closure by FET enlarged the true lumen and promoted thrombus formation in the false lumen, which resulted in aortic remodeling in 29% of patients.[1585] On the other hand, 80% of patients undergoing TEVAR for acute Type B dissection survived 8 years after surgery, and 38% of the surviving patients showed aortic remodeling below the descending aorta. However, they had a high long-term aortic retreatment rate of 33%.[1586] Therefore, the short-term results of TEVAR for Type B dissection patients are comparable to those of non-Marfan syndrome patients; however, it often results in reoperation for retrograde Type A dissection and stent graft-induced new entry. Based on these, the use of TEVAR for hereditary aortic diseases is justified only for the purpose of survival of patients with acute aortic syndrome (rupture and dissection) or patients for whom open surgery is judged to be unsuitable due to the age or high surgical risk.[1586,1587]

On the other hand, in a retrospective observational study of aortic replacement conducted in 2017, thoracoabdominal aortic replacement was performed on 65 patients with hereditary aortic diseases, of whom 86% had a history of aortic surgery and 11% had undergone urgent surgery. Also, their surgical sites were thoracic descending aorta in 15% and thoracoabdominal aorta with Crawford type I in 17%, type II in 40%, type III in 17%, and type IV in 7%. They had an operative mortality rate of 14%, and the causes of death were hemorrhage, nerve injury, heart failure,

Table 50. COR and LOE for Medical Treatment of Marfan Syndrome		
	COR	LOE
It is recommended to perform diagnostic imaging regularly	I	C
It is recommended to perform exercise restriction	I	C
It is recommended to administer β-blockers to prevent the enlargement of aortic diameter[277,1593,1594]	I	B
It is recommended to administer ARB as alternative drugs of β-blockers to prevent the enlargement of aortic diameter[1595–1598]	I	A
The combined use of β-blockers and ARB may be considered to prevent the enlargement of aortic diameter[1415,1598,1599]	IIb	A

ARB, angiotensin II receptor blockers; COR, class of recommendation; LOE, level of evidence.

and respiratory failure. Also, an extended surgery of 7 h or longer was a risk factor for operative death. They had a retreatment avoidance rate of 85% and a 1-year survival rate of 80%.[1572] Therefore, multiple surgeries are usually performed in patients with hereditary aortic diseases, and because of the high surgical risk, treatment in an experienced facility is desirable. In addition, it has a lower long-term aortic retreatment rate than TEVAR, and those patients have a relatively maintained long-term life prognosis.

1.5.3 Loeys–Dietz Syndrome

Loeys–Dietz syndrome is a hereditary aortic disease mainly caused by gene mutations of TGF-β receptors. Due to the higher risk of aortic events in patients with Loeys–Dietz syndrome than in patients with Marfan syndrome, it is recommended to consider surgery for patients with Loeys–Dietz syndrome having a smaller diameter of the aortic root or ascending aorta compared with those with Marfan syndrome.[1539] As in Marfan syndrome, the reimplantation method for annuloaortic ectasia associated with Loeys–Dietz syndrome was reported to have favorable results. In 2011, it was reported that there was no operative death in 31 Loeys–Dietz syndrome patients undergoing the reimplantation method (77% of whom were children). Also, only 3% had a long-term recurrence of a moderate or higher degree of aortic valve insufficiency, and there were no complications with valve replacement, thromboembolism, or infectious endocarditis.[1588] In 2019, it was reported that 33 (62%) of 53 Loeys–Dietz syndrome patients had undergone aortic surgery, 67% of whom did not require reoperation, with an urgent-surgery mortality rate of 6%. On the other hand, 33% underwent multiple aortic surgeries, several of whom were complicated by aortic dissection. In addition, there were no aortic or valve-related complications after root replacement, and they showed favorable results with a 10-year survival rate of 89%.[1589]

A study retrospectively examining patients undergoing aortic surgery showed that 30–40% of patients initially developed dissection regardless of whether they had Marfan syndrome or Loeys–Dietz syndrome; additionally, there was no difference in the long-term survival rate between Marfan syndrome patients and Loeys–Dietz syndrome patients. In addition, total arch replacement was necessary for 12% of Marfan syndrome patients and 22% of Loeys–Dietz syndrome patients.[1590] As with the decision on treatment policy for acute aortic dissection in Marfan syndrome patients, the decision on whether total arch replacement is performed should be made in consideration of the experience of the facility and surgeons and the surgical risk.

1.5.4 Vascular Ehlers-Danlos Syndrome

Vascular Ehlers-Danlos syndrome is caused by abnormalities in type III collagen gene, and it has a high risk of arterial aneurysms and dissections from the aorta to the small and medium arteries. In a retrospective observational study investigating the long-term prognosis, approximately half of the patients underwent surgery, with an operative mortality rate of approximately 10%. A complication with postoperative hemorrhage was observed at a high rate, and 40% of patients developed vascular-related complications even in the late postoperative period.[1591] Therefore, due to the high risks of not only aortic complications but also surgical treatment, there has been no clear standard for preventive aortic surgery, and each patient needs to be responded individually when he/she is judged to have a high survival risk. Some have recently reported stable results of patients undergoing aortic surgery,[1592] and future clinical trials on the surgery are awaited.

1.6 Medical Treatment

1.6.1 Marfan Syndrome (Table 50)

Strenuous exercise needs to be restricted; however, the daily life of Marfan syndrome patients varies depending on the pathological condition. Although restrictions are determined according to changes in the pathological condition, their normal life requires a few restrictions.

Drug therapies for Marfan syndrome include the "control of blood pressure" for heart and arterial diseases. β blockers are currently used as the first choice for the prevention of aortic enlargement in this disease, which is based on the reports showing that they suppressed the enlargement of the aortic root.[277,1593,1594] However, no large-scale studies have been conducted, and there has been only one RCT with a relatively small number of subjects.[277] In addition, there has been no clear evidence of their preventive effect on aortic dissection or rupture.

ARBs, which are TGF-β inhibitors, were reported to clearly suppress the enlargement of the aortic root in mice,[528] and their effects have been investigated in several studies since then. Multiple large-scale RCTs comparing the effects of ARBs and β blockers showed similar results in preventing the progression of aortic diameter enlargement.[1595–1597] A meta-analysis of these trials showed similar results,[1598]

Table 51. COR and LOE for Endovascular Treatment for Genetic Aortic Diseases

	COR	LOE
In patients who have already undergone multiple graft replacements, TEVAR for bridging the non-replaced area should be considered[1582,1601–1603]	IIa	C
As a method of bridging until radical treatment (open surgery) for life-threatening complicated aortic diseases such as AEF, ABF, infected aortic aneurysm, TEVAR should be considered[1604]	IIa	C
TEVAR should be considered for patients with life-threatening acute aortic disease (complicated acute Type B dissection, acute aortic syndrome for which invasive treatment is indicated) and who meet the anatomical requirement for TEVAR[1381,1586,1605]	IIa	C
For patients who are difficult or high-risk for open surgery, TEVAR should be considered if anatomical requirements are met[1381,1586,1601,1602,1604,1606–1608]	IIa	C
In patients with Type A dissection, total arch replacement with the frozen elephant trunk method should be considered[1105,1125,1582,1585,1609,1610]	IIa	C
TEVAR/EVAR may be considered, as indicated for non-genetic aortic diseases	IIb	C

ABF, aorto-bronchial fistula; AEF, aorto-esophageal fistula; COR, class of recommendation; EVAR, endovascular aortic repair; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

suggesting that ARBs are as effective as β blockers in preventing the enlargement of aortic diameter; additionally, ARBs can be used as alternative drugs to β blockers without any problem. However, it is not recommended to actively replace β blockers with ARBs, as they are not more effective than β blockers.

While some large-scale RCTs reported that the addition of ARB administration to baseline treatment (β blockers in many cases) suppressed the progression of aortic diameter enlargement, others did not observe such suppression.[1415,1599] Therefore, there has been no consensus on the effects of the combined use of ARBs with β blockers, and similar results were shown by a meta-analysis.[1598] Thus, the preventive effect of the combined use of ARBs with β blockers on the enlargement of aortic diameter remains unclear at present.

1.6.2 Loeys–Dietz Syndrome

There have been no reports that sufficiently examined the effectiveness of drug therapy for Loeys–Dietz syndrome, and basically, its treatment is based on that for Marfan syndrome.

1.6.3 Vascular Ehlers–Danlos syndrome

Celiprolol, which is a β1 blocker with a β2 stimulating effect, was reported to be effective in preventing the onset of arterial dissection and arterial rupture in patients with vascular Ehlers–Danlos syndrome.[1600]

1.7 Endovascular Treatment (Table 51)

It is considered that stent-graft deployment (TEVAR/EVAR) should be of limited use in patients with hereditary connective tissue diseases.[1587,1611–1613] This is because the incidence of endoleak after TEVAR/EVAR for this disease, additional treatment rate, and incidence of life-threatening complications (such as retrograde Type A dissection) may be higher than in patients with non-hereditary aortic diseases.[416,417,1380,1587,1611,1614,1615] In many patients with hereditary aortic diseases, such as true aneurysms and aortic dissection, the lesion site involves the entire region of the aorta, and invasive treatment must often be performed at several areas of the aorta. In such cases, TEVAR/EVAR for bridging the non-replaced area between proximal and distal synthetic grafts can be recommended.[1582,1601–1603] Furthermore, TEVAR (when anatomical requirements are fulfilled) can also be recommended for complicated acute aortic syndrome (aortic dissection, IMH, PAU) patients requiring emergency treatment for life-saving.[1381,1586,1601,1602,1605,1606] In addition, TEVAR for bridging until open surgery or TEVAR in the patients with high-risk of open surgery can also be recommended.[1582,1604,1607,1608] However, there is no evidence regarding the following issue: whether or not the application/usage of TEVAR/EVAR equivalent to those in patients with non-genetic aortic aneurysms/dissection are permissible in patients with genetic aortic diseases. These procedures cannot be recommended.

On the other hand, total arch replacement with an open stent graft/FET for Type A dissection can be recommended, as its stable early results, a favorable remote-phase prognosis, and aortic remodeling have been obtained even in patients with genetic aortic diseases.[1105,1125,1582,1585,1609,1610]

The extent of invasive treatment for genetic aortic diseases involves the entire region of the aorta and its main branch in many cases. A strategy to systematically combine open surgery with endovascular repair at an adequate timing/extent of treatment may improve the prognosis rather than a strategy to treat these diseases by open surgery alone. It is important to accumulate data in facilities that are skilled in surgical and endovascular procedures now and in the future.[1582,1602,1604,1606,1608,1609,1612,1613,1616]

2. Aortopathy Associated With Bicuspid Aortic Valve

2.1 Pathological Conditions

The enlargement of the ascending aorta (root-arch) and aneurysm formation associated with the bicuspid aortic valve (BAV) are called "bicuspid aortopathy," and it is found in approximately 40% of BAV patients.[1617] Hereditary factors have been identified in only a few percent of all bicuspid aortopathy patients; additionally, several patients are thought to have multifactorial diseases affected by blood flow stress associated with BAV.[1618] Regarding the morphology of BAV, a true bicuspid valve, which divides into two at 180°, is rare, and the left coronary cusp-right coronary cusp fusion type, right coronary cusp-noncoronary cusp fusion type, and left coronary cusp-noncoronary cusp fusion type occur at ratios of 70%, 10–20%, and 5–10%, respectively.[1619] On the other hand, the morphology

Table 52. COR and LOE for Open Surgery for Aortopathy Associated With Bicuspid Aortic Valve		
	COR	LOE
It is recommended to perform open surgery on patients with an aortic root/ascending or arch aortic diameter of ≥55 mm associated with asymptomatic bicuspid aortic valve[543,1626,1633–1635] (See **Table 12**)	I	C
Open surgery should be considered for patients with risk factors for aortic dissection* who have an aortic root/ascending aortic diameter of ≥50 mm associated with asymptomatic bicuspid aortic valve[539,543,1551,1633,1634,1636] (See **Table 12**)	IIa	C
Concomitant open surgery should be considered for patients with an aortic root/ascending aortic diameter of ≥45 mm who are scheduled for aortic valve surgery or other open heart surgery[544–548,1633,1637] (See **Table 12**)	IIa	C
Concomitant open surgery should be considered for patients with an arch aortic diameter of ≥50 mm who are scheduled for aortic valve surgery or other open heart surgery[1620,1635]	IIa	C
Open surgery may be considered for patients with an aortic root/ascending aortic diameter of ≥50 mm due to an asymptomatic bicuspid aortic valve, who do not have risk factors for aortic dissection* and are not scheduled for other open heart surgery[1617,1620,1635,1638]	IIb	C

*Such as a family history of aortic dissection, aortic enlargement rate of ≥5 mm/6 months, severe aortic valve insufficiency, and desire for pregnancy. COR, class of recommendation; LOE, level of evidence.

of bicuspid aortopathy is classified into type I: enlargement of only the aortic root (13%), type II: enlargement of only the ascending aorta (14%), type III: enlargement from the ascending to aortic arch (28%), and type IV: enlargement from the root to aortic arch with a gradual decrease in arch diameter (45%).[1620] Types I and II are common in the left-right coronary cusp fusion type BAV. In contrast, types II and III are common in the right-noncoronary cusp fusion type BAV, and root enlargement rarely occurs.[1621] In addition, approximately 90% of patients with coarctation of the aorta are complicated by left-right coronary cusp fusion type BAV.[1622]

As in patients with other hereditary aortic diseases, BAV patients often develop acute aortic dissection at a young age.[1623] Because of reduced expression of fibrillin-1 in the aortic tissue and enlarged aortic diameter of bicuspid aortopathy patients,[540] the 2010 AHA/ACC guidelines recommended a treatment strategy for bicuspid aortopathy based on that for hereditary aortic diseases, in consideration of its similarity with Marfan syndrome.[95] However, a subsequent comparative study of the aortic diameter showed that although both BAV patients and Marfan syndrome patients had a high enlargement rate of the ascending aorta, aortic enlargement occurred only in approximately half of BAV patients, suggesting the diversity of the pathological conditions of BAV.[1624] A retrospective observational study conducted in 2015 showed that the incidence of aortic dissection after aortic valve replacement was lower in BAV patients (0.5%) than in Marfan syndrome patients (5.5%) and that the incidence of aortic aneurysm surgery was lower in BAV patients (2.5%) than in Marfan syndrome patients (10.4%).[1625] In addition, a prospective clinical study conducted in 2016 showed that both the incidence of aortic dissection and the long-term mortality rate after dissection were lower in BAV patients than in Marfan syndrome patients.[1626] Therefore, as a hereditary aortic disease, bicuspid aortopathy is considered to have a lower risk compared with other hereditary aortic diseases, although the risk is higher than the normal aorta. A recent pathological study has shown decreased expression of fibrillin-1 in the aortic tissue of both Marfan syndrome patients and BAV patients. However, the two diseases have shown differences in some expression markers, suggesting that different genetic abnormalities lie in the background.[1627]

Notch1 was reported to be involved in BAV as its causative gene.[1628,1629] However, the involvement of several other genes has been suggested, and the genetic background of BAV has not been fully elucidated.

With regard to the abnormal blood flow stress associated with BAV, the direction and velocity of blood flow have been visualized by 4-dimensional cardiac MRI, and the aortic wall shear stress can be quantitatively evaluated. Compared with the normal aorta, abnormal clockwise spiral blood flow occurs in the ascending aorta of BAV patients, and it was suggested that the aortic wall shear stress increases when the axis of blood flow is largely tilted, affecting the enlargement of the aorta.[1630] Medial elastic fibers collapse at the site of increased aortic wall shear stress; additionally, it results in abnormalities in the extracellular matrix, such as increased levels of TGF-β and matrix metalloproteinases, suggesting its association with bicuspid aortopathy.[1631] In addition, the directions and velocities of cardiac output jet differ depending on the valve morphology of BAV, suggesting a mechanism that results in different dilated morphologies of the aorta.[1632]

2.2 Surgical Indications (Table 52)

2.2.1 Asymptomatic Patients

Compared with healthy individuals, bicuspid aortopathy patients were reported to have 8.4- and 86-times higher incidences of aortic dissection and aortic aneurysm, respectively,[1633] and early aortic treatment has been considered for bicuspid aortopathy patients.[543] However, it was recently reported that no such difference is observed between bicuspid aortopathy patients and tricuspid valve patients. Surgical treatment for bicuspid aortopathy is relatively safe and contributes to the survival rate and aortic event avoidance.[1617] Therefore, a diameter of 55 mm or larger is recommended as an indication of root/ascending aortic replacement for asymptomatic bicuspid aortopathy. On the other hand, an observational study of the ascending aortic diameter of bicuspid aortopathy reported that patients with a diameter of at least 50 mm or a yearly enlargement rate of at least 5 mm are expected to have a similar prognosis after aortic surgery, as that of healthy individuals.[1634] In a retrospective observational study, the risk of acute aortic dissection was higher in BAV patients

with an ascending aortic diameter of at least 53 mm or an aortic root diameter of at least 50 mm. Thus, surgery in a facility experienced in aortic treatment is recommended for patients with a diameter of 50 mm or larger.[1638]

2.2.2 Concurrent Treatment During Aortic Valve Surgery

It has long been debated whether aortic replacement should be performed concurrently with valve surgery for BAV patients exhibiting a mild enlargement of the ascending aorta. The ascending aorta enlarges faster after aortic valve replacement in BAV patients than in tricuspid valve patients, increasing the risk of dissection.[546,548] In 2004, a retrospective observational study examined the aortic diameter of 201 BAV patients after aortic valve replacement. It showed that the groups of BAV patients with an ascending aortic diameter of below 40 mm, 40–44 mm, and 45–49 mm at the time of surgery had postoperative 15-year aortic event avoidance rates of 86%, 81%, and 43%, respectively; therefore, the study recommended concomitant surgery with valve replacement for bicuspid aortopathy patients with a diameter of 45mm or larger.[544] A study conducted in 2011 examined over 1800 BAV patients who had undergone only aortic valve replacement or ascending aortic replacement in combination, and it showed no difference between the two groups in the operative mortality rate at 1%. Also, the groups showed no difference in the long-term survival rate and incidence of aortic events. However, since patients with an aortic diameter of below 45 mm had a low aortic event incidence of 0.2% even after undergoing only aortic valve replacement, it recommended performing aortic replacement in combination on patients with an aortic diameter of 45 mm or larger.[547]

In addition, 10–25% of Turner syndrome patients are complicated by BAV. However, most of Turner syndrome patients developing aortic dissection were complicated by BAV, and their ascending aortic diameter coefficient at the onset of dissection was 2.7 cm/m^2. Turner syndrome patients are characterized by short height, and there is a concern that the timing of treatment is delayed if the normal aortic diameter is applied. Thus, aortic replacement is considered for Turner syndrome patients over 18 years of age with an aortic diameter coefficient of >2.5 cm/m^2.[1551,1636]

2.2.3 Bicuspid Aortopathy Extending to the Aortic Root and Aortic Arch

The surgical range varies depending on the enlargement range of bicuspid aortopathy. Because aortic dissection of BAV patients often has an entry in the enlarged aortic root,[539] patients with root enlargement are indicated for aortic root replacement. On the other hand, when only aortic valve replacement and ascending aortic replacement are performed in BAV patients having the enlarged ascending aorta without the enlargement of the root, it is unlikely that the root enlargement poses a problem in the late stage after surgery, and aortic root replacement is not recommended.[545,1637] In addition, the AHA/ACC and ESC guidelines have not previously specified treatment for bicuspid aortopathy with enlargement of the aortic arch region. However, the enlarged site of bicuspid aortopathy remains in the root and ascending regions in only approximately 1/4 of all cases.[1620] Surgical indication for arch enlargement was set to 55 mm in the guidelines published in Canada in 2014.[1635]

Given these, surgical indication criteria in **Table 52** are recommended based on the 2010 AHA/ACC guidelines,[95] the 2014 ESC guidelines,[96] the 2016 AHA/ACC statement clarification,[1639] and the 2018 AATS consensus guidelines.[1640] In addition, if a patient is diagnosed with BAV and has an aortic diameter of >40 mm, imaging evaluation, such as yearly echocardiography and CT/MRI examination (every 6 months if there is a tendency of enlargement), needs to be performed regularly, and regular follow-up of aortic diameter is required. Furthermore, it is also desirable to screen first-degree family members (especially males).

3. Atherosclerotic Aortic Diseases

3.1 Thromboembolic Aortic Diseases

Plaques in the aorta consist of lipids that have accumulated in the intima/media layer of the aorta as a result of atherosclerotic plaque extension. Secondary inflammation and fibrous tissue deposition, as well as subsequently formed thrombus and the erosion of the lumen surface, are the factors that cause thrombotic (thromboembolic) or atherosclerotic (cholesterin crystal) embolism.[1641] Thromboembolic embolus is usually large, and it generally occludes medium-large arteries, causing cerebral infarction, transient cerebral ischemic seizure, renal infarction, intestinal ischemia, and peripheral artery thromboembolism. On the other hand, cholesterin crystalline embolus occludes small arteries and arterioles, and it can cause blue toe syndrome and renal failure.

3.1.1 Epidemiology

As in other atherosclerotic plaques in the vascular bed, the risk factors leading to aortic plaque formation include age, gender, hypertension, diabetes mellitus, dyslipidemia, lifestyle with little exercise, smoking, and inflammation. The Offspring Framingham study reported that aortic plaque was found in 46% of individuals with normal blood pressure and that it was more common in women. Large plaques are associated with hypertension; additionally, they were reported to be more common in patients with cardiovascular disease.[1642] Aortic plaques were shown to be involved not only in cerebrovascular but also peripheral arterial embolism by autopsy results,[1643] a study of patients with non-fatal cerebrovascular and peripheral vascular diseases,[1644] and a case study of transesophageal echography and intraoperative echography.[1645,1646]

Atrial fibrillation patients presenting with mobile plaque, ulcer formation in plaque, or plaque with a thickness of at least 4 mm shown by transesophageal echography were reported to have 4 times higher risk of cerebral infarction than those without a plaque.[1647] Also, in cerebral infarction patients, an aortic plaque with a thickness of at least 4 mm was reported to be an independent risk factor for the recurrence of cerebral infarction and the development of all vascular events.[1648] Atherosclerotic (cholesterin crystal) embolism was found in 0.18–2.4% of autopsy cases.[1649] Embolic events are also found during angiography, cardiac catheter examination, intra-aortic balloon pumping (IABP), and cardiac surgery. Cholesterin crystal embolism was found in 12–77% of patients who had received some treatment on the aorta,[1650,1651] and it was reported that cholesterin crystal embolism was found in 22% and 27% of autopsy cases after cardiac surgery[1652] and after aortic contrast imaging,[1653] respectively. In a study that examined 921 cases of cardiac surgery, the incidences of cerebral infarction in patients with and without atherosclerotic

lesions were 8.7% and 1.8%, respectively, showing a significantly higher incidence in the group with lesions.[1654] However, these incidences were lower than that in autopsy.

A meta-analysis showed that the radial arterial approach and femoral artery approach of cardiac catheter examination resulted in low incidences of cerebral infarction at 0.1% and 0.5%, respectively, showing no significant difference between the two.[1655] Also, cardiac catheter examination generally does not have a high risk of developing cerebral infarction. Currently, transcatheter aortic valve implantation (TAVI) is performed in older adults with many complications, mainly atherosclerotic lesions. However, a meta-analysis reported that the apical approach reduced cerebral infarction compared with the (femoral or axillary) arterial approach,[1656] and the risk varies depending on the presence or absence, site, and degree of atherosclerotic lesions.

It was reported that cholesterin crystal embolism was found in 1.3–3.6% of patients undergoing stent deployment in the aortoiliac region during endovascular treatment for peripheral artery disease below the abdominal aorta.[1657–1659] On the other hand, it was reported that embolism was found in 2.9% of patients undergoing open surgery below the renal artery;[1660] additionally, there was no difference in the incidence between endovascular treatment and open surgery. However, endovascular treatment in patients with shaggy aorta or ulcerative plaque has a high risk.[1648]

3.1.2 Treatment

Antithrombotic therapy (antiplatelet agents and anticoagulants) is necessary to reduce the risk of thromboembolism. However, there have been few studies on thromboembolism that occurs in the aorta, many of which are small-scale studies. While some studies showed the effectiveness of warfarin for aortic plaque,[1661–1663] others reported that warfarin was not effective compared with antiplatelet agents.[1664,1665] Conversely, antithrombotic therapy may promote the separation of cholesterin crystal and atheroma.[1666,1667]

a. Lipid-Lowering Therapy (Plaque Stabilization)

Lipid-lowering therapy with statins is useful in reducing the risk of developing symptomatic atherosclerotic diseases.[1668] There have been no RCTs recommending the oral administration of statins in patients with cerebral infarction caused by atheroma embolism. However, it was reported that 19% and 38% of patients with familial hypercholesterolemia showed atheroma extension and reduction of atheroma, respectively, when evaluated for 2 years by transesophageal echography.[1669] In addition, the oral administration of statins for 6 months was reported to reduce aortic atheroma volume by 15% on MRI examination,[1670] and oral administration of statins for 3 months was reported to reduce plaque inflammation on PET examination.[1671] A large-scale retrospective study of patients with severe aortic plaques reported that only statins reduced the risk of developing cerebral infarction by 70%,[1664] and statin administration for the stabilization of atheroma as an embolic source is also considered. However, large-scale RCTs are needed.

b. Revascularization

The surgical approach for lesions causing peripheral embolism is a measure to reduce the risk of embolism recurrence. There have been no large-scale RCTs; several reports on open surgery/endovascular treatment for aortic atheroma were from single centers. Although open surgery for lesions below the renal artery has favorable results,[1672,1673] the involvement of suprarenal lesions increases the operative mortality rate,[1672] and it should be carefully examined as a preventive treatment. In addition, thromboendarterectomy and prosthetic graft replacement for thoracic aortic lesions are considered only for patients with repeated recurrence due to their high surgical invasiveness.[1674,1675] Because endovascular treatment itself triggers embolism in patients with aortic atheroma, careful consideration is needed for its indications and selection. For lesions peripheral to the thoracic descending aorta, a method of covering the lesion site using a stent graft has been reported;[1676,1677] however, no large-scale studies have been conducted at present.

3.2 Thrombus in the Aorta

Transesophageal echography in patients with cerebral infarction or peripheral arterial embolism showed that thrombus was found in the aortic arch of young individuals who did not have extensive atherosclerosis. Also, only 4 of 23 patients with highly mobile thrombus in the aorta showed a thrombus tendency, and the pathophysiology of such lesions remains unclear.[1678] Such thrombus in the aorta that is not adhered to the aortic wall is a life-threatening pathological condition that becomes an embolic source not only for cerebral infarction but also for the splanchnic artery and lower limbs. It often develops after aortic lesions, such as dissection, trauma, and atherosclerotic changes, and it shows a thrombus tendency as its pathological condition, which rarely occurs in normal blood vessels. Transesophageal echography, which allows for the real-time confirmation of the mobility and floatability of thrombus, is the first choice for diagnosis in the distal arch and descending aorta, and CT/MRI examination is also useful in deciding a treatment policy.[1679,1680] In the abdominal aorta, abdominal echography often visualizes a flattering thrombus in real-time, and similarly, CT/MRI examination is useful for detailed diagnosis and decision on treatment policy.

There have been reports of conservative treatment with heparinization,[1679] thrombus aspiration by endovascular treatment,[1681] stent deployment/stent-graft deployment,[1681] thrombectomy,[1679] and open surgery, mainly prosthetic graft replacement;[1682] however, there have been no large-scale comparative studies.

There are increasing reports of not only patients exhibiting venous thrombosis but also those exhibiting thrombus in the aorta as a phenotype of cancer-related thrombosis.[1683] In addition, patients presenting with aortic thrombus during anticancer drug treatment with cisplatin or bevacizumab have been reported in recent years, and attention must be paid to cancer patients receiving chemotherapy.[1684,1685]

3.3 Atherosclerotic Aortic Obstruction

Atherosclerotic (degenerative) occlusion of the thoracic aorta is highly rare, including the acute/chronic stage, and acute occlusion of the abdominal aorta is also rare. On the other hand, if the abdominal aorta has resulted in chronic occlusion, the obstructive lesion may progress to the pararenal artery aortic obstruction. However, due to the extensive development of collateral flow, many patients do not present with acute ischemic symptoms, and clinical symptoms are limited to claudication symptoms in numerous

cases. However, if it develops as acute occlusion, it results in a fatal pathological condition. Its factors include the progression of normal atherosclerosis obliterans and the involvement of the small-diameter aorta (so-called small aorta), as well as saddle embolism and aortic dissection in acute cases.

In acute cases, the symptoms progressively worsen with a sudden disruption of blood flow until the collateral flow results in occlusion. Subsequently, patients present with clinical symptoms caused by acute arterial occlusion of the lower limbs, such as the disappearance of peripheral arterial pulsation, cold sensation, and foot drop, causing severe ischemic symptoms in the lower limbs/spinal nerves, intestinal tract, and kidneys. In numerous cases, diagnosis is made by Doppler echography in addition to clinical symptoms; however, imaging examinations, such as CT and MRI, also provide useful information for deciding a treatment policy. In patients with saddle embolism, thrombectomy can be performed if blood flow is resumed early after onset, and the risk of developing ischemia reperfusion injury (myonephropathic metabolic syndrome) is low. However, if it is delayed, the resumption of blood flow can no longer be achieved, leading to a poor life prognosis.[1686] Bypass surgery or endovascular treatment is performed in chronic cases, and both have favorable results.[1687]

3.4 Aortic Calcification

The presence of the thoracic aorta that exhibits severe atherosclerosis can be easily diagnosed as it is observed as porcelain aorta in an unenhanced image. Similarly, the abdominal aorta exhibits a calcification image along the running of the aorta, which can be easily diagnosed. Patients with maintenance dialysis show severe calcification not only in the peripheral arteries, but also in the aorta. In any region, its range and progression of the pathological condition are diagnosed by CT examination. It has been shown that calcification of the abdominal aorta is not only a risk of embolism in surgery, but also an independent risk factor for cardiovascular/cerebrovascular events.[1688] However, in cardiovascular open surgery, calcification lesions can be not only an obstacle for cannulation, clamping, and various bypass surgeries, but also a risk factor for cerebral infarction and peripheral embolism. For patients with porcelain aorta who have no problem with access routes, endovascular treatment is also selected in consideration of the risks/benefits.

Coral reef aorta is a disease that presents with highly severe calcification and stenosis due to calcification lesions that have extended to the lumen in the aorta at the level of the abdominal splanchnic artery branch, mainly the renal artery. Many of its clinical studies are case reports, and only one study examined over 80 cases.[1689] This is a rare disease that presents with renovascular hypertension, abdominal angina, and lower-limb ischemic symptoms due to severe calcification of the abdominal aorta at the level of the abdominal splanchnic artery branch and stenosis with calcification of each abdominal splanchnic artery. This disease was reported to be more common in women compared with other atherosclerotic diseases, and its etiology and occurrence mechanism remain unknown. Previously, surgical treatment, mainly thromboendarterectomy, was performed for its patients;[1689] however, the operative mortality rate was as high as 11. 6% due to cardiac complications and multiple organ failure.[1690] In recent years, extra-anatomical bypass[1691] and endovascular treatment with stent graft have been performed, especially for high-risk cases;[1692] however, no large-scale studies have been conducted.

Table 53. COR and LOE for Shaggy Aorta

	COR	LOE
Evaluation of the presence or absence of shaggy aorta by contrast-enhanced CT prior to aortic aneurysm treatment intervention should be considered to avoid multiple thromboembolism during treatment	IIa	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence.

3.5 Leriche Syndrome

"Leriche syndrome" is occasionally referred to a general term for occlusive diseases in the aortoiliac region; however, patients having anatomical occlusion of the aortoiliac region alone are not considered to have this syndrome. Those presenting with three symptoms of intermittent claudication, attenuation/disappearance of peripheral arterial pulsation, and sexual dysfunction are referred to as "Leriche syndrome" patients.

Several cases of occlusion of the aortoiliac region are based on atherosclerosis, and it is commonly found in older adults. However, Leriche syndrome patients have sexual dysfunction as the main sign, and they are often diagnosed in the 40s to 60s. Leriche syndrome is treated in the same manner as occlusive diseases of the aortoiliac region caused by normal atherosclerosis obliterans, and surgical revascularization (bilateral aortic iliac artery bypass surgery and bilateral aortic femoral artery bypass surgery) or endovascular treatment is performed for Leriche syndrome patients. The results of its endovascular treatment have improved in recent years, and endovascular treatment is often selected except for patients with high aortic obstruction (pararenal artery aortic obstruction).[1693] In Europe and the United States, stent-graft deployment is performed in addition to bare metal stent, and the primary patency rate was reported to be 87% after 1 year and 82% after 2 years.[1694] Intermittent claudication is improved by bypass surgery and endovascular treatment described above. However, improvement of sexual dysfunction requires an improvement of blood flow in the internal iliac region, and reconstruction of the internal iliac artery is considered if it can be performed.

3.6 Shaggy Aorta (Table 53)

Shaggy aorta refers to the appearance of hemp-like fluff on the inner surface of the aorta due to severe diffuse atherosclerotic lesions in the aorta (**Figure 67**). Clinically, it is often referred to an imaging finding of contrast-enhanced CT or echography.[1695] In addition, shaggy aorta syndrome is a disease group exhibiting various organ damages in which fine cholesterin crystals derived from an unstable and floatable atheroma in the thoracic or abdominal aorta become separated as a natural course without a clear trigger or as a result of catheter operation

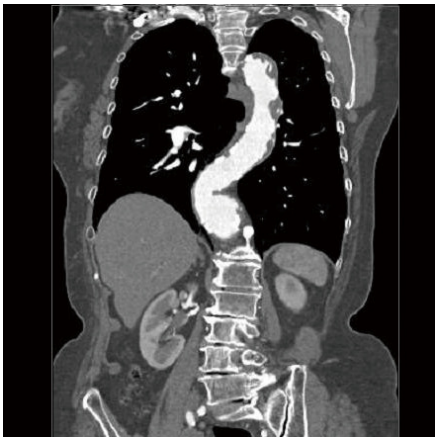


Figure 67. Typical shaggy aorta (contrast-enhanced CT findings, coronal section). An extensive, irregularly shaped, diffuse atherosclerotic lesion is observed in the thoracic aorta.

in the aorta and open surgical operation, which embolizes peripheral arteries.[1696] The uniform definition of shaggy aorta has not been clearly established since its evaluation method differs depending on the modality of diagnostic imaging. However, it generally indicates the aorta with an extensive irregularly-shaped atheroma lesion that has a thickness of at least 4–5 mm and protrudes into the lumen on preoperative contrast-enhanced CT, intraoperative transesophageal echography, and aortic echography. In particular, those with a mobile atheroma are recognized as an aortic atherosclerotic lesion with a high clinical risk of developing organ embolism.[1697]

Its etiology and pathological condition may be regarded as those of vasculitis; nevertheless, many of its aspects, including genetic factors, remain unclear. Regarding its medical treatment, some reported the effect of statins on reducing atheroma and parietal thrombosis;[1698,1699] however, the future progress and results of RCTs are awaited.[1700]

According to a report examining the effect of shaggy aorta on the invasive treatment of aortic aneurysm, shaggy aorta was found in 48 (11%) of 447 AAA patients. Also, the total of the incidence of major complications and mortality rate up to postoperative 30 days was 4.1 times higher in patients with shaggy aorta than in patients without shaggy aorta.[1701] With regard to its preoperative factors, the number of patients with a history of cerebral infarction, chronic kidney injury, or arteriosclerosis obliterans was significantly higher in those with shaggy aorta, although the main cause of the major complications described above, and deaths was multiple thromboembolism. This applies to both open surgery and TEVAR, indicating that the risk of multiple thromboembolism cannot be avoided regardless of the treatment method. Furthermore, even when comparing long-term results up to postoperative 5 years, the survival rate was significantly lower in the patient group with shaggy aorta.

In addition, according to a study that examined 251 patients undergoing prosthetic graft replacement for TAAA, 36 patients (14%) had shaggy aorta among all patients including 139 patients with dissecting aortic aneurysm.[1702] Comparing a total of 112 patients undergoing degenerative aortic aneurysm surgery, including 76 without shaggy aorta and 36 with shaggy aorta, patients with shaggy aorta had approximately 5 and 4 times higher operative mortality rate and incidence of SCI, respectively, than patients without shaggy aorta.[1702] Similarly, in a clinical study of 179 patients undergoing aortic arch prosthetic graft replacement, 34 patients (19%) were found to have shaggy aorta in the ascending or aortic arch.[1703] Although these patients did not have a statistically higher operative mortality rate, their odds ratio for shaggy aorta as a risk factor involved in the development of temporary neurological deficits was 4.4. Furthermore, the long-term survival rate after arch replacement was significantly lower in patients with shaggy aorta.

Scoring of shaggy aorta has been reported in recent years. In this study, on the axial image of reconstructed CT, a shaggy score of 1 point was given to those with (1) ulcer-like thrombus, (2) a maximum thrombus thickness of at least 5 mm, and (3) thrombus occupying at least 2/3 rounds of aortic diameter, and it is expected to be an index of postoperative embolism in the future.[1704]

The complication of multiple thromboembolism at the time of surgery is thought to be the main factor for the deterioration of treatment results of aortic aneurysm surgery due to having shaggy aorta. Therefore, a method of avoiding intraoperative thromboembolism has been devised to improve surgical results.[1705] To avoid cerebral embolism during aortic arch prosthetic graft replacement and to avoid severe complications due to embolism to the intestinal tract and kidneys during TEVAR for thoracic descending-thoracoabdominal aortic aneurysm, it is basically considered to expose those domain blood vessels in advance so that they are temporarily separated from the circulation in the aorta, which is followed by the completion of the surgical operation on the aorta.[1706,1707] On the other hand, considering that the dispersion of debris due to aortic cross-clamping and releasing operation of clamping is the main cause of thromboembolism, a method that uses deep hypothermic circulatory arrest without aortic cross-clamping may also be adopted as a measure against shaggy aorta.[1708] However, even in such cases, attention must be paid to the details of the extracorporeal circulation method, such as the cannulation site of the blood supply tube and the shape of the cannula, and the flow rate balance in the blood supply between the upper and lower body, when establishing extracorporeal circulation.[1697]

4. Aortitis

4.1 Definition and Classification

4.1.1 Inflammatory Aortic Diseases

The Chapel Hill Consensus Conference (CHCC, the 1994 first edition[1709] and the 2012 revised edition[1710]) has gained a worldwide consensus on the classification of vasculitis. Based on this, the "Clinical Practice Guidelines for Vasculitis Syndrome (2017 revised edition)" of the Japanese Circulation Society[1711] classifies vasculitis into large vasculitis (aorta and its major branches), medium vasculitis (organ arteries), small vasculitis (arterioles/small arteries and capillary blood vessels), and other vasculitis (**Table 54**). In addition, ESC published clinical practice guidelines for aortic diseases in 2014,[96] and a disease classification based on a new disease concept of histopathological diagnosis was subsequently shown.[1712]

4.1.2 Takayasu Arteritis

Takayasu arteritis was first reported by the Japanese ophthalmologist Mikito Takayasu as an ocular lesion in 1908, and it is also called Takayasu arteritis in Europe and the United States (**Figures 68** and **69**). It was also called "pulseless disease" due to stenosis lesion of branch blood vessels of the aorta or "aortitis syndrome" because the lesion spreads throughout the aorta. It is common among young women in Eastern countries, mainly in Japan, and it is a rare disease in Europe and the United States.[1710]

a. Macroscopic Images

It typically begins with a stenosis lesion in the lumen of a blood vessel. In particular, the blood vessels of the three branches that ascend from the bifurcation of the aortic arch are easily affected, and it may cause head and upper-limb ischemic symptoms, such as subclavian artery steal syndrome, depending on the stenosis site. The lesion progresses to the major branch blood vessels of the arch and further into the descending aorta. However, it tends to dilate in the ascending aorta, causing ascending aortic aneurysm and aortic valve insufficiency. Inflammation spreads from the aortic valve annulus to the aortic valve in approximately 5% of cases.[1713] Although rare, it may cause aortic dissection, and a lesion may extend to the pulmonary artery. In the scarred stage, the lumen of blood vessels exhibits the lead-pipe appearance due to stenosis and marked calcification.

b. Histological Changes

Histologically, severe infiltration of inflammatory cells from the adventitia to the media is found in the active stage of inflammation, and in particular, lesions with a moth-eaten appearance that disrupt and damage elastic fibers of the media layer are observed. Focal granulomatous lesions are formed mainly in the media, which may develop into small infarction in the media. It may not be easily distinguished from giant cell arteritis, which has multinucleated giant cells that sometimes phagocytose elastic fibers commonly found in patients in Europe and the United States. In the scarred stage, the media becomes thinner, and the adventitia shows fibrous thickening. Also, diffuse intimal hyperplasia occurs in the intima, where plate-like calcification progresses.

Table 54. Categories and Diseases of Vasculitis

Original 2012 CHCC
Large vessel vasculitis (LVV)
Takayasu arteritis (TAK)
Giant cell arteritis (GCA)
Medium vessel vasculitis (MVV)
Polyarteritis nodosa (PAN)
Kawasaki disease (KD)
Small vessel vasculitis (SVV)
Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV)
Microscopic polyangiitis (MPA)
Granulomatosis with polyangiitis (Wegener's) (GPA)
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)
Immune complex SVV
Anti-glomerular basement membrane (anti-GBM) disease Cryoglobulinemic vasculitis (CV)
IgA vasculitis (Henoch-Schonlein) (IgAV)
Hypocomplementemic urticarial vasculitis, HUV (anti-C1q vasculitis)
Variable vessel vasculitis (VVV)
Behcet's disease (BD)
Cogan's syndrome (CS)
Single-organ vasculitis (SOV)
Cutaneous leukocytoclastic angiitis
Cutaneous arteritis
Primary central nervous system vasculitis
Isolated aortitis
Vasculitis associated with systemic disease
Lupus vasculitis
Rheumatoid vasculitis
Sarcoid vasculitis
Vasculitis associated with probable etiology
Hepatitis C virus-associated cryoglobulinemic vasculitis
Hepatitis B virus-associated vasculitis
Syphilis-associated aortitis
Drug-associated immune complex vasculitis
Drug-associated ANCA-associated vasculitis
Cancer-associated vasculitis

(Adopted from the Japanese Circulation Society. 2017,[1711] Jennette JC, et al. 2013.[1710]) © 2013 American College of Rheumatology.

4.1.3 Giant Cell Arteritis

Giant cell arteritis is a common disease in Europe and the United States, while it is relatively rare in Japan (**Figure 70**). Compared with Takayasu arteritis, giant cell arteritis is more commonly found in older adults (60 years or older), and its association with polymyalgia rheumatica has been pointed out. Inflammation of the head arteries, such as the temporal artery and ophthalmic artery, is observed; however, approximately 10–20% of patients have aortic lesions. Histologically, it is often diagnosed by temporal artery biopsy. Infiltration of inflammatory cells, including giant cells, is observed mainly in the external elastic membrane of the media, and the lumen develops concentric stenosis with fibrous thickening of the intima/adventitia. Aortic lesions also show infiltration of inflammatory cells, including multinucleated giant cells, in the media, and they damage elastic fibers, causing fibrous thickening of the intima and adventitia. Its histological difference from Takayasu arteritis is that most patients with giant cell arteritis have multinucleated giant cells and that they have mild infiltration of inflammatory cells and fibrosis in the adventitia. However, it is difficult to distinguish giant cell arteritis from Takayasu arteritis by histological findings alone in some disease stages.

4.1.4 Isolated Aortitis

Isolated aortitis presents with vasculitis localized to the aorta and its branches, and it can be distinguished from Takayasu arteritis or temporal arteritis.[1714] It is classified as single-organ vasculitis in Chapel Hill Consensus Conference.[1710]

4.1.5 Vascular Behçet's Disease

Vascular Behçet's disease was first reported by the Turkish dermatologist Behçet, and it is said to be often seen in the Silk Road countries (**Figure 71**). In Japan, it is said to be often seen in Tohoku/Hokkaido. Although its well-known

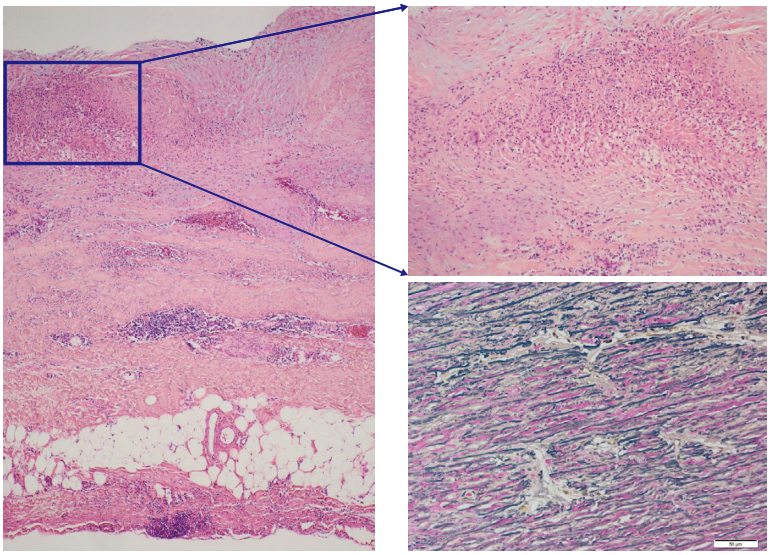


Figure 68. Takayasu arteritis (chronic active stage). Fibrous thickening of the adventitia is prominent, and severe inflammation of the media is also observed (**Left**: All layers. **Upper right**: Enlarged image of medial disruption site caused by inflammation, HE staining). Rupture of the medial elastic membrane is observed around the inflammation (**Lower right**, EVG staining).

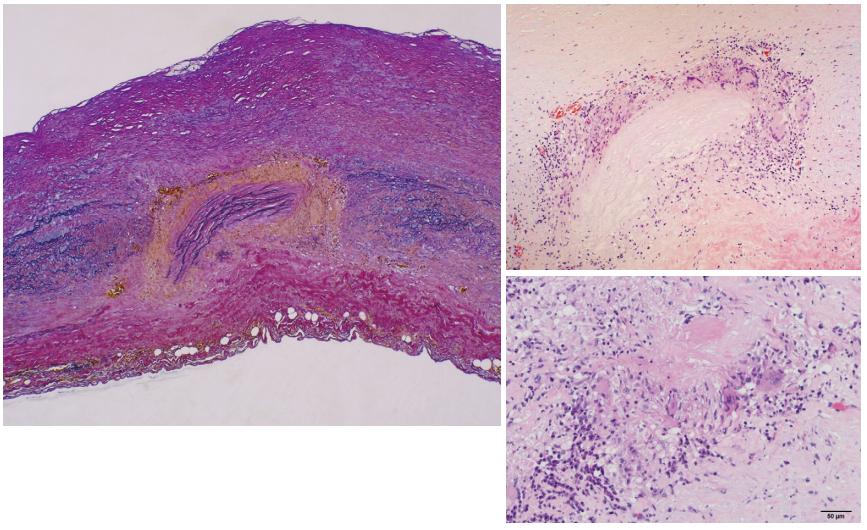


Figure 69. Takayasu arteritis (active stage). The elastic fibers are severely disrupted, and the central part exhibits necrosis (**Left**). The necrotic lesion is surrounded by multinucleated giant cells and lymphocytes (**Upper right**/**Lower right**).

symptoms include oral aphtha and genital ulcer, it is characterized by inflammation of various blood vessels, and its lesions range from occlusive phlebitis with venous thrombus to aortic aneurysm. Inflammation also occurs in the aorta, and severe infiltration of inflammatory cells with many neutrophils progresses disruptively in the media and adventitia. Granulomatous lesions, including multinucleated giant cells, are often found, and cannot be easily distinguished from Takayasu arteritis or giant cell arteritis by the histological image of the aorta alone.

4.1.6 Syphilitic Medialitis (Syphilis-Associated Aortitis)

Until the early 20th century, syphilis was an important cause of aortic aneurysm; however, it is extremely rare today. Its macroscopic characteristic is the crepe-like wrinkles of the intima derived from irregular contractions after inflammation of the media. Severe dilation occurs, often leading to ascending aortic aneurysm. Histologically, it is a granulomatous inflammatory lesion mainly composed of the media, and many plasma cells are found. It may contain multinucleated giant cells. It shows an image of

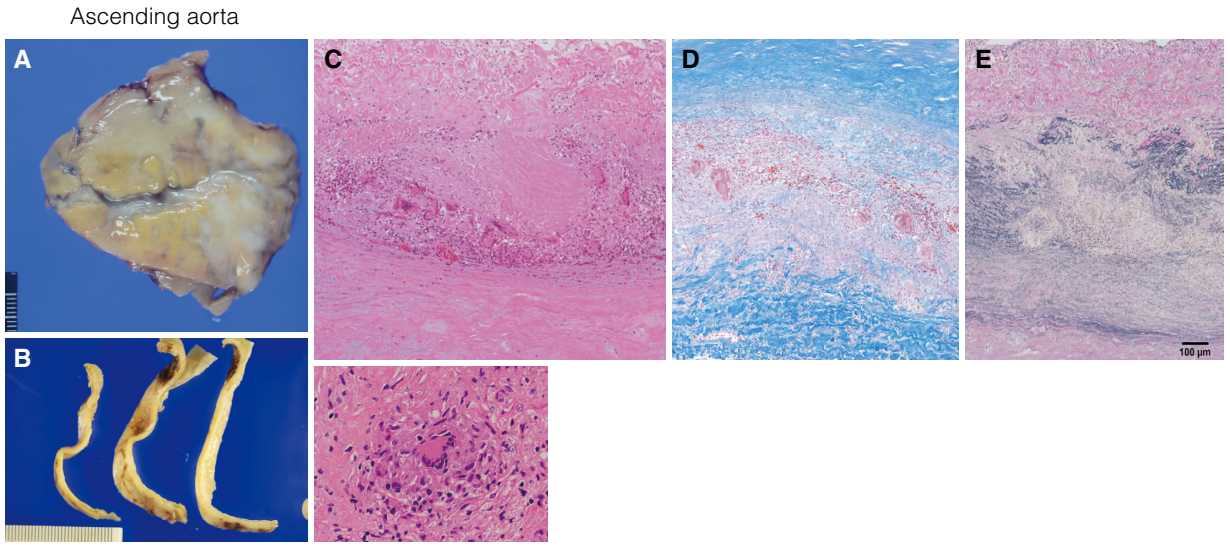


Figure 70. Giant cell arteritis. Macroscopically, atherosclerotic lesions are mainly observed (**A**). Thickening of the adventitia is mild (**B**). A large number of inflammatory cells and multinucleated giant cells are observed around the area of disrupted elastic fibers and coagulative necrosis (**C**–**E**). (**C**) HE staining (lower image shows the high-power field), (**D**) Masson's trichrome staining, (**E**) EVG staining.

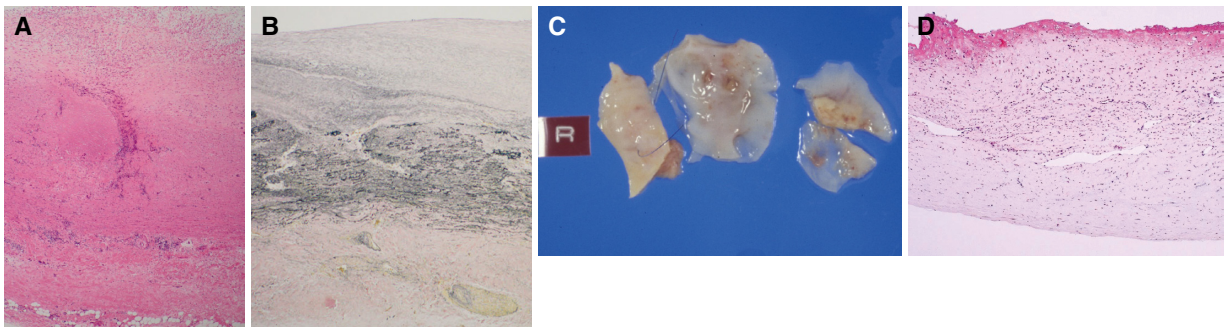


Figure 71. Vascular Behçet's disease. (**A**) Mesoarteritis with medial necrosis (HE staining). (**B**) Rupture of the medial elastic membrane of the aorta (EVG staining). (**C**) Right coronary cusp and its Valsalva sinus. (**D**) Disruption due to inflammation of the right coronary cusp.

rupture of medial elastic fibers exhibiting a moth-eaten appearance due to inflammation.

4.1.7 Inflammatory Abdominal Aortic Aneurysm and IgG4-Related Inflammatory Aortic Aneurysm

Inflammatory AAA was reported as uremia-causing AAA by James in 1935,[1715] and its disease concept was presented by Walker et al. in 1972.[977] In addition to the abdominal aortic aneurysm-like dilation, inflammatory AAA causes marked thickening of the wall and marked infiltration of inflammatory cells, mainly plasma cells, that often form lymphoid follicles in the adventitia, and this aortic aneurysm is characterized by fibrous thickening around the aortic aneurysm and fibrous adhesions to the surrounding tissues. Patients with inflammatory AAA are often complicated by atherosclerotic lesions, which may be a specialized cellular response to atheroma. Infiltration of inflammatory cells in the adventitia may form lymphoid follicles, mainly lymphocytes (**Figure 72**). Patients with inflammatory AAA show little formation of granuloma.

In the recent years, it has been found that infiltrating inflammatory cells contain a large number of IgG4-producing plasma cells in some cases. Similarly, an association with IgG4 has been demonstrated in other organs through autoimmune pancreatitis, atherosclerotic cholangitis, dacryoadenitis/sialadenitis, and thyroiditis, and inflammatory aortic aneurysm has also become recognized as one of the IgG4-related diseases. In a study by Kasashima et al., 13 (56.5%) of 23 patients with inflammatory AAA were diagnosed to be associated with IgG4.[87] Several patients with IgG4-related diseases have high blood IgG and IgG4 levels. Histologically, severe infiltration of

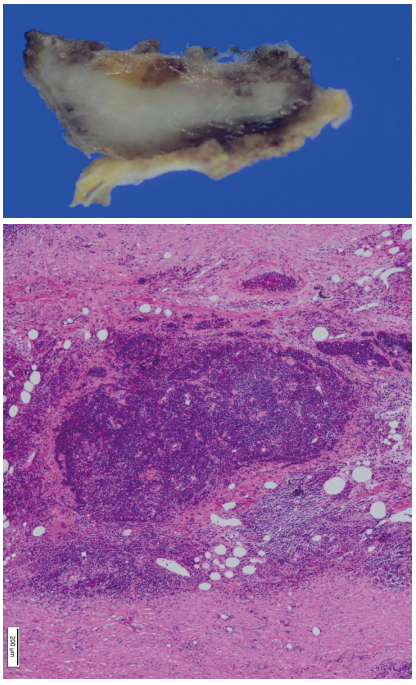


Figure 72. Inflammatory aortic aneurysm. Severe fibrous thickening of the adventitia (**Top**) and infiltration of inflammatory cells with lymphoid follicles mainly in the adventitia (**Bottom**) are observed.

chronic inflammatory cells, especially plasma cells, occurs mainly in the adventitia (**Figure 73**). Also, the formation of lymphoid follicles is observed. In recently published comprehensive diagnostic criteria of IgG4-related diseases, "the IgG4/IgG-positive plasma cells ratio of at least 40%" and "at least 10 IgG4-positive plasma cells in the high-power field" in histopathological specimens are defined as diagnostic criteria.[1716] Although there have been few reports of IgG4-related aortic aneurysm, it was reported to account for 5% of total-resection cases.

4.1.8 Infected Aortic Aneurysm

In 1885, Osler first reported bacterial arterial aneurysm as arterial aneurysm caused by bacterial embolism from infectious endocarditis. Specifically, bacterial arterial aneurysm refers to a fragile arterial aneurysm that forms due to inflammation caused by an infectious embolism attaching to the peripheral artery from an infection focus. However, its concept has now been broadened, and "infected aortic aneurysms" include infection of existing aortic aneurysm and surrounding infection, such as fistula formation, that spread to the aorta.

4.2 Diagnostic Imaging

The diagnosis of Takayasu arteritis needs to be made mainly by diagnostic imaging, and the presence of multiple or diffuse hypertrophic lesion, stenosing lesion (including occlusion), or dilatating lesion (including aneurysm), which are detected in the aorta and/or its primary branch as imaging findings, constitutes one of the diagnostic criteria.[1711] Therefore, the presence of imaging findings described above is essential for the definitive diagnosis of Takayasu arteritis. These evaluations are performed by chest radiography, CT/MRI examination, echography, angiography, or PET/CT examination. However, with the dissemination of CT/MRI examinations, invasive angiography is rarely used for its initial diagnosis. In addition, since April 2018, F-18 FDG PET performed at some PET facilities for patients with large vessel vasculitis has been covered by insurance if the localization or activity of their lesion cannot be determined by other examinations.

Hypertrophic lesions are visualized by echography (macaroni sign of the common carotid artery),[1717] contrast-enhanced CT, contrast-enhanced MRI (contrast imaging effect encircling the arterial wall),[1718] and PET/CT (FDG uptake encircling the arterial wall)[1719] (**Figure 74**). In particular, a double ring-like pattern of the aortic wall thickened in the early stage of Takayasu arteritis is observed in the delayed phase of contrast-enhanced CT (**Figure 75**), which is characteristic of this disease.[1720,1721] In addition, the degree of FDG accumulation also correlates with the clinical activity of Takayasu arteritis,[1719] and it is useful for determining the treatment effect.

Stenosing and dilatating lesions are visualized by chest radiography (wavelike margin of the descending aorta), CTA, MRA, cardiac echography (aortic valve insufficiency), and angiography. The ascending aorta often dilates, resulting in aortic valve insufficiency. In the chronic stage, chest

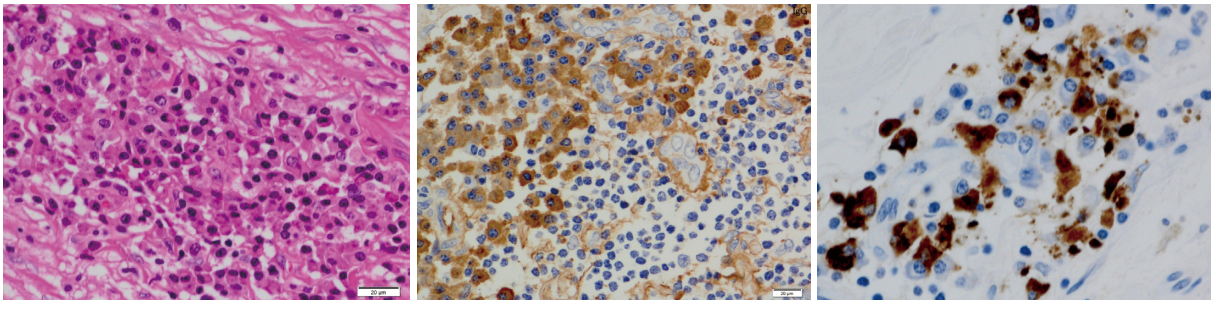


Figure 73. Inflammatory aortic aneurysm as an IgG4-related disease. HE staining of the aortic wall shows the infiltration of several plasma cells (**Left**). Most of them produce IgG (**Middle**), and IgG4 is dominant (40%) (**Right**).

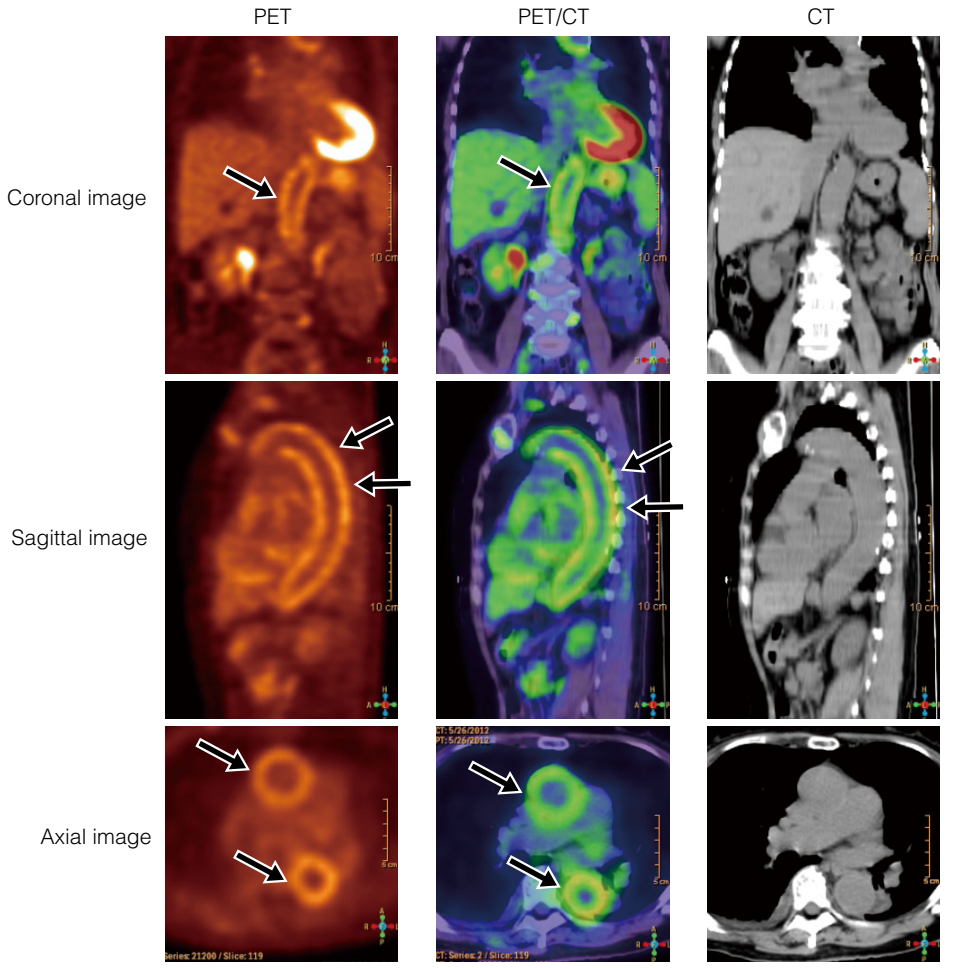
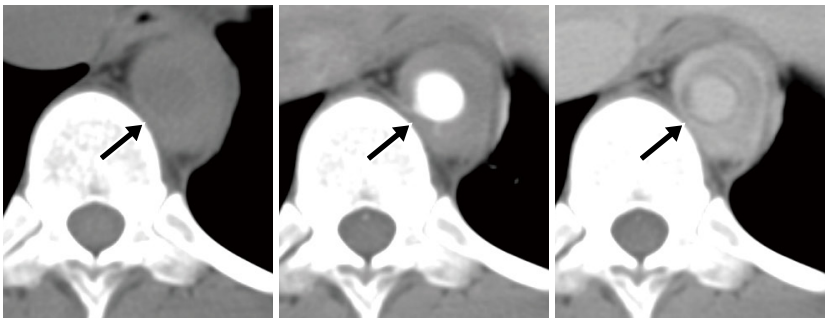


Figure 74. Evaluation of aortitis by PET/CT. Extensive encircling accumulation of FDG is observed on the aortic wall (↑).



A: Unenhanced CT **B:** Contrast-enhanced CT (early-phase) **C:** Contrast-enhanced CT (delayed-phase)

Figure 75. Double-ring like appearance found in the early stage of Takayasu arteritis. Encircling wall thickening is observed around the aorta. Contrast-enhanced CT shows a low-density area on the inside and a high-density area on the outside, showing a double ring-like appearance on the thickened wall (↑).

Table 55. COR and LOE for the Medical Treatment of Aortitis		
	COR	LOE
It is recommended to administer steroids for Takayasu arteritis[1726]	I	B
It is recommended to administer tocilizumab in addition to steroids for Takayasu arteritis[1727]	I	B
It is recommended to administer steroids for giant cell arteritis[1728]	I	B
It is recommended to administer tocilizumab in addition to steroids for giant cell arteritis[1729]	I	B
It is recommended to administer steroids for aortitis as an IgG4-related disease[1730]	I	C
The administration of steroids should be considered for an inflammatory aortic aneurysm whose maximum diameter is not indicated for surgery[1731]	IIa	C
The administration of antimicrobial drugs with sensitivity to infected aortic aneurysms should be considered	IIa	C
Steroid administration + immunosuppressive therapy should be considered for vascular (type) Behcet's disease[1732]	IIa	C

COR, class of recommendation; LOE, level of evidence.

radiography shows linear calcification of the aortic margin and cardiac enlargement due to aortic valve insufficiency, and patients with severe aortic stenosis show rib notching that reflects the development of collateral flow from the intercostal artery. In addition, CT shows encircling calcification of the arterial wall, and CT/MR angiography visualizes localized-diffuse stenosis/dilation of blood vessels and development of collateral flow.

4.3 Invasive Treatment

Indications of aortitis for invasive treatment are the same as those for non-inflammatory stenotic and aneurysmal lesions. However, persistent inflammation increases the risk of insufficient anastomosis with prosthetic graft. Therefore, it is desirable that inflammation is in remission before elective invasive treatment.

Most cases of aortitis in Japan are Takayasu arteritis. Also, the incidence of giant cell arteritis in Japan is considerably low, and evidence for its invasive treatment has been scarce. Thus, this section mainly describes an invasive treatment for Takayasu arteritis. This section focuses on the thoracoabdominal obstruction type and arterial aneurysm type in the classification of Ueno et al.[1722]

4.3.1 Surgical Revascularization

a. Thoracoabdominal Obstructive Type Lesions

Thoracoabdominal obstructive type lesions generally present with atypical coarctation of the aorta and often develops a stenosing lesion from the distal descending aorta to the abdominal aorta. Also, it presents with renovascular hypertension in addition to ischemic symptoms of the major abdominal branch. Aorta-aorta bypass surgery, axillary artery-femoral artery bypass surgery, and aortic replacement are performed in consideration of long-term results and invasiveness. Patients presenting with a lesion in the major intraperitoneal branch and ischemic symptoms of each organ require revascularization of the artery.

b. Aneurysmal Lesion

True aneurysm accounts for the majority of expanded lesions, and the incidence of dissecting aneurysm is low. Its surgical indications are based on those of normal TAA/TAAA, AAA, and peripheral arterial aneurysm, which are degenerative diseases. It often occurs with stenotic lesions described above, and such patients require comprehensive measures, including auxiliary means and surgical procedures.

4.3.2 Endovascular Treatment

Stent-graft deployment for stenotic lesions and arterial aneurysms has been attempted.[1723] However, it is not considered the first treatment choice for stenotic lesions since all layers of the arterial wall are accompanied by scar fibrosis and calcification.[1724] Its long-term results for arterial aneurysm are currently unknown.[1725]

4.4 Medical Treatment (Table 55)

Medical treatment of aortitis is performed with steroids that have an anti-inflammatory effect, immunosuppressants, and biochemical preparations. The medical treatments of Takayasu arteritis, giant cell arteritis, vascular Behçet's disease, inflammatory aortic aneurysm or inflammatory periaortitis, aortitis as one of the IgG4-related diseases, and infected aortic aneurysm are outlined below.

4.4.1 Takayasu Arteritis

a. Steroids

The administration of steroids is a basic treatment that has traditionally been used for aortitis, and it is important as an initial treatment. However, the efficacy rate of steroids alone is approximately 50%.[1726,1733]

i. Indications

Even if Takayasu arteritis is suspected from the clinical course, steroid therapy may not be indicated if the inflammation activity is low. If possible, F-18FDGPET or PET/CT examination is performed to objectively evaluate inflammation.[1719]

ii. Administration Methods

For Takayasu arteritis, "Prednisolone 0.5–1 mg/kg/day×2–4 weeks → Dose reduction of 5 mg per week (up to 30 mg/day) → Dose reduction of 2.5 mg per week (up to 20 mg/day) → Dose reduction that does not exceed 1.2 mg

per month → Maintenance dose: 5–10 mg/day" is recommended as a guide.[1711] For other diseases, there is no guide for the starting dose, and in several cases, the dose is determined based on that for Takayasu arteritis.

iii. Follow-up

Exacerbation is determined by the CRP level using blood collected at the time of follow-up at the outpatient department. Additionally, erythrocyte sedimentation rate, pentraxin 3 (PTX3), and other inflammatory markers have been investigated as indices for follow-up, although none is considered optimal. If a patient exhibits exacerbation of symptoms and imaging findings in addition to CRP levels, treatments, including immunosuppressants and biochemical preparations, as well as steroids, are reexamined at readmission.

iv. Concomitant Drugs

Attention must be paid to hyperglycemia, susceptibility to infection, gastric ulcer, and osteoporosis caused by the administration of steroids. Blood glucose levels need to be strictly managed at the start of steroid administration, and its treatment is performed if necessary. The susceptibility to infection is managed under hospitalization until the dose of steroids is reduced to some extent, and ST-mixed formulations are orally administered. Oral drugs are administered to prevent gastric ulcer and osteoporosis.

v. Patients Complicated by Aortic Aneurysm

It has been reported that 15% of patients with Takayasu arteritis are complicated by aortic aneurysm.[1734] The reoperation rate and the rate of lesions appearing at the surgical and other sites were reported to be significantly higher in patients undergoing surgery with inflammation than in those undergoing surgery after controlling inflammation.[1735] Also, surgery with inflammation leads to problems, such as postoperative pseudoaneurysm. Thus, surgery after controlling inflammation to the possible extent is recommended. On the other hand, it has been reported that the administration of steroids leads to a fragile aortic wall, increasing the risk of rupture.[1736–1738] Thus, the option of performing surgery without steroid therapy must be carefully considered for patients with a large aneurysm diameter.

b. Immunosuppressants and Biological Preparations

If recurrence occurs after steroid therapy, immunosuppressants or biological preparations are administered in combination with steroids, with the expectation of their synergistic effects with steroids or dose reduction effects of steroids. Immunosuppressants include methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, tacrolimus, and cyclosporine, while biological preparations include tocilizumab (anti-IL-6 receptor antibody) and TNF inhibitors. In particular, tocilizumab is expected to become a major therapeutic drug along with steroids in the future. However, it is currently positioned as a drug for recurrence cases after steroid therapy or a drug for recurrence prevention.[1726]

4.4.2 Giant Cell Arteritis

First, steroids are administered,[1728] and if recurrence occurs, a treatment similar to that for Takayasu arteritis, such as steroids + tocilizumab,[1729] is given.

4.4.3 Vascular (Type) Behçet's Disease

Vascular (type) Behçet's disease is a special type of Behçet's disease, and it refers to the one that meets the criteria of complete or incomplete type with pathological conditions, such as arterial aneurysm, arterial occlusion, deep vein thrombosis, and pulmonary embolism. A combination of steroids+immunosuppressants is used;[1732] however, there has been no solid evidence for the management of large artery lesions.

4.4.4 Inflammatory Aortic Aneurysm

Steroid therapy is often successful and is the first treatment choice.[1731] There is no established starting dose of steroids; however, it is often decided based on that for Takayasu arteritis. For aortitis, which is an IgG4-related disease, some have suggested the starting dose of 0.5–0.6 mg/kg/day.[1730] Immunosuppressants may be used for patients with recurrence; however, they are not considered as a sufficiently established treatment at present. If the diameter of inflammatory aortic aneurysm has exceeded the surgical indication, invasive treatment should also be considered regardless of the control of inflammation with steroids.

4.4.5 Infected Aortic Aneurysm

Since patients have a fragile aortic wall due to some infection, open surgery that can remove infected wound is performed as radical treatment, and it should be performed promptly without delay. For medical treatment, antimicrobial drugs are administered to control preoperative infection and prevent recurrence after surgery. However, caution is needed as one may miss the timing of surgery with an undue focus on the control of preoperative infection, which leads to rupture. Steroids are rather contraindicated.

5. Aortic Tumor

5.1 Pathology

Most common aortic tumors are intimal sarcoma that develops into the lumen, and primary tumors originating from the smooth muscle of the aortic wall are highly rare. Intimal sarcoma is a rare malignant soft tissue tumor that develops mainly in the intima of the great arteries, such as the aorta, pulmonary artery, and inferior vena cava, and grows in blood vessels. Approximately 100 cases have been reported to date.[1739] Its prognosis in the aorta is highly poor; however, its detection at early onset is difficult as it grows relatively slowly in the lumen. On the other hand, some patients with intimal sarcoma of the pulmonary artery were reported to have a relatively long prognosis. Intimal sarcoma and thrombus attached to the lumen side of the blood vessel of the tumor may occlude the lumen at the vascular bifurcation, which may be considered thromboembolism (**Figure 76**). Aortic intimal sarcoma causes multi-organ infarction, for which thrombectomy surgery using a catheter is performed, and its pathology may lead to the diagnosis of aortic intimal sarcoma. Intimal sarcoma that developed from the anastomotic site of prosthetic graft was also reported.[1740] Cases of aortic intimal sarcoma that developed as aortic valve stenosis have also been reported.[1741]

Histologically, aortic tumors are classified into "differentiated type (DIS)," which shows tissue differentiation into fibroblasts and myofibroblasts, and "undifferentiated type (UIS)," which shows no obvious tissue differentiation.[1742] The differentiated type is the most common, and there are said to be many cases of epithelioid angiosarcoma that are positive for both endothelial markers (CD31, CD34, and

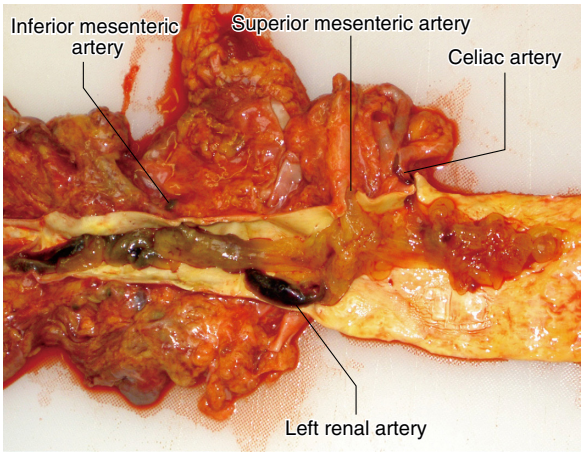


Figure 76. Aortic intimal sarcoma. Tumor invades each branch of the aorta.

factor XIII) and epithelial markers, such as cytokeratin[1743] (**Figure 77**). The undifferentiated type often shows mitosis and exhibits polymorphic nature. Immunohistochemically, the undifferentiated type is positive for vimentin and often positive for α-smooth muscle actin, while it is negative for CD31 and cytokeratin (**Figure 78**). It is also characterized by various histological findings, such as myxomatous, osseous metaplasia, and cartilage matrix. However, histological classification of aortic malignant tumors is difficult, and a definitive diagnosis is challenging because of preceding symptoms caused by the site of occurrence.

Their differential diseases include aortic aneurysm, endovascular thrombosis, thromboembolism, angiosarcoma derived from the vascular wall, and metastatic malignant tumor embolism.

5.2 Diagnostic Imaging

Contrast-enhanced CT examination (**Figure 79**) or contrast-enhanced MRI examination is often used for diagnostic

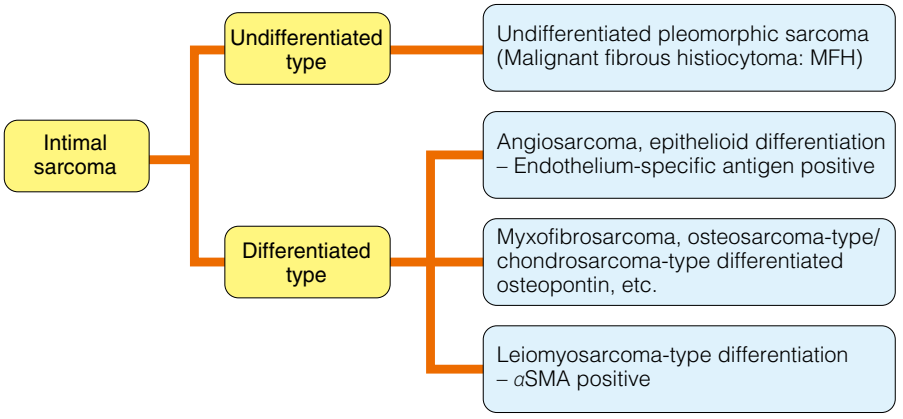


Figure 77. Classification of aortic intimal sarcoma.

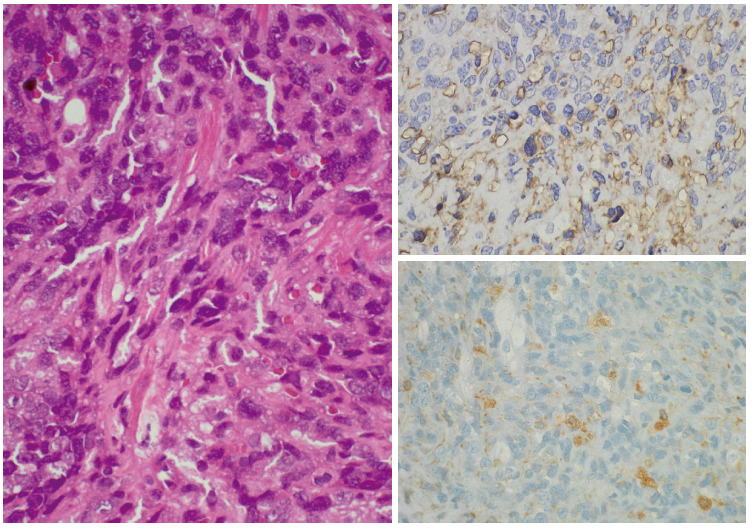


Figure 78. Aortic intimal sarcoma (angiosarcoma type).

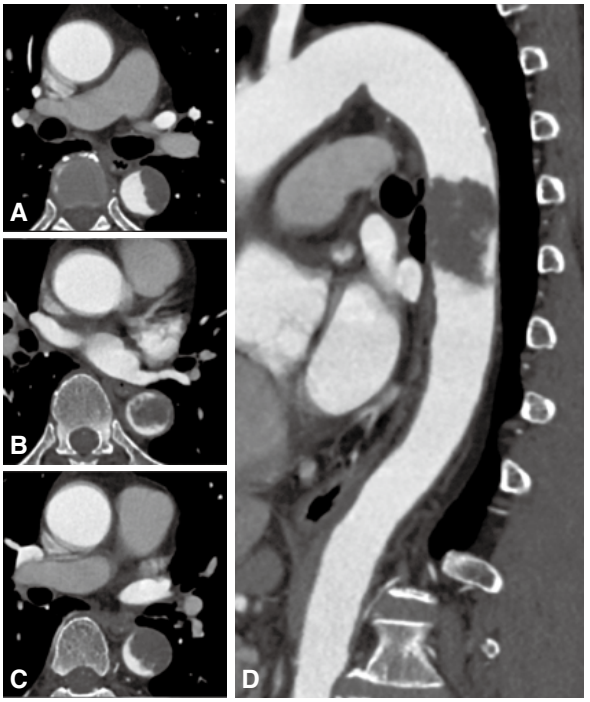


Figure 79. Aortic tumor (intimal sarcoma of the descending aorta). (**A**–**C**) Contrast-enhanced CT, axial images. (**D**) Contrast-enhanced CT, sagittal image.

imaging of primary aortic tumors. However, contrast-enhanced MRI examination, which is superior in evaluating tissue properties and discriminating from thrombi, is considered the gold standard.[1744] However, since some cases are often hypovascular tumors, it may be difficult to determine the contrast imaging effect of the tumor.[1745] In the intimal type, which is derived from the intima, grows protruding toward the aortic lumen, it must be distinguished from atherosclerotic atheroma and parietal thrombosis. On the other hand, in the mural type, which is derived from the media/adventitia, grows outward, it must be distinguished from aortic aneurysm and aortic dissection with thrombosed false lumen. The contrast imaging effect of the tumor becomes clearer as the size of tumor increases. In addition, the tumor exhibits high accumulation in FDG-PET examination, which is useful for discrimination.[1746] Due to the rate of prevalence of distant metastasis, including the bone, bone scintigraphy and PET/CT examination are recommended when it is suspected.[1744]

5.3 Invasive Treatment

Most of its previous reports are case reports of angiosarcoma. Thus, its cases are rare, and there have been no reports that could be evidence. In addition, the role of invasive treatment is not clear. In principle, it is considered desirable to resect the mass together with the aorta. However, it is often diagnosed after metastasis has progressed, and the resection itself is often difficult. Stenosis release by endarterectomy or stent-graft deployment may be useful for improving life prognosis.[1747]

Table 56. COR and LOE for Diagnosis and Treatment of Traumatic Aortic Injury

	COR	LOE
It is recommended to perform CT examination on patients suspected of having aortic injury[1038,1748]	I	C
It is recommended to perform TEVAR on patients with aortic injury[96,1749,1750] (See **Tables 9** and **33**)	I	C

COR, class of recommendation; CT, computed tomography; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

6. Traumatic Aortic Injury (Table 56)

Aortic injury due to blunt trauma is mainly caused by rapid deceleration (traffic accident or fall from a high place).[1751] It is said to occur more commonly at the site where the aorta is fixed, such as the aortic root, the vicinity of ligamentum arteriosum, and diaphragm; additionally, 90% of its cases occur in the aortic isthmus in the vicinity of the ligamentum arteriosum.[1038,1748]

6.1 Pathology

Injury due to traffic accidents is more likely to occur in the thoracic descending aorta, and in particular, many cases develop lateral rupture immediately after the bifurcation of the left subclavian artery. A large rupture results in massive hemorrhage, and it is fatal. However, if the injury is small, a hematoma may form under the adventitia, resulting in a pseudoaneurysm. It may take several months to a year to form an aneurysm after injury.

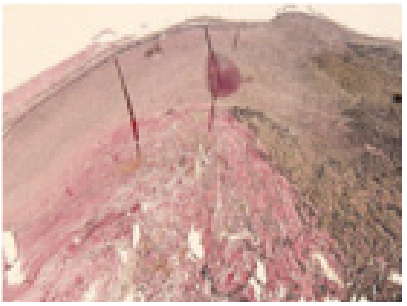
Aortic aneurysms in the chronic stage after an injury often exhibit the morphology of saccular aneurysms. Histopathologically, several cases exhibit a sudden disruption of the normal medial elastic membrane, resulting in a pseudoaneurysm (**Figure 80**). In patients with a pseudoaneurysm, it is important to understand their medical history of traumatic aortic injury. Although rare, the degeneration of the medial smooth muscle layer due to aging may cause dissection when inserting a blood supply tube during surgery.

Rabin et al. has classified these according to the degree of injury as follows:[1751] Grade 1: intimal failure or hematoma in the intima, Grade 2: localized pseudoaneurysm (less than 50% of the entire circumference), Grade 3: extensive pseudoaneurysm (50% or more of entire circumference), and Grade 4: rupture or tear of the blood vessel.

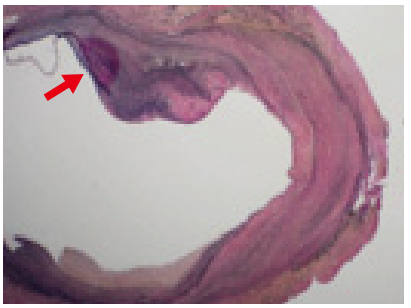
6.2 Diagnostic Imaging

The findings on chest radiography include upper mediastinal dilatation, disappearance of the aortic ridge, left hemothorax, apical cap, 1st/2nd rib fracture, right tracheal deviation, downward deviation of the left main bronchus, and right deviation of the gastric tube; however, there are also false-negative cases.[112]

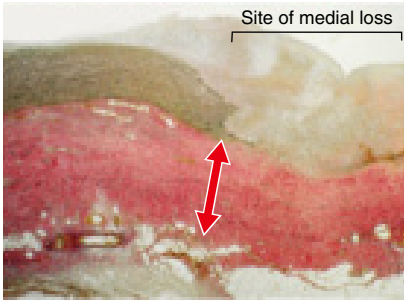
CT examination can be performed quickly with high reproducibility, and its sensitivity and specificity are both approximately 100%. Thus, it is an essential examination if this disease is suspected. CT findings of thoracic aortic injury show the formation of a thin-walled saccular aortic



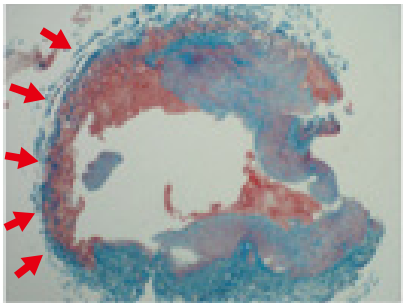
Aortic arch pseudoaneurysm



Pseudoaneurysm after trauma that occurred two years prior. Intimal hyperplasia developed at the site of medial loss (↑), resulting in a pseudoaneurysm

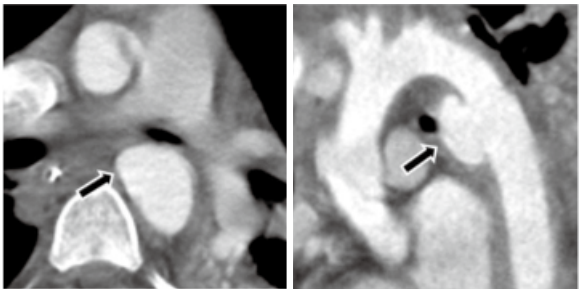


Aortic arch aneurysm has been recently pointed out, which was caused by a traffic accident that occurred 20 years prior. The right half of the medial elastic membrane layer has disappeared due to the trauma, resulting in fibrosis. The adventitia is severely fibrous and thickened (↔)



Iliac artery injury immediately after trauma. The media is completely interrupted, and a thrombus is attached

Figure 80. Traumatic aortic injury.



A: Contrast-enhanced CT **B:** Contrast-enhanced CT, MPR image

Figure 81. Traumatic aortic aneurysm. Both (**A**) and (**B**) show a saccular aneurysm in the thoracic descending aorta (↑), suggesting a traumatic aortic aneurysm.

aneurysm in the aortic isthmus, which is often accompanied by a surrounding hematoma (**Figure 81**). If it is accompanied by aortic dissection or intramural hematoma, it exhibits findings similar to those of acute aortic dissection; however, their range is often localized. In addition, mediastinal hematoma and hemothorax may be observed. 3D CT imaging, such as multi-planar reconstruction (MPR), is useful for preoperative evaluation when performing a treatment with stent graft (SG).

On the other hand, bedside transesophageal echography is useful if CT examination is difficult due to unstable hemodynamics. Also, it is advantageous that it can concurrently evaluate not only aortic injury, but also associated pathological conditions, such as injury to the right ventricle, right atrium, and tricuspid valve, as well as thrombus in the inferior vena cava. However, esophageal injury has been caused by transesophageal echography in some cases, and it is a serious complication to be noted.

6.3 Invasive Treatment

With respect to traffic accident- or falling-related aortic injury, the mortality rate in the scene of an accident is reportedly ≥80%, and multiple trauma is observed in many cases. However, the probability of life-saving in surviving patients transported to a hospital has increased. Such aortic injury is classified into four types: type I (intimal injury), type II (intramural hematoma), type III (pseudoaneurysm), and type IV (rupture).[1749] The most frequent site is the aortic isthmus. To treat traumatic aortic injury of the aortic isthmus or descending aorta, SG treatment should be considered.[96,1750] Aortic injury is a part of multiple trauma

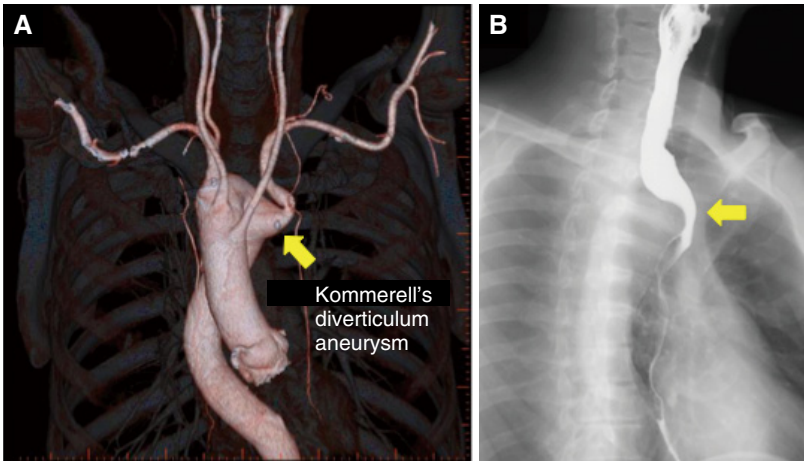


Figure 82. Kommerell's diverticulum aneurysm (**A**) and esophageal stenosis in a patient with dysphagia (**B**).

in many cases, and open surgery using cardiopulmonary bypass is highly risky.[1752–1754] On the other hand, SG treatment does not require cardiopulmonary bypass, facilitating the subsequent, prompt treatment of other concomitant trauma; therefore, this procedure has markedly improved the results of treatment.[1755–1758]

As fatal rupture occurs in the early phase (within 24 h), it has been indicated that the condition should be promptly treated, but a study suggested that treatment should be performed after the general condition becomes stable in type-I patients. The risk should be evaluated based on the degree of rupture or intimal injury, and it is also useful to delay the timing of SG deployment or select noninvasive treatment.[1751,1759–1763]

As the incidence of SG-associated complications is high, SGs have been improved.[1750,1754] In Japan, one device for traumatic aortic injury is approved.

7. Congenital Aortic Diseases

7.1 Kommerell's Diverticulum

7.1.1 Concept and Pathogenesis

In 1936, Kommerell reported a patient in whom the esophagus was compressed by a diverticulum located between the left aortic arch and descending aorta in the presence of aberrant right subclavian artery, leading to dysphagia.[1764] Currently, Kommerell's diverticulum is defined as a "diverticulum at the proximal descending aorta with aberrant subclavian artery". In the embryonic phase, the left aortic arch, right aortic arch, aberrant subclavian artery, and Kommerell's diverticulum related to developmental anomalies of aortic arch branches are formed.[500] Of all births, the left aortic arch with aberrant right subclavian artery accounts for 0.7 to 2.0%, and the right aortic arch with aberrant left subclavian artery accounts for 0.04 to 0.4%.[1765] Of these, Kommerell's diverticulum aneurysm formation is observed in 20 to 60% (**Figure 82A**).

7.1.2 Symptoms

In children, diverticulum aneurysm-related direct compression or vascular rings formed by diverticulum aneurysms induce symptoms. A primary symptom is respiratory disorder related to stenosis of the airway. In most adult patients, this disease is asymptomatic, but dysphagia, thoracic pain, and laterality of the upper limb blood pressure are sometimes observed. With recent advances in imaging procedures, symptom-free patients have been incidentally detected. In adulthood, aneurysmal rupture or aortic dissection occurs in some cases, but no study has reported on the natural history.

7.1.3 Diagnosis

CT/MRI are useful, and the relationship with adjacent organs or presence of a vascular ring can be evaluated. No definite method to measure the diverticulum aneurysm diameter has been established, and no aneurysm-diameter-based criteria for the risk of rupture or dissection have been unified. Furthermore, it is necessary to evaluate the relationship with adjacent organs and presence or absence of compression using imaging procedures. On chest X-ray, a shadow of the deviated aorta is sometimes observed, and barium esophagography reveals its stenosis in some patients with dysphagia (**Figure 82B**).

7.1.4 Surgical Indications

When respiratory disorder related to dysphagia or stenosis of the airway associated with compression by Kommerell's diverticulum aneurysms is present, surgery is indicated. However, the condition is asymptomatic in many patients. Whether or not surgery should be indicated is examined based on the diverticulum aneurysm diameter/morphology. When the aneurysmal diameter exceeds 50 mm, or when the orifice of the subclavian artery with an anomalous origin measures >30 mm in diameter, the indication of surgery may be appropriate.[1766]

7.1.5 Treatment Methods

a. Thoracotomy

The purpose of thoracotomy in childhood and adulthood is to resect Kommerell's diverticulum aneurysms and reconstruct aberrant subclavian artery. In childhood, resection of Kommerell's diverticulum aneurysms, dissection of the arterial ligament, and reconstruction for aberrant subclavian artery are performed.[1767] In adulthood, prosthetic graft replacement is selected rather than closure of diverticulum aneurysms and patch plasty.

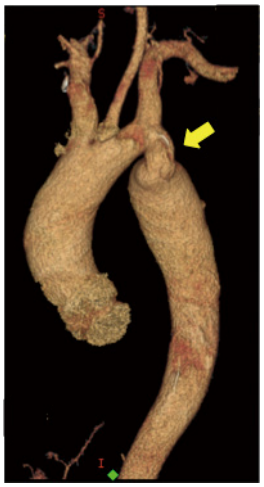


Figure 83. Coarctation of the aorta.

Based on the position of diverticulum aneurysms, descending aortic replacement by right or left lateral thoracotomy is performed. When aberrant subclavian artery is present, reconstruction is conducted. In this case, surgery is possible under partial cardiopulmonary bypass. Furthermore, total arch replacement by median sternotomy is selected in accordance with the type of concomitant diseases. Concerning reconstruction for aberrant subclavian artery, there are two methods: in situ reconstruction and extra-anatomical bypass. However, when selecting extra-anatomical bypass for reconstruction, compression of adjacent organs may persist. The favorable results of approach and treatment methods for diverticulum aneurysms have been reported in both reconstructed ways.[500,1768]

b. Endovascular Treatment

Hybrid TEVAR is selected in some cases, but the number of such sessions is small, and its remote-phase results remain to be clarified. Complications, such as endoleak, AEF, and ischemia of the upper limbs, have been reported, and the indication must be carefully determined.

7.2 Coarctation of the Aorta

This is the most frequent congenital aortic disease that induces stenosis at the distal aortic arch, accounting for 0.5% of all births (**Figure 83**). Based on the positional relationship between the site of stenosis and arterial duct (ligament), this disease is classified into pre-duct (infant type) and post-duct (adult type) types. It is often complicated by patent ductus arteriosus, ventricular septal defect, or other congenital heart diseases. In most cases, coarctation of the aorta is treated prior to adulthood.

Physical findings include an increase in the upper limb blood pressure, a reduction in lower limb pulsation palpability, left scapular murmurs, and thrill palpability. Developmental disorder of the lower limbs, intermittent claudication of the lower limbs, left ventricular hypertrophy, heart failure, nasal bleeding, and rib notching on chest X-ray are sometimes observed. According to a report on the natural history of this disease in ≥1-year-old patients published by Campbell et al., the average life expectancy is 34 years, and the causes of death include heart failure (25%), aortic rupture (21%), infectious endocarditis (18%), intracranial hemorrhage (12%), and others (24%).[1769] Enlargement of an advanced collateral pathway, Abbott's artery, induces spinal cord compression-related SCI or rupture in some cases. Therefore, early invasive treatment is necessary, and in-situ/extra-anatomical bypass is indicated.[1770] Recently, the efficacy and safety of stent graft treatment were reported.[1771]

Pseudocoarctation of the aorta was first reported as a subclinical form of coarctation by Souders et al.[1772] It is sometimes termed "kinking or buckling of the aortic arch" due to its morphological characteristics. This is a congenital anomaly that develops in the initial embryonic phase. The diagnostic criteria prepared by Gay et al. include an abnormal shadow of the left superior mediastinum, a pressure difference of <25 mmHg in the upper and lower limbs, the absence of a collateral pathway, and prolongation of the aortic arch to descending aorta origin.[1773] Furthermore, the position of the aortic arch is high, and the aorta sometimes

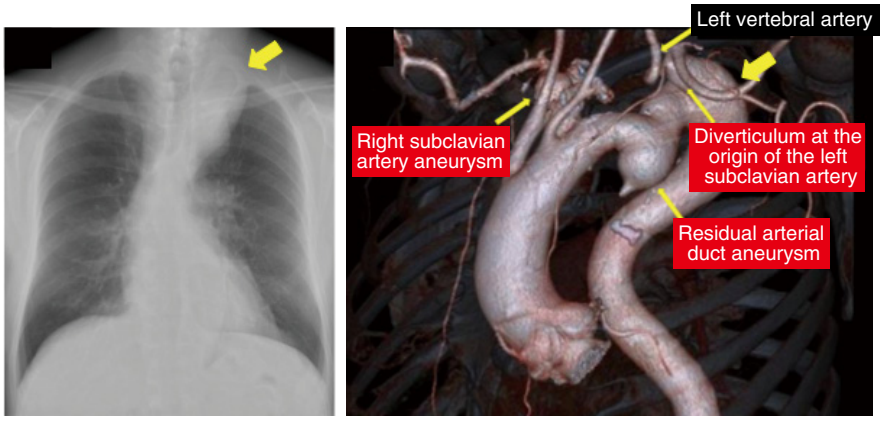


Figure 84. Cervical aortic arch.

kinks at the aortic isthmus. When aneurysm formation is observed, treatment is performed.

Stenosis related to aortitis syndrome (Takayasu arteritis/pulseless disease) is termed "atypical coarctation of the aorta", differing from congenital coarctation of the aorta.

7.3 Cervical Aortic Arch

This is a rare congenital aortic disease. It refers to a developmental anomaly on aortic-arch formation from the fourth branchial arch in the embryonic phase, which is associated with a remaining higher branchial arch. Mullins et al.[1774] defined this disease as a condition in which the vertex of the aortic arch is present in the cervix, with an anomalous origin of an aortic arch branch and abnormality in the descending aorta configulation. However, other investigators defined it as a condition in which the vertex of the aortic arch reaches an area cephalic to the clavicle (**Figure 84**). In some cases, this disease is palpable as a pulsatile cervical mass, or compressive symptoms of the airway or esophagus are observed. Haughton[1775] classified this disease into 5 types (A to E) based on the shape of the aortic arch and arrangement of arch branches. Several studies reported surgery for type D (left cervical aortic arch with a normal cervical branch, with a surplus aortic arch and hypoplastic left descending aorta in some cases).[1776,1777]

8. Aortic Esophageal/Bronchial Fistula (Table 57)

8.1 Aorto-Esophageal Fistula

8.1.1 Concept

Aorto-esophageal fistula (AEF) is a relatively rare disease; however, its prognosis is highly poor. With the increase in endovascular treatment, such as SG deployment, secondary AEF has been increasing in the recent years.[967,1778]

AEF was first reported by Dubrueil in 1818.[1784] In 1914, Chiari reported three clinical signs of AEF, which are (1) pain in the mid-thoracic region, (2) a small amount of bright red hematemesis in the early stage, and (3) subsequent massive hematemesis,[1785] calling it "aortic esophageal syndrome." AEF due to foreign body aspiration, such as fish bone, is most consistent with these clinical findings, and symptoms vary depending on the cause. In 1980, Ctercteko and Mok reported the first successful surgical case of AEF caused by foreign body aspiration.[1786] The first successful case of AEF caused by TAA is said to be the one reported by Snyder and Crawford in 1983.[1787] However, its treatment results are poor even today, and there have been few studies with a large number of cases.

The occurrence mechanism of AEF remains unknown; however, it has been hypothesized that occlusion of the esophageal artery, inflammation of the mediastinum due to a hematoma, and mechanical compression by aneurysm or SG may lead to impaired blood flow in the esophageal wall, causing AEF.[967,1778] On the other hand, some have suggested that infection of SG and prosthetic graft should be considered as the first factor of fistula formation.[1788] Compression necrosis of the esophagus, ischemic necrosis due to occlusion of esophageal feeding blood vessels by SG, collapsed esophageal lumen due to oversizing of SG and repeated TEVAR, confinement of bacteria in the infected aneurysm, and endoleak have been considered as the occurrence mechanism of secondary AEF.[1778,1780,1789]

8.1.2 Epidemiology

The factors of AEF are diverse, as shown in **Table 58**. However, the most common cause of primary AEF is TAA, and its incidence is said to be 0.16%.[1780] The incidence of secondary AEF and aorto-bronchial fistula (ABF) after open surgery for TAA is 1.7%,[641] which is comparable to that after TEVAR of 1.7%.[967] However, TEVAR has a shorter time to AEF onset.[1790]

The most common site is the posterior to left wall of the esophagus (upper/middle) 20–30 cm from the incisors, and its location can be confirmed by esophageal endoscopy. However, there have been few reports accurately describing its location on the aortic side. Based on the studies describing its locations,[126–129] it was found in the arch in 16%, the descending region in 78%, thoracoabdominal region in 6%, indicating that most are in the descending aorta.

Staphylococcus aureus is the most common primary causative organism, followed by hemolytic streptococcus. Others include *Escherichia coli*, *Pseudomonas aeruginosa*, fungus, *Enterococcus*, and *Streptococcus pneumoniae*.[1790] In addition, patients having MRSA as the primary causative organism have a poor prognosis, and their 30-day mortality rate exceeds 70%.[1790]

With regard to its symptoms, the above three signs described by Chiari have long been known; however, the incidences of precursor hematemesis and chest pain are not

Table 57. COR and LOE for the Treatment of Aorto-Esophageal Fistula and Aorto-Bronchial Fistula

	COR	LOE
It is recommended to perform TEVAR as a life-saving measure for aortic rupture associated with aortic infiltration of esophageal or lung cancer[1778]	I	C
When massive hemorrhage occurs due to aorto-esophageal or aorto-bronchial fistula or when there is a concern about massive hemorrhage, performing TEVAR to the earliest extent possible should be considered to prevent massive hemorrhage[1779]	IIa	C
The removal of infected tissue, including artifacts, should be considered[126,127,1778,1780–1783]	IIa	C
Esophagectomy should be considered for aorto-esophageal fistula[126,127,1778,1781,1782]	IIa	C
When the rupture of aorto-esophageal or aorto-bronchial fistula associated with cancer radiation therapy or chemotherapy is concerned, treatment should be considered after preventing the failure with TEVAR in line with the primary aortic esophageal/bronchial fistula or cancer infiltration site[1778]	IIa	C

COR, class of recommendation; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

Table 58. Causes of Aorto-Esophageal Fistula	
After TEVAR	Secondary
After thoracic aorta prosthetic graft replacement	
Thoracic aortic aneurysm	
Foreign body aspiration	
Esophageal cancer	
Esophageal ulcer and regurgitation	
Tuberculosis	
Traumatic pseudo aortic aneurysm	
Accidental ingestion of alkaline solution	
Tracheoesophageal aortic fistula	
Atherosclerotic aortic ulcer	
Congenital aortic arch abnormality	

TEVAR, thoracic endovascular aortic repair. (Source: Prepared based on Hollander JE, et al. 1991.[1780])

considerably high at 65% and 59%, respectively.[1780] Also, Czerny et al. reported that unidentified fever, hematemesis, and shock were found in 81%, 53%, and 22% of AEF patients after TEVAR, respectively,[1778] while Chiesa et al. reported that hematemesis, unidentified fever, shock, and chest pain were found in 68%, 58%, 26%, and 5% of patients, respectively.[967] In a comparative study of open surgery and TEVAR, pain (73% vs. 35%) and fever with the chills (84% vs. 61%) were more common in open surgery, while hematemesis (12% vs. 42%) was more common in TEVAR.[1790]

The view that long-term survival cannot be achieved by conservative therapy alone, such as the administration of antimicrobial drugs, remains unchanged today. Czerny et al. reported that no patients survived for one year without esophagectomy,[1778] and Akashi et al. stated that esophagectomy, prosthetic graft replacement (including homograft), and omentum wrapping are necessary for lifesaving and that the treatment should not be limited to TEVAR.[126] The results of radical surgeries, such as esophagectomy and prosthetic graft replacement, showed favorable in-hospital mortality rates of 14.3%,[1781] 22.2%,[127] and 25%,[1782] while a poor rate of 64% was also reported.[967] However, all patients had poor long-term results, and even a report by Yamazato et al., which showed favorable surgical results, had a 5-year survival rate of 42.4%.[127]

8.1.3 Diagnosis

It often takes time from the stage of initial symptoms, such as unidentified fever, chest pain, and early small hematemesis, to diagnosis. The marked inflammatory findings on blood tests may trigger its detection. CT examination is useful for diagnostic imaging. Fluid accumulation with gas patterns around the aorta and esophagus indicates edema or abscess formation due to inflammation, and it is a finding for strongly suspecting infection. In addition, using esophageal endoscopy, the diagnosis of AEF can be nearly confirmed by a small ulcer image on the esophageal wall or protrusion of a foreign body;[1791] however, it is not always necessary depending on the condition of the patient. Other diagnostic methods include aortography and esophageal barium contrast examination; however, they are not commonly used. In addition, when deciding on the treatment policy, PET/CT examination may be useful in determining the range of infection or inflammation.

8.1.4 Treatment

The patients cannot be saved by conservative therapy with antimicrobial drugs alone, and invasive treatment is required.[1778,1780] Although some reports demonstrated that the patients were saved by TEVAR alone, SG deployment in infected parts poses a major problem in the long-term prognosis. Kan et al. reported that the 1-year survival rate of patients who had undergone TEVAR or EVAR for infected aortic aneurysm was inferior in the persistent-infection group compared with the infection-cured group.[1783] In general, the prognosis of patients undergoing TEVAR alone or esophageal stent alone is poor,[126,127,1778] and esophagectomy, cleaning and sufficient lavage of infected tissue, removal of infected aorta and reconstruction of the aorta, and omentum wrapping of the reconstruction site are all required for long-term survival.[126,127] These treatments may be given in one stage[127] or in stages in consideration of the condition of the patient and the degree of invasiveness.[128,129] Once the postoperative infection is controlled, esophageal reconstruction is finally performed.

a. Antimicrobial Therapy

The administration of intensive antimicrobial drugs is started according to the result of the culture test. If multiple or no bacteria are identified, widely effective antimicrobial drugs are administered as the initial response. However, since an infection focus is present in the mediastinum, its goal is only to control infection until surgery.

b. TEVAR for the Control of Massive Hemorrhage

If there is a massive hemorrhage from AEF or concern about massive hemorrhage, it is essential to first prevent massive hemorrhage with urgent TEVAR (bridging TEVAR).[1779] If the patient is in a state of shock due to massive hemorrhage, the use of SB (Sengstaken-Blakenmore) tubes is useful for hemorrhagic control until TEVAR.[1792]

c. Esophagectomy

If esophagectomy and aortic reconstruction are performed concurrently, the esophagus can be removed after resection of the aorta with the left thoracotomy approach. If a staged approach is selected, the esophagus is resected with right thoracotomy or right thoracic endoscopy for sufficient dissection and lavage of infection focus. In any case, esophageal fistula is created in the cervical region, and gastric fistula is created in the upper abdominal region.

d. Aortic Reconstruction

In principle, a total resection of the prosthetic graft and SG is performed in secondary AEF. It is performed with a left thoracotomy; however, its approach differs depending on the site. If it extends to the aortic arch, a method of expanding the field of view with a trans-sternal incision from anterior lateral thoracotomy or posterior lateral thoracotomy is used. If it extends to the lower descending aorta, a Stoney incision or anterior-lateral linear incision based on thoracoabdominal aortic surgery is used. In any case, the femoral arteries and veins are exposed, and surgery is performed under extracorporeal circulation. If it extends to the aortic arch, the aorta is reconstructed using hypothermia (25–28°C) and anterograde selective cerebral perfusion in combination. If clamping of the aorta beyond distal aortic arch can be performed, the aorta is

reconstructed with the upper body under autologous beating-heart and the lower body under partial extracorporeal circulation. The infected aorta and tissue are removed first. If esophagectomy is performed concurrently, the esophagus is removed after the removal of the aorta, and both stumps are temporarily closed. Subsequently, sufficient lavage is performed.

Previously, revascularization of the lower body was performed by the closure of the aortic stump and ascending aorta-abdominal aorta bypass (extra-anatomical bypass) to avoid transplanting prosthetic graft in the infection focus. However, in-situ prosthetic graft replacement has recently been used as the first choice in several cases. Considering the complications of pseudoaneurysm and hemorrhage of the aortic stump and bypass occlusion that may occur in the late stage of extra-anatomical bypass,[1793] in-situ prosthetic graft replacement is expected to become the standard procedure.

e. Selection of Graft

Vogt et al. reported that homograft (cryopreserved allogeneic graft) was highly effective for infection control in infected aortic aneurysms.[1794] However, homografts cannot be easily obtained in Japan due to the small number of homografts stored in tissue banks, and the diameter of homografts is often small. Lesèche et al. reported that occlusion and aneurysm formation were observed in 17% of patients in an average of 3 years of follow-up after homograft transplantation,[1008] and it still has a problem in its long-term results.[128,1795] Therefore, in Japan, prosthetic graft is commonly used, and several studies have reported cases of using rifampicin-immersed graft prepared intraoperatively.[1796,1797] In addition, there are ePTFE (expanded polytetrafluoroethylene) prosthetic graft, prosthetic graft made from bovine pericardium,[503] and silver-coated prosthetic graft;[1798] however, their effectiveness is unknown.

f. Omentum Wrapping

Omentum, which is a tissue rich in blood flow and lymph, is thought to be effective for infection control, and it is often used for the treatment of mediastinitis after open heart surgery.[1012] In AEF surgery, the area around the prosthetic graft transplanted in situ is covered with omentum to prevent the spread of infection. Pedunculated omentum having either the right or left gastroepiploic artery as vascular pedicle can be used for a wide range of aorta from the arch to the descending region.[911,1013] Akashi et al. reported the usefulness of pedunculated omentum for improving the prognosis of AEF.[126]

g. Postoperative Antimicrobial Drug

Postoperative intensive antimicrobial therapy is essential. Antimicrobial drugs suitable for the primary causative organism are administered intravenously for 4–8 weeks, aiming to achieve a negative inflammatory response. Some have reported that the administration of antimicrobial drugs can subsequently be discontinued without any issues,[1001] whereas others have reported that oral antimicrobial drugs should be administered for a lifetime.[998,1006]

h. Esophageal Reconstruction

Esophageal reconstruction is often performed several weeks to months after aortic revascularization to wait for the complete control of infection and improvement of systemic nutritional status. Gastric tube preparation and colon conduit are used as alternatives to the esophagus. Due to the concerns about suture failure and stenosis of the suture site, it is often prepared in the route before or after the sternum.

AEF has a high mortality rate; however, a prompt preoperative diagnosis and early invasive treatment are thought to lead to an improved lifesaving rate.

8.2 Aorto-Bronchial Fistula

8.2.1 Concept

ABF was first reported by Girardet in 1914.[1799] Although several case reports have been published since then, ABF is reported more often with AEF than by itself, and their complication is relatively common clinically. It is often divided into primary and secondary ABF depending on the cause of occurrence;[1781] additionally, fistulas may be divided into central and peripheral types depending on their location in the airway.[1778]

8.2.2 Epidemiology

The incidence of ABF varies in the range of 0.3–5%; additionally, it is not considerably different from that of AEF. von Segesser et al. reported that ABF occurred in 8 (5.6%) of 145 patients who had undergone surgery for a thoracic descending aortic/thoracoabdominal aortic aneurysm.[1800] The occurrence of ABF is also increasing in parallel with the dissemination of TEVAR. Luehr,[1782] Chiesa,[967] and Czerny[1778] reported that the incidence of ABF after TEVAR was 0.5%, 0.4%, and 0.6%, respectively. The occurrence mechanism of ABF is different from that of AEF; additionally, it is caused by perforation due to the compression of SG and aneurysm rupture in several cases.

8.2.3 Diagnosis

Common initial symptoms of ABF are fever and hemoptysis or hematemesis of swallowed hemoptysis, and CT examination often shows pulmonary infiltrative shadow. It is easily diagnosed if a large hematoma is present in the lungs, however, its differentiation of airway hemorrhage from atelectasis due to compression of an aneurysm is often difficult with diagnostic imaging. In such cases, bronchoscopy is recommended; however, its invasiveness is not low. In addition, its definitive diagnosis can be made if a fistula can be observed directly. However, because the diagnosis of the peripheral type is difficult, endoscopic examination of ABF is not as useful as that of AEF. If there is an airway hemorrhage that deteriorates respiratory condition, aneurysm resection and bronchial fistula closure should be performed at an early stage, rather than spending time on a definitive diagnosis.

8.2.4 Treatment

As with AEF, the results of conservative treatment for ABF are poor, and aortic aneurysm resection, SG removal, bronchial fistula closure, and pulmonary resection are the standard treatments. The treatment results of ABF are more favorable than those of AEF. It is because the airway has less resident flora than the inside of the esophagus; additionally, the airway does not require reconstruction like the esophagus. In addition, some cases can be treated with TEVAR alone. Canaud conducted a meta-analysis of 134 patients treated with TEVAR and showed a 30-day mortality rate of 5.9%, an aorta-related mortality rate after 18 months of 14.3%, and an ABF recurrence rate of

11.1%, reporting favorable results.[1781] Czerny examined 26 cases of ABF after TEVAR in the European Registry of Endovascular Aortic Repair Complications (EuREC), which showed 5 cases undergoing follow-up, 2 cases undergoing pulmonary bronchial surgery alone, 9 cases undergoing TEVAR alone, and 8 cases undergoing SG removal, pulmonary bronchial surgery, and in-situ aortic reconstruction.[1778] The survival rate after 2 years was reported to be 63% in the active treatment group, which was more favorable than in those undergoing palliative surgery at 21%. As described above, early radical surgery is, in principle, performed for ABF, as with AEF; however, TEVAR is also an option in some cases.

8.3 Aortic Fistula Associated With Aortic Infiltration of Esophageal/Lung Cancer

Primary aortic esophageal/bronchial fistula associated with aortic infiltration of esophageal or lung cancer is outside the indication for TEVAR, although TEVAR as a life-support (lifesaving) measure through the prevention of rupture has been attracting attention as a new approach.[1801] If the rupture of aortic esophageal/bronchial fistula associated with radiation therapy or chemotherapy is concerned, patients may be treated with radiation therapy or chemotherapy after undergoing TEVAR as a preventive measure for fistula rupture in accordance with the primary aortic esophageal/bronchial fistula or the infiltration site of cancer. However, such treatment, including the use of TEVAR outside the indication, is given at the discretion of each facility. Thus, its treatment results are unclear due to the limited number of cases and the lack of research at the national level.

PQ 12.
Is TEVAR Effective for Aortic Infiltration of Esophageal Cancer?

Recommendation
Emergency TEVAR should be performed to treat symptomatic AEF with hemorrhage. Furthermore, preventive TEVAR for avoiding hemorrhage or aortic rupture before esophagectomy or radio-/chemotherapy is effective.

Anatomically, the esophagus is adjacent to the thoracic descending aorta. In approximately 17% of patients with advanced esophageal cancer, aortic infiltration is observed.[1780] Advanced esophageal cancer with aortic infiltration may progress to an AEF, causing serious hemorrhage.[1779,1802] TEVAR for AEF was first reported in 1994.[1803] Subsequently, many studies reported that TEVAR prevented serious hemorrhage in advanced esophageal cancer patients with aortic infiltration, suggesting the usefulness of TEVAR for the treatment of advanced esophageal cancer with the risk of hemorrhage.[732,1801,1804,1805]

The timing of TEVAR for advanced esophageal cancer with aortic infiltration is classified into two based on its purpose. One is emergency TEVAR for achieving hemostasis for symptomatic conditions. In symptomatic advanced esophageal cancer patients with hematemesis, aortic replacement and esophagectomy are necessary. When such esophageal cancer progresses to AEF, a series of open surgery, consisting of aortic replacement with a rifampicin-immersed synthetic graft, omentum wrapping, and esophagectomy, is an option, but is extremely invasive. The perioperative mortality rate is 45.4–55%.[406,1806] On the other hand, TEVAR facilitates hemorrhage control through stent-graft deployment into the thoracic aorta with tumor infiltration alone. This is a minimally invasive, effective method that can be conducted in a short time.[1807] In the case of progression to AEF, the above open surgery may be required, but TEVAR is also effective as bridge surgery. The mortality rates within 30 days after TEVAR or open surgery are reportedly 9.4 and 27.5%, respectively; the results of TEVAR are favorable.[1806]

The other is preventive TEVAR before esophagectomy or radiochemotherapy. In advanced esophageal cancer patients with aortic infiltration, the aortic wall that tumor cells infiltrate may be damaged during open surgery. Furthermore, necrosis of infiltrating tumor cells on radiochemotherapy may induce aortic-wall rupture.[732] If pretreatment CT suggests the aortic infiltration of a tumorous thoracic lesion, the risk of hemorrhage or rupture may be reduced by conducting preventive TEVAR, facilitating safe surgery or radiochemotherapy for esophageal cancer.[732,1808]

Similarly, ABF are observed in some patients with pulmonary diseases, including lung cancer.[1809–1812] In this case, serious hemorrhage may also occur. A primary symptom is hemoptysis, but the perioperative mortality rate is reportedly 15–24%.[1813,1814] Several studies indicated that TEVAR for ABF also facilitated minimally invasive, effective closure of the fistula site and hemorrhage control, suggesting its efficacy on emergencies.[1815–1817]

After TEVAR for AEF or ABF, remote-phase stent graft infection may occur. Broad-spectrum antimicrobial drugs should be administered for 6–8 weeks after insertion, followed by the oral administration of antimicrobial drugs over the lifetime.[406] A study reported that the results of adequate antimicrobial drug administration were relatively favorable: the incidence of postoperative stent-graft infection was 2.9%.[732]

Both emergency TEVAR for hemorrhage in AEF patients and preventive TEVAR before surgery/radiochemotherapy in patients in whom aortic infiltration is suspected are useful. However, these types of TEVAR are not covered by health insurance, and instructions for use (IFU) is not applicable. Currently, the expenditure is borne by hospitals. In the future, these should become covered by health insurance earlier.

IX. Rehabilitation

1. Rehabilitation for Aortic Dissection (Table 59)

The evidence for rehabilitation for aortic dissection has been scarce compared to that for the cardiac region; additionally, there has been no fixed method/effect (evaluation) for rehabilitation. This section describes aortic dissection indicated for conservative treatment, that is, uncomplicated Type B dissection. Cases in which invasive treatment (TEVAR or prosthetic graft replacement) has been performed in the acute phase are discussed in the section on perioperative rehabilitation.

There have been few reports of standardized rehabilitation for acute dissection. However, as part of a multicenter study on the specific medical procedures for acute aortic dissection, a rehabilitation program has been created for the standardization of diagnostic treatment after hospitalization and early bed-leaving, leading to the introduction of clinical pathways in clinical settings, with the support of the Projects for Establishing and Promoting Effective Medical Technology in Clinical Research under the 2002 Ministry of Health, Labour and Welfare Scientific Research Fund.[1818] Since acute/subacute complications in acute dissection (rupture/impending rupture, organ ischemia, uncontrollable hypertension, and enlarged state or rapid enlargement) have different prognoses depending on the disease type and pathological condition, they cannot be easily managed with one rehabilitation program. Shorter rehabilitation courses are recommended for pathological conditions that are less likely to cause aortic dissection complications. Early bed-leaving reduces pneumonia and restlessness requiring the use of drugs. Thus, the active promotion of rehabilitation in low-risk patients is expected to shorten the lengths of their ICU stay and hospitalization,[1397,1819] which also allows for the safe implementation of a short-term rehabilitation program.[1395] The condition may worsen during rehabilitation, and complications may occur. Thus, if a patient has developed complications, rehabilitation is discontinued, and invasive treatment is reconsidered. Short-term rehabilitation programs are not appropriate for patients with complications from the time of onset and patients complicated by DIC, and they require individual responses. The indication criteria for short-term rehabilitation programs are shown in **Table 60**.

1.1 From the Acute Phase to the Recovery Stage

Previously, patients who had not undergone invasive treatment during the acute phase were required to rest in bed for 7 days to prevent acute aortic dissection-related

Table 59. COR and LOE for Rehabilitation in the Acute Phase of Aortic Dissection

	COR	LOE
In patients with acute aortic dissection subject to medical treatment (mainly uncomplicated Type B), promotion of leaving the bed and return to daily living according to a rehabilitation program under heart rate/blood pressure management should be considered[1395,1397]	IIa	C

COR, class of recommendation; LOE, level of evidence.

Table 60. Indication Criteria for Short-Term Rehabilitation Programs for Aortic Dissection

Patients with acute Type B dissection who:

- do not have rupture or impending rupture
- do not have malperfusion
- have been able to achieve pain control
- have achieved the control of blood pressure and heart rate
- do not have enlargement of aortic diameter (complicated by thoracic aortic aneurysm)
- are not complicated by DIC

DIC, disseminated intravascular coagulation syndrome.

Table 61. Example of a Short-Term Rehabilitation Program for Aortic Dissection

Day of disease	Level of rest	Excretion	Cleanliness	Meal
Day of onset	Bed rest	On bed	Bed bath (with assistance), face washing (with assistance)	None
Day 2	Sitting on bed	On bed	Bed bath (with assistance), face washing (without assistance)	With assistance
Day 3	Walking around the bed	Indoor bathroom	Bed bath (with assistance), face washing in the room	↓
Day 4	↓	↓	Bed bath (without assistance), face washing in the room	Without assistance
Day 5	Walking in the hospital ward	Bathroom in the hospital ward	Bed bath (without assistance), face washing in the hospital ward	↓
Day 6	↓	↓	↓	↓
Day 7	No restriction in the hospital	↓	↓	↓
Day 8	↓	↓	Shower is allowed	↓

(Source: Prepared based on Niino T, et al. 2009.[1395])

Table 62. Criteria for Starting Rehabilitation for Aortic Dissection	
• Conscious state	−2≤RASS≤1 There is no restlessness requiring sedation within 30 min
• Breathing	Breathing frequency of <35 times/min lasts for a certain period of time SaO_2 of 90% or higher lasts for a certain period of time FiO_2 of <0.6
• Circulation	Control of blood pressure and heart rate has been achieved There is no appearance of new severe arrhythmia There are no electrocardiogram changes suggestive of new myocardial ischemia
• Fever	There is no fever above 38.5°C

FiO_2, fraction of inspiratory oxygen; RASS, Richmond Agitation Sedation Scale; SaO_2, oxygen saturation. (Source: Prepared based on the Japanese Society of Intensive Care Medicine. 2017.[1820])

Table 63. Criteria for Discontinuing the Rehabilitation of Aortic Dissection	
• Consciousness disturbance	Consciousness/sedation level is RASS≤−3 RASS>2 requiring an increased dose or new administration of sedative Dyspnea during exertion, rejection by patients
• Respiratory condition	Respiratory Rate <5 times/min or ≥40 times/min SpO_2 is 88–90% or >4% decrease
• Circulatory dynamics	Heart rate of ≥100/min and systolic blood pressure of >140 mmHg under exercise therapy Appearance of new severe arrhythmia Electrocardiogram changes suggestive of new myocardial ischemia

RASS, Richmond Agitation Sedation Scale; SpO_2, saturation of percutaneous oxygen. (Source: Prepared based on Adler J, et al. 2012.[1821])

complications. Today, however, they undergo a program of early rehabilitation as soon as their circulation condition is settled.[1395,1397,1819] **Table 61** shows an example of a short-term rehabilitation program.[1395]

Patients must have stable hemodynamics, respiratory condition, and state of consciousness at the start of rehabilitation. In the acute phase, it is recommended to control the systolic blood pressure to 100–120 mmHg and adjust the heart rate to below 60 beats/min by the administration of various antihypertensive drugs.[1270] The blood pressure should be sufficiently controlled, actively focusing on the level of rest. The criteria for starting rehabilitation are shown in **Table 62**.[1820]

If the condition worsens while rehabilitation is in progress, rehabilitation must be discontinued. The discontinuation criteria are shown in **Table 63**.[1821] We set the load pass criterion to a systolic blood pressure of 140 mmHg or lower after loading. If the patient does not pass the criterion, the dose of antihypertensive drugs is increased, and the procedure is repeated the subsequent day. If the patient cannot take the prescribed rest due to delirium, the rehabilitation load is limited to the stage at which the prescribed rest can be taken. Also, if the patient has decreased activities of daily life (ADL) due to cerebrovascular disease or locomotive disorder before the onset of aortic dissection, it is desirable to avoid a load higher than the ADL before the onset of dissection.

1.1.1 Initial Resting Time

Basically, early rehabilitation is crucial, and it aims for the prevention of atelectasis due to inflammatory pleural effusion, the prevention of lower-limb venous thrombosis due to long-term bed rest, and the prevention of restlessness and dementia exacerbation in older adults due to obligatory rest.[1819] The patients are required to rest in bed for the first 24 h to prevent acute aorta-related complications; however, to facilitate drinking and oral drug administration by widening the field of view of the patient, passive postural change is allowed from the first day.

1.1.2 Excretion

The patients with aortic dissection may develop paralytic ileus due to decreased intestinal tract blood flow. Furthermore, excretion on the bed is difficult, and they are likely to develop constipation due to the difficulty in defecation control, which is also a factor for ileus.[1389,1822] In a rehabilitation program, since the bedside toilet (indoor toilet) can be used after the bedside standing training, early standing is desired in patients with a stable condition.

1.1.3 Cleanliness

Bed bath with assistance is started from the time of hospitalization; additionally, rehabilitation is sequentially advanced to hair washing and then to shower bath. The maintenance of physical cleanliness is important not only for the prevention of infections, but also for mental stability and QOL during hospitalization.

1.2 From the Recovery Stage to the Return to Daily Living

Rehabilitation in the recovery stage is performed mainly for the purpose of improving decreased physical function associated with rest during hospitalization. It is considered to correspond to one month after discharge; however, the healing process of acute dissection during this period is not fully understood. Thus, rehabilitation should be limited to light walking of shorter than 500 m.

Social (workplace) return and daily living are focused after 2–3 months from the onset, and the period has a great impact on the QOL, requiring detailed guidance. As blood pressure control is of the most importance, it is necessary to evaluate the blood pressure and activity range by exercise stress testing, such as the treadmill, using the blood pressure value as the endpoint. Blood pressure control is performed with a target resting blood pressure of below 130/80 mmHg.[1263]

In the chronic stage, it is recommended to perform aerobic exercise of 3–5 METs, which is effective in lowering the systolic blood pressure, regularly exercising for at least 30 min per day and at least 150 min per week as a guide.[1416,1823,1824] It is desirable to avoid physical load involving effort (exercise with force close to 100% of the person: bench press and intense isometric load).[1416,1823] It

has been reported that supervised exercise therapy improves exercise tolerance even in patients after surgery of Type A dissection.[1824,1825]

2. Perioperative Rehabilitation of the Aorta (Table 64)

There has been fewer evidence for rehabilitation in the aortic region than that in the cardiac region. However, patients receiving aortic treatment are older and have higher frailty than those receiving treatment for the cardiac region, and they develop complications and comorbidities associated with treatment more commonly. Thus, early rehabilitation is expected to prevent postoperative complications, shorten the length of hospitalization, and improve the life prognosis.

Table 64. COR and LOE for Perioperative Rehabilitation of a Large Artery

	COR	LOE
It is recommended to perform exercise therapy to strengthen the cardiopulmonary function prior to surgery for abdominal aortic aneurysm while the circulatory dynamics is monitored[1826–1829]	I	A
Exercise therapy and respiratory rehabilitation according to the site/treatment (open surgery or TEVAR/EVAR) of the arterial aneurysm should be considered from an early stage after invasive treatment of the aorta[1830]	IIa	C

COR, class of recommendation; EVAR, endovascular aortic repair; LOE, level of evidence; TEVAR, thoracic endovascular aortic repair.

2.1 Preoperative Rehabilitation

The main objectives of rehabilitation before elective surgery are to avoid postoperative acute phase complications and to achieve early social rehabilitation. Patients with aortic diseases are generally older than those undergoing cardiac surgery; additionally, several patients are complicated by occlusive pulmonary disease associated with a smoking history.[1831,1832] It was reported that patients who had had exercise habits before surgery achieved earlier rehabilitation,[1833] and preoperative smoking cessation, physical therapy, and exercise programs improved the respiratory function,[1834] contributing to a decrease in postoperative complications. There has been evidence from multiple RCTs that respiratory rehabilitation before open surgery improves the respiratory function and reduces postoperative respiratory complications, and it is recommended.[1835–1842] In particular, it is recommended for patients complicated by COPD and those exhibiting abnormalities on preoperative respiratory function tests.

Multiple RCTs, systematic reviews, and meta-analyses of preoperative exercise therapy for AAA patients have been reported. Cardiopulmonary exercise stress tests can be safely carried out by AAA patients;[1843] additionally, it has been reported that exercise therapy in AAA patients scheduled for surgery improves exercise tolerance, such as oxygen uptake and anaerobic threshold,[1826–1828,1844] and reduces the perioperative complications and the length of hospital stay.[1829] In addition, exercise therapy does not enlarge the aneurysm diameter, and conversely, it has been shown that rehabilitation in AAA patients before surgical indication may suppress aneurysm enlargement.[1845] Several results support preoperative exercise therapy, and supervised exercise therapy before elective surgery (especially for AAA patients) is recommended.

In addition, preoperative mild cognitive impairment (MCI) and dementia, which are observed at a certain rate with the aging of surgical patients, are associated with postoperative cognitive dysfunction (POCD), postoperative delirium, respiratory complications, and advisability of postoperative return to home.[1830,1846–1848] In such cases, rehabilitation is often delayed, and it is advisable to carry out an objective cognitive function assessment, such as the Mini Mental State Examination (MMSE). If a decrease in the motor function or cognitive function is observed, it may be difficult for the patient to return home after surgery. Thus, a multi-disciplinary survey, understanding, and sharing of information on their social environments, such as the usage status of long-term care insurance, residence status of the family, and employment situation, should be started before surgery.

2.2 Postoperative Rehabilitation

The objectives of postoperative rehabilitation are the prevention of and recovery from disuse syndrome. In addition, it has been reported that the period until ADL elevation and ADL-inhibiting factors differ depending on the site of aortic aneurysm;[1849,1850] additionally, perioperative rehabilitation according to the surgical site is required.

As a result of postoperative rehabilitation, the improvement of physical function shortens the length of hospital stay and enables early rehabilitation; additionally, it also reduces the incidence of postoperative complications, such as infection, pneumonia, pleural effusion retention, and delirium.[1851–1854] Moreover, it results in early social rehabilitation and an improvement of social rehabilitation rate, leading to the improvement of life prognosis and QOL, as well as the improvement of the early recovery rate of older adults.

Older adults and patients with high frailty are more likely to be complicated by postoperative dysphagia;[1416,1823,1825,1855] additionally, dysphagia rehabilitation may contribute to the reduction of postoperative respiratory complications and improvement of QOL and life prognosis in the chronic stage.

2.3 Responses According to the Pathological Condition/Treatment Method

2.3.1 Post-Aortic Dissection Surgery

Most open surgeries for Type A dissection are urgent surgeries, and patients with extensive dissection develop organ damage associated with impaired blood flow. Thus, the general condition after surgery and risk at the time of rehabilitation vary significantly among patients. Therefore, it is desirable to judge the start time of rehabilitation individually according to the course of treatment and general condition. In addition, lesions often remain after the surgery of Type A dissection (residual dissection), and it is common to set certain restrictions on their daily living and physical activity. In the postoperative chronic stage, it is recommended to perform an aerobic exercise of 3–5 METs for approximately 30 min/day (150 min/week) as a

guide;[1416,1823] additionally, a high-intensity physical load involving effort, aerobic exercise to the extent of breathlessness (6 METs or higher), and defecation with straining should be avoided. An improvement in exercise tolerance by supervised exercise therapy was reported in patients who had undergone surgery for Type A dissection.[1825,1855]

Several patients with acute aortic dissection caused by Marfan syndrome are younger adults; additionally, the complication rate of atherosclerotic diseases of other organs is low. However, due to the fragility of tissues, high-intensity exercise, isometric exercise, and contact sports with heart rates above 100 beats/min are not recommended.[1823]

2.3.2 Abdominal Aortic Aneurysm

a. After Open Surgery

Open surgery of AAA has a large impact on the intestinal tract, and gastrointestinal symptoms become ADL-inhibiting factors.[1849] Patients who have developed ileus due to the exacerbation of abdominal pain or distension may need to discontinue rehabilitation and require rest. It has been reported that rehabilitation that is started early after prosthetic graft replacement for AAA reduces the risk of intestinal obstruction and promotes dietary intake, affects wound healing, shortens the hospital stay, aids in early rehabilitation, and reduces the occurrence of respiratory complications.[1850–1853]

b. After EVAR

The surgical wound after EVAR is usually found only in the inguinal region; additionally, active rehabilitation begins the day after surgery to maintain ADL. In patients undergoing internal iliac arterial embolization, attention must be paid to buttock claudication symptoms during rehabilitation. In addition, in patients with a narrowed aortic terminal or iliac artery with severe calcification, attention needs to be paid to limb occlusion and stenosis. Also, it is necessary to compare the preoperative/postoperative ankle-brachial blood pressure ratio and pay attention to the appearance of intermittent claudication.

2.3.3 Thoracic Aortic Aneurysm

a. After Open Surgery

Attention must be paid to cerebral infarction and dysphagia in ascending/aortic arch replacement, while paraplegia and respiration disorder require caution in descending/thoracoabdominal aortic replacement. According to a report in Japan, the proportions of cases leading to early postoperative independence after arch and descending/thoracoabdominal replacement are low at 39% and 30%, respectively, while that after ascending replacement is 75%.[1850] As a cause of delay in independence, cerebrovascular diseases are common in arch replacement, while postoperative pleural effusion retention and SCI are common in thoracic descending/thoracoabdominal replacement. After descending replacement, attention must be paid to oxygenation and carbon dioxide retention, focusing on the presence or absence of pleural effusion management and atelectasis. The swallowing function often declines after arch replacement or in older adults after surgery.[1856–1859] Thus, the evaluation of the swallowing function and swallowing training should be considered even before surgery, and the swallowing/ingesting therapy, such as the introduction of thickened food, should be actively introduced after surgery.

ADL in patients undergoing coronary artery revascularization in arch replacement or ascending replacement should be expanded by carrying out a staged walking load and shower load occasionally, while paying attention to the changes in the electrocardiograms before and after rehabilitation.

b. After TEVAR

The surgical wound after TEVAR is localized in the inguinal region, and its effect is not considerably different from that after EVAR. However, more strict blood pressure management and diagnostic imaging are recommended. In patients with a high risk of being complicated by SCI or patients transiently presenting with symptoms of paraplegia, there is concern that symptoms may be induced/exacerbated by lowering the blood pressure, and they require a relatively high blood pressure target.

Since the rest level cannot be increased during the insertion of the spinal cord drainage, rehabilitation is started from the standing position after drainage removal. In rehabilitation, attention should be paid to the decrease in blood pressure, the appearance of paraplegia, and the onset of intracranial hypotension syndrome.

2.3.4 Paraplegia After Treatment for Thoracic Aortic Aneurysm

Patients developing SCI, such as paraplegia, after open surgery or TEVAR for TAA require a specialized rehabilitation program according to the degree of the injury.[1860] Patients with complete paraplegia are confined to the bed as they have difficulty in maintaining a sitting position. It is necessary to regularly change the position of the patient to prevent the development of decubitus and to promptly manage urination/defecation due to bladder and rectal disorders. Patients with paraparesis undergo physical therapy from the early stage of onset to maintain/improve residual function.

2.3.5 Non-Ruptured Cases (Elective Surgery Cases) and Ruptured Cases (Urgent Surgery Cases)

The risk management differs between non-ruptured and ruptured cases as they have different pathological conditions. In ruptured cases, the general condition is poor, and postoperative complications often occur. In addition, since their preoperative evaluation is insufficient, rehabilitation is started without fully understanding comorbidities, such as coronary artery disease, cerebrovascular disease, and pulmonary disease.

2.4 Implementation of Perioperative Rehabilitation

Early walking exercise is useful. ADL is expanded in stages, proceeding to low-intensity exercise therapy, such as a bicycle ergometer.

Patients undergoing open surgery can carry out position change, half-sitting, and pulmonary physiotherapy under analgesia while they are in the intensive care unit, if they meet the criteria for starting rehabilitation (**Table 65**). Inhalation therapy and respiratory drainage therapy in a sitting position are recommended for patients producing a lot of sputum. Various complications appear when bed rest is prolonged. Thus, continuous infusion is discontinued for early bed-leaving, and the number of inserted/attached lines, such as balloon catheters, is minimized. After working on analgesia, walking exercise is started using a walking aid.

Table 65. Criteria for Starting Postoperative Rehabilitation for Aortic Disease

Rehabilitation can be started if the following are absent:

1. Due to low (cardiac) output syndrome (LOS):
   (1) Life supporting devices, such as ventilator, IABP, and PCPS, are installed
   (2) Large doses of inotropic drugs, such as noradrenaline and catecholamine preparations, have been administered
   (3) Systolic blood pressure is 80–90 mmHg or lower (even with the administration of inotropic drugs)
   (4) Cold sensation of limbs and cyanosis are observed
   (5) Metabolic acidosis
   (6) Urinary volume: Hourly urine remains 0.5–1.0 mL/kg/h or lower for at least 2 h
2. The Swan–Ganz catheter has been inserted
3. The resting heart rate is 120/min or higher
4. Blood pressure is unstable (hypotension symptoms appear simply by changing positions)
5. Arrhythmia with unstable hemodynamics (newly developed atrial fibrillation or premature ventricle contraction of Lown IVb or higher)
6. Dyspnea or tachypnea at rest (breathing frequency of <30 times/min)
7. Postoperative hemorrhagic tendency remains

IABP, intra-aortic balloon pumping; PCPS, percutaneous cardiopulmonary support.

Table 66. Criteria for Discontinuing Postoperative Rehabilitation for Aortic Disease

1. Inflammation
   - Fever above 37.5°C
   - Inflammatory findings (acute exacerbation period of CRP)
2. Circulatory dynamics
   - Appearance of new severe arrhythmia
   - A doctor is consulted if the patient has tachycardiac atrial fibrillation
   - Resting systolic blood pressure of 130 mmHg or higher
   - Decrease in systolic blood pressure by 30 mmHg or more upon rehabilitation
   - New ischemic electrocardiogram changes: heart rate of 120/min or higher
3. Anemia
   - Acute exacerbation to a Hb level of 8.0 g/dL or lower
   - A doctor is consulted if the Hb level of the patient undergoing surgery without blood transfusion is in the 7.0 g/dL range
4. Respiratory condition
   - Decrease in SpO_2 (92% or lower during oxygen inhalation or exercise-induced decrease in SpO_2 by 4% or more)
   - Respiratory Rate of 40 times or more
5. State of consciousness
   - Consciousness/sedation level is RASS ≤–3
   - RASS >2 requiring increased dose or new administration of sedative
   - Rejection by patients

CRP, C-reactive protein; RASS, Richmond Agitation Sedation Scale; SpO_2, saturation of percutaneous oxygen.

2.4.1 Blood Pressure Control

Consideration should be given to the maintenance of urine volume and cerebral blood flow immediately after surgery; however, it should be aimed at hypotension to the most possible extent. With the expansion of postoperative ADL, the target blood pressure needs to be adjusted for each case; however, the resting systolic blood pressure should be maintained below 130 mmHg.

2.4.2 Exercise Stress

ADL is sequentially expanded from sitting, standing, walking in the hospital ward, showering, and bathing. Also, exercise with a treadmill or bicycle ergometer is performed in addition to normal walking.

2.4.3 Criteria for Discontinuation

Attention must be paid to items in **Table 66** when performing postoperative rehabilitation. If the discontinuation criteria are met, the rehabilitation is discontinued or not performed.

2.4.4 Guidance for Discharge

Guidance for discharge is given not only to patients, but also to their family members, which includes symptoms and their management at recurrence, precautions for daily living after discharge (management of blood pressure and defecation, salt restriction, need for fluid intake, and sternum protection), postoperative complications (prosthetic graft infection/wound infection and adverse reaction of blood transfusion), and emergency consultation methods.

A management index for outpatient systolic blood pressure is set, and guidance on the method for measuring blood pressure, time zones, and recording methods is provided. Even if the patient is transferred to another hospital due to prolonged postoperative management for various reasons, social rehabilitation is pursued by requesting the hospital for the patient to perform appropriate rehabilitation.[1861]

X. Various Issues of Medical Treatment for Aortic Diseases

1. Disease Prevention

1.1 Current Status of Treatment Results and Survival Rate

The treatment results of acute aortic dissection and aortic aneurysm rupture have improved with operative deaths of 9.6% and 17.6%, respectively.[42] However, it has also been reported that approximately half of the patients die before arriving at a hospital,[1862] and in reality, the true survival rate is significantly low. The methods for resolving this situation differ for the two diseases. Since the enlargement/rupture of aortic aneurysms takes time, their detection and treatment before rupture are important, which require screening by radiography or echography.

On the other hand, since aortic dissection itself does not exist until its onset, it is necessary to avoid its onset and treat it to the earliest extent possible after the onset. While the latter is discussed in **Chapter VI** of the present guideline, it is important to avoid the factors that trigger the onset of the former because of the lack of reliable preventive measures. If it is difficult, we should prepare for its onset by understanding the situation in which the onset is likely to occur.

1.2 Risk Factors of Aortic Dissection

1.2.1 Aortic Diameter

Both dissection and rupture are likely to occur when the thoracic aortic diameter exceeds 60 mm.[535,635,1863] Therefore, it is effective to detect aortic enlargement and treat it in a preventive manner. However, dissection may develop with a diameter of 40 mm or smaller even in non-Marfan syndrome patients,[1864–1866] suggesting the involvement of other factors.

1.2.2 Physical/Psychological Stress

Weightlifting and strenuous exercise may be involved in the development of dissection.[1867,1868] Lifting a barbell leads to blood pressure of over 300 mmHg, and its repetition causes cystic medial degeneration in the aortic wall.[1869] Dissection may occur with strenuous exercise even if the size is below 50 mm and has not reached the surgical indication.[1870] The International Olympic Committee proposed screening for Olympic athletes exposed to such physical stress. However, due to the social circumstances, examinations, such as echocardiography, were performed only on approximately 30% of athletes in the 2016 Rio de Janeiro Olympics.[1871] In addition, not only physical stress but also emotional stress, such as exasperation, is said to be involved in the onset of dissection.[1872]

1.2.3 Hypertension

While 80% of patients with aortic dissection are complicated by hypertension,[68,1873] those with hypertension have a high incidence of dissection.[1873] The incidence of dissection per 100,000 population was 21 in those with hypertension and 5 in those without hypertension. A blood pressure of at least 180 mmHg was recorded several times before the onset in approximately half of the patients with dissection, and blood pressure before the onset was significantly high in patients who died before arriving at the hospital.[1862] Thus, hypertension is considered as a treatable risk factor. In addition, several dissection patients exhibit large fluctuations in blood pressure, and it has been reported that an increase or no decrease in blood pressure at night is associated with the onset of Type B dissection at night.[1874]

1.2.4 Seasons, Time Zones, and Day of the Week

The onset of dissection is said to be more common in winter;[1875–1883] however, some reports have denied this statement.[1884,1885] Its onset is thought to be affected by a decrease in temperature, and some reported that its onset was more common when the temperature remained low for 3 days,[1877] while others reported that there was no such association.[1884,1885] With regard to the atmospheric pressure, some have reported that there was an association,[1880] while others reported that there was no association.[1886] Some have reported that its onset is more common on Mondays of the week and that its mortality rate is higher on weekends,[45,1882,1887–1889] while it was also reported that no such difference was observed.[46] A higher mortality rate on weekends may be affected by the shortage of the emergency medical care system on weekends. Its onset is more common in the morning during the day.[46,47,1875,1882,1890–1892] A similar tendency has been observed in acute myocardial infarction[1893–1895] and stroke.[1896,1897] Additionally, it may be affected by increased blood pressure, increased heart rate, sympathetic nerve tension, the hormones involved in vasoconstriction, and circadian variation that elevates platelet aggregation in the morning.[1898]

1.2.5 Sleep Disorder

Approximately half of the patients with Type A dissection suffer from sleep disorder.[1899] Sleep disorder increases the incidence of hypertension,[1900] and it is a risk factor for coronary artery lesion.[1901] Also, several patients with sleep disorder die from cardiovascular diseases.[1902] Sleep disorder includes insomnia, lack of sleep, and obstructive sleep apnea syndrome (OSAS), and OSAS may be affected by a decrease in intrathoracic pressure to approximately –50 mmHg that occurs during inspiration. According to the apnea hypopnea index (AHI), approximately half of the dissection patients have severe OSAS.[1903] In addition, there is a strong association between enlargement of the false lumen in the descending aorta and the severity of OSAS, and the aorta enlargement rate, which is normally 1–3 mm/year, increased to 7.5 mm/year in the group with AHI of >30 events/h.

1.3 Prevention of Aortic Dissection

Family doctors and general practitioners play an important role in reducing the risk of developing aortic dissection described above. First, the screening for aortic diseases in patients with background factors, such as hypertension and family history, should cover the entire aorta if there is an opportunity to perform CT examination. More than 90% of aortic aneurysms are detected incidentally, and it is also useful for detecting lung cancer as the majority of its cases are detected incidentally. Although it has a problem of radiation exposure, it is advantageous that CT examination is widely used in Japan, which should be fully utilized. If there is an opportunity to perform echocardiography, it should not only cover the aortic root, but also the abdominal aorta (See "**Chapter III. Symptoms, Examinations, and Diagnoses**").

Subsequently, it is necessary to accurately grasp the elevation and fluctuation in blood pressure. Fluctuation in the blood pressure is a treatable risk factor, and the prevention of the onset of dissection by blood pressure management is important. In particular, circadian variation should be observed by the self-measurement of blood pressure. In addition, public awareness needs to be raised regarding sports, emotional stress, and seasons/circadian variation, which may affect the fluctuation of blood pressure, along with smoking cessation; moreover, a multifaceted approach that includes the government and the news media is desired.

Finally, the management of sleep disorders is important; additionally, the active diagnosis/treatment of OSAS and its public awareness are needed. Since insomnia and lack of sleep are greatly affected by work stress, it is necessary to take wide measures, including those by an improved work environment, family doctors, and government. Work-style

reform is thought to be important from the viewpoint of not only labor but also by the avoidance of the onset of dissection.

2. Surveillance (Tables 67 and 68)

Patients with aortic diseases require lifelong surveillance, regardless of whether they are treated with medical treatment or invasive treatment (prosthetic graft replacement or TEVAR/EVAR). The surveillance includes the evaluation of clinical symptoms, evaluation of oral drugs, evaluation of disease transition by imaging examinations, identification of treatment goals at each disease condition/stage, and active diagnosis and intervention for comorbidities.[96]

2.1 Classification of Disease Stages and Pathological Conditions

The disease stages of aortic dissection are clinically classified into the acute phase, which is 2 weeks from onset, the subacute phase, which is from 2 weeks to 3 months after onset, and the chronic stage, which is after 3 months of onset. In contrast, the pathological conditions of aortic

Table 67. COR and LOE for the Risk Management of Chronic Aortic Diseases

	COR	LOE
It is recommended to administer effective antihypertensive drugs to patients with aortic dissection to reduce the risk of aortic disease-related deaths[276,1364]	I	C
It is recommended to give antihypertensive therapy, lipid management with statins, administration of antiplatelet agents, and guidance for smoking cessation to patients with chronic aortic dissection to reduce the risk of cardiovascular death in the late stage[1330,1904]	I	C
It is recommended to administer β-blockers for uncomplicated chronic Type B dissection for a long period of time[276]	I	C
It is recommended to perform strict blood pressure management (below 130/80 mmHg) for chronic aortic diseases[96]	I	C
It is recommended to manage cardiovascular risk after open surgery for abdominal aortic aneurysm with antiplatelet agents, in addition to the management of blood pressure and lipid levels[929,1905–1911]	I	B
Antihypertensive therapy, lipid management with statins, and cardiovascular risk management with antiplatelet agents should be considered for abdominal aortic aneurysm[1905,1912–1915]	IIa	B

COR, class of recommendation; LOE, level of evidence.

Table 68. COR and LOE for the Surveillance of Aortic Diseases

	COR	LOE
It is recommended to perform surveillance of thoracic aortic diseases by CT examination[69,143]	I	C
It is recommended to perform echography as the first choice for the diagnosis and surveillance of small-diameter abdominal aortic aneurysms[1916–1919] (See **Table 22**)	I	B
It is recommended to perform surveillance of abdominal aortic aneurysm by echography or CT every 1–2 years if the aneurysm diameter is 30–40 mm, every 6 months-1 year if the aneurysm diameter is 40–50 mm, or every 3–6 months if the aneurysm diameter is 50–55 mm[795] (See **Table 22**)	I	B
It is recommended to use CT for diagnosing and deciding on the treatment methods for the rupture of abdominal aortic aneurysm[1701,1918,1920]	I	C
Regarding surveillance at an early stage after TEVAR/EVAR (within 30 days), it is recommended to use diagnostic imaging to evaluate endoleaks and confirm stent deployment sites and joints[889,1921–1923]	I	B
If the patient presents with abdominal pain or recurrence after the onset of acute Type B dissection and is suspected of having malperfusion of the abdominal branch, it is recommended to perform another CT examination[1363]	I	C
During the medical treatment of uncomplicated chronic Type B dissection, it is recommended to perform continuous evaluation by regular diagnostic imaging[1050,1924]	I	C
The evaluation of descending aortic diseases by MDCT from the thoracic aorta to the common femoral artery should be considered[1925,1926]	IIa	C
CT examination should be considered as diagnostic imaging for the surveillance of acute thoracic aortic diseases[1925]	IIa	C
Prompt invasive treatment should be considered for type I/III endoleaks after TEVAR[658,1927]	IIa	C
Continuous surveillance by CT or MRI should be considered after TEVAR/EVAR[658]	IIa	C

COR, class of recommendation; CT, computed tomography; EVAR, endovascular aortic repair; LOE, level of evidence; MDCT, multidetector row CT; TEVAR, thoracic endovascular aortic repair.

diseases are classified into three types: (1) stable disease condition without complications, (2) unstable disease condition (progressive increase in aneurysm diameter, chronic malperfusion of the pelvis/lower limb, or complications with persistent/recurrent symptoms), and (3) disease condition with residual dissection after invasive treatment for ascending aortic dissection.[96]

2.2 Clinical Phase

The clinical phase can be divided into two types: those in which acute aortic disease has transitioned to chronic disease and those found to be chronic at the time of the initial diagnosis (asymptomatic in most cases). In the latter, mediastinal/aortic arch enlargement is often detected incidentally by chest radiography, or it is detected by echography or CT examination for the evaluation of other diseases. It is difficult to identify a definite time of onset in these cases; however, the confirmation and evaluation of symptoms that appear in the acute/subacute phase and physical/laboratory findings after diagnosis are important. In rare cases, the progression of TAA or dissecting TAA causes symptoms, such as hoarseness/chest pain associated with enlargement and intermittent claudication/abdominal pain/deterioration of renal function due to malperfusion.

2.3 Diagnosis

Aortic diseases are diagnosed by sectional imaging of contrast-enhanced/non-contrast-enhanced CT examination, MRI examination, or transesophageal echography. Chronic aortic diseases are diagnosed based on the images of wall thickening, non-mobile dissected intima, the formation of false lumen thrombosis, and aneurysm formation in chronic dissection (mainly distal arch). In symptomatic patients, multimodal therapy is immediately considered if mediastinal hematoma, pericardial effusion/pleural effusion, and retroperitoneal hematoma due to rupture are found by various imaging examinations.

2.4 Preoperative Surveillance

Preoperative surveillance for aortic diseases is planned by considering the disease to be targeted and the modality to be used, as well as its intervals and purposes. Aortic diseases include TAA, AAA, acute/subacute aortic dissection, and dissecting aortic aneurysms. However, in AAA and TAA (arch/descending aorta), which have a stronger atherosclerotic predisposition, management against other atherosclerotic diseases and risk factors is essential, rather than focusing only on aortic diseases.

Evaluation by CT is recommended for the preoperative surveillance for TAA; additionally, CT examination is required annually for patients with an aneurysm diameter of below 45 mm or every 3–6 months for patients with an aneurysm diameter of 45–55 mm. Invasive treatment is considered if imaging examinations for TAA show an increase in enlargement rate of aneurysm diameter by at least 5 mm in half a year or an aneurysm diameter of 55 mm. On the other hand, it is recommended to use echography for the preoperative surveillance of AAA and to use CT examination for deciding a treatment policy. Surveillance using echography or CT is recommended every 1–2 years for patients with an aneurysm diameter of 30–40 mm, every 6–12 months for patients with an aneurysm diameter of 40–50 mm, or every 3–6 months for patients with an aneurysm diameter of 50–55 mm.[321] Invasive treatment is considered if imaging examinations for AAA show an increase in the enlargement rate of aneurysm diameter by at least 5 mm in half a year or an aneurysm diameter of >55 mm (men) or >50 mm (women). In addition, the definition of small-diameter aortic aneurysms and accurate surveillance intervals in Japan are discussed in **PQ 13**.

Acute aortic dissection is clinically classified into the acute phase, which is 2 weeks from onset, subacute phase, which is from 2 weeks to 3 months after onset, and chronic stage, which is after 3 months of onset. Type A/B dissection patients having complications in the acute phase are subject to urgent/semi-urgent invasive treatment (prosthetic graft replacement/TEVAR). On the other hand, invasive treatment may be performed on patients with Type A dissection (dissection with thrombosed false lumen) or uncomplicated Type B dissection several weeks after onset, if the diameter is 40 mm or smaller. In such cases, it is important to accurately evaluate the disease condition based on detailed surveillance in the course of the acute to subacute/chronic stage, making efforts not to miss the timing of surgery. The surveillance for aneurysmal chronic aortic dissection is performed based on that for aortic aneurysms (TAA or AAA). However, dissecting TAA is indicated for invasive treatment if it is 60 mm or larger, and invasive treatment for dissecting TAA at 55–60 mm is discussed by a specialized team based on the general condition of the patient, anatomical requirements, and expected surgical invasiveness.

PQ 13.

How Often Should CT Examinations Be Performed After Abdominal Aortic Aneurysm or Chronic Aortic Dissection?

Recommendation

In AAA patients, the aneurysm diameter is evaluated by CT examination every 1–2 years if it is 30–39 mm, every 6 months–1 year if it is 40–49 mm, or every 3–6 months if it is 50–55 mm. Chronic dissection is evaluated every 1 year if it is below 45 mm or every 3–6 months if it is 45–55 mm.

A meta-analysis showed that the risk of AAA rupture increased 1.91 times for every 5 mm of aneurysm diameter enlargement. On the other hand, AAAs with a small aneurysm diameter were shown to pose no issue even when they were followed up every few years.[795] The SVS and ESVS guidelines recommend the evaluation of aneurysm diameter every 3 years if it is 30–39 mm, every year if it is 40–49 mm, or every 3–6 months if it is 50 mm or larger. CT examination is more easily performed in Japan than in Europe and the United States, and due to social circumstances, the evaluation of the aneurysm diameter has been frequently performed. In several cases, the aneurysm diameter is evaluated every 1–2 years if it is 30–39 mm, every 6 months–1 year if it is 40–49 mm, or every 3–6 months if it is 50–55 mm.

On the other hand, the evidence of follow-up intervals for aneurysm formation after chronic aortic dissection is scarce. Although studies on aneurysm diameter and rupture risk are also scarce, rupture at an aneurysm diameter of <45 mm is rare, for which annual CT examination is sufficient. However, continuous CT examinations are

performed every 3–6 months for aneurysms with a diameter of 45–55 mm. Patients with risk factors for aneurysm formation, such as heritable connective tissue disorder, require a more careful follow-up.

2.5 Follow-up After Invasive Treatment

2.5.1 Thoracic Aortic Diseases

In principle, follow-up by imaging examinations is performed 1, 6, and 12 months after invasive treatment and annually thereafter. In addition, the regular observation of clinical symptoms is concurrently needed. In particular, the strict management of blood pressure is required as the past literature showed that approximately 50% of patients had treatment-resistant hypertension.[1928] The symptoms rarely appear in the chronic stage after treatment, and the disease specificity is low. However, attention must be paid to the appearance of hoarseness/dysphagia associated with aneurysm enlargement, exacerbation of symptoms associated with chronic hypoperfusion, such as intermittent claudication/abdominal pain, and the appearance of chest and back pain associated with rupture.

a. After TEVAR

A lifelong follow-up by CT examination is required. MRI examination may be alternatively used to prevent radiation exposure; however, currently, it poses a problem of extensive artifact caused by stainless steel.[1929] On the other hand, MRI examination can be performed if it is nitinol-based;[1930] however, because it cannot visualize stent struts, the structural failure of the stent graft skeleton is evaluated using chest radiography. In Japan, medical devices, including implantable devices and metals, are classified into different types, such as "MRI contraindicated," "MRI compatible," and "those that can be imaged depending on the condition".[146,147] An examination is performed after confirming a compatibility online with the "MR compatibility search system for medical devices" (MEDIE Co. Ltd.), in addition to the confirmation by the package insert. Patients with severe renal dysfunction who cannot undergo CT/MRI examination are evaluated by using non-contrast-enhanced CT, transesophageal echography, and chest radiography in combination.

CT examination is recommended 1, 6, and 12 months after TEVAR and annually thereafter. Electrocardiogram gated imaging has superior image quality. In patients showing no endoleaks after TEVAR for TAA and continuing to have stable condition beyond 24 months, imaging follow-up interval may be extended to 2 years; however, the symptoms of the patients and oral medical treatment are followed up annually. On the other hand, several patients who have undergone TEVAR for aortic dissection exhibit patent false lumen at the level of the abdominal aorta. Additionally, they may show exacerbation of the disease due to temporal changes in hemodynamics. Thus, patients who have undergone TEVAR for TAA require surveillance at the same interval as a follow-up or more strict surveillance.

b. After Open Surgery

It is necessary to evaluate the complications specific to open surgery (prosthetic graft replacement), such as anastomotic aneurysm and prosthetic graft infection, and exacerbation/new onset of aortic diseases at a distance from the site of prosthetic graft replacement. Several patients who have undergone open surgery for Type A dissection have residual dissection in the thoracic descending/abdominal aortic region, and they require follow-up on re-dissection/dissection-cavity enlargement. Imaging examinations are performed 1, 3, 6, 12, 18, and 24 months after surgery and at least annually thereafter.

2.5.2 Abdominal Aortic Aneurysm

The follow-up interval after EVAR is different from that after prosthetic graft replacement. Since AAA is strongly associated with atherosclerotic factors, lifelong drug therapy, including smoking cessation, is needed to suppress cardiovascular events.

a. After EVAR

In principle, CT examination is recommended after 1, 6, and 12 months, and annually thereafter. On the other hand, a recent meta-analysis reported that contrast echography is useful in diagnosing type II endoleaks.[1931] Type I/III endoleaks requiring retreatment can be well identified by ordinary echography. Retreatment for a type II endoleak is considered if the aneurysm diameter enlarges 10 mm or more after EVAR. MRI examination for patients who have undergone EVAR is performed in the same manner as that for patients who have undergone TEVAR.

b. After Open Surgery

CT examination and echography are performed at least every 5 years to evaluate anastomotic aneurysms. In addition, attention must be paid to abdominal wall incisional hernia after open surgery. An observational study with Medicare in the United States showed that 5.8% of patients required treatment of hernia within 4 years. A study on the 5-year and 15-year follow-up found anastomotic aneurysms in 1% and 12% of patients, respectively, and limb occlusion in 1% and 5% of patients, respectively. In addition, at the 5-year follow-up, graft infection was found in 0.5–5% of patients, and a secondary aortic gastrointestinal fistula was found in less than 1% of patients.[321]

PQ 14.

Should Exercise Restriction Be Performed for Patients With Chronic Aortic Dissection?

Recommendation

In daily life, regular mild/moderate aerobic exercise without excessive restrictions is desirable for patients with chronic aortic dissection.

There has been little evidence of exercise in patients with chronic aortic dissection. However, they are recommended to perform mild/moderate aerobic exercise (equivalent to 3–5 METs), such as walking, light running, and biking, which are highly effective in lowering systolic blood pressure, at least 30 min per day and 150 min per week.[1416,1823] Excessive weight lifting that increases intrathoracic pressure should be avoided as it significantly elevates the blood pressure.[1416,1823] Supervised exercise therapy was reported to improve the exercise tolerability of patients after surgery of Type A dissection.[1825,1855] The exercise intensity of the therapy was mild rehabilitation with approximately Borg Scale 11, and the maximum blood pressure during exercise

Table 69. COR and LOE for Contrast-Enhanced CT in Patients With Aortic Diseases		
	COR	LOE
Contrast-enhanced CT may be considered for patients with severe renal dysfunction (eGFR <30 mL/min/1.73 m^2) after taking preventive measures against contrast medium-induced nephropathy[494,1935,1936]	IIb	C

COR, class of recommendation; CT, computed tomography; eGFR, estimated glemerular filtration rate; LOE, level of evidence.

was maintained at approximately 150 mmHg.[1855] Patients who had received appropriate exercise therapy were able to resume carrying heavy objects of approximately 20 kg, as well as outdoor activities, such as mountain climbing and diving.[1932] There are no restrictions on daily living and sexual life in patients who have undergone appropriate rehabilitation, and stepping the stairs, biking, gardening, shopping, and carrying heavy objects up to approximately 50% of the body weight are allowed.[1824]

3. Notes on Diagnostic Imaging

Diagnostic imaging plays a major role in the follow-up of aortic aneurysm/dissection. However, it is necessary to fully understand the characteristics of examination methods to properly perform diagnostic imaging. This section mainly describes the considerations for frequently performed CT/MRI examinations.

3.1 Radiation Exposure by CT Examination

With the advancement in CT devices, radiation exposure associated with examination has been reduced. However, when performing CT examination repeatedly as follow-up diagnostic imaging for young individuals, especially women capable of pregnancy and children, it is necessary to fully consider the accompanying medical X-ray exposure and to judge its indications carefully. If possible, alternative methods, such as echography and MRA examination, are also considered. The risk of developing cancer associated with radiation exposure is said to be higher in women than in men. However, its risk decreases after the age of 50.[1933]

Regarding CT radiation exposure, it is important to know whether the exposure dose of one's own facility is higher than that of others, for which the diagnostic reference level (DRL) is used as a judgment criterion. The DRLs of CT examination set for adults with a standard physical constitution (50–60 kg) in 2015 are 15 mGy for 1 phase of thoracic region, 20 mGy for 1 phase of thoracic region-pelvis, and 20 mGy for 1 phase of upper abdominal region-pelvis.[1934] If the dose at one's facility exceeds this level, it needs to be reduced within the range that does not affect medical treatment.

3.2 Contrast Medium-Induced Nephropathy by Iodine Contrast-Enhanced CT Examination (Table 69)

Patients with mild-moderate renal dysfunction (eGFR ≥30 mL/min/1.73 m^2) are not likely to develop contrast medium-induced nephropathy (CIN) after the administration of contrast medium. On the other hand, when performing a contrast-enhanced CT examination for a patient with severe renal dysfunction (eGFR <30 mL/min/1.73 m^2), the risk of developing CIN should be explained to the patient, and appropriate preventive measures must be taken as needed.[494,1935,1936] The reduction of the amount of contrast medium in contrast-enhanced CT may decrease the risk of developing CIN. Thus, it is recommended to use the minimum amount of contrast medium within the range that can maintain the diagnostic ability, especially for patients at high risk of CIN.

When reducing the amount of contrast medium, the combined use of low tube voltage CT imaging and successive approximation image reconstruction is desirable. In addition, repeated contrast-enhanced CT examinations within a short period of time (24–48 h) require caution as they may increase the risk of CIN.

PQ 15.
Can Contrast-Enhanced CT Examination Be Performed on Patients With Impaired Renal Function/Renal Failure?

Recommendation

In patients with severe renal dysfunction (eGFR <30 mL/min/1.73 m^2), attention must be paid to the development of contrast medium-induced nephropathy after contrast-enhanced CT examination, and preventive measures need to be taken with the administration of isotonic transfusion. Alternatively, a reduction in the number of examinations or the amount of contrast medium may be considered.

Contrast-enhanced CT examination may be performed in patients with mild-moderate renal dysfunction (eGFR ≥30 mL/min/1.73 m^2) as they are not likely to develop contrast medium-induced nephropathy (CIN) after the administration of contrast medium. On the other hand, the risk of CIN is thought to be low even in patients with severe renal dysfunction (eGFR <30 mL/min/1.73 m^2). However, due to its insufficient evidence, appropriate preventive measures need to be taken while explaining the risk of developing CIN to the patient.[494] In addition, patients requiring critical care and severe emergency outpatients have a high risk of developing acute kidney injury, regardless of the administration of a contrast medium. Thus, even in patients with moderate renal dysfunction (eGFR <45 mL/min/1.73 m^2), appropriate preventive measures need to be taken while providing sufficient explanation to the patient. On the other hand, contrast-enhanced CT examination may be considered for patients with life-threatening unstable circulatory dynamics who are strongly suspected of having aortic aneurysm rupture or acute aortic dissection, regardless of the presence or absence of renal dysfunction.

With regard to the transfusion method for the prevention of CIN, 0.9% saline solution (physiological saline solution), which is an isotonic transfusion, is transfused at 1 mL/kg/h from 6 h before the start of contrast imaging, and it is transfused at 1 mL/kg/h for 6–12 h after the completion of contrast imaging. In urgent cases with limited transfusion time, sodium bicarbonate solution (1.26%, 152 mEq/L) is transfused at 3 mL/kg/h from 1 h before the start of contrast imaging, and it is transfused at 1 mL/kg/h for 6 h after the completion of contrast imaging.[494] However, the volume of

transfusion may be reduced if there is a possibility of heart failure due to transfusion. In addition, the effectiveness of any drug therapy in preventing CIN has not been established, and blood purification therapy is not recommended.

3.3 Gadolinium Contrast MRA Examination

Contrast-enhanced MRA examination using gadolinium contrast medium is contraindicated for patients with severe renal dysfunction (eGFR <30 mL/min/1.73 m^2), dialysis, or acute renal failure due to the risk of developing nephrogenic systemic fibrosis.[1937] The preventive effect of transfusion and dialysis has not been demonstrated, and their alternatives need to be considered.

3.4 Compatibility of Medical Devices With MRI Examination

Medical devices, including implantable devices and metals, are classified into different types, such as "MRI contraindicated," "MRI compatible," and "those that can be imaged depending on the condition".[147] It is important to perform examinations after confirming compatibility online with the "MR compatibility search system for medical devices" (MEDIE Co. Ltd.), in addition to the confirmation by the package insert.

Acknowledgments

The preparation of the English version of this guideline was made possible with the generous support of the Japanese Society for Vascular Surgery. We would like to express our deepest gratitude to the society.

References

1. Takamoto S, Ishimaru S, Kato M, Kuribayashi S, Matsuo H, Miyata T, et al; JCS Joint Working Group. Guidelines for diagnosis and treatment of aortic aneurysm and aortic dissection (JCS 2011): Digest version. *Circ J* 2013; **77:** 789–828.
2. Johnston KW, Rutherford RB, Tilson MD, Shah DM, Hollier L, Stanley JC. Suggested standards for reporting on arterial aneurysms. *J Vasc Surg* 1991; **13:** 452–458.
3. Thompson RW, Geraghty PJ, Lee JK. Abdominal aortic aneurysms: Basic mechanisms and clinical implications. *Curr Probl Surg* 2002; **39:** 110–230.
4. Matsumoto T, Uekusa T, Fukuda Y. Vasculo-Behçet's disease: A pathologic study of eight cases. *Hum Pathol* 1991; **22:** 45–51.
5. Lakhanpal S, Tani K, Lie JT, Katoh K, Ishigatsubo Y, Ohokubo T. Pathologic features of Behçet's syndrome: A review of Japanese autopsy registry data. *Hum Pathol* 1985; **16:** 790–795.
6. Hotchi M. Pathological studies on Takayasu arteritis. *Heart Vessels Suppl* 1992; **7:** 11–17.
7. Matsumura K, Hirano T, Takeda K, Matsuda A, Nakagawa T, Yamaguchi N, et al. Incidence of aneurysms in Takayasu's arteritis. *Angiology* 1991; **42:** 308–315.
8. Takayama T, Miyata T, Nagawa H. True abdominal aortic aneurysm in Marfan syndrome. *J Vasc Surg* 2009; **49:** 1162–1165.
9. Roberts WC, Honig HS. The spectrum of cardiovascular disease in the Marfan syndrome: A clinico-morphologic study of 18 necropsy patients and comparison to 151 previously reported necropsy patients. *Am Heart J* 1982; **104:** 115–135.
10. Isselbacher EM. Thoracic and abdominal aortic aneurysms. *Circulation* 2005; **111:** 816–828.
11. Zarins CK, Xu C, Glagov S. Atherosclerotic enlargement of the human abdominal aorta. *Atherosclerosis* 2001; **155:** 157–164.
12. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): A collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006; **113:** e463–e654.
13. Tilson MD, Stansel HC. Differences in results for aneurysm vs occlusive disease after bifurcation grafts: Results of 100 elective grafts. *Arch Surg* 1980; **115:** 1173–1175.
14. Clifton MA. Familial abdominal aortic aneurysms. *Br J Surg* 1977; **64:** 765–766.
15. Verloes A, Sakalihasan N, Koulischer L, Limet R. Aneurysms of the abdominal aorta: Familial and genetic aspects in three hundred thirteen pedigrees. *J Vasc Surg* 1995; **21:** 646–655.
16. Blanchard JF. Epidemiology of abdominal aortic aneurysms. *Epidemiol Rev* 1999; **21:** 207–221.
17. Wilmink AB, Quick CR. Epidemiology and potential for prevention of abdominal aortic aneurysm. *Br J Surg* 1998; **85:** 155–162.
18. Golledge J, van Bockxmeer F, Jamrozik K, McCann M, Norman PE. Association between serum lipoproteins and abdominal aortic aneurysm. *Am J Cardiol* 2010; **105:** 1480–1484.
19. Ailawadi G, Eliason JL, Upchurch GR. Current concepts in the pathogenesis of abdominal aortic aneurysm. *J Vasc Surg* 2003; **38:** 584–588.
20. Shimizu K, Mitchell RN, Libby P. Inflammation and cellular immune responses in abdominal aortic aneurysms. *Arterioscler Thromb Vasc Biol* 2006; **26:** 987–994.
21. Matsuo H. 定義・分類. [in Japanese] *In:* Yutani C, Matsuo H, editors. 大動脈瘤・大動脈解離の臨床と病理. Igaku-Shoin, 2004; 2–4.

21a. Hao H. Pathology of aortic aneurysm and aortic dissection. [in Japanese] *Jpn J Vasc Surg* 2014; **23:** 957–963.

22. Nienaber CA, Eagle KA. Aortic dissection: New frontiers in diagnosis and management: Part I: From etiology to diagnostic strategies. *Circulation* 2003; **108:** 628–635.
23. Erbel R, Alfonso F, Boileau C, Dirsch O, Eber B, Haverich A, et al. Diagnosis and management of aortic dissection: Recommendation of the task force on aortic dissection, European Society of Cardiology. *Eur Heart J* 2001; **22:** 1642–1681.
24. Hirst AE Jr, Johns VJ Jr, Kime SW Jr. Dissecting aneurysm of the aorta: A review of 505 cases. *Medicine (Baltimore)* 1958; **37:** 217–279.
25. Nakashima Y, Kurozumi T, Sueishi K, Tanaka K. Dissecting aneurysm: A clinicopathologic and histopathologic study of 111 autopsied cases. *Hum Pathol* 1990; **21:** 291–296.
26. Kageyama N, Ro A, Tanifuji T, Kumagai T, Murai T, Fukunaga T. The histophathologic study of elastic laminar and interconnecting elastic fiber in aortic media: Implications for aortic dissection. [in Japanese] *J Jpn Coll Angiol* 2005; **45:** 1003–1009.
27. Nakashima Y, Shiokawa Y, Sueishi K. Alterations of elastic architecture in human aortic dissecting aneurysm. *Lab Invest* 1990; **62:** 751–760.
28. Larson EW, Edwards WD. Risk factors for aortic dissection: A necropsy study of 161 cases. *Am J Cardiol* 1984; **53:** 849–855.
29. Angouras D, Sokolis DP, Dosios T, Kostomitsopoulos N, Boudoulas H, Skalkeas G, et al. Effect of impaired vasa vasorum flow on the structure and mechanics of the thoracic aorta: Implications for the pathogenesis of aortic dissection. *Eur J Cardiothorac Surg* 2000; **17:** 468–473.
30. Gao F, Guo Z, Sakamoto M, Matsuzawa T. Fluid-structure interaction within a layered aortic arch model. *J Biol Phys* 2006; **32:** 435–454.
31. Beller CJ, Labrosse MR, Thubrikar MJ, Robicsek F. Role of aortic root motion in the pathogenesis of aortic dissection.

Circulation 2004; **109:** 763–769.
32. Vilacosta I, San Román JA. Acute aortic syndrome. *Heart* 2001; **85:** 365–368.
33. Stanson AW, Kazmier FJ, Hollier LH, Edwards WD, Pairolero PC, Sheedy PF, et al. Penetrating atherosclerotic ulcers of the thoracic aorta: Natural history and clinicopathologic correlations. *Ann Vasc Surg* 1986; **1:** 15–23.
34. Murai T. Aortic dissection and sudden death--statistical analysis on 1320 cases autopsied at Tokyo-to Medical Examiner Office. [in Japanese] *Jpn J Legal Med* 1988; **42:** 564–577.
35. Daily PO, Trueblood HW, Stinson EB, Wuerflein RD, Shumway NE. Management of acute aortic dissections. *Ann Thorac Surg* 1970; **10:** 237–247.
36. DeBakey ME, Henly WS, Cooley DA, Morris GC, Crawford ES, Beall AC. Surgical management of dissecting aneurysms of the aorta. *J Thorac Cardiovasc Surg* 1965; **49:** 130–149.
37. Fukumoto H. ERにおける急性大動脈解離の管理. [in Japanese] *Jpn J Acute Med* 2002; **26:** 1462–1467.
38. Amano J, Kuwano H, Yokomise H. Thoracic and cardiovascular surgery in Japan during 2011: Annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2013; **61:** 578–607.
39. Masuda M, Kuwano H, Okumura M, Amano J, Arai H, Endo S, et al; Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery. Thoracic and cardiovascular surgery in Japan during 2012: Annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2014; **62:** 734–764.
40. Masuda M, Kuwano H, Okumura M, Arai H, Endo S, Doki Y, et al; Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery. Thoracic and cardiovascular surgery in Japan during 2013: Annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2015; **63:** 670–701.
41. Masuda M, Okumura M, Doki Y, Endo S, Hirata Y, Kobayashi J, et al; Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery. Thoracic and cardiovascular surgery in Japan during 2014: Annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2016; **64:** 665–697.
42. Masuda M, Endo S, Natsugoe S, Shimizu H, Doki Y, Hirata Y, et al; Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery. Thoracic and cardiovascular surgery in Japan during 2015: Annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2018; **66:** 581–615.
43. Shimizu H, Endo S, Natsugoe S, Doki Y, Hirata Y, Kobayashi J, et al; Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery. Thoracic and cardiovascular surgery in Japan in 2016: Annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2019; **67:** 377–411.
43a. Shimizu H, Okada M, Tangoku A, Doki Y, Endo S, et al; Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery. Thoracic and cardiovascular surgeries in Japan during 2017: Annual report by the Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2020; **68:** 414–449.
43b. Japanese Society for Vascular Surgery. NCD登録症例に基づく日本の血管外科手術例数集計結果. [in Japanese] Available at: http://www.jsvs.org/ja/enquete/report2011/index.html (accessed July 31, 2020).
44. Japanese Society of Pathology. 日本病理剖検輯報 46輯 (2003)–51輯 (2008). [in Japanese]
45. Sumiyoshi M, Kojima S, Arima M, Suwa S, Nakazato Y, Sakurai H, et al. Circadian, weekly, and seasonal variation at the onset of acute aortic dissection. *Am J Cardiol* 2002; **89:** 619–623.
46. Mehta RH, Manfredini R, Hassan F, Sechtem U, Bossone E, Oh JK, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. Chronobiological patterns of acute aortic dissection. *Circulation* 2002; **106:** 1110–1115.
47. Kojima S, Sumiyoshi M, Nakata Y, Daida H. Triggers and circadian distribution of the onset of acute aortic dissection. *Circ J* 2002; **66:** 232–235.
48. Taylor BV, Kalman PG. Saccular aortic aneurysms. *Ann Vasc Surg* 1999; **13:** 555–559.
49. Natsume K, Shiiya N, Takehara Y, Sugiyama M, Satoh H, Yamashita K, et al. Characterizing saccular aortic arch aneurysms from the geometry-flow dynamics relationship. *J Thorac Cardiovasc Surg* 2017; **153:** 1413–1420.
50. Boyd AJ, Kuhn DC, Lozowy RJ, Kulbisky GP. Low wall shear stress predominates at sites of abdominal aortic aneurysm rupture. *J Vasc Surg* 2016; **63:** 1613–1619.
51. Akai T, Hoshina K, Yamamoto S, Takeuchi H, Nemoto Y, Ohshima M, et al. Biomechanical analysis of an aortic aneurysm model and its clinical application to thoracic aortic aneurysms for defining "saccular" aneurysms. *J Am Heart Assoc* 2015; **4:** e001547.
52. Shang EK, Nathan DP, Boonn WW, Lys-Dobradin IA, Fairman RM, Woo EY, et al. A modern experience with saccular aortic aneurysms. *J Vasc Surg* 2013; **57:** 84–88.
53. Shang EK, Nathan DP, Sprinkle SR, Fairman RM, Bavaria JE, Gorman RC, et al. Impact of wall thickness and saccular geometry on the computational wall stress of descending thoracic aortic aneurysms. *Circulation* 2013; **128 Suppl:** S157–S162.
54. Karthaus EG, Tong TML, Vahl A, Hamming JF. Dutch society of vascular surgery, the steering committee of the Dutch surgical aneurysm audit and the Dutch institute for clinical auditing: Saccular abdominal aortic aneurysms: Patient characteristics, clinical presentation, treatment, and outcomes in the Netherlands. *Ann Surg* 2019; **270:** 852–858.
55. Sheppard MN. Diseases of the Aorta. *In:* Practical Cardiovascular Pathology, 2nd edn. CRC Press, 2011; 258–259.
56. Stary HC, Blankenhorn DH, Chandler AB, Glagov S, Insull W, Richardson M, et al. A definition of the intima of human arteries and of its atherosclerosis-prone regions: A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Circulation* 1992; **85:** 391–405.
57. Stary HC, Chandler AB, Glagov S, Guyton JR, Insull W, Rosenfeld ME, et al. A definition of initial, fatty streak, and intermediate lesions of atherosclerosis: A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Arterioscler Thromb* 1994; **14:** 840–856.
58. Stary HC, Chandler AB, Dinsmore RE, Fuster V, Glagov S, Insull W, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis: A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Arterioscler Thromb Vasc Biol* 1995; **15:** 1512–1531.
59. Movsowitz HD, Lampert C, Jacobs LE, Kotler MN. Penetrating atherosclerotic aortic ulcers. *Am Heart J* 1994; **128:** 1210–1217.
60. Evangelista A, Mukherjee D, Mehta RH, O'Gara PT, Fattori R, Cooper JV, et al; International Registry of Aortic Dissection (IRAD) Investigators. Acute intramural hematoma of the aorta: A mystery in evolution. *Circulation* 2005; **111:** 1063–1070.
61. Jang YM, Seo JB, Lee YK, Chae EJ, Park SH, Kang JW, et al. Newly developed ulcer-like projection (ULP) in aortic intramural haematoma on follow-up CT: Is it different from the ULP seen on the initial CT? *Clin Radiol* 2008; **63:** 201–206.
62. Bossone E, Suzuki T, Eagle KA, Weinsaft JW. Diagnosis of acute aortic syndromes: Imaging and beyond. *Herz* 2013; **38:** 269–276.
63. Nienaber CA, Powell JT. Management of acute aortic syndromes. *Eur Heart J* 2012; **33:** 26–35.
64. Hallinan JT, Anil G. Multi-detector computed tomography in the diagnosis and management of acute aortic syndromes. *World J Radiol* 2014; **6:** 355–365.
65. Cooke JC, Cambria RP. Simultaneous tracheobronchial and esophageal obstruction caused by a descending thoracic aneurysm. *J Vasc Surg* 1993; **18:** 90–94.
66. Furukawa H, Tsuchiya K, Osawa H, Saito H, Iida Y. Saccular descending thoracic aortic aneurysm with dysphagia. *Jpn J Thorac Cardiovasc Surg* 1999; **47:** 277–280.
67. Park SW, Hutchison S, Mehta RH, Isselbacher EM, Cooper JV, Fang J, et al. Association of painless acute aortic dissection with increased mortality. *Mayo Clin Proc* 2004; **79:** 1252–1257.
68. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, et al. The International Registry of Acute Aortic Dissection (IRAD): New insights into an old disease. *JAMA* 2000; **283:** 897–903.
69. Klompas M. Does this patient have an acute thoracic aortic dissection? *JAMA* 2002; **287:** 2262–2272.
70. Tyson MD. Dissecting Aneurysms. *Am J Pathol* 1931; **7:** 581–603.
71. Zull DN, Cydulka R. Acute paraplegia: A presenting manifestation of aortic dissection. *Am J Med* 1988; **84:** 765–770.
72. Matsuo H. Pathophysiology and complications of aortic

dissection. *J Jpn Surg Soc* 1996; **97:** 879–883.
73. Ikeda K, Abe T, Itou M, Fukuda J, Tamiya Y, Tanaka T, et al. Surgical management for acute aortic dissection with organ ischemia. *Jpn J Thorac Surg* 1999; **52:** 89–93.
74. Spittell PC, Spittell JA Jr, Joyce JW, Tajik AJ, Edwards WD, Schaff HV, et al. Clinical features and differential diagnosis of aortic dissection: Experience with 236 cases (1980 through 1990). *Mayo Clin Proc* 1993; **68:** 642–651.
75. Fann JI, Sarris GE, Mitchell RS, Shumway NE, Stinson EB, Oyer PE, et al. Treatment of patients with aortic dissection presenting with peripheral vascular complications. *Ann Surg* 1990; **212:** 705–713.
76. Horie T. Clinicopathological study in cases with dissecting aneurysm of the aorta--with special reference to coronary artery dissection. [in Japanese] *Jpn Circ J* 1993; **57 Suppl:** 1283–1286.
77. Di Eusanio M, Trimarchi S, Patel HJ, Hutchison S, Suzuki T, Peterson MD, et al. Clinical presentation, management, and short-term outcome of patients with type A acute dissection complicated by mesenteric malperfusion: Observations from the International Registry of Acute Aortic Dissection. *J Thorac Cardiovasc Surg* 2013; **145:** 385–390.
78. Stather PW, Sidloff DA, Dattani N, Gokani VJ, Choke E, Sayers RD, et al. Meta-analysis and meta-regression analysis of biomarkers for abdominal aortic aneurysm. *Br J Surg* 2014; **101:** 1358–1372.
79. Folsom AR, Yao L, Alonso A, Lutsey PL, Missov E, Lederle FA, et al. Circulating biomarkers and abdominal aortic aneurysm incidence: The Atherosclerosis Risk in Communities (ARIC) Study. *Circulation* 2015; **132:** 578–585.
80. Wang Y, Shen G, Wang H, Yao Y, Sun Q, Jing B, et al. Association of high sensitivity C-reactive protein and abdominal aortic aneurysm: A meta-analysis and systematic review. *Curr Med Res Opin* 2017; **33:** 2145–2152.
81. Sidloff DA, Stather PW, Choke E, Bown MJ, Sayers RD. A systematic review and meta-analysis of the association between markers of hemostasis and abdominal aortic aneurysm presence and size. *J Vasc Surg* 2014; **59:** 528–535.
82. Aboulafia DM, Aboulafia ED. Aortic aneurysm-induced disseminated intravascular coagulation. *Ann Vasc Surg* 1996; **10:** 396–405.
83. Fisher DF, Yawn DH, Crawford ES. Preoperative disseminated intravascular coagulation associated with aortic aneurysms: A prospective study of 76 cases. *Arch Surg* 1983; **118:** 1252–1255.
84. Miyashita T, Ando M, Hanafusa Y, Onishi Y, Kuro M. An analysis of risk factors of perioperative bleeding in surgical repair of abdominal aortic aneurysm. *J Cardiovasc Surg (Torino)* 2000; **41:** 595–599.
85. Japanese Society on Thrombosis and Hemostasis 学術標準化委員会DIC部会. Expert consensus based on the evidence for the treatment of disseminated intravascular coaglation due to infection intravascular. [in Japanese] *Jpn J Thromb Hemost* 2009; **20:** 77–113.
86. Asakura H. Classifying types of disseminated intravascular coagulation: Clinical and animal models. *J Intensive Care* 2014; **2:** 20.
87. Kasashima S, Zen Y, Kawashima A, Endo M, Matsumoto Y, Kasashima F. A new clinicopathological entity of IgG4-related inflammatory abdominal aortic aneurysm. *J Vasc Surg* 2009; **49:** 1264–1271.
88. Marill KA. Serum D-dimer is a sensitive test for the detection of acute aortic dissection: A pooled meta-analysis. *J Emerg Med* 2008; **34:** 367–376.
89. Suzuki T, Distante A, Zizza A, Trimarchi S, Villani M, Salerno Uriarte JA, et al; IRAD-Bio Investigators. Diagnosis of acute aortic dissection by D-dimer: The International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) experience. *Circulation* 2009; **119:** 2702–2707.
90. Taylor RA, Iyer NS. A decision analysis to determine a testing threshold for computed tomographic angiography and D-dimer in the evaluation of aortic dissection. *Am J Emerg Med* 2013; **31:** 1047–1055.
91. Asha SE, Miers JW. A systematic review and meta-analysis of D-dimer as a rule-out test for suspected acute aortic dissection. *Ann Emerg Med* 2015; **66:** 368–378.
92. Paparella D, Malvindi PG, Scrascia G, de Ceglia D, Rotunno C, Tunzi F, et al. D-dimers are not always elevated in patients with acute aortic dissection. *J Cardiovasc Med (Hagerstown)* 2009; **10:** 212–214.
93. Sutherland A, Escano J, Coon TP. D-dimer as the sole screening test for acute aortic dissection: A review of the literature. *Ann Emerg Med* 2008; **52:** 339–343.
94. Rogers AM, Hermann LK, Booher AM, Nienaber CA, Williams DM, Kazerooni EA, et al; IRAD Investigators. Sensitivity of the aortic dissection detection risk score, a novel guideline-based tool for identification of acute aortic dissection at initial presentation: Results from the international registry of acute aortic dissection. *Circulation* 2011; **123:** 2213–2218.
95. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation* 2010; **121:** e266–e369.
96. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult: The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). *Eur Heart J* 2014; **35:** 2873–2926.
97. Suzuki T, Bossone E, Sawaki D, Jánosi RA, Erbel R, Eagle K, et al. Biomarkers of aortic diseases. *Am Heart J* 2013; **165:** 15–25.
98. Watanabe H, Horita N, Shibata Y, Minegishi S, Ota E, Kaneko T. Diagnostic test accuracy of D-dimer for acute aortic syndrome: Systematic review and meta-analysis of 22 studies with 5000 subjects. *Sci Rep* 2016; **6:** 26893.
99. Nazerian P, Mueller C, Soeiro AM, Leidel BA, Salvadeo SAT, Giachino F, et al; ADvISED Investigators. Diagnostic accuracy of the aortic dissection detection risk score plus D-dimer for acute aortic syndromes: The ADvISED prospective multicenter study. *Circulation* 2018; **137:** 250–258.
100. Yoshimuta T, Yokoyama H, Okajima T, Tanaka H, Toyoda K, Nagatsuka K, et al. Impact of elevated D-dimer on diagnosis of acute aortic dissection with isolated neurological symptoms in ischemic stroke. *Circ J* 2015; **79:** 1841–1845.
101. Sakamoto Y, Koga M, Ohara T, Ohyama S, Matsubara S, Minatoya K, et al. Frequency and detection of Stanford type A aortic dissection in hyperacute stroke management. *Cerebrovasc Dis* 2016; **42:** 110–116.
102. Harris KM, Strauss CE, Eagle KA, Hirsch AT, Isselbacher EM, Tsai TT, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. Correlates of delayed recognition and treatment of acute type A aortic dissection: The International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2011; **124:** 1911–1918.
103. Inoue Arita Y, Akutsu K, Yamamoto T, Kawanaka H, Kitamura M, Murata H, et al. A fever in acute aortic dissection is caused by endogenous mediators that influence the extrinsic coagulation pathway and do not elevate procalcitonin. *Intern Med* 2016; **55:** 1845–1852.
104. Paparella D, Rotunno C, Guida P, Malvindi PG, Scrascia G, De Palo M, et al. Hemostasis alterations in patients with acute aortic dissection. *Ann Thorac Surg* 2011; **91:** 1364–1369.
105. Guan X, Li J, Gong M, Lan F, Zhang H. The hemostatic disturbance in patients with acute aortic dissection: A prospective observational study. *Medicine (Baltimore)* 2016; **95:** e4710.
106. Guan X, Gong M, Wang X, Zhu J, Liu Y, Sun L, et al. Low preoperative fibrinogen level is risk factor for neurological complications in acute aortic dissection. *Medicine (Baltimore)* 2018; **97:** e10830.
107. Scott J, Humphreys DR. Dissecting aortic aneurysm and disseminated intravascular coagulation. *Br Med J* 1977; **1:** 24.
108. Fine NL, Applebaum J, Elguezabal A, Castleman L. Multiple coagulation defects in association with dissecting aneurysm. *Arch Intern Med* 1967; **119:** 522–526.
109. Japanese Society on Thrombosis and Hemostasis 学術標準化委員会DIC部会. Supplement of expert consensus based on the evidence for the treatment of disseminated intravascular coagulation due to infection. [in Japanese] *Jpn J Thromb Hemost* 2014; **25:** 123–125.
110. NAEYE RL. Thrombotic state after a hemorrhagic diathesis, a possible complication of therapy with epsilon-aminocapproic acid. *Blood* 1962; **19:** 694–701.

111. Kawano H, Hata T, Uda A, Maemura K. Use of rivaroxaban for the effective management of disseminated intravascular coagulation associated with abdominal aortic aneurysm. *Intern Med* 2015; **54:** 2625–2628.
112. Eyler WR, Clark MD. Dissecting aneurysms of the aorta: Roentgen manifestations including a comparison with other types of aneurysms. *Radiology* 1965; **85:** 1047–1057.
113. Earnest F, Muhm JR, Sheedy PF. Roentgenographic findings in thoracic aortic dissection. *Mayo Clin Proc* 1979; **54:** 43–50.
114. Mehard WB, He1186iken JP, Sicard GA. High-attenuating crescent in abdominal aortic aneurysm wall at CT: A sign of acute or impending rupture. *Radiology* 1994; **192:** 359–362.
115. Boos J, Brook OR, Fang J, Temin N, Brook A, Raptopoulos V. What is the optimal abdominal aortic aneurysm sac measurement on CT images during follow-up after endovascular repair? *Radiology* 2017; **285:** 1032–1041.
116. Ihara T, Komori K, Yamamoto K, Kobayashi M, Banno H, Kodama A. Three-dimensional workstation is useful for measuring the correct size of abdominal aortic aneurysm diameters. *Ann Vasc Surg* 2013; **27:** 154–161.
117. Rudarakanchana N, Bicknell CD, Cheshire NJ, Burfitt N, Chapman A, Hamady M, et al. Variation in maximum diameter measurements of descending thoracic aortic aneurysms using unformatted planes versus images corrected to aortic centerline. *Eur J Vasc Endovasc Surg* 2014; **47:** 19–26.
118. Hirose Y, Hamada S, Takamiya M, Imakita S, Naito H, Nishimura T. Aortic aneurysms: Growth rates measured with CT. *Radiology* 1992; **185:** 249–252.
119. Takase K, Sawamura Y, Igarashi K, Chiba Y, Haga K, Saito H, et al. Demonstration of the artery of Adamkiewicz at multi-detector row helical CT. *Radiology* 2002; **223:** 39–45.
120. Gomes MN, Davros WJ, Zeman RK. Preoperative assessment of abdominal aortic aneurysm: The value of helical and three-dimensional computed tomography. *J Vasc Surg* 1994; **20:** 367–376.
121. Rubin GD, Walker PJ, Dake MD, Napel S, Jeffrey RB, McDonnell CH, et al. Three-dimensional spiral computed tomographic angiography: An alternative imaging modality for the abdominal aorta and its branches. *J Vasc Surg* 1993; **18:** 656–665.
122. Van Hoe L, Baert AL, Gryspeerdt S, Marchal G, Lacroix H, Wilms G, et al. Supra- and juxtarenal aneurysms of the abdominal aorta: Preoperative assessment with thin-section spiral CT. *Radiology* 1996; **198:** 443–448.
123. Matsuo H, Honma S, Hayashi T, Tsushima N, Takamoto S, Andou M, et al. "Inflammatory" abdominal aortic aneurysm: Clinical features and clinical significance. [in Japanese] *J Jpn Coll Angiol* 1996; **36:** 295–301.
124. Iino M, Kuribayashi S, Imakita S, Takamiya M, Matsuo H, Ookita Y, et al. Sensitivity and specificity of CT in the diagnosis of inflammatory abdominal aortic aneurysms. *J Comput Assist Tomogr* 2002; **26:** 1006–1012.
125. Rakita D, Newatia A, Hines JJ, Siegel DN, Friedman B. Spectrum of CT findings in rupture and impending rupture of abdominal aortic aneurysms. *Radiographics* 2007; **27:** 497–507.
126. Akashi H, Kawamoto S, Saiki Y, Sakamoto T, Sawa Y, Tsukube T, et al. Therapeutic strategy for treating aortoesophageal fistulas. *Gen Thorac Cardiovasc Surg* 2014; **62:** 573–580.
127. Yamazato T, Nakamura T, Abe N, Yokawa K, Ikeno Y, Koda Y, et al. Surgical strategy for the treatment of aortoesophageal fistula. *J Thorac Cardiovasc Surg* 2018; **155:** 32–40.
128. Kawamoto S, Sato M, Motoyoshi N, Kumagai K, Adachi O, Saito T, et al. Outcomes of a staged surgical treatment strategy for aortoesophageal fistula. *Gen Thorac Cardiovasc Surg* 2015; **63:** 147–152.
129. Yamanaka K, Nishina T, Miwa S, Sakaguchi H, Hirose K, Mizuno A, et al. A Staged surgical treatment strategy for aortoesophageal fistula. [in Japanese] *J Jpn Coll Angiol* 2016; **56:** 59–64.
130. Vu QD, Menias CO, Bhalla S, Peterson C, Wang LL, Balfe DM. Aortoenteric fistulas: CT features and potential mimics. *Radiographics* 2009; **29:** 197–209.
131. Halliday KE, al-Kutoubi A. Draped aorta: CT sign of contained leak of aortic aneurysms. *Radiology* 1996; **199:** 41–43.
132. Siegel CL, Cohan RH. CT of abdominal aortic aneurysms. *AJR Am J Roentgenol* 1994; **163:** 17–29.
133. Beales L, Wolstenhulme S, Evans JA, West R, Scott DJ. Reproducibility of ultrasound measurement of the abdominal aorta. *Br J Surg* 2011; **98:** 1517–1525.
134. Mora C, Marcus C, Barbe C, Ecarnot F, Long A. Measurement of maximum diameter of native abdominal aortic aneurysm by angio-CT: Reproducibility is better with the semi-automated method. *Eur J Vasc Endovasc Surg* 2014; **47:** 139–150.
135. Yamada T, Tada S, Harada J. Aortic dissection without intimal rupture: Diagnosis with MR imaging and CT. *Radiology* 1988; **168:** 347–352.
136. Williams DM, Joshi A, Dake MD, Deeb GM, Miller DC, Abrams GD. Aortic cobwebs: An anatomic marker identifying the false lumen in aortic dissection--imaging and pathologic correlation. *Radiology* 1994; **190:** 167–174.
137. Hamada S, Takamiya M, Kimura K, Imakita S, Nakajima N, Naito H. Type A aortic dissection: Evaluation with ultrafast CT. *Radiology* 1992; **183:** 155–158.
138. Kawamata H, Kumazaki T; Ulcerlike Projections of the Thrombosed Type Aortic Dissection. Their incidence, locations and natural history. [in Japanese] *J Jpn Coll Angiol* 1994; **34:** 1017–1032.
139. Wu MT, Wang YC, Huang YL, Chang RS, Li SC, Yang P, et al. Intramural blood pools accompanying aortic intramural hematoma: CT appearance and natural course. *Radiology* 2011; **258:** 705–713.
140. Williams DM, Lee DY, Hamilton BH, Marx MV, Narasimham DL, Kazanjian SN, et al. The dissected aorta: Part III. Anatomy and radiologic diagnosis of branch-vessel compromise. *Radiology* 1997; **203:** 37–44.
141. Ohtaki M, Kuribayashi Y, Tsuji M, et al. 大動脈瘤に合併した急性大動脈解離. [in Japanese] *Jpn J Clin Radiol* 1991; **36:** 97–102.
142. Saito H, Honma K, Sukekawa H, et al. 大動脈瘤に合併した急性大動脈解離. [in Japanese] *Jpn J Med Imaging* 1993; **12:** 179–185.
143. Goldstein SA, Evangelista A, Abbara S, Arai A, Asch FM, Badano LP, et al. Multimodality imaging of diseases of the thoracic aorta in adults: From the American Society of Echocardiography and the European Association of Cardiovascular Imaging: Endorsed by the Society of Cardiovascular Computed Tomography and Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 2015; **28:** 119–182.
144. 撮像法およびCQ：(4) 心血管—心血管領域の標準的撮像法. [in Japanese] Japan Radiological Society. 画像診断ガイドライン 2016年版. Kanehara-Shuppan, 2016; 210–254.
145. Morris SA, Orbach DB, Geva T, Singh MN, Gauvreau K, Lacro RV. Increased vertebral artery tortuosity index is associated with adverse outcomes in children and young adults with connective tissue disorders. *Circulation* 2011; **124:** 388–396.
146. Shellock F. Reference manual for magnetic resonance safety, implants, and devices, 2018 edn. Biomedical Research Publishing Group, 2018.
147. Levine GN, Gomes AS, Arai AE, Bluemke DA, Flamm SD, Kanal E, et al. Safety of magnetic resonance imaging in patients with cardiovascular devices: An American Heart Association scientific statement from the Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology, and the Council on Cardiovascular Radiology and Intervention: Endorsed by the American College of Cardiology Foundation, the North American Society for Cardiac Imaging, and the Society for Cardiovascular Magnetic Resonance. *Circulation* 2007; **116:** 2878–2891.
148. Krinsky GA, Rofsky NM, DeCorato DR, Weinreb JC, Earls JP, Flyer MA, et al. Thoracic aorta: Comparison of gadolinium-enhanced three-dimensional MR angiography with conventional MR imaging. *Radiology* 1997; **202:** 183–193.
149. Ferreira PF, Gatehouse PD, Mohiaddin RH, Firmin DN. Cardiovascular magnetic resonance artefacts. *J Cardiovasc Magn Reson* 2013; **15:** 41.
150. Kramer CM, Barkhausen J, Flamm SD, Kim RJ, Nagel E; Society for Cardiovascular Magnetic Resonance Board of Trustees Task Force on Standardized Protocols. Standardized cardiovascular magnetic resonance (CMR) protocols 2013 update. *J Cardiovasc Magn Reson* 2013; **15:** 91.
151. Korosec FR, Frayne R, Grist TM, Mistretta CA. Time-resolved contrast-enhanced 3D MR angiography. *Magn Reson Med* 1996; **36:** 345–351.
152. Guo Q, Zhao J, Huang B, Yuan D, Yang Y, Zeng G, et al. A systematic review of ultrasound or magnetic resonance imaging compared with computed tomography for endoleak detection and aneurysm diameter measurement after endovascular aneurysm repair. *J Endovasc Ther* 2016; **23:** 936–943.
153. Urata J, Miyazaki M, Wada H, Nakaura T, Yamashita Y, Takahashi M. Clinical evaluation of aortic diseases using nonenhanced MRA with ECG-triggered 3D half-fourier FSE.

J Magn Reson Imaging 2001; **14:** 113–119.
154. Krishnam MS, Tomasian A, Deshpande V, Tran L, Laub G, Finn JP, et al. Noncontrast 3D steady-state free-precession magnetic resonance angiography of the whole chest using nonselective radiofrequency excitation over a large field of view: Comparison with single-phase 3D contrast-enhanced magnetic resonance angiography. *Invest Radiol* 2008; **43:** 411–420.
155. Fayad ZA, Nahar T, Fallon JT, Goldman M, Aguinaldo JG, Badimon JJ, et al. In vivo magnetic resonance evaluation of atherosclerotic plaques in the human thoracic aorta: A comparison with transesophageal echocardiography. *Circulation* 2000; **101:** 2503–2509.
156. Zhu C, Tian B, Leach JR, Liu Q, Lu J, Chen L, et al. Non-contrast 3D black blood MRI for abdominal aortic aneurysm surveillance: Comparison with CT angiography. *Eur Radiol* 2017; **27:** 1787–1794.
157. Treitl KM, Maurus S, Sommer NN, Kooijman-Kurfuerst H, Coppenrath E, Treitl M, et al. 3D-black-blood 3T-MRI for the diagnosis of thoracic large vessel vasculitis: A feasibility study. *Eur Radiol* 2017; **27:** 2119–2128.
158. Koh DM, Collins DJ. Diffusion-weighted MRI in the body: Applications and challenges in oncology. *AJR Am J Roentgenol* 2007; **188:** 1622–1635.
159. Utz JA, Herfkens RJ, Heinsimer JA, Shimakawa A, Glover G, Pelc N. Valvular regurgitation: Dynamic MR imaging. *Radiology* 1988; **168:** 91–94.
160. Lotz J, Meier C, Leppert A, Galanski M. Cardiovascular flow measurement with phase-contrast MR imaging: Basic facts and implementation. *Radiographics* 2002; **22:** 651–671.
161. Dogui A, Redheuil A, Lefort M, DeCesare A, Kachenoura N, Herment A, et al. Measurement of aortic arch pulse wave velocity in cardiovascular MR: Comparison of transit time estimators and description of a new approach. *J Magn Reson Imaging* 2011; **33:** 1321–1329.
162. Dyverfeldt P, Bissell M, Barker AJ, Bolger AF, Carlhäll CJ, Ebbers T, et al. 4D flow cardiovascular magnetic resonance consensus statement. *J Cardiovasc Magn Reson* 2015; **17:** 72.
163. Clough RE, Waltham M, Giese D, Taylor PR, Schaeffter T. A new imaging method for assessment of aortic dissection using four-dimensional phase contrast magnetic resonance imaging. *J Vasc Surg* 2012; **55:** 914–923.
164. Amano Y, Sekine T, Suzuki Y, Tanaka K, Takagi R, Kumita S. Time-resolved three-dimensional magnetic resonance velocity mapping of chronic thoracic aortic dissection: A preliminary investigation. *Magn Reson Med Sci* 2011; **10:** 93–99.
165. Tanaka H, Ogino H, Minatoya K, Matsui Y, Higami T, Okabayashi H, et al; Japanese Study of Spinal Cord Protection in Descending and Thoracoabdominal Aortic Repair investigators. The impact of preoperative identification of the Adamkiewicz artery on descending and thoracoabdominal aortic repair. *J Thorac Cardiovasc Surg* 2016; **151:** 122–128.
166. Yoshioka K, Niinuma H, Ohira A, Nasu K, Kawakami T, Sasaki M, et al. MR angiography and CT angiography of the artery of Adamkiewicz: Noninvasive preoperative assessment of thoracoabdominal aortic aneurysm. *Radiographics* 2003; **23:** 1215–1225.
167. Yoshioka K, Niinuma H, Ehara S, Nakajima T, Nakamura M, Kawazoe K. MR angiography and CT angiography of the artery of Adamkiewicz: State of the art. *Radiographics* 2006; **26 Suppl 1:** S63–S73.
168. Utsunomiya D, Yamashita Y, Okumura S, Urata J. Demonstration of the Adamkiewicz artery in patients with descending or thoracoabdominal aortic aneurysm: Optimization of contrast-medium application for 64-detector-row CT angiography. *Eur Radiol* 2008; **18:** 2684–2690.
169. Nishida J, Kitagawa K, Nagata M, Yamazaki A, Nagasawa N, Sakuma H. Model-based iterative reconstruction for multi-detector row CT assessment of the Adamkiewicz artery. *Radiology* 2014; **270:** 282–291.
170. Shimoyama S, Nishii T, Watanabe Y, Kono AK, Kagawa K, Takahashi S, et al. Advantages of 70-kV CT angiography for the visualization of the Adamkiewicz artery: Comparison with 120-kV imaging. *AJNR Am J Neuroradiol* 2017; **38:** 2399–2405.
171. Yoshioka K, Tanaka R, Takagi H, Ueyama Y, Kikuchi K, Chiba T, et al. Ultra-high-resolution CT angiography of the artery of Adamkiewicz: A feasibility study. *Neuroradiology* 2018; **60:** 109–115.
172. Yamada N, Takamiya M, Kuribayashi S, Okita Y, Minatoya K, Tanaka R. MRA of the Adamkiewicz artery: A preoperative study for thoracic aortic aneurysm. *J Comput Assist Tomogr* 2000; **24:** 362–368.
173. Hyodoh H, Kawaharada N, Akiba H, Tamakawa M, Hyodoh K, Fukada J, et al. Usefulness of preoperative detection of artery of Adamkiewicz with dynamic contrast-enhanced MR angiography. *Radiology* 2005; **236:** 1004–1009.
174. Yoshioka K, Tanaka R, Takagi H, Ueyama Y, Sugawara T, Chiba T, et al. Systematic evaluation of collateral pathways to the artery of Adamkiewicz using computed tomography. *Eur J Cardiothorac Surg* 2018; **54:** 19–25.
175. Takagi H, Ota H, Natsuaki Y, Komori Y, Ito K, Saiki Y, et al. Identifying the Adamkiewicz artery using 3-T time-resolved magnetic resonance angiography: Its role in addition to multi-detector computed tomography angiography. *Jpn J Radiol* 2015; **33:** 749–756.
176. Bastos MG, Novaes AKB, Pazeli JMP. Traditional and ultrasound physical examinations: A hybrid approach to improve clinical care. *Rev Assoc Med Bras (1992)* 2018; **64:** 474–480.
177. Mancuso FJ, Siqueira VN, Moisés VA, Gois AF, Paola AA, Carvalho AC, et al. Focused cardiac ultrasound using a pocket-size device in the emergency room. *Arq Bras Cardiol* 2014; **103:** 530–537.
178. Orihashi K. 携帯エコーを使った「超」身体所見—外来・救急・在宅、どこでも「超」診断. [in Japanese] Medicus Shuppan, 2015.
179. Yamaguchi S, Murakami H, Kudo T, Otokozawa C, Sasaki S, Yuda S, et al. Usefulness of the echocardiographic paravertebral approach for the diagnosis of descending thoracic aortic dissection. *J Echocardiogr* 2017; **15:** 127–134.
180. Nishigami K. Update on cardiovascular echo in aortic aneurysm and dissection. *Ann Vasc Dis* 2018; **11:** 437–442.
181. Nishigami K. Point-of-care echocardiography for aortic dissection, pulmonary embolism and acute coronary syndrome in patients with killer chest pain: EASY screening focused on the assessment of effusion, aorta, ventricular size and shape and ventricular asynergy. *J Echocardiogr* 2015; **13:** 141–144.
182. Bernett J, Strony R. Diagnosing acute aortic dissection with aneurysmal degeneration with point of care ultrasound. *Am J Emerg Med* 2017; **35:** 1384.e3–1384.
183. D'Abate F, Oladokun D, La Leggia A, Hinchliffe R, Thompson M, Holt P, et al. Transthoracic ultrasound evaluation of arch and descending thoracic aortic pathology. *Eur J Vasc Endovasc Surg* 2018; **55:** 658–665.
184. Perkins AM, Liteplo A, Noble VE. Ultrasound diagnosis of type A aortic dissection. *J Emerg Med* 2010; **38:** 490–493.
185. American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Thoracic Aortic Dissection. Diercks DB, Promes SB, Schuur JD, Shah K, Valente JH, Cantrill SV. Clinical policy: Critical issues in the evaluation and management of adult patients with suspected acute nontraumatic thoracic aortic dissection. *Ann Emerg Med* 2015; **65:** 32–42.
186. Zhan S, Hong S, Shan-Shan L, Chen-Ling Y, Lai W, Dong-Wei S, et al. Misdiagnosis of aortic dissection: Experience of 361 patients. *J Clin Hypertens (Greenwich)* 2012; **14:** 256–260.
187. Ansari-Ramandi MM, Alemzadeh-Ansari MJ, Firoozi A. Acute type A aortic dissection missed as acute coronary syndrome. *J Clin Diagn Res* 2016; **10:** OD33–OD34.
188. Tsigkas G, Kasimis G, Theodoropoulos K, Chouchoulis K, Baikoussis NG, Apostolakis E, et al. A successfully thrombolysed acute inferior myocardial infarction due to type A aortic dissection with lethal consequences: The importance of early cardiac echocardiography. *J Cardiothorac Surg* 2011; **6:** 101.
189. Pourafkari L, Tajlil A, Ghaffari S, Parvizi R, Chavoshi M, Kolahdouzan K, et al. The frequency of initial misdiagnosis of acute aortic dissection in the emergency department and its impact on outcome. *Intern Emerg Med* 2017; **12:** 1185–1195.
190. Pare JR, Liu R, Moore CL, Sherban T, Kelleher MS, Thomas S, et al. Emergency physician focused cardiac ultrasound improves diagnosis of ascending aortic dissection. *Am J Emerg Med* 2016; **34:** 486–492.
191. National Cerebral and Cardiovascular Center. 脳梗塞患者の中に急性大動脈解離患者が隠れている～適切な診断を行うための指針を提案～ (平成30年1月25日). Available at: http://www.ncvc.go.jp/pr/release/post_34.html (accessed July 31, 2020).
192. Orihashi K. Cerebral malperfusion in acute aortic dissection. *Surg Today* 2016; **46:** 1353–1361.
193. Gologorsky E, Karras R, Gologorsky A, Ricci M, Salerno TA. Transesophageal echocardiography after contrast-enhanced CT angiography in the diagnosis of type A aortic dissection. *J Card Surg* 2011; **26:** 495–500.

194. Baliga RR, Nienaber CA, Bossone E, Oh JK, Isselbacher EM, Sechtem U, et al. The role of imaging in aortic dissection and related syndromes. *JACC Cardiovasc Imaging* 2014; **7:** 406–424.
195. Kim CM, Yu SC, Hong SJ. Cardiac tamponade during transesophageal echocardiography in the patient of circumferential aortic dissection. *J Korean Med Sci* 1997; **12:** 266–268.
196. Dalby Kristensen S, Ramlov Ivarsen H, Egeblad H. Rupture of aortic dissection during attempted transesophageal echocardiography. *Echocardiography* 1996; **13:** 405–406.
197. Chavanon O, Baguet JP, Albaladéjo P, Blin D, Vanzetto G. Direct admission to the operating room: an efficient strategy for patients with diagnosed or highly suspected acute type A aortic dissection. *Can J Cardiol* 2011; **27:** 685–691.
198. Thorsgard ME, Morrissette GJ, Sun B, Eales F, Kshettry V, Flavin T, et al. Impact of intraoperative transesophageal echocardiography on acute type-A aortic dissection. *J Cardiothorac Vasc Anesth* 2014; **28:** 1203–1207.
199. MacKnight BM, Maldonado Y, Augoustides JG, Cardenas RA, Patel PA, Ghadimi K, et al. Advances in imaging for the management of acute aortic syndromes: Focus on transesophageal echocardiography and type-A aortic dissection for the perioperative echocardiographer. *J Cardiothorac Vasc Anesth* 2016; **30:** 1129–1141.
200. Orihashi K, Matsuura Y, Sueda T, Watari M, Okada K, Sugawara Y, et al. Aortic arch branches are no longer a blind zone for transesophageal echocardiography: A new eye for aortic surgeons. *J Thorac Cardiovasc Surg* 2000; **120:** 466–472.
201. Patil TA, Ambli SK. Transesophageal echocardiography evaluation of the aortic arch branches. *Ann Card Anaesth* 2018; **21:** 53–56.
202. Orihashi K, Matsuura Y, Sueda T, Shikata H, Morita S, Hirai S, et al. Abdominal aorta and visceral arteries visualized with transesophageal echocardiography during operations on the aorta. *J Thorac Cardiovasc Surg* 1998; **115:** 945–947.
203. Tampo A, Kunisawa T, Kurosawa A, Takahata O, Iwasaki H. Intraoperative evaluation of visceral arteries by transesophageal echocardiography in Stanford B thoracic aortic dissection. *J Cardiothorac Vasc Anesth* 2011; **25:** 589–590.
204. Orihashi K, Sueda T, Okada K, Imai K. Identification by transesophageal echocardiography of intramural hematoma and the site of aortic rupture. *J Thorac Cardiovasc Surg* 2008; **136:** 1089–1091.
205. Orihashi K, Ozawa M, Takahashi S, Takasaki T, Sato K, Kurosaki T, et al. Treatment strategy for acute type A aortic dissection complicated with organ ischemia. *Ann Vasc Dis* 2011; **4:** 293–298.
206. Orihashi K. 経食道心エコー法マニュアル (改訂第5版). [in Japanese] Nankodo, 2019; 260.
207. Orihashi K, Matsuura Y, Sueda T, Shikata H, Watari M, Okada K. Clinical implication of orbital ultrasound monitoring during selective cerebral perfusion. *Ann Thorac Surg* 2001; **71:** 673–677.
208. Orihashi K, Sueda T, Okada K, Takahashi S. Compressed true lumen in the innominate artery: A pitfall of right axillary arterial perfusion in acute aortic dissection. *J Thorac Cardiovasc Surg* 2009; **137:** 242–243.
209. Güllü AU, Nurkalem Z, Akçar M, Eren M. Acute type A aortic dissection and left main coronary artery obstruction detected by transesophageal echocardiography. *Turk Kardiyol Dern Ars* 2010; **38:** 211–214.
210. Orihashi K. Malperfusion in acute type A aortic dissection: Unsolved problem. *Ann Thorac Surg* 2013; **95:** 1570–1576.
211. Orihashi K, Sueda T, Okada K, Imai K. Detection and monitoring of complications associated with femoral or axillary arterial cannulation for surgical repair of aortic dissection. *J Cardiothorac Vasc Anesth* 2006; **20:** 20–25.
212. Orihashi K, Takasaki T, Ozawa M, Sueda T. Intraoperative occlusion of left coronary ostium after aortic repair detected by transesophageal echocardiography. *J Thorac Cardiovasc Surg* 2011; **142:** e205–e206.
213. Orihashi K. Mesenteric ischemia in acute aortic dissection. *Surg Today* 2016; **46:** 509–516.
214. Orihashi K. Mesenteric ischemia in acute aortic dissection. *Gen Thorac Cardiovasc Surg* 2018; **66:** 557–564.
215. Orihashi K, Sueda T, Okada K, Imai K. Perioperative diagnosis of mesenteric ischemia in acute aortic dissection by transesophageal echocardiography. *Eur J Cardiothorac Surg* 2005; **28:** 871–876.
216. Earl TJ, Poppas A. Type A aortic dissection presenting with acute lower extremity vascular insufficiency in the absence of chest pain. *Open J Cardiovasc Surg* 2012; **5:** 1–4.
217. Hara H, Tanabe K, Tanimoto S, Aoki J, Yachi S, Kishi S, et al. Aortic regurgitation due to back-and-forth intimal flap movement detected by both multidetector computed tomography and transesophageal echocardiography. *J Cardiol Cases* 2013; **7:** e161–e163.
218. Chow JL, Mariano ER, Liang D. Transesophageal echocardiography assessment of severe aortic regurgitation in type A aortic dissection caused by a prolapsed circumferential intimal flap. *J Cardiothorac Vasc Anesth* 2007; **21:** 85–87.
219. Yamada Y, Kanazawa Y, Takei Y, Fukuda H. Type A aortic dissection with intimal intussusception. *J Card Surg* 2016; **31:** 693–694.
220. Cirillo M, Conti E, Tasca G, Troise G; Images in cardiovascular medicine. A 360-degree aortic dissection tear mimicking massive aortic regurgitation. *Circulation* 2005; **112:** e366.
221. Noiseux N, Couture P, Sheridan P, Cartier R. Aortic cannulation for type A dissection: Guidance by transesophageal echocardiography. *Interact Cardiovasc Thorac Surg* 2003; **2:** 178–180.
222. Ma H, Xiao Z, Shi J, Liu L, Qin C, Guo Y. Aortic arch cannulation with the guidance of transesophageal echocardiography for Stanford type A aortic dissection. *J Cardiothorac Surg* 2018; **13:** 106.
223. Demertzis S, Casso G, Torre T, Siclari F. Direct epiaortic ultrasound scanning for the rapid confirmation of intraoperative aortic dissection. *Interact Cardiovasc Thorac Surg* 2008; **7:** 725–726.
224. Varghese D, Riedel BJ, Fletcher SN, Al-Momatten MI, Khaghani A. Successful repair of intraoperative aortic dissection detected by transesophageal echocardiography. *Ann Thorac Surg* 2002; **73:** 953–955.
225. Assaad S, Geirsson A, Rousou L, Sherman B, Perrino A. The dual modality use of epiaortic ultrasound and transesophageal echocardiography in the diagnosis of intraoperative iatrogenic type-A aortic dissection. *J Cardiothorac Vasc Anesth* 2013; **27:** 326–328.
226. Orihashi K, Kihara K, Yamamoto M, Nishimori H. Iatrogenic subintimal aortic dissection that disappeared without a trace. *Eur J Cardiothorac Surg* 2017; **52:** 825–826.
227. Orihashi K, Sueda T, Okada K, Imai K. Newly developed aortic dissection in the abdominal aorta after femoral arterial perfusion. *Ann Thorac Surg* 2005; **79:** 1945–1949.
228. Kainuma A, Ihara M, Miyawaki I, Mima H, Koyama T, Yamazaki K. Usefulness of transesophageal echocardiography in guiding acute aortic dissection management during open repair of an abdominal aortic aneurysm. *J Cardiothorac Vasc Anesth* 2016; **30:** 725–728.
229. Gamo M, Goto M, Yazawa R, Hirose Y. Acute aortic dissection detected by transesophageal echocardiography during abdominal aortic aneurysmectomy. *J Anesth* 2007; **21:** 523–524.
230. Wallet F, Perbet S, Fléron MH, De Castro V, Godet G, Bertrand M, et al. Elephant trunk prosthesis kinking: Transesophageal echocardiography diagnosis. *Anesth Analg* 2008; **106:** 67–69.
231. Giuseppe Pino P, Zampi G, Pergolini A, Cao P, Musumeci F. Endovascular aortic repair after elephant trunk: A three-dimensional echocardiography sight. *Eur Heart J Cardiovasc Imaging* 2013; **14:** 836.
232. Hirose N, Orihashi K, Miyashita K, Tashiro M, Kihara K, Yamamoto M. Advantages of transesophageal echocardiography during stent grafting for aortic dissection: A report of three cases. *Ann Vasc Dis* 2018; **11:** 557–561.
233. Yamanaka K, Ishii H. Three-step method for transesophageal echocardiography-guided implantation of the frozen elephant trunk: How to prevent spinal cord injury. *Gen Thorac Cardiovasc Surg* 2019; **67:** 340–343.
234. Orihashi K, Matsuura Y, Sueda T, Watari M, Okada K, Sugawara Y, et al. Echocardiography-assisted surgery in transaortic endovascular stent grafting: Role of transesophageal echocardiography. *J Thorac Cardiovasc Surg* 2000; **120:** 672–678.
235. Inoue H, Morita M, Ota T, Ito J, Uchida H. Thoracic aortic stent migration to false lumen in aortic dissection detected by intraoperative transesophageal echocardiography. *Anesth Analg* 2016; **122:** 963–966.
236. Orihashi K, Tashiro M, Kondo N, Kihara K, Yamamoto M, Wariishi S, et al. Intraoperative migration of open stent graft detected by transesophageal echocardiography: Report of two cases. *Ann Vasc Dis* 2014; **7:** 75–78.
237. Rapezzi C, Rocchi G, Fattori R, Caldarera I, Ferlito M, Napoli G, et al. Usefulness of transesophageal echocardiographic monitoring to improve the outcome of stent-graft treatment of

thoracic aortic aneurysms. *Am J Cardiol* 2001; **87:** 315–319.
238. Rocchi G, Lofiego C, Biagini E, Piva T, Bracchetti G, Lovato L, et al. Transesophageal echocardiography-guided algorithm for stent-graft implantation in aortic dissection. *J Vasc Surg* 2004; **40:** 880–885.
239. Mufty H, Rex S, Fourneau I, Maleux G. Echocardiography-guided false lumen catheterization for "Cheese-Wire" technique in complicated type A aortic dissection. *Ann Vasc Surg* 2019; **56:** 340–344.
240. Kronzon I, Tunick PA, Riles T, Rosen R. Transesophageal echocardiography in intimal flap fenestration. *J Am Soc Echocardiogr* 2001; **14:** 934–936.
241. Yamamoto M, Fukutomi T, Noguchi T, Orihashi K. Distal re-entry closure with neobranching technique after thoracic endovascular aortic repair of Type B aortic dissection. *Eur J Cardiothorac Surg* 2018; **53:** 881–883.
242. Abe S, Ono S, Murata K, Tomochika Y, Kimura K, Fujino T, et al. Usefulness of transesophageal echocardiographic monitoring in transluminal endovascular stent-graft repair for thoracic aortic aneurysm. *Jpn Circ J* 2000; **64:** 960–964.
243. Drelich-Zbroja A, Sojka M, Kuczyńska M, Światłowski Ł, Kuklik E, Sobstyl J, et al. Diagnostic imaging in patients after endovascular aortic aneurysm repair with special focus on ultrasound contrast agents. *Pol Arch Intern Med* 2018; **129:** 80–87.
244. Pecoraro F, Bracale UM, Farina A, Badalamenti G, Ferlito F, Lachat M, et al. Single-center experience and preliminary results of intravascular ultrasound in endovascular aneurysm repair. *Ann Vasc Surg* 2019; **56:** 209–215.
245. Prasad Gaurav KK, Kumar B, Thingnam SKS. Traumatic aortic dissection pseudoaneurysm with multiple entry: Role of transesophageal echocardiography. *Ann Card Anaesth* 2018; **21:** 427–429.
246. Vignon P, Guéret P, Vedrinne JM, Lagrange P, Cornu E, Abrieu O, et al. Role of transesophageal echocardiography in the diagnosis and management of traumatic aortic disruption. *Circulation* 1995; **92:** 2959–2968.
247. Saranteas T, Mavrogenis AF, Mandila C, Poularas J, Panou F. Ultrasound in cardiac trauma. *J Crit Care* 2017; **38:** 144–151.
248. Griffee MJ, Singleton A, Zimmerman JM, Morgan DE, Nirula R. The effect of perioperative rescue transesophageal echocardiography on the management of trauma patients. *A A Case Rep* 2016; **6:** 387–390.
249. Gerstein NS. A word of caution regarding transesophageal echocardiography and penetrating chest trauma. *J Cardiothorac Vasc Anesth* 2012; **26:** e3.
250. Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, et al; Multicentre Aneurysm Screening Study Group. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: A randomised controlled trial. *Lancet* 2002; **360:** 1531–1539.
251. Davis M, Harris M, Earnshaw JJ. Implementation of the national health service abdominal aortic aneurysm screening program in England. *J Vasc Surg* 2013; **57:** 1440–1445.
252. Ali MU, Fitzpatrick-Lewis D, Miller J, Warren R, Kenny M, Sherifali D, et al. Screening for abdominal aortic aneurysm in asymptomatic adults. *J Vasc Surg* 2016; **64:** 1855–1868.
253. Liisberg M, Diederichsen AC, Lindholt JS. Abdominal ultrasound-scanning versus non-contrast computed tomography as screening method for abdominal aortic aneurysm: A validation study from the randomized DANCAVAS study. *BMC Med Imaging* 2017; **17:** 14.
254. Ohlsson H, Gottsäter A, Resch T, Sonesson B, Malina M, Kjellin P, et al. On the complexity of screening detected abdominal aortic aneurysms: A retrospective observational multicenter cohort study. *Int Angiol* 2017; **36:** 261–267.
255. Bennett D, Stewart D, Kearns D, Mairs A, Ellis P. Non-visualized aorta in abdominal aortic aneurysm screening: Screening outcomes and the influence of subject and programme characteristics. *J Med Screen* 2017; **24:** 214–219.
256. Glover MJ, Kim LG, Sweeting MJ, Thompson SG, Buxton MJ. Cost-effectiveness of the national health service abdominal aortic aneurysm screening programme in England. *Br J Surg* 2014; **101:** 976–982.
257. Benson RA, Meecham L, Fisher O, Loftus IM. Ultrasound screening for abdominal aortic aneurysm: Current practice, challenges and controversies. *Br J Radiol* 2018; **91:** 20170306.
258. Corrado G, Durante A, Genchi V, Trabattoni L, Beretta S, Rovelli E, et al. Prevalence of previously undiagnosed abdominal aortic aneurysms in the area of Como: The ComoCuore "looking for AAA" ultrasonography screening. *Int J Cardiovasc Imaging* 2016; **32:** 1213–1217.
259. Canadian Task Force on Preventive Health Care. Recommendations on screening for abdominal aortic aneurysm in primary care. *CMAJ* 2017; **189:** E1137–E1145.
260. Bird AN, Davis AM. Screening for abdominal aortic aneurysm. *JAMA* 2015; **313:** 1156–1157.
261. Linné A, Forsberg J, Lindström D, Ideskog E, Hultgren R. Age at detection of abdominal aortic aneurysms in siblings of patients with abdominal aortic aneurysms. *J Vasc Surg* 2016; **63:** 883–887.
262. Jones GT, Hill BG, Curtis N, Kabir TD, Wong LE, Tilyard MW, et al. Comparison of three targeted approaches to screening for abdominal aortic aneurysm based on cardiovascular risk. *Br J Surg* 2016; **103:** 1139–1146.
263. Argyriou C, Georgiadis GS, Kontopodis N, Pherwani AD, Van Herwaarden JA, Hazenberg CEVB, et al. Screening for abdominal aortic aneurysm during transthoracic echocardiography: A systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2018; **55:** 475–491.
264. Matsumura Y, Wada M, Hirakawa D, Yasuoka Y, Morimoto N, Takeuchi H, et al. Clinical utility of transthoracic echocardiography for screening abdominal aortic aneurysm: A prospective study in a Japanese population. *Cardiovasc Ultrasound* 2016; **14:** 8.
265. Bown MJ, Sutton AJ, Bell PR, Sayers RD. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair. *Br J Surg* 2002; **89:** 714–730.
266. Hoornweg LL, Storm-Versloot MN, Ubbink DT, Koelemay MJ, Legemate DA, Balm R. Meta analysis on mortality of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2008; **35:** 558–570.
267. Thompson SG, Ashton HA, Gao L, Buxton MJ, Scott RA; Multicentre Aneurysm Screening Study (MASS) Group. Final follow-up of the Multicentre Aneurysm Screening Study (MASS) randomized trial of abdominal aortic aneurysm screening. *Br J Surg* 2012; **99:** 1649–1656.
268. Hemminki K, Li X, Johansson SE, Sundquist K, Sundquist J. Familial risks of aortic aneurysms among siblings in a nationwide Swedish study. *Genet Med* 2006; **8:** 43–49.
269. Larsson E, Granath F, Swedenborg J, Hultgren R. A population-based case-control study of the familial risk of abdominal aortic aneurysm. *J Vasc Surg* 2009; **49:** 47–51.
270. Sakalihasan N, Limet R, Defawe OD. Abdominal aortic aneurysm. *Lancet* 2005; **365:** 1577–1589.
271. MacSweeney ST, Ellis M, Worrell PC, Greenhalgh RM, Powell JT. Smoking and growth rate of small abdominal aortic aneurysms. *Lancet* 1994; **344:** 651–652.
272. Wilmink TB, Quick CR, Day NE. The association between cigarette smoking and abdominal aortic aneurysms. *J Vasc Surg* 1999; **30:** 1099–1105.
273. Sode BF, Nordestgaard BG, Grønbæk M, Dahl M. Tobacco smoking and aortic aneurysm: Two population-based studies. *Int J Cardiol* 2013; **167:** 2271–2277.
274. Elefteriades JA. Indications for aortic replacement. *J Thorac Cardiovasc Surg* 2010; **140 Suppl:** S5–S9.
275. Nienaber CA, Eagle KA. Aortic dissection: New frontiers in diagnosis and management: Part II: Therapeutic management and follow-up. *Circulation* 2003; **108:** 772–778.
276. Genoni M, Paul M, Jenni R, Graves K, Seifert B, Turina M. Chronic beta-blocker therapy improves outcome and reduces treatment costs in chronic type B aortic dissection. *Eur J Cardiothorac Surg* 2001; **19:** 606–610.
277. Shores J, Berger KR, Murphy EA, Pyeritz RE. Progression of aortic dilatation and the benefit of long-term beta-adrenergic blockade in Marfan's syndrome. *N Engl J Med* 1994; **330:** 1335–1341.
278. Kokje VB, Hamming JF, Lindeman JH. Editor's choice - Pharmaceutical management of small abdominal aortic aneurysms: A systematic review of the clinical evidence. *Eur J Vasc Endovasc Surg* 2015; **50:** 702–713.
279. Rughani G, Robertson L, Clarke M. Medical treatment for small abdominal aortic aneurysms. *Cochrane Database Syst Rev* 2012: CD009536.
280. Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, et al. The Japanese society of hypertension guidelines for the management of hypertension (JSH 2019). *Hypertens Res* 2019; **42:** 1235–1481.
281. Peters R, Beckett N, Burch L, de Vernejoul MC, Liu L, Duggan

J, et al. The effect of treatment based on a diuretic (indapamide) ± ACE inhibitor (perindopril) on fractures in the Hypertension in the Very Elderly Trial (HYVET). *Age Ageing* 2010; **39:** 609–616.
282. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001; **358:** 1033–1041.
283. Heidenreich PA, McDonald KM, Hastie T, Fadel B, Hagan V, Lee BK, et al. Meta-analysis of trials comparing beta-blockers, calcium antagonists, and nitrates for stable angina. *JAMA* 1999; **281:** 1927–1936.
284. Dargie HJ. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: The CAPRICORN randomised trial. *Lancet* 2001; **357:** 1385–1390.
285. Pfeffer MA, Braunwald E, Moyé LA, Basta L, Brown EJ, Cuddy TE, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: Results of the survival and ventricular enlargement trial. *N Engl J Med* 1992; **327:** 669–677.
286. Køber L, Torp-Pedersen C, Carlsen JE, Bagger H, Eliasen P, Lyngborg K, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 1995; **333:** 1670–1676.
287. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation* 2017; **136:** e137–e161.
288. Ezekowitz JA, McAlister FA. Aldosterone blockade and left ventricular dysfunction: A systematic review of randomized clinical trials. *Eur Heart J* 2009; **30:** 469–477.
289. Wachtell K, Lehto M, Gerdts E, Olsen MH, Hornestam B, Dahlöf B, et al. Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol: The Losartan Intervention For End Point Reduction in Hypertension (LIFE) study. *J Am Coll Cardiol* 2005; **45:** 712–719.
290. Lindholt JS, Henneberg EW, Juul S, Fasting H. Impaired results of a randomised double blinded clinical trial of propranolol versus placebo on the expansion rate of small abdominal aortic aneurysms. *Int Angiol* 1999; **18:** 52–57.
291. Nishimura K, Okamura T, Watanabe M, Nakai M, Takegami M, Higashiyama A, et al. Predicting coronary heart disease using risk factor categories for a Japanese urban population, and comparison with the Framingham risk score: The Suita study. *J Atheroscler Thromb* 2016; **23:** 1138–1139.
292. Imamura T, Doi Y, Arima H, Yonemoto K, Hata J, Kubo M, et al. LDL cholesterol and the development of stroke subtypes and coronary heart disease in a general Japanese population: The Hisayama study. *Stroke* 2009; **40:** 382–388.
293. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2019; **139:** e1082–e1143.
294. Kinoshita M, Yokote K, Arai H, Iida M, Ishigaki Y, Ishibashi S, et al. Japan Atherosclerosis Society (JAS) guidelines for prevention of atherosclerotic cardiovascular diseases 2017. *J Atheroscler Thromb* 2018; **25:** 846–984.
295. Grundy SM, Stone NJ. 2018 American Heart Association/American College of Cardiology/Multisociety guideline on the management of blood cholesterol-secondary prevention. *JAMA Cardiol* 2019; **4:** 589–591.
296. Takagi H, Yamamoto H, Iwata K, Goto S, Umemoto T; ALICE (All-Literature Investigation of Cardiovascular Evidence) Group. Effects of statin therapy on abdominal aortic aneurysm growth: A meta-analysis and meta-regression of observational comparative studies. *Eur J Vasc Endovasc Surg* 2012; **44:** 287–292.
297. Jovin IS, Duggal M, Ebisu K, Paek H, Oprea AD, Tranquilli M, et al. Comparison of the effect on long-term outcomes in patients with thoracic aortic aneurysms of taking versus not taking a statin drug. *Am J Cardiol* 2012; **109:** 1050–1054.
298. Twine CP, Williams IM. Systematic review and meta-analysis of the effects of statin therapy on abdominal aortic aneurysms. *Br J Surg* 2011; **98:** 346–353.
299. Tazaki J, Morimoto T, Sakata R, Okabayashi H, Yamazaki F, Nishiwaki N, et al; CREDO-Kyoto PCI/CABG registry cohort-2 investigators. Impact of statin therapy on patients with coronary heart disease and aortic aneurysm or dissection. *J Vasc Surg* 2014; **60:** 604–612.
300. Sato T, Arakawa M, Tashima Y, Tsuboi E, Burdon G, Trojan J, et al. Statins reduce thoracic aortic aneurysm growth in Marfan syndrome mice via inhibition of the ras-induced ERK (Extracellular Signal-Regulated Kinase) signaling pathway. *J Am Heart Assoc* 2018; **7:** e008543.
301. McLoughlin D, McGuinness J, Byrne J, Terzo E, Huuskonen V, McAllister H, et al. Pravastatin reduces Marfan aortic dilation. *Circulation* 2011; **124 Suppl:** S168–S173.
302. Dawson JA, Choke E, Loftus IM, Cockerill GW, Thompson MM. A randomised placebo-controlled double-blind trial to evaluate lipid-lowering pharmacotherapy on proteolysis and inflammation in abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2011; **41:** 28–35.
303. Raffort J, Lareyre F, Clément M, Hassen-Khodja R, Chinetti G, Mallat Z. Diabetes and aortic aneurysm: Current state of the art. *Cardiovasc Res* 2018; **114:** 1702–1713.
304. 日本糖尿病学会編. 糖尿病治療ガイド2018–2019. [in Japanese] 文光堂, 2018.
305. Brady AR, Thompson SG, Fowkes FG, Greenhalgh RM, Powell JT; UK Small Aneurysm Trial Participants. Abdominal aortic aneurysm expansion: Risk factors and time intervals for surveillance. *Circulation* 2004; **110:** 16–21.
306. Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Makaroun MS, et al. The aneurysm detection and management study screening program: Validation cohort and final results. *Arch Intern Med* 2000; **160:** 1425–1430.
307. Kent KC, Zwolak RM, Egorova NN, Riles TS, Manganaro A, Moskowitz AJ, et al. Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. *J Vasc Surg* 2010; **52:** 539–548.
308. Forsdahl SH, Singh K, Solberg S, Jacobsen BK. Risk factors for abdominal aortic aneurysms: A 7-year prospective study: The Tromsø Study, 1994–2001. *Circulation* 2009; **119:** 2202–2208.
309. Cornuz J, Sidoti Pinto C, Tevaearai H, Egger M. Risk factors for asymptomatic abdominal aortic aneurysm: Systematic review and meta-analysis of population-based screening studies. *Eur J Public Health* 2004; **14:** 343–349.
310. Kihara T, Yamagishi K, Iso H, Tamakoshi A; JACC Study Group. Passive smoking and mortality from aortic dissection or aneurysm. *Atherosclerosis* 2017; **263:** 145–150.
311. Sweeting MJ, Thompson SG, Brown LC, Powell JT, Thompson SG; RESCAN collaborators. Meta-analysis of individual patient data to examine factors affecting growth and rupture of small abdominal aortic aneurysms. *Br J Surg* 2012; **99:** 655–665.
312. Hartmann-Boyce J, Aveyard P. Drugs for smoking cessation. *BMJ* 2016; **352:** i571.
313. LeFevre ML, LeFevre ML. Screening for abdominal aortic aneurysm: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2014; **161:** 281–290.
314. Arinze N, Farber A, Levin SR, Cheng TW, Jones DW, Siracuse CG, et al. The effect of the duration of preoperative smoking cessation timing on outcomes after elective open abdominal aortic aneurysm repair and lower extremity bypass. *J Vasc Surg* 2019; **70:** 1851–1861.
315. Chaikof EL, Dalman RL, Eskandari MK, Jackson BM, Lee WA, Mansour MA, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. *J Vasc Surg* 2018; **67:** 2–77.
316. Lederle FA, Kyriakides TC, Stroupe KT, Freischlag JA, Padberg FT, Matsumura JS, et al; OVER Veterans Affairs Cooperative Study Group. Open versus endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2019; **380:** 2126–2135.
317. Patel R, Sweeting MJ, Powell JT, Greenhalgh RM; EVAR trial investigators. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): A randomised controlled trial. *Lancet* 2016; **388:** 2366–2374.
318. Orr NT, Davenport DL, Minion DJ, Xenos ES. Comparison of perioperative outcomes in endovascular versus open repair for juxtarenal and pararenal aortic aneurysms: A propensity-matched analysis. *Vascular* 2017; **25:** 339–345.
319. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ,

Polanczyk CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; **100:** 1043–1049.
320. Gupta PK, Gupta H, Sundaram A, Kaushik M, Fang X, Miller WJ, et al. Development and validation of a risk calculator for prediction of cardiac risk after surgery. *Circulation* 2011; **124:** 381–387.
321. Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's choice - European Society for Vascular Surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg* 2019; **57:** 8–93.
322. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; **130:** 2215–2245.
323. Kristensen SD, Knuuti J. New ESC/ESA guidelines on noncardiac surgery: Cardiovascular assessment and management. *Eur Heart J* 2014; **35:** 2344–2345.
324. Allen LA, Stevenson LW, Grady KL, Goldstein NE, Matlock DD, Arnold RM, et al. Decision making in advanced heart failure: A scientific statement from the American Heart Association. *Circulation* 2012; **125:** 1928–1952.
325. Lancellotti P. Grading aortic stenosis severity when the flow modifies the gradientvalve area correlation. *Cardiovasc Diagn Ther* 2012; **2:** 6–9.
326. McFalls EO, Ward HB, Moritz TE, Goldman S, Krupski WC, Littooy F, et al. Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med* 2004; **351:** 2795–2804.
327. Devereaux PJ, Chan MT, Alonso-Coello P, Walsh M, Berwanger O, Villar JC, et al; Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) Study Investigators. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012; **307:** 2295–2304.
328. Karkos CD. What is appropriate coronary assessment prior to abdominal aortic surgery? *Eur J Vasc Endovasc Surg* 2003; **25:** 487–492.
329. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; **130:** e278–e333.
330. Kurvers HA, van der Graaf Y, Blankensteijn JD, Visseren FL, Eikelboom B; SMART Study Group. Screening for asymptomatic internal carotid artery stenosis and aneurysm of the abdominal aorta: Comparing the yield between patients with manifest atherosclerosis and patients with risk factors for atherosclerosis only. *J Vasc Surg* 2003; **37:** 1226–1233.
331. Liapis CD, Kakisis JD, Dimitroulis DA, Daskalopoulos M, Nikolaou A, Kostakis AG. Carotid ultrasound findings as a predictor of long-term survival after abdominal aortic aneurysm repair: A 14-year prospective study. *J Vasc Surg* 2003; **38:** 1220–1225.
332. Jonas DE, Feltner C, Amick HR, Sheridan S, Zheng ZJ, Watford DJ, et al. Screening for asymptomatic carotid artery stenosis: A systematic review and meta-analysis for the U.S. Preventive Services Task Force. *Ann Intern Med* 2014; **161:** 336–346.
333. Naylor AR, Ricco JB, de Borst GJ, Debus S, de Haro J, Halliday A, et al. Editor's choice - Management of atherosclerotic carotid and vertebral artery disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2018; **55:** 3–81.
334. Baxter BT, Pearce WH, Waltke EA, Littooy FN, Hallett JW, Kent KC, et al. Prolonged administration of doxycycline in patients with small asymptomatic abdominal aortic aneurysms: Report of a prospective (Phase II) multicenter study. *J Vasc Surg* 2002; **36:** 1–12.
335. Meijer CA, Stijnen T, Wasser MN, Hamming JF, van Bockel JH, Lindeman JH; Pharmaceutical Aneurysm Stabilisation Trial Study Group. Doxycycline for stabilization of abdominal aortic aneurysms: A randomized trial. *Ann Intern Med* 2013; **159:** 815–823.
336. Daneman N, Lu H, Redelmeier DA. Fluoroquinolones and collagen associated severe adverse events: A longitudinal cohort study. *BMJ Open* 2015; **5:** e010077.
337. Pasternak B, Inghammar M, Svanström H. Fluoroquinolone use and risk of aortic aneurysm and dissection: Nationwide cohort study. *BMJ* 2018; **360:** k678.
338. Lee CC, Lee MG, Hsieh R, Porta L, Lee WC, Lee SH, et al. Oral fluoroquinolone and the risk of aortic dissection. *J Am Coll Cardiol* 2018; **72:** 1369–1378.
339. Fillinger MF, Greenberg RK, McKinsey JF, Chaikof EL; Society for Vascular Surgery Ad Hoc Committee on TEVAR Reporting Standards. Reporting standards for thoracic endovascular aortic repair (TEVAR). *J Vasc Surg* 2010; **52:** 1022–1033.
340. Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al; Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of The Society for Vascular Surgery/American Association for Vascular Surgery. Reporting standards for endovascular aortic aneurysm repair. *J Vasc Surg* 2002; **35:** 1048–1060.
341. Biancari F, Mariscalco G, Mariani S, Saari P, Satta J, Juvonen T. Endovascular treatment of degenerative aneurysms involving only the descending thoracic aorta: Systematic review and meta-analysis. *J Endovasc Ther* 2016; **23:** 387–392.
342. Zhang L, Zhao Z, Chen Y, Sun Y, Bao J, Jing Z, et al. Reintervention after endovascular repair for aortic dissection: A systematic review and meta-analysis. *J Thorac Cardiovasc Surg* 2016; **152:** 1279–1288.
343. Kouvelos GN, Oikonomou K, Antoniou GA, Verhoeven EL, Katsargyris A. A systematic review of proximal neck dilatation after endovascular repair for abdominal aortic aneurysm. *J Endovasc Ther* 2017; **24:** 59–67.
344. Mangialardi N, Orrico M, Ronchey S, Praquin B, Alberti V, Setacci C. Towards an entirely endovascular aortic world: An update of techniques and outcomes for endovascular and open treatment of type I, II, and III endoleaks. *J Cardiovasc Surg (Torino)* 2016; **57:** 698–711.
345. Perini P, Bianchini Massoni C, Mariani E, Ucci A, Fanelli M, Azzarone M, et al. Systematic review and meta-analysis of the outcome of different treatments for type 1a endoleak after EVAR. *Ann Vasc Surg* 2019; **60:** 435–446.
346. Spanos K, Rohlffs F, Panuccio G, Eleshra A, Tsilimparis N, Kölbel T. Outcomes of endovascular treatment of endoleak type Ia after EVAR: A systematic review of the literature. *J Cardiovasc Surg (Torino)* 2019; **60:** 175–185.
347. Bianchini Massoni C, Perini P, Tecchio T, Azzarone M, de Troia A, Freyrie A. A systematic review of treatment modalities and outcomes of type Ib endoleak after endovascular abdominal aneurysm repair. *Vascular* 2018; **26:** 90–98.
348. Ultee KHJ, Büttner S, Huurman R, Bastos Gonçalves F, Hoeks SE, Bramer WM, et al. Editor's choice - Systematic review and meta-analysis of the outcome of treatment for type II endoleak following endovascular aneurysm repair. *Eur J Vasc Endovasc Surg* 2018; **56:** 794–807.
349. Jonker FH, Verhagen HJ, Lin PH, Heijmen RH, Trimarchi S, Lee WA, et al. Open surgery versus endovascular repair of ruptured thoracic aortic aneurysms. *J Vasc Surg* 2011; **53:** 1210–1216.
350. Yamaguchi T, Nakai M, Sumita Y, Nishimura K, Tazaki J, Kyuragi R, et al. Editor's choice - Endovascular repair versus surgical repair for Japanese patients with ruptured thoracic and abdominal aortic aneurysms: A nationwide study. *Eur J Vasc Endovasc Surg* 2019; **57:** 779–786.
351. Gopaldas RR, Dao TK, LeMaire SA, Huh J, Coselli JS. Endovascular versus open repair of ruptured descending thoracic aortic aneurysms: A nationwide risk-adjusted study of 923 patients. *J Thorac Cardiovasc Surg* 2011; **142:** 1010–1018.
352. Jonker FH, Trimarchi S, Verhagen HJ, Moll FL, Sumpio BE, Muhs BE. Meta-analysis of open versus endovascular repair for ruptured descending thoracic aortic aneurysm. *J Vasc Surg* 2010; **51:** 1026–1032.
353. Etienne H, Majewski M, Cochennec F, Segaux L, Becquemin JP. Emergency endovascular interventions for ruptured descending thoracic aortic aneurysm. *Ann Vasc Surg* 2017; **39:** 160–166.
354. Pang D, Hildebrand D, Bachoo P. Thoracic endovascular repair (TEVAR) versus open surgery for blunt traumatic thoracic aortic injury. *Cochrane Database Syst Rev* 2019: CD006642.
355. van der Zee CP, Vainas T, van Brussel FA, Tielliu IF, Zeebregts CJ, van der Laan MJ. Endovascular treatment of traumatic

thoracic aortic lesions: A systematic review and meta-analysis. *J Cardiovasc Surg (Torino)* 2019; **60:** 100–110.
356. Ho XN, Wee IJ, Syn N, Harrison M, Wilson L, Choong AM. The endovascular repair of blunt traumatic thoracic aortic injury in Asia: A systematic review and meta-analysis. *Vascular* 2019; **27:** 213–223.
357. Steuer J, Björck M, Sonesson B, Resch T, Dias N, Hultgren R, et al. Editor's choice – Durability of endovascular repair in blunt traumatic thoracic aortic injury: Long-term outcome from four tertiary referral centers. *Eur J Vasc Endovasc Surg* 2015; **50:** 460–465.
358. Grigorian A, Spencer D, Donayre C, Nahmias J, Schubl S, Gabriel V, et al. National trends of thoracic endovascular aortic repair versus open repair in blunt thoracic aortic injury. *Ann Vasc Surg* 2018; **52:** 72–78.
359. Harky A, Bleetman D, Chan JSK, Eriksen P, Chaplin G, MacCarthy-Ofosu B, et al. A systematic review and meta-analysis of endovascular versus open surgical repair for the traumatic ruptured thoracic aorta. *J Vasc Surg* 2020; **71:** 270–282.
360. Walsh SR, Tang TY, Sadat U, Naik J, Gaunt ME, Boyle JR, et al. Endovascular stenting versus open surgery for thoracic aortic disease: Systematic review and meta-analysis of perioperative results. *J Vasc Surg* 2008; **47:** 1094–1098.
361. Cheng D, Martin J, Shennib H, Dunning J, Muneretto C, Schueler S, et al. Endovascular aortic repair versus open surgical repair for descending thoracic aortic disease a systematic review and meta-analysis of comparative studies. *J Am Coll Cardiol* 2010; **55:** 986–1001.
362. Abraha I, Romagnoli C, Montedori A, Cirocchi R. Thoracic stent graft versus surgery for thoracic aneurysm. *Cochrane Database Syst Rev* 2016: CD006796.
363. Harky A, Kai Chan JS, Ming Wong CH, Bashir M. Open versus endovascular repair of descending thoracic aortic aneurysm disease: A systematic review and meta-analysis. *Ann Vasc Surg* 2019; **54:** 304–315.
364. Goodney PP, Travis L, Lucas FL, Fillinger MF, Goodman DC, Cronenwett JL, et al. Survival after open versus endovascular thoracic aortic aneurysm repair in an observational study of the medicare population. *Circulation* 2011; **124:** 2661–2669.
365. Coady MA, Ikonomidis JS, Cheung AT, Matsumoto AH, Dake MD, Chaikof EL, et al. Surgical management of descending thoracic aortic disease: Open and endovascular approaches: A scientific statement from the American Heart Association. *Circulation* 2010; **121:** 2780–2804.
366. Wong CS, Healy D, Canning C, Coffey JC, Boyle JR, Walsh SR. A systematic review of spinal cord injury and cerebrospinal fluid drainage after thoracic aortic endografting. *J Vasc Surg* 2012; **56:** 1438–1447.
367. Awad H, Ramadan ME, El Sayed HF, Tolpin DA, Tili E, Collard CD. Spinal cord injury after thoracic endovascular aortic aneurysm repair. *Can J Anaesth* 2017; **64:** 1218–1235.
368. Miranda V, Sousa J, Mansilha A. Spinal cord injury in endovascular thoracoabdominal aortic aneurysm repair: Prevalence, risk factors and preventive strategies. *Int Angiol* 2018; **37:** 112–126.
369. Rong LQ, Kamel MK, Rahouma M, White RS, Lichtman AD, Pryor KO, et al. Cerebrospinal-fluid drain-related complications in patients undergoing open and endovascular repairs of thoracic and thoraco-abdominal aortic pathologies: A systematic review and meta-analysis. *Br J Anaesth* 2018; **120:** 904–913.
370. Amabile P, Grisoli D, Giorgi R, Bartoli JM, Piquet P. Incidence and determinants of spinal cord ischaemia in stent-graft repair of the thoracic aorta. *Eur J Vasc Endovasc Surg* 2008; **35:** 455–461.
371. Schlösser FJ, Verhagen HJ, Lin PH, Verhoeven EL, van Herwaarden JA, Moll FL, et al. TEVAR following prior abdominal aortic aneurysm surgery: Increased risk of neurological deficit. *J Vasc Surg* 2009; **49:** 308–314.
372. Belczak SQ, Silva ES, Klajner R, Puech-Leão P, De Luccia N. Type II endoleaks, left-arm complications, and need of revascularization after left subclavian artery coverage for thoracic aortic aneurysms endovascular repair: A systematic review. *Ann Vasc Surg* 2017; **41:** 294–299.
373. Huang Q, Chen XM, Yang H, Lin QN, Qin X. Effect of left subclavian artery revascularisation in thoracic endovascular aortic repair: A systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2018; **56:** 644–651.
374. Ferrer C, Cao P, De Rango P, Tshomba Y, Verzini F, Melissano G, et al. A propensity-matched comparison for endovascular and open repair of thoracoabdominal aortic aneurysms. *J Vasc Surg* 2016; **63:** 1201–1207.
375. Hu Z, Li Y, Peng R, Liu J, Jia X, Liu X, et al. Multibranched stent-grafts for the treatment of thoracoabdominal aortic aneurysms: A systematic review and meta-analysis. *J Endovasc Ther* 2016; **23:** 626–633.
376. Spanos K, Tsilimparis N, Rohlffs F, Wipper S, Detter C, Behrendt CA, et al. Total endovascular arch repair is the procedure of the future. *J Cardiovasc Surg (Torino)* 2018; **59:** 559–571.
377. Ferrer C, Cao P, Coscarella C, Ferri M, Lovato L, Camparini S, et al; TRIUmPH Registry Investigators. iTalian RegIstry of doUble inner branch stent graft for arch PatHology (the TRIUmPH Registry). *J Vasc Surg* 2019; **70:** 672–682.
378. Rocha RV, Friedrich JO, Elbatarny M, Yanagawa B, Al-Omran M, Forbes TL, et al. A systematic review and meta-analysis of early outcomes after endovascular versus open repair of thoracoabdominal aortic aneurysms. *J Vasc Surg* 2018; **68:** 1936–1945.
379. Antoniou GA, El Sakka K, Hamady M, Wolfe JH. Hybrid treatment of complex aortic arch disease with supra-aortic debranching and endovascular stent graft repair. *Eur J Vasc Endovasc Surg* 2010; **39:** 683–690.
380. Moulakakis KG, Mylonas SN, Markatis F, Kotsis T, Kakisis J, Liapis CD. A systematic review and meta-analysis of hybrid aortic arch replacement. *Ann Cardiothorac Surg* 2013; **2:** 247–260.
381. Carter R, Wee IJY, Petrie K, Syn N, Choong AM. Chimney parallel grafts and thoracic endovascular aortic repair for blunt traumatic thoracic aortic injuries: A systematic review. *Vascular* 2019; **27:** 204–212.
382. Chakos A, Jbara D, Yan TD, Tian DH. Long-term survival and related outcomes for hybrid versus traditional arch repair-a meta-analysis. *Ann Cardiothorac Surg* 2018; **7:** 319–327.
383. Glorion M, Coscas R, McWilliams RG, Javerliat I, Goëau-Brissonniere O, Coggia M. A comprehensive review of in situ fenestration of aortic endografts. *Eur J Vasc Endovasc Surg* 2016; **52:** 787–800.
384. Svensson LG, Kouchoukos NT, Miller DC, Bavaria JE, Coselli JS, Curi MA, et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. *Ann Thorac Surg* 2008; **85 Suppl:** S1–S41.
385. Mussa FF, Horton JD, Moridzadeh R, Nicholson J, Trimarchi S, Eagle KA. Acute aortic dissection and intramural hematoma: A systematic review. *JAMA* 2016; **316:** 754–763.
386. Harky A, Chan JSK, Wong CHM, Francis N, Grafton-Clarke C, Bashir M. Systematic review and meta-analysis of acute type B thoracic aortic dissection, open, or endovascular repair. *J Vasc Surg* 2019; **69:** 1599–1609.
387. Li L, Jiao Y, Zou J, Zhang X, Yang H, Ma H. Thoracic endovascular aortic repair versus best medical treatment for high-risk type B intramural hematoma: A systematic review of clinical studies. *Ann Vasc Surg* 2018; **52:** 273–279.
388. Muetterties CE, Menon R, Wheatley GH. A systematic review of primary endovascular repair of the ascending aorta. *J Vasc Surg* 2018; **67:** 332–342.
389. Nienaber CA, Sakalihasan N, Clough RE, Aboukoura M, Mancuso E, Yeh JS, et al. Thoracic endovascular aortic repair (TEVAR) in proximal (type A) aortic dissection: Ready for a broader application? *J Thorac Cardiovasc Surg* 2017; **153:** S3–S11.
390. Luebke T, Brunkwall J. Type B aortic dissection: A review of prognostic factors and meta-analysis of treatment options. *Aorta (Stamford)* 2014; **2:** 265–278.
391. Famularo M, Meyermann K, Lombardi JV. Aneurysmal degeneration of type B aortic dissections after thoracic endovascular aortic repair: A systematic review. *J Vasc Surg* 2017; **66:** 924–930.
392. Krol E, Panneton JM. Uncomplicated acute type B aortic dissection: Selection guidelines for TEVAR. *Ann Vasc Dis* 2017; **10:** 165–169.
393. Iannuzzi JC, Stapleton SM, Bababekov YJ, Chang D, Lancaster RT, Conrad MF, et al. Favorable impact of thoracic endovascular aortic repair on survival of patients with acute uncomplicated type B aortic dissection. *J Vasc Surg* 2018; **68:** 1649–1655.
394. Yuan X, Mitsis A, Ghonem M, Iakovakis I, Nienaber CA. Conservative management versus endovascular or open surgery in the spectrum of type B aortic dissection. *J Vis Surg* 2018; **4:** 59.
395. Wang GJ, Cambria RP, Lombardi JV, Azizzadeh A, White RA, Abel DB, et al. Thirty-day outcomes from the Society for

Vascular Surgery Vascular Quality Initiative thoracic endovascular aortic repair for type B dissection project. *J Vasc Surg* 2019; **69:** 680–691.
396. Kato M, Bai H, Sato K, Kawamoto S, Kaneko M, Ueda T, et al. Determining surgical indications for acute type B dissection based on enlargement of aortic diameter during the chronic phase. *Circulation* 1995; **92 Suppl:** II107–II112.
397. Marui A, Mochizuki T, Mitsui N, Koyama T, Kimura F, Horibe M. Toward the best treatment for uncomplicated patients with type B acute aortic dissection: A consideration for sound surgical indication. *Circulation* 1999; **100 Suppl:** II275–II280.
398. van Bogerijen GH, Tolenaar JL, Rampoldi V, Moll FL, van Herwaarden JA, Jonker FH, et al. Predictors of aortic growth in uncomplicated type B aortic dissection. *J Vasc Surg* 2014; **59:** 1134–1143.
399. Reutersberg B, Trenner M, Haller B, Geisbüsch S, Reeps C, Eckstein HH. The incidence of delayed complications in acute type B aortic dissections is underestimated. *J Vasc Surg* 2018; **68:** 356–363.
400. Spinelli D, Benedetto F, Donato R, Piffaretti G, Marrocco-Trischitta MM, Patel HJ, et al. Current evidence in predictors of aortic growth and events in acute type B aortic dissection. *J Vasc Surg* 2018; **68:** 1925–1935.
401. Stanford aortic dissection risk calculator. Available at: http://web.stanford.edu/group/3dq/cgi-bin/typeb-aortic-dissection-and-risk-calculator/calc-absolute/index.html (accessed July 31, 2020).
402. Tian DH, De Silva RP, Wang T, Yan TD. Open surgical repair for chronic type B aortic dissection: A systematic review. *Ann Cardiothorac Surg* 2014; **3:** 340–350.
403. Kamman AV, de Beaufort HW, van Bogerijen GH, Nauta FJ, Heijmen RH, Moll FL, et al. Contemporary management strategies for chronic type B aortic dissections: A systematic review. *PLoS One* 2016; **11:** e0154930.
404. Boufi M, Patterson BO, Grima MJ, Karthikesalingam A, Hudda MT, Holt PJ, et al. Systematic review of reintervention after thoracic endovascular repair for chronic type B dissection. *Ann Thorac Surg* 2017; **103:** 1992–2004.
405. Boufi M, Patterson BO, Loundou AD, Boyer L, Grima MJ, Loftus IM, et al. Endovascular versus open repair for chronic type B dissection treatment: A meta-analysis. *Ann Thorac Surg* 2019; **107:** 1559–1570.
406. Canaud L, Ozdemir BA, Bee WW, Bahia S, Holt P, Thompson M. Thoracic endovascular aortic repair in management of aortoesophageal fistulas. *J Vasc Surg* 2014; **59:** 248–254.
407. Kanaoka Y, Ohki T, Maeda K, Baba T, Fujita T. Multivariate analysis of risk factors of cerebral infarction in 439 patients undergoing thoracic endovascular aneurysm repair. *Medicine (Baltimore)* 2016; **95:** e3335.
408. Huang WH, He PC, Luo JF, Liu Y, Chen JY, Tan N, et al. A randomized controlled trial of rapid artificial cardiac pacing in thoracic endovascular aortic repair. [Article in Chinese] *Zhonghua Yi Xue Za Zhi* 2011; **91:** 1668–1672.
409. Chen J, Huang W, Luo S, Yang D, Xu Z, Luo J. Application of rapid artificial cardiac pacing in thoracic endovascular aortic repair in aged patients. *Clin Interv Aging* 2014; **9:** 73–78.
410. 日本ステントグラフト実施基準管理委員会. 胸部大動脈瘤ステントグラフト治療成績 (治療実施期間：2016年1月1日～12月31日). [in Japanese] Available at: http://stentgraft.jp/pro/result/pirnt/JACSM2016_1.pdf (accessed July 31, 2020).
411. Nienaber JJ, Duncan AA, Oderich GS, Pruthi RK, Nichols WL. Operative and nonoperative management of chronic disseminated intravascular coagulation due to persistent aortic endoleak. *J Vasc Surg* 2014; **59:** 1426–1429.
412. Kanaoka Y, Ohki T, Maeda K, Baba T. Analysis of risk factors for early type I endoleaks after thoracic endovascular aneurysm repair. *J Endovasc Ther* 2017; **24:** 89–96.
413. Kudo T, Kuratani T, Shimamura K, Sakamoto T, Kin K, Masada K, et al. Type 1a endoleak following Zone 1 and Zone 2 thoracic endovascular aortic repair: Effect of bird-beak configuration. *Eur J Cardiothorac Surg* 2017; **52:** 718–724.
414. von Allmen RS, Gahl B, Powell JT. Editor's choice - Incidence of stroke following thoracic endovascular aortic repair for descending aortic aneurysm: A systematic review of the literature with meta-analysis. *Eur J Vasc Endovasc Surg* 2017; **53:** 176–184.
415. Spanos K, Kellert L, Rantner B, Banafsche R, Tsilimparis N. The importance of definitions and reporting standards for cerebrovascular events after thoracic endovascular aortic repair. *J Endovasc Ther* 2018; **25:** 737–739.
416. Canaud L, Ozdemir BA, Patterson BO, Holt PJ, Loftus IM, Thompson MM. Retrograde aortic dissection after thoracic endovascular aortic repair. *Ann Surg* 2014; **260:** 389–395.
417. Chen Y, Zhang S, Liu L, Lu Q, Zhang T, Jing Z. Retrograde type A aortic dissection after thoracic endovascular aortic repair: A systematic review and meta-analysis. *J Am Heart Assoc* 2017; **6:** e004649.
418. Perera AH, Riga CV, Monzon L, Gibbs RG, Bicknell CD, Hamady M. Robotic arch catheter placement reduces cerebral embolization during Thoracic Endovascular Aortic Repair (TEVAR). *Eur J Vasc Endovasc Surg* 2017; **53:** 362–369.
419. Gandet T, Canaud L, Ozdemir BA, Ziza V, Demaria R, Albat B, et al. Factors favoring retrograde aortic dissection after endovascular aortic arch repair. *J Thorac Cardiovasc Surg* 2015; **150:** 136–142.
420. Grover G, Perera AH, Hamady M, Rudarakanchana N, Barras CD, Singh A, et al. Cerebral embolic protection in thoracic endovascular aortic repair. *J Vasc Surg* 2018; **68:** 1656–1666.
421. Sueda T, Takahashi S. Spinal cord injury as a complication of thoracic endovascular aneurysm repair. *Surg Today* 2018; **48:** 473–477.
422. Hosaka A, Motoki M, Kato M, Sugai H, Okubo N. Quantification of aortic shagginess as a predictive factor of perioperative stroke and long-term prognosis after endovascular treatment of aortic arch disease. *J Vasc Surg* 2019; **69:** 15–23.
423. Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al; ACE trialists. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *J Vasc Surg* 2011; **53:** 1167–1173.
424. Dangas G, O'Connor D, Firwana B, Brar S, Ellozy S, Vouyouka A, et al. Open versus endovascular stent graft repair of abdominal aortic aneurysms: A meta-analysis of randomized trials. *JACC Cardiovasc Interv* 2012; **5:** 1071–1080.
425. EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): Randomised controlled trial. *Lancet* 2005; **365:** 2179–2186.
426. Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, et al; Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004; **351:** 1607–1618.
427. Blankensteijn JD, de Jong SE, Prinssen M, van der Ham AC, Buth J, van Sterkenburg SM, et al; Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2005; **352:** 2398–2405.
428. Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT, Matsumura JS, Kohler TR, et al; Open Versus Endovascular Repair (OVER) Veterans Affairs Cooperative Study Group. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: A randomized trial. *JAMA* 2009; **302:** 1535–1542.
429. Chen ZG, Tan SP, Diao YP, Wu ZY, Miao YQ, Li YJ. The long-term outcomes of open and endovascular repair for abdominal aortic aneurysm: A meta-analysis. *Asian J Surg* 2019; **42:** 899–906.
430. Schermerhorn ML, Buck DB, O'Malley AJ, Curran T, McCallum JC, Darling J, et al. Long-term outcomes of abdominal aortic aneurysm in the medicare population. *N Engl J Med* 2015; **373:** 328–338.
431. van Schaik TG, Yeung KK, Verhagen HJ, de Bruin JL, van Sambeek MRHM, Balm R, et al; DREAM trial participants. Long-term survival and secondary procedures after open or endovascular repair of abdominal aortic aneurysms. *J Vasc Surg* 2017; **66:** 1379–1389.
432. Powell JT, Sweeting MJ, Ulug P, Blankensteijn JD, Lederle FA, Becquemin JP, et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *Br J Surg* 2017; **104:** 166–178.
433. Bulder RMA, Bastiaannet E, Hamming JF, Lindeman JHN. Meta-analysis of long-term survival after elective endovascular or open repair of abdominal aortic aneurysm. *Br J Surg* 2019; **106:** 523–533.
434. Li B, Khan S, Salata K, Hussain MA, de Mestral C, Greco E, et al. A systematic review and meta-analysis of the long-term outcomes of endovascular versus open repair of abdominal

aortic aneurysm. *J Vasc Surg* 2019; **70:** 954–969.
435. Stather PW, Sidloff D, Dattani N, Choke E, Bown MJ, Sayers RD. Systematic review and meta-analysis of the early and late outcomes of open and endovascular repair of abdominal aortic aneurysm. *Br J Surg* 2013; **100:** 863–872.
436. Kontopodis N, Antoniou SA, Georgakarakos E, Ioannou CV. Endovascular vs open aneurysm repair in the young: Systematic review and meta-analysis. *J Endovasc Ther* 2015; **22:** 897–904.
437. EVAR trial participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): Randomised controlled trial. *Lancet* 2005; **365:** 2187–2192.
438. Patel R, Powell JT, Sweeting MJ, Epstein DM, Barrett JK, Greenhalgh RM. The UK EndoVascular Aneurysm Repair (EVAR) randomised controlled trials: Long-term follow-up and cost-effectiveness analysis. *Health Technol Assess* 2018; **22:** 1–132.
439. Brown LC, Greenhalgh RM, Thompson SG, Powell JT; EVAR Trial Participants. Does EVAR alter the rate of cardiovascular events in patients with abdominal aortic aneurysm considered unfit for open repair?: Results from the randomised EVAR trial 2. *Eur J Vasc Endovasc Surg* 2010; **39:** 396–402.
440. Hoshina K, Ishimaru S, Sasabuchi Y, Yasunaga H, Komori K; Japan Committee for Stentgraft Management (JACSM). Outcomes of endovascular repair for abdominal aortic aneurysms: A nationwide survey in Japan. *Ann Surg* 2019; **269:** 564–573.
441. Oliveira-Pinto J, Oliveira N, Bastos-Gonçalves F, Hoeks S, VAN Rijn MJ, Ten Raa S, et al. Long-term results of outside "instructions for use" EVAR. *J Cardiovasc Surg (Torino)* 2017; **58:** 252–260.
442. van Noort K, Boersen JT, Zoethout AC, Schuurmann RCL, Heyligers JMM, Reijnen MMPJ, et al; DEVASS (Dutch Endovascular Aneurysm Sealing Study) Group. Anatomical predictors of endoleaks or migration after endovascular aneurysm sealing. *J Endovasc Ther* 2018; **25:** 719–725.
443. Goudeketting SR, Fung Kon Jin PHP, Ünlü Ç, de Vries JPM. Systematic review and meta-analysis of elective and urgent late open conversion after failed endovascular aneurysm repair. *J Vasc Surg* 2019; **70:** 615–628.
444. Patel SR, Allen C, Grima MJ, Brownrigg JRW, Patterson BO, Holt PJE, et al. A systematic review of predictors of reintervention after EVAR: Guidance for risk-stratified surveillance. *Vasc Endovascular Surg* 2017; **51:** 417–428.
445. Hicks CW, Canner JK, Arhuidese I, Obeid T, Black JH, Malas MB. Comprehensive assessment of factors associated with in-hospital mortality after elective abdominal aortic aneurysm repair. *JAMA Surg* 2016; **151:** 838–845.
446. Zacharias N, Warner CJ, Taggert JB, Roddy SP, Kreienberg PB, Ozsvath KJ, et al. Anatomic characteristics of abdominal aortic aneurysms presenting with delayed rupture after endovascular aneurysm repair. *J Vasc Surg* 2016; **64:** 1629–1632.
447. Antoniou GA, Georgiadis GS, Antoniou SA, Neequaye S, Brennan JA, Torella F, et al. Late rupture of abdominal aortic aneurysm after previous endovascular repair: A systematic review and meta-analysis. *J Endovasc Ther* 2015; **22:** 734–744.
448. Kansal V, Nagpal S, Jetty P. Editor's choice - Late open surgical conversion after endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg* 2018; **55:** 163–169.
449. Kouvelos GN, Antoniou G, Spanos K, Giannoukas A, Matsagkas M. Endovascular aneurysm repair in patients with a wide proximal aortic neck: A systematic review and meta-analysis of comparative studies. *J Cardiovasc Surg (Torino)* 2019; **60:** 167–174.
450. Beckerman WE, Tadros RO, Faries PL, Torres M, Wengerter SP, Vouyouka AG, et al. No major difference in outcomes for endovascular aneurysm repair stent grafts placed outside of instructions for use. *J Vasc Surg* 2016; **64:** 63–74.
451. Di X, Ye W, Liu CW, Jiang J, Han W, Liu B. Fenestrated endovascular repair for pararenal abdominal aortic aneurysms: A systematic review and meta-analysis. *Ann Vasc Surg* 2013; **27:** 1190–1200.
452. Linsen MA, Jongkind V, Nio D, Hoksbergen AW, Wisselink W. Pararenal aortic aneurysm repair using fenestrated endografts. *J Vasc Surg* 2012; **56:** 238–246.
453. Donas KP, Torsello G, Bisdas T, Osada N, Schönefeld E, Pitoulias GA. Early outcomes for fenestrated and chimney endografts in the treatment of pararenal aortic pathologies are not significantly different: A systematic review with pooled data analysis. *J Endovasc Ther* 2012; **19:** 723–728.
454. Ou J, Chan YC, Cheng SW. A systematic review of fenestrated endovascular repair for juxtarenal and short-neck aortic aneurysm: Evidence so far. *Ann Vasc Surg* 2015; **29:** 1680–1688.
455. Asakura T. Recent development and long-term results of open vs EVAR for pararenal abdominal aortic aneurysms. *Ann Vasc Dis* 2018; **11:** 458–463.
456. Tinelli G, Crea MA, de Waure C, Di Tanna GL, Becquemin JP, Sobocinski J, et al. A propensity-matched comparison of fenestrated endovascular aneurysm repair and open surgical repair of pararenal and paravisceral aortic aneurysms. *J Vasc Surg* 2018; **68:** 659–668.
457. Locham S, Dakour-Aridi H, Bhela J, Nejim B, Bhavana Challa A, Malas M. Thirty-day outcomes of fenestrated and chimney endovascular repair and open repair of juxtarenal, pararenal, and suprarenal abdominal aortic aneurysms using national surgical quality initiative program database (2012–2016). *Vasc Endovascular Surg* 2019; **53:** 189–198.
458. Fiorucci B, Speziale F, Kölbel T, Tsilimparis N, Sirignano P, Capoccia L, et al. Short- and midterm outcomes of open repair and fenestrated endografting of pararenal aortic aneurysms in a concurrent propensity-adjusted comparison. *J Endovasc Ther* 2019; **26:** 105–112.
459. D'Oria M, Mastrorilli D, DeMartino R, Lepidi S. Current status of endovascular preservation of the internal iliac artery with Iliac Branch Devices (IBD). *Cardiovasc Intervent Radiol* 2019; **42:** 935–948.
460. Bosanquet DC, Wilcox C, Whitehurst L, Cox A, Williams IM, Twine CP, et al; British Society of Endovascular therapy (BSET). Systematic review and meta-analysis of the effect of internal iliac artery exclusion for patients undergoing EVAR. *Eur J Vasc Endovasc Surg* 2017; **53:** 534–548.
461. Kouvelos GN, Katsargyris A, Antoniou GA, Oikonomou K, Verhoeven EL. Outcome after interruption or preservation of internal iliac artery flow during endovascular repair of abdominal aorto-iliac aneurysms. *Eur J Vasc Endovasc Surg* 2016; **52:** 621–634.
462. Gaudric J, Tresson P, Derycke L, Tezenas Du Montcel S, Couture T, Davaine JM, et al. Surgical internal iliac artery preservation associated with endovascular repair of infrarenal aortoiliac aneurysms to avoid buttock claudication and distal type I endoleaks. *J Vasc Surg* 2018; **68:** 1736–1743.
463. Robalo C, Sousa J, Mansilha A. Internal iliac artery preservation strategies in the endovascular treatment of aortoiliac aneurysms. *Int Angiol* 2018; **37:** 346–355.
464. Mansukhani NA, Havelka GE, Helenowski IB, Rodriguez HE, Hoel AW, Eskandari MK. Hybrid endovascular aortic aneurysm repair: Preservation of pelvic perfusion with external to internal iliac artery bypass. *Ann Vasc Surg* 2017; **42:** 162–168.
465. Lee MJ, Daniels SL, Drake TM, Adam IJ. Risk factors for ischaemic colitis after surgery for abdominal aortic aneurysm: A systematic review and observational meta-analysis. *Int J Colorectal Dis* 2016; **31:** 1273–1281.
466. Moulakakis KG, Alexiou VG, Karaolanis G, Sfyroeras GS, Theocharopoulos GN, Lazaris AM, et al. Spinal cord ischemia following elective endovascular repair of infrarenal aortic aneurysms: A systematic review. *Ann Vasc Surg* 2018; **52:** 280–291.
467. Hosaka A, Kato M, Kato I, Isshiki S, Okubo N. Outcome after concomitant unilateral embolization of the internal iliac artery and contralateral external-to-internal iliac artery bypass grafting during endovascular aneurysm repair. *J Vasc Surg* 2011; **54:** 960–964.
468. Jean-Baptiste E, Brizzi S, Bartoli MA, Sadaghianloo N, Baqué J, Magnan PE, et al. Pelvic ischemia and quality of life scores after interventional occlusion of the hypogastric artery in patients undergoing endovascular aortic aneurysm repair. *J Vasc Surg* 2014; **60:** 40–49.
469. 日本ステントグラフト実施基準管理委員会. 腹部大動脈瘤ステントグラフト治療成績 (治療実施期間：2016年1月1日～12月31日). [in Japanese] Available at: http://stentgraft.jp/pro/result/pirnt/JACSM2016_2.pdf (accessed July 31, 2020).
470. Ajalat M, Williams R, Wilson SE. The natural history of type 2 endoleaks after endovascular aneurysm repair justifies conservative management. *Vascular* 2018; **26:** 524–530.
471. Kumar L, Cowled P, Boult M, Howell S, Fitridge R. Type II endoleak after endovascular aneurysm repair: Natural history and treatment outcomes. *Ann Vasc Surg* 2017; **44:** 94–102.
472. Sidloff DA, Stather PW, Choke E, Bown MJ, Sayers RD. Type II endoleak after endovascular aneurysm repair. *Br J Surg* 2013; **100:** 1262–1270.
473. Hajibandeh S, Ahmad N, Antoniou GA, Torella F. Is intervention

better than surveillance in patients with type 2 endoleak post-endovascular abdominal aortic aneurysm repair? *Interact Cardiovasc Thorac Surg* 2015; **20:** 128–134.
474. Cieri E, De Rango P, Isernia G, Simonte G, Ciucci A, Parlani G, et al. Type II endoleak is an enigmatic and unpredictable marker of worse outcome after endovascular aneurysm repair. *J Vasc Surg* 2014; **59:** 930–937.
475. Yang B, Rosati CM, Norton EL, Kim KM, Khaja MS, Dasika N, et al. Endovascular fenestration/stenting first followed by delayed open aortic repair for acute type A aortic dissection with malperfusion syndrome. *Circulation* 2018; **138:** 2091–2103.
476. Yang B, Norton EL, Rosati CM, Wu X, Kim KM, Khaja MS, et al. Managing patients with acute type A aortic dissection and mesenteric malperfusion syndrome: A 20-year experience. *J Thorac Cardiovasc Surg* 2019; **158:** 675–687.
477. Deeb GM, Patel HJ, Williams DM. Treatment for malperfusion syndrome in acute type A and B aortic dissection: A long-term analysis. *J Thorac Cardiovasc Surg* 2010; **140 Suppl:** S98–S100.
478. Midulla M, Renaud A, Martinelli T, Koussa M, Mounier-Vehier C, Prat A, et al. Endovascular fenestration in aortic dissection with acute malperfusion syndrome: Immediate and late follow-up. *J Thorac Cardiovasc Surg* 2011; **142:** 66–72.
479. Gargiulo M, Bianchini Massoni C, Gallitto E, Freyrie A, Trimarchi S, Faggioli G, et al. Lower limb malperfusion in type B aortic dissection: A systematic review. *Ann Cardiothorac Surg* 2014; **3:** 351–367.
480. Puippe GD. Complicated acute type B aortic dissection-what does endovascular therapy contribute? [Article in German] *Radiologe* 2018; **58:** 822–828.
481. Arata K, Imagama I, Shigehisa Y, Mukaihara K, Toyokawa K, Matsuba T, et al. Aortic fenestration for type B chronic aortic dissection complicated with lower limb malperfusion induced by walking exercise. *Ann Vasc Dis* 2015; **8:** 29–32.
482. Nguyen BN, Neville RF, Rahbar R, Amdur R, Sidawy AN. Comparison of outcomes for open abdominal aortic aneurysm repair and endovascular repair in patients with chronic renal insufficiency. *Ann Surg* 2013; **258:** 394–399.
483. Patel VI, Lancaster RT, Mukhopadhyay S, Aranson NJ, Conrad MF, LaMuraglia GM, et al. Impact of chronic kidney disease on outcomes after abdominal aortic aneurysm repair. *J Vasc Surg* 2012; **56:** 1206–1213.
484. Marrocco-Trischitta MM, Melissano G, Kahlberg A, Calori G, Setacci F, Chiesa R. Chronic kidney disease classification stratifies mortality risk after elective stent graft repair of the thoracic aorta. *J Vasc Surg* 2009; **49:** 296–301.
485. Wang GJ, Fairman RM, Jackson BM, Szeto WY, Pochettino A, Woo EY. The outcome of thoracic endovascular aortic repair (TEVAR) in patients with renal insufficiency. *J Vasc Surg* 2009; **49:** 42–46.
486. Walsh SR, Tang T, Gaunt ME, Boyle JR. Contrast-induced nephropathy. *J Endovasc Ther* 2007; **14:** 92–100.
487. Gurm HS, Seth M, Mehran R, Cannon L, Grines CL, LaLonde T, et al; Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2). Impact of contrast dose reduction on incidence of Acute Kidney Injury (AKI) among patients undergoing PCI: A modeling study. *J Invasive Cardiol* 2016; **28:** 142–146.
488. Saratzis AN, Goodyear S, Sur H, Saedon M, Imray C, Mahmood A. Acute kidney injury after endovascular repair of abdominal aortic aneurysm. *J Endovasc Ther* 2013; **20:** 315–330.
489. Pisimisis GT, Bechara CF, Barshes NR, Lin PH, Lai WS, Kougias P. Risk factors and impact of proximal fixation on acute and chronic renal dysfunction after endovascular aortic aneurysm repair using glomerular filtration rate criteria. *Ann Vasc Surg* 2013; **27:** 16–22.
490. Surowiec SM, Davies MG, Fegley AJ, Tanski WJ, Pamoukian VN, Sternbach Y, et al. Relationship of proximal fixation to postoperative renal dysfunction in patients with normal serum creatinine concentration. *J Vasc Surg* 2004; **39:** 804–810.
491. Alric P, Hinchliffe RJ, Picot MC, Braithwaite BD, MacSweeney ST, Wenham PW, et al. Long-term renal function following endovascular aneurysm repair with infrarenal and suprarenal aortic stent-grafts. *J Endovasc Ther* 2003; **10:** 397–405.
492. Minami K, Sugiyama Y, Iida H. A retrospective observational cohort study investigating the association between acute kidney injury and all-cause mortality among patients undergoing endovascular repair of abdominal aortic aneurysms. *J Anesth* 2017; **31:** 686–691.
493. Piffaretti G, Mariscalco G, Bonardelli S, Sarcina A, Gelpi G, Bellosta R, et al. Predictors and outcomes of acute kidney injury after thoracic aortic endograft repair. *J Vasc Surg* 2012; **56:** 1527–1534.
494. Isaka Y, Hayashi H, Aonuma K, Horio M, Terada Y, Doi K, et al; Japanese Society of Nephrology, Japan Radiological Society, and Japanese Circulation Society Joint Working Group. Guideline on the use of iodinated contrast media in patients with kidney disease 2018. *Jpn J Radiol* 2020; **38:** 3–46.
495. Trivedi HS, Moore H, Nasr S, Aggarwal K, Agrawal A, Goel P, et al. A randomized prospective trial to assess the role of saline hydration on the development of contrast nephrotoxicity. *Nephron Clin Pract* 2003; **93:** C29–C34.
496. Nijssen EC, Rennenberg RJ, Nelemans PJ, Essers BA, Janssen MM, Vermeeren MA, et al. Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): A prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. *Lancet* 2017; **389:** 1312–1322.
497. De Angelis C, Sardanelli F, Perego M, Alì M, Casilli F, Inglese L, et al. Carbon dioxide (CO_2) angiography as an option for endovascular abdominal aortic aneurysm repair (EVAR) in patients with chronic kidney disease (CKD). *Int J Cardiovasc Imaging* 2017; **33:** 1655–1662.
498. Saratzis A, Bath MF, Harrison S, Sayers RD, Mahmood A, Sarafidis P, et al. Long-term renal function after endovascular aneurysm repair. *Clin J Am Soc Nephrol* 2015; **10:** 1930–1936.
499. Al Adas Z, Shepard AD, Nypaver TJ, Weaver MR, Maatman T, Yessayan LT, et al. Long-term decline in renal function is more significant after endovascular repair of infrarenal abdominal aortic aneurysms. *J Vasc Surg* 2018; **68:** 739–748.
500. Tanaka A, Milner R, Ota T. Kommerell's diverticulum in the current era: A comprehensive review. *Gen Thorac Cardiovasc Surg* 2015; **63:** 245–259.
501. Lancaster G, Lovoulos CJ, Moussouttas M, Goldstein AH, Leifer D, Fayad PB, et al. Aortic arch replacement for recurrent cerebral embolization. *Ann Thorac Surg* 2002; **73:** 291–294.
502. Janko MR, Bose S, Lawrence PF. Current status of treatment for aortic graft infection: When should cryopreserved allografts be used? *Semin Vasc Surg* 2019; **32:** 81–87.
503. Czerny M, von Allmen R, Opfermann P, Sodeck G, Dick F, Stellmes A, et al. Self-made pericardial tube graft: A new surgical concept for treatment of graft infections after thoracic and abdominal aortic procedures. *Ann Thorac Surg* 2011; **92:** 1657–1662.
504. Kubota H, Endo H, Noma M, Ishii H, Tsuchiya H, Yoshimoto A, et al. Xenopericardial roll graft replacement for infectious pseudoaneurysms and graft infections of the aorta. *J Cardiothorac Surg* 2015; **10:** 133.
505. Kreibich M, Siepe M, Morlock J, Beyersdorf F, Kondov S, Scheumann J, et al. Surgical treatment of native and prosthetic aortic infection with xenopericardial tube grafts. *Ann Thorac Surg* 2018; **106:** 498–504.
506. Robicsek F, Cook JW, Reames MK, Skipper ER. Size reduction ascending aortoplasty: Is it dead or alive? *J Thorac Cardiovasc Surg* 2004; **128:** 562–570.
507. Arsan S, Akgun S, Kurtoglu N, Yildirim T, Tekinsoy B. Reduction aortoplasty and external wrapping for moderately sized tubular ascending aortic aneurysm with concomitant operations. *Ann Thorac Surg* 2004; **78:** 858–861.
508. Feindt P, Litmathe J, Börgens A, Boeken U, Kurt M, Gams E. Is size-reducing ascending aortoplasty with external reinforcement an option in modern aortic surgery? *Eur J Cardiothorac Surg* 2007; **31:** 614–617.
509. Kiessling AH, Odwody E, Miskovic A, Stock UA, Zierer A, Moritz A. Midterm follow up in patients with reduction ascending aortoplasty. *J Cardiothorac Surg* 2014; **9:** 120.
510. Treasure T, Petrou M, Rosendahl U, Austin C, Rega F, Pirk J, et al. Personalized external aortic root support: A review of the current status. *Eur J Cardiothorac Surg* 2016; **50:** 400–404.
511. Yamamoto M, Iguchi M, Yamamoto M, Hiroi M. Loeys-Dietz syndrome with aortic wall necrosis secondary to external wrapping. *Eur J Cardiothorac Surg* 2018; **53:** 1288–1289.
512. Gambardella I, Antoniou GA, Torella F, Spadaccio C, Oo AY, Gaudino M, et al. Secondary open aortic procedure following thoracic endovascular aortic repair: Meta-analytic state of the art. *J Am Heart Assoc* 2017; **6:** e006618.
513. Joo HC, Kwon JH, Kim JH, Lee SH, Lee S, Youn YN, et al. Late open conversion after thoracic endovascular aortic repair. *J Vasc Surg* 2019; **70:** 439–448.
514. Davidovic L, Sladojevic M, Koncar I, Markovic M, Ulus T, Ilic N, et al. Late complication after thoracic endovascular aortic

repair: What is the role of an open surgical conversion? *Ann Vasc Surg* 2018; **47:** 238–246.
515. Japanese Society for Vascular Surgery. 血管外科手術例数アニュアルレポート2014. [in Japanese] Available at: http://www.jsvs.org/ja/enquete/aggregate_2014re2.pdf (accessed July 31, 2020).
516. Danyi P, Elefteriades JA, Jovin IS. Medical therapy of thoracic aortic aneurysms: Are we there yet? *Circulation* 2011; **124:** 1469–1476.
517. Svensjö S, Bengtsson H, Bergqvist D. Thoracic and thoracoabdominal aortic aneurysm and dissection: An investigation based on autopsy. *Br J Surg* 1996; **83:** 68–71.
518. Cambria RP, Davison JK, Zannetti S, L'Italien G, Brewster DC, Gertler JP, et al. Clinical experience with epidural cooling for spinal cord protection during thoracic and thoracoabdominal aneurysm repair. *J Vasc Surg* 1997; **25:** 234–243.
519. Chun AS, Elefteriades JA, Mukherjee SK. Medical treatment for thoracic aortic aneurysm: Much more work to be done. *Prog Cardiovasc Dis* 2013; **56:** 103–108.
520. Braverman AC. Medical management of thoracic aortic aneurysm disease. *J Thorac Cardiovasc Surg* 2013; **145 Suppl:** S2–S6.
521. Elefteriades JA. Does medical therapy for thoracic aortic aneurysms really work?: Are beta-blockers truly indicated? PRO. *Cardiol Clin* 2010; **28:** 255–260.
522. Groenink M, de Roos A, Mulder BJ, Spaan JA, van der Wall EE. Changes in aortic distensibility and pulse wave velocity assessed with magnetic resonance imaging following beta-blocker therapy in the Marfan syndrome. *Am J Cardiol* 1998; **82:** 203–208.
523. Pyeritz RE, Loeys B. The 8th international research symposium on the Marfan syndrome and related conditions. *Am J Med Genet A* 2012; **158A:** 42–49.
524. Habashi JP, Doyle JJ, Holm TM, Aziz H, Schoenhoff F, Bedja D, et al. Angiotensin II type 2 receptor signaling attenuates aortic aneurysm in mice through ERK antagonism. *Science* 2011; **332:** 361–365.
525. Lindsay ME, Dietz HC. Lessons on the pathogenesis of aneurysm from heritable conditions. *Nature* 2011; **473:** 308–316.
526. Yetman AT, Bornemeier RA, McCrindle BW. Usefulness of *enalapril* versus *propranolol* or *atenolol* for prevention of aortic dilation in patients with the Marfan syndrome. *Am J Cardiol* 2005; **95:** 1125–1127.
527. Brooke BS, Habashi JP, Judge DP, Patel N, Loeys B, Dietz HC. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. *N Engl J Med* 2008; **358:** 2787–2795.
528. Habashi JP, Judge DP, Holm TM, Cohn RD, Loeys BL, Cooper TK, et al. Losartan, an AT1 antagonist, prevents aortic aneurysm in a mouse model of Marfan syndrome. *Science* 2006; **312:** 117–121.
529. Stein LH, Berger J, Tranquilli M, Elefteraides JA. Effect of statin drugs on thoracic aortic aneurysms. *Am J Cardiol* 2013; **112:** 1240–1245.
530. Les AS, Shadden SC, Figueroa CA, Park JM, Tedesco MM, Herfkens RJ, et al. Quantification of hemodynamics in abdominal aortic aneurysms during rest and exercise using magnetic resonance imaging and computational fluid dynamics. *Ann Biomed Eng* 2010; **38:** 1288–1313.
531. Sohn DW, Jung JW, Oh BH, Lee MM, Park YB, Choi YS, et al. Should ascending aortic intramural hematoma be treated surgically? *Am J Cardiol* 2001; **87:** 1024–1026.
532. Riambau V, Böckler D, Brunkwall J, Cao P, Chiesa R, Coppi G, et al. Editor's choice - Management of descending thoracic aorta diseases: Clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2017; **53:** 4–52.
533. Svensson LG, Adams DH, Bonow RO, Kouchoukos NT, Miller DC, O'Gara PT, et al. Aortic valve and ascending aorta guidelines for management and quality measures. *Ann Thorac Surg* 2013; **95 Suppl:** S1–S66.
534. Albornoz G, Coady MA, Roberts M, Davies RR, Tranquilli M, Rizzo JA, et al. Familial thoracic aortic aneurysms and dissections--incidence, modes of inheritance, and phenotypic patterns. *Ann Thorac Surg* 2006; **82:** 1400–1405.
535. Coady MA, Rizzo JA, Hammond GL, Mandapati D, Darr U, Kopf GS, et al. What is the appropriate size criterion for resection of thoracic aortic aneurysms? *J Thorac Cardiovasc Surg* 1997; **113:** 476–491.
535a. Zafar MA, Li Y, Rizzo JA, Charilaou P, Saeyeldin A, Velasquez CA, et al. Height alone, rather than body surface area, suffices for risk estimation in ascending aortic aneurysm. *J Thorac Cardiovasc Surg* 2018; **155:** 1938–1950.
535b. Masri A, Kalahasti V, Svensson LG, Roselli EE, Johnston D, Hammer D, et al. Aortic cross-sectional area/height ratio and outcomes in patients with a trileaflet aortic valve and a dilated aorta. *Circulation* 2016; **134:** 1724–1737.
536. Jondeau G, Detaint D, Tubach F, Arnoult F, Milleron O, Raoux F, et al. Aortic event rate in the Marfan population: A cohort study. *Circulation* 2012; **125:** 226–232.
537. Pearson GD, Devereux R, Loeys B, Maslen C, Milewicz D, Pyeritz R, et al. Report of the National Heart, Lung, and Blood Institute and National Marfan Foundation Working Group on research in Marfan syndrome and related disorders. *Circulation* 2008; **118:** 785–791.
538. Eleid MF, Forde I, Edwards WD, Maleszewski JJ, Suri RM, Schaff HV, et al. Type A aortic dissection in patients with bicuspid aortic valves: Clinical and pathological comparison with tricuspid aortic valves. *Heart* 2013; **99:** 1668–1674.
539. Etz CD, von Aspern K, Hoyer A, Girrbach FF, Leontyev S, Bakhtiary F, et al. Acute type A aortic dissection: Characteristics and outcomes comparing patients with bicuspid versus tricuspid aortic valve. *Eur J Cardiothorac Surg* 2015; **48:** 142–150.
540. Fedak PW, de Sa MP, Verma S, Nili N, Kazemian P, Butany J, et al. Vascular matrix remodeling in patients with bicuspid aortic valve malformations: Implications for aortic dilatation. *J Thorac Cardiovasc Surg* 2003; **126:** 797–806.
541. Grewal N, Gittenberger-de Groot AC, Poelmann RE, Klautz RJ, Lindeman JH, Goumans MJ, et al. Ascending aorta dilation in association with bicuspid aortic valve: A maturation defect of the aortic wall. *J Thorac Cardiovasc Surg* 2014; **148:** 1583–1590.
542. Pasta S, Phillippi JA, Gleason TG, Vorp DA. Effect of aneurysm on the mechanical dissection properties of the human ascending thoracic aorta. *J Thorac Cardiovasc Surg* 2012; **143:** 460–467.
543. Davies RR, Kaple RK, Mandapati D, Gallo A, Botta DM, Elefteriades JA, et al. Natural history of ascending aortic aneurysms in the setting of an unreplaced bicuspid aortic valve. *Ann Thorac Surg* 2007; **83:** 1338–1344.
544. Borger MA, Preston M, Ivanov J, Fedak PW, Davierwala P, Armstrong S, et al. Should the ascending aorta be replaced more frequently in patients with bicuspid aortic valve disease? *J Thorac Cardiovasc Surg* 2004; **128:** 677–683.
545. Park CB, Greason KL, Suri RM, Michelena HI, Schaff HV, Sundt TM. Fate of nonreplaced sinuses of Valsalva in bicuspid aortic valve disease. *J Thorac Cardiovasc Surg* 2011; **142:** 278–284.
546. Russo CF, Mazzetti S, Garatti A, Ribera E, Milazzo A, Bruschi G, et al. Aortic complications after bicuspid aortic valve replacement: Long-term results. *Ann Thorac Surg* 2002; **74:** S1773–S1776.
547. Svensson LG, Kim KH, Blackstone EH, Rajeswaran J, Gillinov AM, Mihaljevic T, et al. Bicuspid aortic valve surgery with proactive ascending aorta repair. *J Thorac Cardiovasc Surg* 2011; **142:** 622–629.
548. Yasuda H, Nakatani S, Stugaard M, Tsujita-Kuroda Y, Bando K, Kobayashi J, et al. Failure to prevent progressive dilation of ascending aorta by aortic valve replacement in patients with bicuspid aortic valve: Comparison with tricuspid aortic valve. *Circulation* 2003; **108 Suppl:** II291–II294.
549. Kouchoukos NT, Karp RB, Blackstone EH, Kirklin JW, Pacifico AD, Zorn GL. Replacement of the ascending aorta and aortic valve with a composite graft: Results in 86 patients. *Ann Surg* 1980; **192:** 403–413.
550. Musci M, Weng Y, Hübler M, Amiri A, Pasic M, Kosky S, et al. Homograft aortic root replacement in native or prosthetic active infective endocarditis: Twenty-year single-center experience. *J Thorac Cardiovasc Surg* 2010; **139:** 665–673.
551. El-Hamamsy I, Eryigit Z, Stevens LM, Sarang Z, George R, Clark L, et al. Long-term outcomes after autograft versus homograft aortic root replacement in adults with aortic valve disease: A randomised controlled trial. *Lancet* 2010; **376:** 524–531.
552. Boodhwani M, de Kerchove L, Glineur D, Poncelet A, Rubay J, Astarci P, et al. Repair-oriented classification of aortic insufficiency: Impact on surgical techniques and clinical outcomes. *J Thorac Cardiovasc Surg* 2009; **137:** 286–294.
553. David TE, Feindel CM, Armstrong S, Maganti M. Replacement of the ascending aorta with reduction of the diameter of the sinotubular junction to treat aortic insufficiency in patients with ascending aortic aneurysm. *J Thorac Cardiovasc Surg* 2007; **133:** 414–418.

554. Bavaria JE, Woo YJ, Hall RA, Wahl PM, Acker MA, Gardner TJ. Circulatory management with retrograde cerebral perfusion for acute type A aortic dissection. *Circulation* 1996; **94 Suppl:** II173–II176.
555. Bentall H, De Bono A. A technique for complete replacement of the ascending aorta. *Thorax* 1968; **23:** 338–339.
556. Cabrol C, Pavie A, Gandjbakhch I, Villemot JP, Guiraudon G, Laughlin L, et al. Complete replacement of the ascending aorta with reimplantation of the coronary arteries: New surgical approach. *J Thorac Cardiovasc Surg* 1981; **81:** 309–315.
557. Piehler JM, Pluth JR. Replacement of the ascending aorta and aortic valve with a composite graft in patients with nondisplaced coronary ostia. *Ann Thorac Surg* 1982; **33:** 406–409.
558. Svensson LG, Crawford ES, Hess KR, Coselli JS, Safi HJ. Composite valve graft replacement of the proximal aorta: Comparison of techniques in 348 patients. *Ann Thorac Surg* 1992; **54:** 427–439.
559. Mestres CA, Betriu A, Pomar JL. Occlusion of the coronary perfusion graft: An exceptional complication after reconstruction of the ascending aorta with the Cabrol technique. *J Thorac Cardiovasc Surg* 1989; **98:** 302–303.
560. Izumi C, Eishi K, Ashihara K, Arita T, Otsuji Y, Kunihara T, et al; Japanese Circulation Society Joint Working Group. JCS/JSCS/JATS/JSVS 2020 guidelines on the management of valvular heart disease. *Circ J* 2020; **84:** 2037–2119.
561. Sarsam MA, Yacoub M. Remodeling of the aortic valve anulus. *J Thorac Cardiovasc Surg* 1993; **105:** 435–438.
562. Yacoub MH, Gehle P, Chandrasekaran V, Birks EJ, Child A, Radley-Smith R. Late results of a valve-preserving operation in patients with aneurysms of the ascending aorta and root. *J Thorac Cardiovasc Surg* 1998; **115:** 1080–1090.
563. David TE, Feindel CM. An aortic valve-sparing operation for patients with aortic incompetence and aneurysm of the ascending aorta. *J Thorac Cardiovasc Surg* 1992; **103:** 617–622.
564. De Paulis R, De Matteis GM, Nardi P, Scaffa R, Buratta MM, Chiariello L. Opening and closing characteristics of the aortic valve after valve-sparing procedures using a new aortic root conduit. *Ann Thorac Surg* 2001; **72:** 487–494.
565. David TE, Feindel CM, Webb GD, Colman JM, Armstrong S, Maganti M. Aortic valve preservation in patients with aortic root aneurysm: Results of the reimplantation technique. *Ann Thorac Surg* 2007; **83:** S732–S735.
566. Demers P, Miller DC. Simple modification of "T. David-V" valve-sparing aortic root replacement to create graft pseudo-sinuses. *Ann Thorac Surg* 2004; **78:** 1479–1481.
567. Takamoto S, Nawata K, Morota T. A simple modification of 'David-V' aortic root reimplantation. *Eur J Cardiothorac Surg* 2006; **30:** 560–562.
568. Beckmann E, Martens A, Pertz J, Kaufeld T, Umminger J, Hanke JS, et al. Valve-sparing David I procedure in acute aortic type A dissection: A 20-year experience with more than 100 patients. *Eur J Cardiothorac Surg* 2017; **52:** 319–324.
569. Kunihara T, Neumann N, Kriechbaum SD, Aicher D, Schäfers HJ. Aortic root remodeling leads to good valve stability in acute aortic dissection and preexistent root dilatation. *J Thorac Cardiovasc Surg* 2016; **152:** 430–436.
570. Rosenblum JM, Leshnower BG, Moon RC, Lasanajak Y, Binongo J, McPherson L, et al. Durability and safety of David V valve-sparing root replacement in acute type A aortic dissection. *J Thorac Cardiovasc Surg* 2019; **157:** 14–23.
571. Sievers HH, Richardt D, Diwoky M, Auer C, Bucsky B, Nasseri B, et al. Survival and reoperation after valve-sparing root replacement and root repair in acute type A dissection. *J Thorac Cardiovasc Surg* 2018; **156:** 2076–2082.
572. Flynn CD, Tian DH, Wilson-Smith A, David T, Matalanis G, Misfeld M, et al. Systematic review and meta-analysis of surgical outcomes in Marfan patients undergoing aortic root surgery by composite-valve graft or valve sparing root replacement. *Ann Cardiothorac Surg* 2017; **6:** 570–581.
573. Gaudino M, Lau C, Munjal M, Avgerinos D, Girardi LN. Contemporary outcomes of surgery for aortic root aneurysms: A propensity-matched comparison of valve-sparing and composite valve graft replacement. *J Thorac Cardiovasc Surg* 2015; **150:** 1120–1129.
574. Ouzounian M, Rao V, Manlhiot C, Abraham N, David C, Feindel CM, et al. Valve-sparing root replacement compared with composite valve graft procedures in patients with aortic root dilation. *J Am Coll Cardiol* 2016; **68:** 1838–1847.
575. Franke UF, Isecke A, Nagib R, Breuer M, Wippermann J, Tigges-Limmer K, et al. Quality of life after aortic root surgery: Reimplantation technique versus composite replacement. *Ann Thorac Surg* 2010; **90:** 1869–1875.
576. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease: The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2017; **38:** 2739–2791.
577. Akashi H, Tayama K, Fujino T, Fukunaga S, Tanaka A, Hayashi S, et al. Cerebral protection selection in aortic arch surgery for patients with preoperative complications of cerebrovascular disease. *Jpn J Thorac Cardiovasc Surg* 2000; **48:** 782–788.
578. Ehrlich MP, Fang WC, Grabenwöger M, Kocher A, Ankersmit J, Laufer G, et al. Impact of retrograde cerebral perfusion on aortic arch aneurysm repair. *J Thorac Cardiovasc Surg* 1999; **118:** 1026–1032.
579. Di Eusanio M, Wesselink RM, Morshuis WJ, Dossche KM, Schepens MA. Deep hypothermic circulatory arrest and antegrade selective cerebral perfusion during ascending aorta-hemiarch replacement: A retrospective comparative study. *J Thorac Cardiovasc Surg* 2003; **125:** 849–854.
580. Hagl C, Ergin MA, Galla JD, Lansman SL, McCullough JN, Spielvogel D, et al. Neurologic outcome after ascending aorta-aortic arch operations: Effect of brain protection technique in high-risk patients. *J Thorac Cardiovasc Surg* 2001; **121:** 1107–1121.
581. Reich DL, Uysal S, Sliwinski M, Ergin MA, Kahn RA, Konstadt SN, et al. Neuropsychologic outcome after deep hypothermic circulatory arrest in adults. *J Thorac Cardiovasc Surg* 1999; **117:** 156–163.
582. Reich DL, Uysal S, Ergin MA, Bodian CA, Hossain S, Griepp RB. Retrograde cerebral perfusion during thoracic aortic surgery and late neuropsychological dysfunction. *Eur J Cardiothorac Surg* 2001; **19:** 594–600.
583. Guo S, Sun Y, Ji B, Liu J, Wang G, Zheng Z. Similar cerebral protective effectiveness of antegrade and retrograde cerebral perfusion during deep hypothermic circulatory arrest in aortic surgery: A meta-analysis of 7023 patients. *Artif Organs* 2015; **39:** 300–308.
584. Usui A, Miyata H, Ueda Y, Motomura N, Takamoto S. Risk-adjusted and case-matched comparative study between antegrade and retrograde cerebral perfusion during aortic arch surgery: Based on the Japan Adult Cardiovascular Surgery Database: The Japan Cardiovascular Surgery Database Organization. *Gen Thorac Cardiovasc Surg* 2012; **60:** 132–139.
585. Okita Y, Miyata H, Motomura N, Takamoto S; Japan Cardiovascular Surgery Database Organization. A study of brain protection during total arch replacement comparing antegrade cerebral perfusion versus hypothermic circulatory arrest, with or without retrograde cerebral perfusion: Analysis based on the Japan Adult Cardiovascular Surgery Database. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S65–S73.
586. Greenberg RK, Haddad F, Svensson L, O'Neill S, Walker E, Lyden SP, et al. Hybrid approaches to thoracic aortic aneurysms: The role of endovascular elephant trunk completion. *Circulation* 2005; **112:** 2619–2626.
587. Svensson LG. The elephant trunk procedure: Uses in complex aortic diseases. *Curr Opin Cardiol* 2005; **20:** 491–495.
588. Svensson LG, Kim KH, Blackstone EH, Alster JM, McCarthy PM, Greenberg RK, et al. Elephant trunk procedure: Newer indications and uses. *Ann Thorac Surg* 2004; **78:** 109–116.
589. Shrestha M, Martens A, Krüger H, Maeding I, Ius F, Fleissner F, et al. Total aortic arch replacement with the elephant trunk technique: Single-centre 30-year results. *Eur J Cardiothorac Surg* 2014; **45:** 289–296.
590. Settepani F, Cappai A, Basciu A, Barbone A, Tarelli G. Outcome of open total arch replacement in the modern era. *J Vasc Surg* 2016; **63:** 537–545.
591. Okada K, Tanaka A, Munakata H, Matsumori M, Morimoto Y, Tanaka Y, et al. Extended replacement of aortic arch aneurysms through left posterolateral thoracotomy. *Eur J Cardiothorac Surg* 2009; **35:** 270–275.
592. Karck M, Chavan A, Hagl C, Friedrich H, Galanski M, Haverich A. The frozen elephant trunk technique: A new treatment for thoracic aortic aneurysms. *J Thorac Cardiovasc Surg* 2003; **125:** 1550–1553.
593. Tian DH, Wan B, Di Eusanio M, Black D, Yan TD. A systematic review and meta-analysis on the safety and efficacy of the frozen elephant trunk technique in aortic arch surgery. *Ann Cardiothorac*

Surg 2013; **2:** 581–591.
594. Katayama K, Uchida N, Katayama A, Takahashi S, Takasaki T, Kurosaki T, et al. Multiple factors predict the risk of spinal cord injury after the frozen elephant trunk technique for extended thoracic aortic disease. *Eur J Cardiothorac Surg* 2015; **47:** 616–620.
595. Griepp RB, Stinson EB, Hollingsworth JF, Buehler D. Prosthetic replacement of the aortic arch. *J Thorac Cardiovasc Surg* 1975; **70:** 1051–1063.
596. Kazui T, Inoue N, Yamada O, Komatsu S. Selective cerebral perfusion during operation for aneurysms of the aortic arch: A reassessment. *Ann Thorac Surg* 1992; **53:** 109–114.
597. Kazui T, Washiyama N, Muhammad BA, Terada H, Yamashita K, Takinami M, et al. Total arch replacement using aortic arch branched grafts with the aid of antegrade selective cerebral perfusion. *Ann Thorac Surg* 2000; **70:** 3–8.
598. Ueda Y, Miki S, Kusuhara K, Okita Y, Tahata T, Yamanaka K. Surgical treatment of aneurysm or dissection involving the ascending aorta and aortic arch, utilizing circulatory arrest and retrograde cerebral perfusion. *J Cardiovasc Surg (Torino)* 1990; **31:** 553–558.
599. Ueda Y, Miki S, Okita Y, Tahata T, Ogino H, Sakai T, et al. Protective effect of continuous retrograde cerebral perfusion on the brain during deep hypothermic systemic circulatory arrest. *J Card Surg* 1994; **9:** 584–595.
600. Ogino H, Ando M, Sasaki H, Minatoya K. Total arch replacement using a stepwise distal anastomosis for arch aneurysms with distal extension. *Eur J Cardiothorac Surg* 2006; **29:** 255–257.
601. Rokkas CK, Kouchoukos NT. Single-stage extensive replacement of the thoracic aorta: The arch-first technique. *J Thorac Cardiovasc Surg* 1999; **117:** 99–105.
602. Nishimura M, Ohtake S, Sawa Y, Takahashi T, Matsumiya G, Kagisaki K, et al. Arch-first technique for aortic arch aneurysm repair through median sternotomy. *Ann Thorac Surg* 2002; **74:** 1264–1266.
603. Minatoya K, Ogino H, Matsuda H, Sasaki H, Tanaka H, Kobayashi J, et al. Evolving selective cerebral perfusion for aortic arch replacement: High flow rate with moderate hypothermic circulatory arrest. *Ann Thorac Surg* 2008; **86:** 1827–1831.
604. Iwakoshi S, Ichihashi S, Itoh H, Tabayashi N, Sakaguchi S, Yoshida T, et al. Clinical outcomes of thoracic endovascular aneurysm repair using commercially available fenestrated stent graft (Najuta endograft). *J Vasc Surg* 2015; **62:** 1473–1478.
605. Bavaria J, Vallabhajosyula P, Moeller P, Szeto W, Desai N, Pochettino A. Hybrid approaches in the treatment of aortic arch aneurysms: Postoperative and midterm outcomes. *J Thorac Cardiovasc Surg* 2013; **145 Suppl:** S85–S90.
606. Iba Y, Minatoya K, Matsuda H, Sasaki H, Tanaka H, Oda T, et al. How should aortic arch aneurysms be treated in the endovascular aortic repair era?: A risk-adjusted comparison between open and hybrid arch repair using propensity score-matching analysis. *Eur J Cardiothorac Surg* 2014; **46:** 32–39.
607. Redlinger RE, Ahanchi SS, Panneton JM. In situ laser fenestration during emergent thoracic endovascular aortic repair is an effective method for left subclavian artery revascularization. *J Vasc Surg* 2013; **58:** 1171–1177.
608. Tse LW, Lindsay TF, Roche-Nagle G, Oreopoulos GD, Ouzounian M, Tan KT. Radiofrequency in situ fenestration for aortic arch vessels during thoracic endovascular repair. *J Endovasc Ther* 2015; **22:** 116–121.
609. Qin J, Zhao Z, Wang R, Ye K, Li W, Liu X, et al. In situ laser fenestration is a feasible method for revascularization of aortic arch during thoracic endovascular aortic repair. *J Am Heart Assoc* 2017; **6:** e004542.
610. Voskresensky I, Scali ST, Feezor RJ, Fatima J, Giles KA, Tricarico R, et al. Outcomes of thoracic endovascular aortic repair using aortic arch chimney stents in high-risk patients. *J Vasc Surg* 2017; **66:** 9–20.
611. Wang T, Shu C, Li M, Li QM, Li X, Qiu J, et al. Thoracic endovascular aortic repair with single/double chimney technique for aortic arch pathologies. *J Endovasc Ther* 2017; **24:** 383–393.
612. Hughes GC, Daneshmand MA, Balsara KR, Achneck HA, Sileshi B, Lee SM, et al. "Hybrid" repair of aneurysms of the transverse aortic arch: Midterm results. *Ann Thorac Surg* 2009; **88:** 1882–1888.
613. Saleh HM, Inglese L. Combined surgical and endovascular treatment of aortic arch aneurysms. *J Vasc Surg* 2006; **44:** 460–466.
614. Kato M, Kaneko M, Kuratani T, Horiguchi K, Ikushima H, Ohnishi K. New operative method for distal aortic arch aneurysm: Combined cervical branch bypass and endovascular stent-graft implantation. *J Thorac Cardiovasc Surg* 1999; **117:** 832–834.
615. Weigang E, Parker J, Czerny M, Peivandi AA, Dorweiler B, Beyersdorf F, et al. Endovascular aortic arch repair after aortic arch de-branching. *Ann Thorac Surg* 2009; **87:** 603–607.
616. Hughes GC, Nienaber JJ, Bush EL, Daneshmand MA, McCann RL. Use of custom Dacron branch grafts for "hybrid" aortic debranching during endovascular repair of thoracic and thoracoabdominal aortic aneurysms. *J Thorac Cardiovasc Surg* 2008; **136:** 21–28.
617. Buth J, Penn O, Tielbeek A, Mersman M. Combined approach to stent-graft treatment of an aortic arch aneurysm. *J Endovasc Surg* 1998; **5:** 329–332.
618. Quiñones-Baldrich WJ, Panetta TF, Vescera CL, Kashyap VS. Repair of type IV thoracoabdominal aneurysm with a combined endovascular and surgical approach. *J Vasc Surg* 1999; **30:** 555–560.
619. Shigemura N, Kato M, Kuratani T, Funakoshi Y, Kaneko M. New operative method for acute type B dissection: Left carotid artery-left subclavian artery bypass combined with endovascular stent-graft implantation. *J Thorac Cardiovasc Surg* 2000; **120:** 406–408.
620. Chiesa R, Melissano G, Tshomba Y, Civilini E, Marone EM, Bertoglio L, et al. Ten years of endovascular aortic arch repair. *J Endovasc Ther* 2010; **17:** 1–11.
621. Preventza O, Garcia A, Cooley DA, Haywood-Watson RJ, Simpson K, Bakaeen FG, et al. Total aortic arch replacement: A comparative study of zone 0 hybrid arch exclusion versus traditional open repair. *J Thorac Cardiovasc Surg* 2015; **150:** 1591–1600.
622. Kotelis D, Geisbüsch P, Attigah N, Hinz U, Hyhlik-Dürr A, Böckler D. Total vs hemi-aortic arch transposition for hybrid aortic arch repair. *J Vasc Surg* 2011; **54:** 1182–1186.
623. Baldwin ZK, Chuter TA, Hiramoto JS, Reilly LM, Schneider DB. Double-barrel technique for endovascular exclusion of an aortic arch aneurysm without sternotomy. *J Endovasc Ther* 2008; **15:** 161–165.
624. Gehringhoff B, Torsello G, Pitoulias GA, Austermann M, Donas KP. Use of chimney grafts in aortic arch pathologies involving the supra-aortic branches. *J Endovasc Ther* 2011; **18:** 650–655.
625. Patel HJ, Dake MD, Bavaria JE, Singh MJ, Filinger M, Fischbein MP, et al. Branched endovascular therapy of the distal aortic arch: Preliminary results of the feasibility multicenter trial of the Gore thoracic branch endoprosthesis. *Ann Thorac Surg* 2016; **102:** 1190–1198.
626. Jacobs MJ, de Mol BA, Elenbaas T, Mess WH, Kalkman CJ, Schurink GW, et al. Spinal cord blood supply in patients with thoracoabdominal aortic aneurysms. *J Vasc Surg* 2002; **35:** 30–37.
627. Backes WH, Nijenhuis RJ, Mess WH, Wilmink FA, Schurink GW, Jacobs MJ. Magnetic resonance angiography of collateral blood supply to spinal cord in thoracic and thoracoabdominal aortic aneurysm patients. *J Vasc Surg* 2008; **48:** 261–271.
628. Eagle KA, Rihal CS, Mickel MC, Holmes DR, Foster ED, Gersh BJ. Cardiac risk of noncardiac surgery: Influence of coronary disease and type of surgery in 3368 operations. *Circulation* 1997; **96:** 1882–1887.
629. Poldermans D, Schouten O, Vidakovic R, Bax JJ, Thomson IR, Hoeks SE, et al; DECREASE Study Group. A clinical randomized trial to evaluate the safety of a noninvasive approach in high-risk patients undergoing major vascular surgery: The DECREASE-V Pilot Study. *J Am Coll Cardiol* 2007; **49:** 1763–1769.
630. Svensson LG, Hess KR, Coselli JS, Safi HJ, Crawford ES. A prospective study of respiratory failure after high-risk surgery on the thoracoabdominal aorta. *J Vasc Surg* 1991; **14:** 271–282.
631. Safi HJ, Harlin SA, Miller CC, Iliopoulos DC, Joshi A, Mohasci TG, et al. Predictive factors for acute renal failure in thoracic and thoracoabdominal aortic aneurysm surgery. *J Vasc Surg* 1996; **24:** 338–345.
632. Goldstein LJ, Davies RR, Rizzo JA, Davila JJ, Cooperberg MR, Shaw RK, et al. Stroke in surgery of the thoracic aorta: Incidence, impact, etiology, and prevention. *J Thorac Cardiovasc Surg* 2001; **122:** 935–945.
633. Mitchell RS. Stent grafts for the thoracic aorta: A new paradigm? *Ann Thorac Surg* 2002; **74:** S1818–S1820.
634. Cambria RA, Gloviczki P, Stanson AW, Cherry KJ, Bower TC, Hallett JW, et al. Outcome and expansion rate of 57 thoracoabdominal aortic aneurysms managed nonoperatively. *Am J Surg*

1995; **170:** 213–217.
635. Davies RR, Goldstein LJ, Coady MA, Tittle SL, Rizzo JA, Kopf GS, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: Simple prediction based on size. *Ann Thorac Surg* 2002; **73:** 17–28.
636. Khoynezhad A, Donayre CE, Bui H, Kopchok GE, Walot I, White RA. Risk factors of neurologic deficit after thoracic aortic endografting. *Ann Thorac Surg* 2007; **83:** S882–S889.
637. Czerny M, Eggebrecht H, Sodeck G, Verzini F, Cao P, Maritati G, et al. Mechanisms of symptomatic spinal cord ischemia after TEVAR: Insights from the European Registry of Endovascular Aortic Repair Complications (EuREC). *J Endovasc Ther* 2012; **19:** 37–43.
638. Mehta VK, Lafaro RJ, De Vincenzo S. Successful management of an aneurysmal aortoesophageal fistula. *J Cardiovasc Surg (Torino)* 2000; **41:** 721–723.
639. Kawaharada N, Morishita K, Hyodoh H, Fujisawa Y, Fukada J, Hachiro Y, et al. Magnetic resonance angiographic localization of the artery of Adamkiewicz for spinal cord blood supply. *Ann Thorac Surg* 2004; **78:** 846–851.
640. Coselli JS, LeMaire SA, Conklin LD, Adams GJ. Left heart bypass during descending thoracic aortic aneurysm repair does not reduce the incidence of paraplegia. *Ann Thorac Surg* 2004; **77:** 1298–1303.
641. Svensson LG, Crawford ES, Hess KR, Coselli JS, Safi HJ. Experience with 1509 patients undergoing thoracoabdominal aortic operations. *J Vasc Surg* 1993; **17:** 357–370.
642. Fehrenbacher JW, Hart DW, Huddleston E, Siderys H, Rice C. Optimal end-organ protection for thoracic and thoracoabdominal aortic aneurysm repair using deep hypothermic circulatory arrest. *Ann Thorac Surg* 2007; **83:** 1041–1046.
643. Patel HJ, Shillingford MS, Mihalik S, Proctor MC, Deeb GM. Resection of the descending thoracic aorta: Outcomes after use of hypothermic circulatory arrest. *Ann Thorac Surg* 2006; **82:** 90–96.
644. Minatoya K, Ogino H, Matsuda H, Sasaki H, Yagihara T, Kitamura S. Replacement of the descending aorta: Recent outcomes of open surgery performed with partial cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 2008; **136:** 431–435.
645. Schermerhorn ML, Giles KA, Hamdan AD, Dalhberg SE, Hagberg R, Pomposelli F. Population-based outcomes of open descending thoracic aortic aneurysm repair. *J Vasc Surg* 2008; **48:** 821–827.
646. Coselli JS, LeMaire SA, Conklin LD, Köksoy C, Schmittling ZC. Morbidity and mortality after extent II thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 2002; **73:** 1107–1116.
647. Suzuki S, Davis CA, Miller CC, Huynh TT, Estrera AL, Porat EE, et al. Cardiac function predicts mortality following thoracoabdominal and descending thoracic aortic aneurysm repair. *Eur J Cardiothorac Surg* 2003; **24:** 119–124.
648. LeMaire SA, Miller CC, Conklin LD, Schmittling ZC, Köksoy C, Coselli JS. A new predictive model for adverse outcomes after elective thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 2001; **71:** 1233–1238.
649. Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal aortic aneurysms. *Ann Thorac Surg* 2007; **83:** S862–S864.
650. Lemaire SA, Jones MM, Conklin LD, Carter SA, Criddell MD, Wang XL, et al. Randomized comparison of cold blood and cold crystalloid renal perfusion for renal protection during thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 2009; **49:** 11–19.
651. Khan SN, Stansby G. Cerebrospinal fluid drainage for thoracic and thoracoabdominal aortic aneurysm surgery. *Cochrane Database Syst Rev* 2012: CD003635.
652. Coselli JS, LeMaire SA, Köksoy C, Schmittling ZC, Curling PE. Cerebrospinal fluid drainage reduces paraplegia after thoracoabdominal aortic aneurysm repair: Results of a randomized clinical trial. *J Vasc Surg* 2002; **35:** 631–639.
653. Fedorow CA, Moon MC, Mutch WA, Grocott HP. Lumbar cerebrospinal fluid drainage for thoracoabdominal aortic surgery: Rationale and practical considerations for management. *Anesth Analg* 2010; **111:** 46–58.
654. Bicknell CD, Riga CV, Wolfe JH. Prevention of paraplegia during thoracoabdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg* 2009; **37:** 654–660.
655. Cowan JA, Dimick JB, Henke PK, Huber TS, Stanley JC, Upchurch GR. Surgical treatment of intact thoracoabdominal aortic aneurysms in the United States: Hospital and surgeon volume-related outcomes. *J Vasc Surg* 2003; **37:** 1169–1174.
656. Karthikesalingam A, Hinchliffe RJ, Loftus IM, Thompson MM, Holt PJ. Volume-outcome relationships in vascular surgery: The current status. *J Endovasc Ther* 2010; **17:** 356–365.
657. Estrera AL, Miller CC, Huynh TT, Porat E, Safi HJ. Neurologic outcome after thoracic and thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 2001; **72:** 1225–1231.
658. Crawford ES, Crawford JL, Safi HJ, Coselli JS, Hess KR, Brooks B, et al. Thoracoabdominal aortic aneurysms: Preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. *J Vasc Surg* 1986; **3:** 389–404.
659. Safi HJ, Winnerkvist A, Miller CC, Iliopoulos DC, Reardon MJ, Espada R, et al. Effect of extended cross-clamp time during thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 1998; **66:** 1204–1209.
660. Svensson LG, Crawford ES, Hess KR, Coselli JS, Safi HJ. Dissection of the aorta and dissecting aortic aneurysms: Improving early and long-term surgical results. *Circulation* 1990; **82 Suppl:** IV24–IV38.
661. Minatoya K, Seike Y, Itonaga T, Oda T, Inoue Y, Kawamoto N, et al. Straight incision for extended descending and thoracoabdominal aortic replacement: Novel and simple exposure with rib-cross thoracotomy. *Interact Cardiovasc Thorac Surg* 2016; **23:** 367–370.
662. Kazui T, Yamashita K, Terada H, Washiyama N. Retrograde segmental aortic repair for type II thoracoabdominal aortic aneurysm. *J Thorac Cardiovasc Surg* 2004; **127:** 1827–1829.
663. Frank SM, Parker SD, Rock P, Gorman RB, Kelly S, Beattie C, et al. Moderate hypothermia, with partial bypass and segmental sequential repair for thoracoabdominal aortic aneurysm. *J Vasc Surg* 1994; **19:** 687–697.
664. Henmi S, Ikeno Y, Yokawa K, Gotake Y, Nakai H, Yamanaka K, et al. Comparison of early patency rate and long-term outcomes of various techniques for reconstruction of segmental arteries during thoracoabdominal aortic aneurysm repair. *Eur J Cardiothorac Surg* 2019; **56:** 313–320.
665. Carrel TP, Signer C. Separate revascularization of the visceral arteries in thoracoabdominal aneurysm repair. *Ann Thorac Surg* 1999; **68:** 573–575.
666. Coselli JS. The use of left heart bypass in the repair of thoracoabdominal aortic aneurysms: Current techniques and results. *Semin Thorac Cardiovasc Surg* 2003; **15:** 326–332.
667. Kouchoukos NT, Daily BB, Rokkas CK, Murphy SF, Bauer S, Abboud N. Hypothermic bypass and circulatory arrest for operations on the descending thoracic and thoracoabdominal aorta. *Ann Thorac Surg* 1995; **60:** 67–77.
668. Okita Y, Takamoto S, Ando M, Morota T, Yamaki F, Matsukawa R, et al. Repair for aneurysms of the entire descending thoracic aorta or thoracoabdominal aorta using a deep hypothermia. *Eur J Cardiothorac Surg* 1997; **12:** 120–126.
669. Hanssen SJ, Derikx JP, Vermeulen Windsant IC, Heijmans JH, Koeppel TA, Schurink GW, et al. Visceral injury and systemic inflammation in patients undergoing extracorporeal circulation during aortic surgery. *Ann Surg* 2008; **248:** 117–125.
670. Conrad MF, Crawford RS, Davison JK, Cambria RP. Thoracoabdominal aneurysm repair: A 20-year perspective. *Ann Thorac Surg* 2007; **83:** S856–S861.
671. Jacobs MJ, Mess W, Mochtar B, Nijenhuis RJ, Statius van Eps RG, Schurink GW. The value of motor evoked potentials in reducing paraplegia during thoracoabdominal aneurysm repair. *J Vasc Surg* 2006; **43:** 239–246.
672. Ogino H, Sasaki H, Minatoya K, Matsuda H, Yamada N, Kitamura S. Combined use of adamkiewicz artery demonstration and motor-evoked potentials in descending and thoracoabdominal repair. *Ann Thorac Surg* 2006; **82:** 592–596.
673. de Haan P, Kalkman CJ, de Mol BA, Ubags LH, Veldman DJ, Jacobs MJ. Efficacy of transcranial motor-evoked myogenic potentials to detect spinal cord ischemia during operations for thoracoabdominal aneurysms. *J Thorac Cardiovasc Surg* 1997; **113:** 87–101.
674. Meylaerts SA, Jacobs MJ, van Iterson V, De Haan P, Kalkman CJ. Comparison of transcranial motor evoked potentials and somatosensory evoked potentials during thoracoabdominal aortic aneurysm repair. *Ann Surg* 1999; **230:** 742–749.
675. Rigberg DA, McGory ML, Zingmond DS, Maggard MA, Agustin M, Lawrence PF, et al. Thirty-day mortality statistics underestimate the risk of repair of thoracoabdominal aortic aneurysms: A statewide experience. *J Vasc Surg* 2006; **43:** 217–222.
676. Alsawas M, Zaiem F, Larrea-Mantilla L, Almasri J, Erwin PJ,

Upchurch GR, et al. Effectiveness of surgical interventions for thoracic aortic aneurysms: A systematic review and meta-analysis. *J Vasc Surg* 2017; **66:** 1258–1268.
677. Gopaldas RR, Huh J, Dao TK, LeMaire SA, Chu D, Bakaeen FG, et al. Superior nationwide outcomes of endovascular versus open repair for isolated descending thoracic aortic aneurysm in 11,669 patients. *J Thorac Cardiovasc Surg* 2010; **140:** 1001–1010.
678. Nation DA, Wang GJ. TEVAR: Endovascular repair of the thoracic aorta. *Semin Intervent Radiol* 2015; **32:** 265–271.
679. Ullery BW, Cheung AT, Fairman RM, Jackson BM, Woo EY, Bavaria J, et al. Risk factors, outcomes, and clinical manifestations of spinal cord ischemia following thoracic endovascular aortic repair. *J Vasc Surg* 2011; **54:** 677–684.
680. Desai ND, Burtch K, Moser W, Moeller P, Szeto WY, Pochettino A, et al. Long-term comparison of thoracic endovascular aortic repair (TEVAR) to open surgery for the treatment of thoracic aortic aneurysms. *J Thorac Cardiovasc Surg* 2012; **144:** 604–611.
681. Martin DJ, Martin TD, Hess PJ, Daniels MJ, Feezor RJ, Lee WA. Spinal cord ischemia after TEVAR in patients with abdominal aortic aneurysms. *J Vasc Surg* 2009; **49:** 302–306.
682. Chiesa R, Melissano G, Marrocco-Trischitta MM, Civilini E, Setacci F. Spinal cord ischemia after elective stent-graft repair of the thoracic aorta. *J Vasc Surg* 2005; **42:** 11–17.
683. Leon LR, Mills JL, Jordan W, Morasch MM, Kovacs M, Becker GJ, et al. The risks of celiac artery coverage during endoluminal repair of thoracic and thoracoabdominal aortic aneurysms. *Vasc Endovascular Surg* 2009; **43:** 51–60.
684. Jonker FH, Schlösser FJ, Moll FL, van Herwaarden JA, Indes JE, Verhagen HJ, et al. Outcomes of thoracic endovascular aortic repair for aortobronchial and aortoesophageal fistulas. *J Endovasc Ther* 2009; **16:** 428–440.
685. Patel HJ, Williams DM, Upchurch GR, Dasika NL, Eliason JL, Deeb GM. Late outcomes of endovascular aortic repair for the infected thoracic aorta. *Ann Thorac Surg* 2009; **87:** 1366–1372.
686. Sörelius K, Mani K, Björck M, Nyman R, Wanhainen A. Endovascular repair of mycotic aortic aneurysms. *J Vasc Surg* 2009; **50:** 269–274.
687. Riesenman PJ, Brooks JD, Farber MA. Thoracic endovascular aortic repair of aortobronchial fistulas. *J Vasc Surg* 2009; **50:** 992–998.
688. Buth J, Harris PL, Hobo R, van Eps R, Cuypers P, Duijm L, et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: Incidence and risk factors: A study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. *J Vasc Surg* 2007; **46:** 1103–1111.
689. Maldonado TS, Dexter D, Rockman CB, Veith FJ, Garg K, Arko F, et al. Left subclavian artery coverage during thoracic endovascular aortic aneurysm repair does not mandate revascularization. *J Vasc Surg* 2013; **57:** 116–124.
690. Matsumura JS, Lee WA, Mitchell RS, Farber MA, Murad MH, Lumsden AB, et al. The society for vascular surgery practice guidelines: Management of the left subclavian artery with thoracic endovascular aortic repair. *J Vasc Surg* 2009; **50:** 1155–1158.
691. Rizvi AZ, Murad MH, Fairman RM, Erwin PJ, Montori VM. The effect of left subclavian artery coverage on morbidity and mortality in patients undergoing endovascular thoracic aortic interventions: A systematic review and meta-analysis. *J Vasc Surg* 2009; **50:** 1159–1169.
692. Cooper DG, Walsh SR, Sadat U, Noorani A, Hayes PD, Boyle JR. Neurological complications after left subclavian artery coverage during thoracic endovascular aortic repair: A systematic review and meta-analysis. *J Vasc Surg* 2009; **49:** 1594–1601.
693. Libicher M, Reichert V, Aleksic M, Brunkwall J, Lackner KJ, Gawenda M. Balloon occlusion of the celiac artery: A test for evaluation of collateral circulation prior endovascular coverage. *Eur J Vasc Endovasc Surg* 2008; **36:** 303–305.
694. Lee WA, Brown MP, Martin TD, Seeger JM, Huber TS. Early results after staged hybrid repair of thoracoabdominal aortic aneurysms. *J Am Coll Surg* 2007; **205:** 420–431.
695. Alonso Pérez M, Llaneza Coto JM, Del Castro Madrazo JA, Fernández Prendes C, González Gay M, Zanabili Al-Sibbai A. Debranching aortic surgery. *J Thorac Dis* 2017; **9 Suppl:** S465–S477.
696. Shuto T, Wada T, Miyamoto S, Kamei N, Hongo N, Mori H. Ten-year experience of the thoraco-abdominal aortic aneurysm treatment using a hybrid thoracic endovascular aortic repair. *Interact Cardiovasc Thorac Surg* 2018; **26:** 951–956.
697. Chiesa R, Tshomba Y, Marone EM, Logaldo D, Bertoglio L, Kahlberg A, et al. Hybrid procedures for the treatment of thoracoabdominal aortic aneurysms and dissections. *J Cardiovasc Surg (Torino)* 2010; **51:** 821–832.
698. Benrashid E, Wang H, Andersen ND, Keenan JE, McCann RL, Hughes GC. Complementary roles of open and hybrid approaches to thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 2016; **64:** 1228–1238.
699. Hawkins RB, Mehaffey JH, Narahari AK, Jain A, Ghanta RK, Kron IL, et al. Improved outcomes and value in staged hybrid extent II thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 2017; **66:** 1357–1363.
700. Shahverdyan R, Gawenda M, Brunkwall J. Five-year patency rates of renal and visceral bypasses after abdominal debranching for thoraco-abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2013; **45:** 648–656.
701. Bisdas T, Donas KP, Bosiers MJ, Torsello G, Austermann M. Custom-made versus off-the-shelf multibranched endografts for endovascular repair of thoracoabdominal aortic aneurysms. *J Vasc Surg* 2014; **60:** 1186–1195.
702. Maurel B, Delclaux N, Sobocinski J, Hertault A, Martin-Gonzalez T, Moussa M, et al. Editor's choice - The impact of early pelvic and lower limb reperfusion and attentive peri-operative management on the incidence of spinal cord ischemia during thoracoabdominal aortic aneurysm endovascular repair. *Eur J Vasc Endovasc Surg* 2015; **49:** 248–254.
703. Orr N, Minion D, Bobadilla JL. Thoracoabdominal aortic aneurysm repair: Current endovascular perspectives. *Vasc Health Risk Manag* 2014; **10:** 493–505.
704. Verhoeven EL, Katsargyris A, Bekkema F, Oikonomou K, Zeebregts CJ, Ritter W, et al. Editor's choice - Ten-year experience with endovascular repair of thoracoabdominal aortic aneurysms: Results from 166 consecutive patients. *Eur J Vasc Endovasc Surg* 2015; **49:** 524–531.
705. Mastracci TM, Greenberg RK, Eagleton MJ, Hernandez AV. Durability of branches in branched and fenestrated endografts. *J Vasc Surg* 2013; **57:** 926–933.
706. Haulon S, Barillà D, Tyrrell M. Part one: For the motion: Fenestrated endografts should be restricted to a small number of specialized centers. *Eur J Vasc Endovasc Surg* 2013; **45:** 200–203.
707. Clough RE, Modarai B, Bell RE, Salter R, Sabharwal T, Taylor PR, et al. Total endovascular repair of thoracoabdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2012; **43:** 262–267.
708. Semba CP, Kato N, Kee ST, Lee GK, Mitchell RS, Miller DC, et al. Acute rupture of the descending thoracic aorta: Repair with use of endovascular stent-grafts. *J Vasc Interv Radiol* 1997; **8:** 337–342.
709. Joyeux F, Canaud L, Hireche K, Berthet JP, Marty-Ane C, Alric P. Temporary extra-anatomic brain perfusion followed by total rerouting of the supra-aortic vessels for hybrid repair of a ruptured aortic arch aneurysm. *J Vasc Surg* 2011; **54:** 1145–1147.
710. Kim JH, Yang JS, Oh SS, Na CY. Emergency one-stage hybrid surgery for ruptured aneurysm of the distal aortic arch. *Tex Heart Inst J* 2013; **40:** 343–346.
711. Shimizu H, Hirahara N, Motomura N, Miyata H, Takamoto S. Current status of cardiovascular surgery in Japan, 2015 and 2016: Analysis of data from Japan Cardiovascular Surgery Database: 4-Thoracic aortic surgery. *Gen Thorac Cardiovasc Surg* 2019; **67:** 751–757.
712. Johansson G, Markström U, Swedenborg J. Ruptured thoracic aortic aneurysms: A study of incidence and mortality rates. *J Vasc Surg* 1995; **21:** 985–988.
713. Yiu RS, Cheng SW. Natural history and risk factors for rupture of thoracic aortic arch aneurysms. *J Vasc Surg* 2016; **63:** 1189–1194.
714. Bashir M, Fok M, Hammoud I, Rimmer L, Shaw M, Field M, et al. A perspective on natural history and survival in nonoperated thoracic aortic aneurysm Patients. *Aorta (Stamford)* 2013; **1:** 182–189.
715. Kawatani Y, Hayashi Y, Ito Y, Kurobe H, Nakamura Y, Suda Y, et al. A case of ruptured aortic arch aneurysm successfully treated by thoracic endovascular aneurysm repair with chimney graft. *Case Rep Surg* 2015; **2015:** 780147.
716. Prêtre R, Murith N, Delay D, Kalonji T. Surgical management of hemorrhage from rupture of the aortic arch. *Ann Thorac*

Surg 1998; **65:** 1291–1295.
717. Melnitchouk S, Pfammatter T, Kadner A, Dave H, Witzke H, Trentz O, et al. Emergency stent-graft placement for hemorrhage control in acute thoracic aortic rupture. *Eur J Cardiothorac Surg* 2004; **25:** 1032–1038.
718. Doevendans PA, Geskes GG, van Aarnhem G, van Suylen R. Ruptured aneurysm of the left sinus of Valsalva into the pericardium. *Neth Heart J* 2001; **9:** 346–348.
719. Marroush TS, Boshara AR, Botros B, Vendittelli P, Ahmed Z, Dawood L, et al. Rupture of sinus of Valsalva aneurysm: Two case reports and a concise review of the literature. *Heart Lung* 2018; **47:** 131–135.
720. Luo X, Zhang D, Li B, Qi L, Gong L, Tang Y, et al. Surgical repair of a ruptured congenital sinus of Valsalva aneurysm: 10-year experience with 286 cases. *Eur J Cardiothorac Surg* 2019; **55:** 1211–1218.
721. Murashita T, Kubota T, Kamikubo Y, Shiiya N, Yasuda K. Long-term results of aortic valve regurgitation after repair of ruptured sinus of valsalva aneurysm. *Ann Thorac Surg* 2002; **73:** 1466–1471.
722. Lin TT, Tsai HE, Lin L, Chen TY, Lee CP, Wu CC. Very late recurrence of sinus of Valsalva aneurysm rupture after patch repair. *BMC Surg* 2014; **14:** 73.
723. Kuriakose EM, Bhatla P, McElhinney DB. Comparison of reported outcomes with percutaneous versus surgical closure of ruptured sinus of Valsalva aneurysm. *Am J Cardiol* 2015; **115:** 392–398.
724. Zhang B, Sun Y, Wu J, Zhu JY, Cao R, Liu XL, et al. Failed transcatheter closure of a giant ruptured sinus of Valsalva aneurysm. *Chin Med J (Engl)* 2015; **128:** 1985–1986.
725. Saeyeldin A, Zafar MA, Velasquez CA, Ip K, Gryaznov A, Brownstein AJ, et al. Natural history of aortic root aneurysms in Marfan syndrome. *Ann Cardiothorac Surg* 2017; **6:** 625–632.
726. Chu MWA, Losenno KL, Dubois LA, Jones PM, Ouzounian M, Whitlock R, et al; Canadian Thoracic Aortic Collaborative (CTAC) Investigators. Early clinical outcomes of hybrid arch frozen elephant trunk repair with the thoraflex hybrid graft. *Ann Thorac Surg* 2019; **107:** 47–53.
727. Harky A, Chan JSK, Wong CHM, Francis C, Bashir M. Current challenges in open versus endovascular repair of ruptured thoracic aortic aneurysm. *J Vasc Surg* 2018; **68:** 1582–1592.
728. Cambria RP, Crawford RS, Cho JS, Bavaria J, Farber M, Lee WA, et al; GORE TAG Investigators. A multicenter clinical trial of endovascular stent graft repair of acute catastrophes of the descending thoracic aorta. *J Vasc Surg* 2009; **50:** 1255–1264.
729. Patel HJ, Williams DM, Upchurch GR, Dasika NL, Deeb GM. A comparative analysis of open and endovascular repair for the ruptured descending thoracic aorta. *J Vasc Surg* 2009; **50:** 1265–1270.
730. McCallum JC, Limmer KK, Perricone A, Bandyk D, Kansal N. Case report and review of the literature total endovascular repair of acute ascending aortic rupture: A case report and review of the literature. *Vasc Endovascular Surg* 2013; **47:** 374–378.
731. Milewski RK, Szeto WY, Pochettino A, Moser GW, Moeller P, Bavaria JE. Have hybrid procedures replaced open aortic arch reconstruction in high-risk patients?: A comparative study of elective open arch debranching with endovascular stent graft placement and conventional elective open total and distal aortic arch reconstruction. *J Thorac Cardiovasc Surg* 2010; **140:** 590–597.
732. Matsumoto A, Kanaoka Y, Baba T, Takizawa R, Hara M, Maeda K, et al. Result of thoracic endovascular aortic repair for patients with esophageal cancer. *World J Surg* 2018; **42:** 1551–1558.
733. Marulli G, Rea F, Zampieri D, Antonello M, Maurizi G, Venuta F, et al. Safe resection of the aortic wall infiltrated by lung cancer after placement of an endoluminal prosthesis. *Ann Thorac Surg* 2015; **99:** 1768–1773.
734. Collaud S, Waddell TK, Yasufuku K, Oreopoulos G, Rampersaud R, Rubin B, et al. Thoracic aortic endografting facilitates the resection of tumors infiltrating the aorta. *J Thorac Cardiovasc Surg* 2014; **147:** 1178–1182.
735. Cowan JA, Dimick JB, Wainess RM, Henke PK, Stanley JC, Upchurch GR. Ruptured thoracoabdominal aortic aneurysm treatment in the United States: 1988 to 1998. *J Vasc Surg* 2003; **38:** 319–322.
736. Gaudino M, Lau C, Munjal M, Girardi LN. Open repair of ruptured descending thoracic and thoracoabdominal aortic aneurysms. *J Thorac Cardiovasc Surg* 2015; **150:** 814–821.
737. Locham SS, Grimm JC, Arhuidese IJ, Nejim B, Obeid T, Black JH, et al. Perioperative outcomes of open versus endovascular repair for ruptured thoracoabdominal aneurysms. *Ann Vasc Surg* 2017; **44:** 128–135.
738. Minami T, Imoto K, Uchida K, Karube N, Yasuda S, Choh T, et al. Thoracic endovascular aortic repair for ruptured descending thoracic aortic aneurysm. *J Card Surg* 2015; **30:** 163–169.
739. Kilic A, Shah AS, Black JH, Whitman GJ, Yuh DD, Cameron DE, et al. Trends in repair of intact and ruptured descending thoracic aortic aneurysms in the United States: A population-based analysis. *J Thorac Cardiovasc Surg* 2014; **147:** 1855–1860.
740. Ultee KHJ, Zettervall SL, Soden PA, Buck DB, Deery SE, Shean KE, et al. The impact of endovascular repair on management and outcome of ruptured thoracic aortic aneurysms. *J Vasc Surg* 2017; **66:** 343–352.
741. Pecoraro F, Pfammatter T, Mayer D, Frauenfelder T, Papadimitriou D, Hechelhammer L, et al. Multiple periscope and chimney grafts to treat ruptured thoracoabdominal and pararenal aortic aneurysms. *J Endovasc Ther* 2011; **18:** 642–649.
742. Gallitto E, Gargiulo M, Freyrie A, Pini R, Mascoli C, Ancetti S, et al. Off-the-shelf multibranched endograft for urgent endovascular repair of thoracoabdominal aortic aneurysms. *J Vasc Surg* 2017; **66:** 696–704.
743. Bisdas T, Donas KP, Bosiers M, Torsello G, Austermann M. One-year follow-up after total endovascular repair of a contained-ruptured thoracoabdominal aortic aneurysm with the sandwich technique. *J Vasc Surg* 2013; **58:** 482–485.
744. Oderich GS, Mendes BC, Gloviczki P, Kalra M, Duncan AA, Bower TC. Current role and future directions of hybrid repair of thoracoabdominal aortic aneurysms. *Perspect Vasc Surg Endovasc Ther* 2012; **24:** 14–22.
745. Gkremoutis A, Schmandra T, Meyn M, Schmitz-Rixen T, Keese M. Hybrid approach to emergent and urgent treatment of complex thoracoabdominal aortic pathology. *Eur J Vasc Endovasc Surg* 2014; **48:** 407–413.
746. Usui A, Fujimoto K, Ishiguchi T, Yoshikawa M, Akita T, Ueda Y. Cerebrospinal dysfunction after endovascular stent-grafting via a median sternotomy: The frozen elephant trunk procedure. *Ann Thorac Surg* 2002; **74:** S1821–S1824.
747. Di Eusanio M, Pantaleo A, Murana G, Pellicciari G, Castrovinci S, Berretta P, et al. Frozen elephant trunk surgery-the Bologna's experience. *Ann Cardiothorac Surg* 2013; **2:** 597–605.
748. Deleted in proof.
749. Kato M, Ohnishi K, Kaneko M, Ueda T, Kishi D, Mizushima T, et al. New graft-implanting method for thoracic aortic aneurysm or dissection with a stented graft. *Circulation* 1996; **94 Suppl:** II188–II193.
750. Borst HG, Walterbusch G, Schaps D. Extensive aortic replacement using "elephant trunk" prosthesis. *Thorac Cardiovasc Surg* 1983; **31:** 37–40.
751. Patel HJ, Nguyen C, Diener AC, Passow MC, Salata D, Deeb GM. Open arch reconstruction in the endovascular era: Analysis of 721 patients over 17 years. *J Thorac Cardiovasc Surg* 2011; **141:** 1417–1423.
752. Koizumi K, Ueda T, Shimizu H, Yozu R. Pull-through technique for entire thoracic aortic dissection without additional left thoracotomy. *Interact Cardiovasc Thorac Surg* 2011; **12:** 339–340.
753. Kieffer E, Petitjean C, Richard T, Godet G, Dhobb M, Ruotolo C. Exclusion-bypass for aneurysms of the descending thoracic and thoracoabdominal aorta. *Ann Vasc Surg* 1986; **1:** 182–195.
754. Tokuda Y, Oshima H, Narita Y, Abe T, Mutsuga M, Fujimoto K, et al. Extended total arch replacement via the L-incision approach: Single-stage repair for extensive aneurysms of the aortic arch. *Interact Cardiovasc Thorac Surg* 2016; **22:** 750–755.
755. Tominaga R, Kurisu K, Ochiai Y, Nakashima A, Masuda M, Morita S, et al. Total aortic arch replacement through the L-incision approach. *Ann Thorac Surg* 2003; **75:** 121–125.
756. Ishikawa N, Omoto T, Ono M, Miyauchi T, Oi M, Maruta K, et al. Antero-lateral partial sternotomy for extensive thoracic aortic aneurysm. *Interact Cardiovasc Thorac Surg* 2013; **16:** 327–331.
757. Kollias VD, Lozos V, Angouras D, Toumpoulis I, Rokkas CK. Single-stage, off-pump hybrid repair of extensive aneurysms of the aortic arch and the descending thoracic aorta. *Hellenic J Cardiol* 2014; **55:** 355–360.
758. Matsueda T, Ikeno Y, Yokawa K, Koda Y, Henmi S, Inoue T, et al. One-stage replacement of the aorta from arch to thoracoabdominal region. *J Thorac Cardiovasc Surg* 2018; **155:** 498–504.
759. Tokuda Y, Oshima H, Narita Y, Abe T, Araki Y, Mutsuga M,

et al. Hybrid versus open repair of aortic arch aneurysms: comparison of postoperative and mid-term outcomes with a propensity score-matching analysis. *Eur J Cardiothorac Surg* 2016; **49:** 149–156.
760. Tokuda Y, Narita Y, Fujimoto K, Mutsuga M, Terazawa S, Ito H, et al. Neurologic deficit after aortic arch replacement: The influence of the aortic atherosclerosis. *Ann Thorac Surg* 2019; **108:** 107–114.
761. Vardulaki KA, Prevost TC, Walker NM, Day NE, Wilmink AB, Quick CR, et al. Growth rates and risk of rupture of abdominal aortic aneurysms. *Br J Surg* 1998; **85:** 1674–1680.
762. Chang JB, Stein TA, Liu JP, Dunn ME. Risk factors associated with rapid growth of small abdominal aortic aneurysms. *Surgery* 1997; **121:** 117–122.
763. Brown LC, Powell JT. Risk factors for aneurysm rupture in patients kept under ultrasound surveillance: UK Small Aneurysm Trial Participants. *Ann Surg* 1999; **230:** 289–296.
764. Strachan DP. Predictors of death from aortic aneurysm among middle-aged men: The Whitehall study. *Br J Surg* 1991; **78:** 401–404.
765. Sprouse LR, Meier GH, Lesar CJ, Demasi RJ, Sood J, Parent FN, et al. Comparison of abdominal aortic aneurysm diameter measurements obtained with ultrasound and computed tomography: Is there a difference? *J Vasc Surg* 2003; **38:** 466–471.
766. Salata K, Syed M, Hussain MA, de Mestral C, Greco E, Mamdani M, et al. Statins reduce abdominal aortic aneurysm growth, rupture, and perioperative mortality: A systematic review and meta-analysis. *J Am Heart Assoc* 2018; **7:** e008657.
767. Thompson SG, Brown LC, Sweeting MJ, Bown MJ, Kim LG, Glover MJ, et al. Systematic review and meta-analysis of the growth and rupture rates of small abdominal aortic aneurysms: Implications for surveillance intervals and their cost-effectiveness. *Health Technol Assess* 2013; **17:** 1–118.
768. Lederle FA, Freischlag JA, Kyriakides TC, Matsumura JS, Padberg FT, Kohler TR, et al; OVER Veterans Affairs Cooperative Study Group. Long-term comparison of endovascular and open repair of abdominal aortic aneurysm. *N Engl J Med* 2012; **367:** 1988–1997.
769. Hertzer NR, Mascha EJ, Karafa MT, O'Hara PJ, Krajewski LP, Beven EG. Open infrarenal abdominal aortic aneurysm repair: The Cleveland Clinic experience from 1989 to 1998. *J Vasc Surg* 2002; **35:** 1145–1154.
770. Hirose K, Chikamori T, Hida S, Tanaka H, Igarashi Y, Watanabe Y, et al. Prevalence of coronary heart disease in patients with aortic aneurysm and/or peripheral artery disease. *Am J Cardiol* 2009; **103:** 1215–1220.
771. Hackam DG, Thiruchelvam D, Redelmeier DA. Angiotensin-converting enzyme inhibitors and aortic rupture: A population-based case-control study. *Lancet* 2006; **368:** 659–665.
772. Sweeting MJ, Thompson SG, Brown LC, Greenhalgh RM, Powell JT. Use of angiotensin converting enzyme inhibitors is associated with increased growth rate of abdominal aortic aneurysms. *J Vasc Surg* 2010; **52:** 1–4.
773. Thompson A, Cooper JA, Fabricius M, Humphries SE, Ashton HA, Hafez H. An analysis of drug modulation of abdominal aortic aneurysm growth through 25 years of surveillance. *J Vasc Surg* 2010; **52:** 55–61.
774. Bicknell CD, Kiru G, Falaschetti E, Powell JT, Poulter NR, Poulter N; AARDVARK Collaborators. An evaluation of the effect of an angiotensin-converting enzyme inhibitor on the growth rate of small abdominal aortic aneurysms: A randomized placebo-controlled trial (AARDVARK). *Eur Heart J* 2016; **37:** 3213–3221.
775. Myers J, McElrath M, Jaffe A, Smith K, Fonda H, Vu A, et al. A randomized trial of exercise training in abdominal aortic aneurysm disease. *Med Sci Sports Exerc* 2014; **46:** 2–9.
776. Gadowski GR, Pilcher DB, Ricci MA. Abdominal aortic aneurysm expansion rate: Effect of size and beta-adrenergic blockade. *J Vasc Surg* 1994; **19:** 727–731.
777. Powell JT, Greenhalgh RM. Small abdominal aortic aneurysms. *N Engl J Med* 2003; **348:** 1895–1901.
778. Brewster DC, Cronenwett JL, Hallett JW, Johnston KW, Krupski WC, Matsumura JS. Guidelines for the treatment of abdominal aortic aneurysms: Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. *J Vasc Surg* 2003; **37:** 1106–1117.
779. Sterpetti AV, Cavallaro A, Cavallari N, Allegrucci P, Tamburelli A, Agosta F, et al. Factors influencing the rupture of abdominal aortic aneurysms. *Surg Gynecol Obstet* 1991; **173:** 175–178.
780. Faggioli GL, Stella A, Gargiulo M, Tarantini S, D'Addato M, Ricotta JJ. Morphology of small aneurysms: Definition and impact on risk of rupture. *Am J Surg* 1994; **168:** 131–135.
781. Hunter GC, Smyth SH, Aguirre ML, Baxter BT, Bull DA, King DD, et al. Incidence and histologic characteristics of blebs in patients with abdominal aortic aneurysms. *J Vasc Surg* 1996; **24:** 93–101.
782. Fillinger MF, Marra SP, Raghavan ML, Kennedy FE. Prediction of rupture risk in abdominal aortic aneurysm during observation: Wall stress versus diameter. *J Vasc Surg* 2003; **37:** 724–732.
783. Lederle FA, Johnson GR, Wilson SE, Gordon IL, Chute EP, Littooy FN, et al; The Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Investigators. Relationship of age, gender, race, and body size to infrarenal aortic diameter. *J Vasc Surg* 1997; **26:** 595–601.
784. Lederle FA, Johnson GR, Wilson SE, Chute EP, Littooy FN, Bandyk D, et al; Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Group. Prevalence and associations of abdominal aortic aneurysm detected through screening. *Ann Intern Med* 1997; **126:** 441–449.
785. Singh K, Bønaa KH, Jacobsen BK, Bjørk L, Solberg S. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: The Tromsø Study. *Am J Epidemiol* 2001; **154:** 236–244.
786. Lord JW, Rossi G, Daliana M, Drago JR, Schwartz AM. Unsuspected abdominal aortic aneurysms as the cause of peripheral arterial occlusive disease. *Ann Surg* 1973; **177:** 767–771.
787. Nemir P, Micozzi MS. Combined aneurysmal and occlusive arterial disease. *Circulation* 1977; **56 Suppl:** II169–II170.
788. Baxter BT, McGee GS, Flinn WR, McCarthy WJ, Pearce WH, Yao JS. Distal embolization as a presenting symptom of aortic aneurysms. *Am J Surg* 1990; **160:** 197–201.
789. Rinckenbach S, Albertini JN, Thaveau F, Steinmetz E, Camin A, Ohanessian L, et al. Prehospital treatment of infrarenal ruptured abdominal aortic aneurysms: A multicentric analysis. *Ann Vasc Surg* 2010; **24:** 308–314.
790. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet* 1998; **352:** 1649–1655.
791. Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al; Aneurysm Detection and Management Veterans Affairs Cooperative Study Group. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 2002; **346:** 1437–1444.
792. Cao P, De Rango P, Verzini F, Parlani G, Romano L, Cieri E, et al; CAESAR Trial Group. Comparison of surveillance versus aortic endografting for small aneurysm repair (CAESAR): Results from a randomised trial. *Eur J Vasc Endovasc Surg* 2011; **41:** 13–25.
793. Ouriel K, Clair DG, Kent KC, Zarins CK; Positive Impact of Endovascular Options for treating Aneurysms Early (PIVOTAL) Investigators. Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg* 2010; **51:** 1081–1087.
794. Japanese Society for Vascular Surgery Database Management Committee Member, NCD Vascular Surgery Data Analysis Team. Vascular surgery in Japan: 2013 annual report by the Japanese society for vascular surgery. [in Japanese] *Jpn J Vasc Surg* 2019; **28:** 273–292.
795. Bown MJ, Sweeting MJ, Brown LC, Powell JT, Thompson SG, Thompson SG; RESCAN Collaborators. Surveillance intervals for small abdominal aortic aneurysms: A meta-analysis. *JAMA* 2013; **309:** 806–813.
796. Filardo G, Powell JT, Martinez MA, Ballard DJ. Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database Syst Rev* 2015: CD001835.
797. CAESAR Trial Collaborators. Comparison of surveillance *vs* Aortic Endografting for Small Aneurysm Repair (CAESAR) trial: Study design and progress. *Eur J Vasc Endovasc Surg* 2005; **30:** 245–251.
798. Ouriel K. The PIVOTAL study: A randomized comparison of endovascular repair versus surveillance in patients with smaller abdominal aortic aneurysms. *J Vasc Surg* 2009; **49:** 266–269.
799. Hatakeyama T, Shigematsu H, Muto T. Risk factors for rupture of abdominal aortic aneurysm based on three-dimensional study. *J Vasc Surg* 2001; **33:** 453–461.
800. Sharp MA, Collin J. A myth exposed: Fast growth in diameter does not justify precocious abdominal aortic aneurysm repair.

Eur J Vasc Endovasc Surg 2003; **25:** 408–411.
801. Soden PA, Zettervall SL, Ultee KH, Darling JD, Buck DB, Hile CN, et al. Outcomes for symptomatic abdominal aortic aneurysms in the American College of Surgeons National Surgical Quality Improvement Program. *J Vasc Surg* 2016; **64:** 297–305.
802. Ten Bosch JA, Koning SW, Willigendael EM, VAN Sambeek MR, Stokmans RA, Prins MH, et al. Symptomatic abdominal aortic aneurysm repair: To wait or not to wait. *J Cardiovasc Surg (Torino)* 2016; **57:** 830–838.
803. Sullivan CA, Rohrer MJ, Cutler BS. Clinical management of the symptomatic but unruptured abdominal aortic aneurysm. *J Vasc Surg* 1990; **11:** 799–803.
804. Kvilekval KH, Best IM, Mason RA, Newton GB, Giron F. The value of computed tomography in the management of symptomatic abdominal aortic aneurysms. *J Vasc Surg* 1990; **12:** 28–33.
805. Nevitt MP, Ballard DJ, Hallett JW. Prognosis of abdominal aortic aneurysms: A population-based study. *N Engl J Med* 1989; **321:** 1009–1014.
806. Sörelius K, Wanhainen A, Furebring M, Björck M, Gillgren P, Mani K, et al; Swedish Collaborator Group for Mycotic Abdominal Aortic Aneurysms. Nationwide study of the treatment of mycotic abdominal aortic aneurysms comparing open and endovascular repair. *Circulation* 2016; **134:** 1822–1832.
807. Laine MT, Björck M, Beiles CB, Szeberin Z, Thomson I, Altreuther M, et al. Few internal iliac artery aneurysms rupture under 4 cm. *J Vasc Surg* 2017; **65:** 76–81.
808. Olsen PS, Schroeder T, Agerskov K, Røder O, Sørensen S, Perko M, et al. Surgery for abdominal aortic aneurysms: A survey of 656 patients. *J Cardiovasc Surg (Torino)* 1991; **32:** 636–642.
809. Crawford ES, Cohen ES. Aortic aneurysm: A multifocal disease: Presidential address. *Arch Surg* 1982; **117:** 1393–1400.
810. Dent TL, Lindenauer SM, Ernst CB, Fry WJ. Multiple arteriosclerotic arterial aneurysms. *Arch Surg* 1972; **105:** 338–344.
811. Steyerberg EW, Kievit J, de Mol Van Otterloo JC, van Bockel JH, Eijkemans MJ, Habbema JD. Perioperative mortality of elective abdominal aortic aneurysm surgery: A clinical prediction rule based on literature and individual patient data. *Arch Intern Med* 1995; **155:** 1998–2004.
812. Nitecki SS, Hallett JW, Stanson AW, Ilstrup DM, Bower TC, Cherry KJ, et al. Inflammatory abdominal aortic aneurysms: A case-control study. *J Vasc Surg* 1996; **23:** 860–869.
813. Pearce WH, Parker MA, Feinglass J, Ujiki M, Manheim LM. The importance of surgeon volume and training in outcomes for vascular surgical procedures. *J Vasc Surg* 1999; **29:** 768–778.
814. Brady AR, Fowkes FG, Greenhalgh RM, Powell JT, Ruckley CV, Thompson SG; UK Small Aneurysm Trial participants. Risk factors for postoperative death following elective surgical repair of abdominal aortic aneurysm: Results from the UK Small Aneurysm Trial. *Br J Surg* 2000; **87:** 742–749.
815. Tu JV, Austin PC, Johnston KW. The influence of surgical specialty training on the outcomes of elective abdominal aortic aneurysm surgery. *J Vasc Surg* 2001; **33:** 447–452.
816. Sarac TP, Clair DG, Hertzer NR, Greenberg RK, Krajewski LP, O'Hara PJ, et al. Contemporary results of juxtarenal aneurysm repair. *J Vasc Surg* 2002; **36:** 1104–1111.
817. Eslami MH, Rybin DV, Doros G, Siracuse JJ, Farber A. External validation of Vascular Study Group of New England risk predictive model of mortality after elective abdominal aorta aneurysm repair in the Vascular Quality Initiative and comparison against established models. *J Vasc Surg* 2018; **67:** 143–150.
818. Durazzo AE, Machado FS, Ikeoka DT, De Bernoche C, Monachini MC, Puech-Leão P, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: A randomized trial. *J Vasc Surg* 2004; **39:** 967–975.
819. Lindenauer PK, Pekow P, Wang K, Gutierrez B, Benjamin EM. Lipid-lowering therapy and in-hospital mortality following major noncardiac surgery. *JAMA* 2004; **291:** 2092–2099.
820. Schouten O, Boersma E, Hoeks SE, Benner R, van Urk H, van Sambeek MR, et al; Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. Fluvastatin and perioperative events in patients undergoing vascular surgery. *N Engl J Med* 2009; **361:** 980–989.
821. Brady AR, Gibbs JS, Greenhalgh RM, Powell JT, Sydes MR; POBBLE trial investigators. Perioperative β-blockade (POBBLE) for patients undergoing infrarenal vascular surgery: Results of a randomized double-blind controlled trial. *J Vasc Surg* 2005; **41:** 602–609.
822. Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, Villar JC, et al; POISE Study Group. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): A randomised controlled trial. *Lancet* 2008; **371:** 1839–1847.
823. Yang H, Raymer K, Butler R, Parlow J, Roberts R. The effects of perioperative β-blockade: Results of the Metoprolol after Vascular Surgery (MaVS) study, a randomized controlled trial. *Am Heart J* 2006; **152:** 983–990.
824. Mehta M, Veith FJ, Darling RC, Roddy SP, Ohki T, Lipsitz EC, et al. Effects of bilateral hypogastric artery interruption during endovascular and open aortoiliac aneurysm repair. *J Vasc Surg* 2004; **40:** 698–702.
825. Marconi M, Ceragioli S, Mocellin DM, Alberti A, Tomei F, Adami D, et al. Open surgical management of hypogastric artery during aortic surgery: Ligate or not ligate? *Ann Vasc Surg* 2015; **29:** 780–785.
826. Arko FR, Lee WA, Hill BB, Fogarty TJ, Zarins CK. Hypogastric artery bypass to preserve pelvic circulation: Improved outcome after endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2004; **39:** 404–408.
827. Chong T, Nguyen L, Owens CD, Conte MS, Belkin M. Suprarenal aortic cross-clamp position: A reappraisal of its effects on outcomes for open abdominal aortic aneurysm repair. *J Vasc Surg* 2009; **49:** 873–880.
828. Knott AW, Kalra M, Duncan AA, Reed NR, Bower TC, Hoskin TL, et al. Open repair of juxtarenal aortic aneurysms (JAA) remains a safe option in the era of fenestrated endografts. *J Vasc Surg* 2008; **47:** 695–701.
829. Sugimoto M, Takahashi N, Niimi K, Kodama A, Banno H, Komori K. Long-term fate of renal function after open surgery for juxtarenal and pararenal aortic aneurysm. *J Vasc Surg* 2018; **67:** 1042–1050.
830. Stewart AH, Eyers PS, Earnshaw JJ. Prevention of infection in peripheral arterial reconstruction: A systematic review and meta-analysis. *J Vasc Surg* 2007; **46:** 148–155.
831. Zelenock GB, Strodel WE, Knol JA, Messina LM, Wakefield TW, Lindenauer SM, et al. A prospective study of clinically and endoscopically documented colonic ischemia in 100 patients undergoing aortic reconstructive surgery with aggressive colonic and direct pelvic revascularization, compared with historic controls. *Surgery* 1989; **106:** 771–779.
832. Seeger JM, Coe DA, Kaelin LD, Flynn TC. Routine reimplantation of patent inferior mesenteric arteries limits colon infarction after aortic reconstruction. *J Vasc Surg* 1992; **15:** 635–641.
833. Mitchell KM, Valentine RJ. Inferior mesenteric artery reimplantation does not guarantee colon viability in aortic surgery. *J Am Coll Surg* 2002; **194:** 151–155.
834. Becquemin JP, Majewski M, Fermani N, Marzelle J, Desgrandes P, Allaire E, et al. Colon ischemia following abdominal aortic aneurysm repair in the era of endovascular abdominal aortic repair. *J Vasc Surg* 2008; **47:** 258–263.
835. Senekowitsch C, Assadian A, Assadian O, Hartleb H, Ptakovsky H, Hagmüller GW. Replanting the inferior mesentery artery during infrarenal aortic aneurysm repair: Influence on postoperative colon ischemia. *J Vasc Surg* 2006; **43:** 689–694.
836. Johnston KW, Scobie TK. Multicenter prospective study of nonruptured abdominal aortic aneurysms: I. Population and operative management. *J Vasc Surg* 1988; **7:** 69–81.
837. Bosanquet DC, Ansell J, Abdelrahman T, Cornish J, Harries R, Stimpson A, et al. Systematic review and meta-regression of factors affecting midline incisional hernia rates: Analysis of 14,618 patients. *PLoS One* 2015; **10:** e0138745.
838. Deery SE, Lancaster RT, Baril DT, Indes JE, Bertges DJ, Conrad MF, et al. Contemporary outcomes of open complex abdominal aortic aneurysm repair. *J Vasc Surg* 2016; **63:** 1195–1200.
839. Henriksen NA, Helgstrand F, Vogt KC, Jorgensen LN, Bisgaard T; Danish Hernia Database. Risk factors for incisional hernia repair after aortic reconstructive surgery in a nationwide study. *J Vasc Surg* 2013; **57:** 1524–1530.
840. Edwards JM, Teefey SA, Zierler RE, Kohler TR. Intraabdominal paraanastomotic aneurysms after aortic bypass grafting. *J Vasc Surg* 1992; **15:** 344–353.
841. Dardik A, Lin JW, Gordon TA, Williams GM, Perler BA. Results of elective abdominal aortic aneurysm repair in the 1990s: A population-based analysis of 2335 cases. *J Vasc Surg* 1999; **30:** 985–995.
842. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, Batista I, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med* 2002; **346:** 1128–1137.

843. De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven EL, Cuypers PW, et al; DREAM Study Group. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2010; **362:** 1881–1889.
844. Lederle FA, Stroupe KT, Kyriakides TC, Ge L, Freischlag JA; Open vs Endovascular Repair (OVER) Veterans Affairs Cooperative Study Group. Long-term cost-effectiveness in the veterans affairs open vs endovascular repair study of aortic abdominal aneurysm: A randomized clinical trial. *JAMA Surg* 2016; **151:** 1139–1144.
845. Herman CR, Charbonneau P, Hongku K, Dubois L, Hossain S, Lee K, et al. Any nonadherence to instructions for use predicts graft-related adverse events in patients undergoing elective endovascular aneurysm repair. *J Vasc Surg* 2018; **67:** 126–133.
846. Abbruzzese TA, Kwolek CJ, Brewster DC, Chung TK, Kang J, Conrad MF, et al. Outcomes following endovascular abdominal aortic aneurysm repair (EVAR): An anatomic and device-specific analysis. *J Vasc Surg* 2008; **48:** 19–28.
847. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. *Circulation* 2011; **123:** 2848–2855.
848. Stanley BM, Semmens JB, Mai Q, Goodman MA, Hartley DE, Wilkinson C, et al. Evaluation of patient selection guidelines for endoluminal AAA repair with the Zenith Stent-Graft: The Australasian experience. *J Endovasc Ther* 2001; **8:** 457–464.
849. Zarins CK, Bloch DA, Crabtree T, Matsumoto AH, White RA, Fogarty TJ. Stent graft migration after endovascular aneurysm repair: Importance of proximal fixation. *J Vasc Surg* 2003; **38:** 1264–1272.
850. Sampaio SM, Panneton JM, Mozes GI, Andrews JC, Bower TC, Karla M, et al. Proximal type I endoleak after endovascular abdominal aortic aneurysm repair: Predictive factors. *Ann Vasc Surg* 2004; **18:** 621–628.
851. Leurs LJ, Hobo R, Buth J; EUROSTAR Collaborators. The multicenter experience with a third-generation endovascular device for abdominal aortic aneurysm repair: A report from the EUROSTAR database. *J Cardiovasc Surg (Torino)* 2004; **45:** 293–300.
852. Hobo R, Kievit J, Leurs LJ, Buth J; EUROSTAR Collaborators. Influence of severe infrarenal aortic neck angulation on complications at the proximal neck following endovascular AAA repair: A EUROSTAR study. *J Endovasc Ther* 2007; **14:** 1–11.
853. Waasdorp EJ, de Vries JP, Hobo R, Leurs LJ, Buth J, Moll FL; EUROSTAR Collaborators. Aneurysm diameter and proximal aortic neck diameter influence clinical outcome of endovascular abdominal aortic repair: A 4-year EUROSTAR experience. *Ann Vasc Surg* 2005; **19:** 755–761.
854. Lal BK, Zhou W, Li Z, Kyriakides T, Matsumura J, Lederle FA, et al; OVER Veterans Affairs Cooperative Study Group. Predictors and outcomes of endoleaks in the Veterans Affairs Open Versus Endovascular Repair (OVER) Trial of Abdominal Aortic Aneurysms. *J Vasc Surg* 2015; **62:** 1394–1404.
855. Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG; EVAR trial participants. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: Randomised controlled trial. *Lancet* 2004; **364:** 843–848.
856. Mani K, Björck M, Lundkvist J, Wanhainen A. Improved long-term survival after abdominal aortic aneurysm repair. *Circulation* 2009; **120:** 201–211.
857. Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Greenhalgh RM; United Kingdom EVAR Trial Investigators. Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *N Engl J Med* 2010; **362:** 1872–1880.
858. Sweeting MJ, Patel R, Powell JT, Greenhalgh RM; EVAR Trial Investigators. Endovascular repair of abdominal aortic aneurysm in patients physically ineligible for open repair: Very long-term follow-up in the EVAR-2 randomized controlled trial. *Ann Surg* 2017; **266:** 713–719.
859. Samura M, Morikage N, Otsuka R, Mizoguchi T, Takeuchi Y, Nagase T, et al. Endovascular aneurysm repair with inferior mesenteric artery embolization for preventing type II endoleak: A prospective randomized controlled trial. *Ann Surg* 2020; **271:** 238–244.
860. Rao R, Lane TR, Franklin IJ, Davies AH. Open repair versus fenestrated endovascular aneurysm repair of juxtarenal aneurysms. *J Vasc Surg* 2015; **61:** 242–255.
861. Donas KP, Lee JT, Lachat M, Torsello G, Veith FJ, Dalman RL; PERICLES investigators. Collected world experience about the performance of the snorkel/chimney endovascular technique in the treatment of complex aortic pathologies: The PERICLES registry. *Ann Surg* 2015; **262:** 546–553.
862. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg* 1991; **5:** 491–499.
863. Böckler D, Holden A, Thompson M, Hayes P, Krievins D, de Vries JP, et al. Multicenter Nellix EndoVascular Aneurysm Sealing system experience in aneurysm sac sealing. *J Vasc Surg* 2015; **62:** 290–298.
864. Buth J, van Marrewijk CJ, Harris PL, Hop WC, Riambau V, Laheij RJ; EUROSTAR Collaborators. Outcome of endovascular abdominal aortic aneurysm repair in patients with conditions considered unfit for an open procedure: A report on the EUROSTAR experience. *J Vasc Surg* 2002; **35:** 211–221.
865. Japanese Society for Vascular Surgery. 日本における血管外科手術例数調査2006. [in Japanese] Available at: http://jsvs.jp/enquete/result/index.html (accessed October 3, 2019).
866. Kristensen SD, Knuuti J, Saraste A, Anker S, Bøtker HE, Hert SD, et al. 2014 ESC/ESA guidelines on non-cardiac surgery: Cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: Cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J* 2014; **35:** 2383–2431.
867. Parker MV, O'Donnell SD, Chang AS, Johnson CA, Gillespie DL, Goff JM, et al. What imaging studies are necessary for abdominal aortic endograft sizing?: A prospective blinded study using conventional computed tomography, aortography, and three-dimensional computed tomography. *J Vasc Surg* 2005; **41:** 199–205.
868. Ruppert V, Leurs LJ, Steckmeier B, Buth J, Umscheid T. Influence of anesthesia type on outcome after endovascular aortic aneurysm repair: An analysis based on EUROSTAR data. *J Vasc Surg* 2006; **44:** 16–21.
869. Nelson PR, Kracjer Z, Kansal N, Rao V, Bianchi C, Hashemi H, et al. A multicenter, randomized, controlled trial of totally percutaneous access versus open femoral exposure for endovascular aortic aneurysm repair (the PEVAR trial). *J Vasc Surg* 2014; **59:** 1181–1193.
870. Bobadilla JL, Hoch JR, Leverson GE, Tefera G. The effect of warfarin therapy on endoleak development after endovascular aneurysm repair (EVAR) of the abdominal aorta. *J Vasc Surg* 2010; **52:** 267–271.
871. Schlösser FJ, Gusberg RJ, Dardik A, Lin PH, Verhagen HJ, Moll FL, et al. Aneurysm rupture after EVAR: Can the ultimate failure be predicted? *Eur J Vasc Endovasc Surg* 2009; **37:** 15–22.
872. Wyss TR, Brown LC, Powell JT, Greenhalgh RM. Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair: Data from the EVAR Trials. *Ann Surg* 2010; **252:** 805–812.
873. Fransen GA, Vallabhaneni SR, van Marrewijk CJ, Laheij RJ, Harris PL, Buth J. Rupture of infra-renal aortic aneurysm after endovascular repair: A series from EUROSTAR registry. *Eur J Vasc Endovasc Surg* 2003; **26:** 487–493.
874. Katsargyris A, Yazar O, Oikonomou K, Bekkema F, Tielliu I, Verhoeven EL. Fenestrated stent-grafts for salvage of prior endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg* 2013; **46:** 49–56.
875. Naughton PA, Garcia-Toca M, Rodriguez HE, Keeling AN, Resnick SA, Morasch MD, et al. Endovascular treatment of delayed type 1 and 3 endoleaks. *Cardiovasc Intervent Radiol* 2011; **34:** 751–757.
876. Jordan WD, Mehta M, Varnagy D, Moore WM, Arko FR, Joye J, et al; Aneurysm Treatment using the Heli-FX Aortic Securement System Global Registry (ANCHOR) Workgroup Members. Results of the ANCHOR prospective, multicenter registry of EndoAnchors for type Ia endoleaks and endograft migration in patients with challenging anatomy. *J Vasc Surg* 2014; **60:** 885–892.
877. Kim JK, Noll RE, Tonnessen BH, Sternbergh WC. A technique for increased accuracy in the placement of the "giant" Palmaz stent for treatment of type IA endoleak after endovascular abdominal aneurysm repair. *J Vasc Surg* 2008; **48:** 755–757.
878. Donas KP, Telve D, Torsello G, Pitoulias G, Schwindt A, Austermann M. Use of parallel grafts to save failed prior endovascular aortic aneurysm repair and type Ia endoleaks. *J Vasc Surg* 2015; **62:** 578–584.
879. Lo RC, Buck DB, Herrmann J, Hamdan AD, Wyers M, Patel

VI, et al; Vascular Study Group of New England. Risk factors and consequences of persistent type II endoleaks. *J Vasc Surg* 2016; **63:** 895–901.
880. Marchiori A, von Ristow A, Guimaraes M, Schönholz C, Uflacker R. Predictive factors for the development of type II endoleaks. *J Endovasc Ther* 2011; **18:** 299–305.
881. Couchet G, Pereira B, Carrieres C, Maumias T, Ribal JP, Ben Ahmed S, et al. Predictive factors for type II endoleaks after treatment of abdominal aortic aneurysm by conventional endovascular aneurysm repair. *Ann Vasc Surg* 2015; **29:** 1673–1679.
882. Otsu M, Ishizaka T, Watanabe M, Hori T, Kohno H, Ishida K, et al. Analysis of anatomical risk factors for persistent type II endoleaks following endovascular abdominal aortic aneurysm repair using CT angiography. *Surg Today* 2016; **46:** 48–55.
883. Sarac TP, Gibbons C, Vargas L, Liu J, Srivastava S, Bena J, et al. Long-term follow-up of type II endoleak embolization reveals the need for close surveillance. *J Vasc Surg* 2012; **55:** 33–40.
884. Biancari F, Mäkelä J, Juvonen T, Venermo M. Is inferior mesenteric artery embolization indicated prior to endovascular repair of abdominal aortic aneurysm? *Eur J Vasc Endovasc Surg* 2015; **50:** 671–674.
885. Lagios K, Karaolanis G, Bazinas T, Perdikides T, Bountouris I. Translumbar infusion of *N*-Butyl cyanoacrylate for the treatment of type II endoleaks. *J Vasc Interv Radiol* 2018; **29:** 826–832.
886. White GH, May J, Waugh RC, Chaufour X, Yu W. Type III and type IV endoleak: Toward a complete definition of blood flow in the sac after endoluminal AAA repair. *J Endovasc Surg* 1998; **5:** 305–309.
887. Lin PH, Bush RL, Katzman JB, Zemel G, Puente OA, Katzen BT, et al. Delayed aortic aneurysm enlargement due to endotension after endovascular abdominal aortic aneurysm repair. *J Vasc Surg* 2003; **38:** 840–842.
888. Faure EM, Becquemin JP, Cochennec F, Garcia Monaco R; ENGAGE collaborators. Predictive factors for limb occlusions after endovascular aneurysm repair. *J Vasc Surg* 2015; **61:** 1138–1145.
889. Karthikesalingam A, Holt PJ, Hinchliffe RJ, Nordon IM, Loftus IM, Thompson MM. Risk of reintervention after endovascular aortic aneurysm repair. *Br J Surg* 2010; **97:** 657–663.
890. Mantas GK, Antonopoulos CN, Sfyroeras GS, Moulakakis KG, Kakisis JD, Mylonas SN, et al. Factors predisposing to endograft limb occlusion after endovascular aortic repair. *Eur J Vasc Endovasc Surg* 2015; **49:** 39–44.
891. Cochennec F, Becquemin JP, Desgranges P, Allaire E, Kobeiter H, Roudot-Thoraval F. Limb graft occlusion following EVAR: Clinical pattern, outcomes and predictive factors of occurrence. *Eur J Vasc Endovasc Surg* 2007; **34:** 59–65.
892. Wang G, Zhai S, Li T, Li X, Lu D, Wang B, et al. Limb graft occlusion following endovascular aortic repair: Incidence, causes, treatment and prevention in a study cohort. *Exp Ther Med* 2017; **14:** 1763–1768.
893. Conway AM, Modarai B, Taylor PR, Carrell TW, Waltham M, Salter R, et al. Stent-graft limb deployment in the external iliac artery increases the risk of limb occlusion following endovascular AAA repair. *J Endovasc Ther* 2012; **19:** 79–85.
894. Mertens J, Houthoofd S, Daenens K, Fourneau I, Maleux G, Lerut P, et al. Long-term results after endovascular abdominal aortic aneurysm repair using the Cook Zenith endograft. *J Vasc Surg* 2011; **54:** 48–57.
895. Stokmans RA, Teijink JA, Forbes TL, Böckler D, Peeters PJ, Riambau V, et al. Early results from the ENGAGE registry: Real-world performance of the Endurant Stent Graft for endovascular AAA repair in 1262 patients. *Eur J Vasc Endovasc Surg* 2012; **44:** 369–375.
896. Taudorf M, Jensen LP, Vogt KC, Grønvall J, Schroeder TV, Lönn L. Endograft limb occlusion in EVAR: Iliac tortuosity quantified by three different indices on the basis of preoperative CTA. *Eur J Vasc Endovasc Surg* 2014; **48:** 527–533.
897. Cao P, Verzini F, Zannetti S, De Rango P, Parlani G, Lupattelli L, et al. Device migration after endoluminal abdominal aortic aneurysm repair: Analysis of 113 cases with a minimum follow-up period of 2 years. *J Vasc Surg* 2002; **35:** 229–235.
898. Pintoux D, Chaillou P, Azema L, Bizouarn P, Costargent A, Patra P, et al. Long-term influence of suprarenal or infrarenal fixation on proximal neck dilatation and stentgraft migration after EVAR. *Ann Vasc Surg* 2011; **25:** 1012–1019.
899. Tonnessen BH, Sternbergh WC, Money SR. Mid- and long-term device migration after endovascular abdominal aortic aneurysm repair: A comparison of AneuRx and Zenith endografts. *J Vasc Surg* 2005; **42:** 392–401.
900. Sternbergh WC III, Money SR, Greenberg RK, Chuter TA; Zenith Investigators. Influence of endograft oversizing on device migration, endoleak, aneurysm shrinkage, and aortic neck dilation: Results from the Zenith Multicenter Trial. *J Vasc Surg* 2004; **39:** 20–26.
901. van Prehn J, Schlösser FJ, Muhs BE, Verhagen HJ, Moll FL, van Herwaarden JA. Oversizing of aortic stent grafts for abdominal aneurysm repair: A systematic review of the benefits and risks. *Eur J Vasc Endovasc Surg* 2009; **38:** 42–53.
902. Bastos Gonçalves F, Oliveira NF, Josee van Rijn M, Ultee KH, Hoeks SE, Ten Raa S, et al. Iliac seal zone dynamics and clinical consequences after endovascular aneurysm repair. *Eur J Vasc Endovasc Surg* 2017; **53:** 185–192.
903. Roos H, Sandström C, Koutouzi G, Jeppsson A, Falkenberg M. Predisposing factors for re-interventions with additional iliac stent grafts after endovascular aortic repair. *Eur J Vasc Endovasc Surg* 2017; **53:** 89–94.
904. May J, White GH, Yu W, Waugh R, Stephen M, Sieunarine K, et al. Conversion from endoluminal to open repair of abdominal aortic aneurysms: A hazardous procedure. *Eur J Vasc Endovasc Surg* 1997; **14:** 4–11.
905. Lipsitz EC, Ohki T, Veith FJ, Suggs WD, Wain RA, Rhee SJ, et al. Delayed open conversion following endovascular aortoiliac aneurysm repair: Partial (or complete) endograft preservation as a useful adjunct. *J Vasc Surg* 2003; **38:** 1191–1198.
906. Nabi D, Murphy EH, Pak J, Zarins CK. Open surgical repair after failed endovascular aneurysm repair: Is endograft removal necessary? *J Vasc Surg* 2009; **50:** 714–721.
907. Argyriou C, Georgiadis GS, Lazarides MK, Georgakarakos E, Antoniou GA. Endograft infection after endovascular abdominal aortic aneurysm repair: A systematic review and meta-analysis. *J Endovasc Ther* 2017; **24:** 688–697.
908. Smeds MR, Duncan AA, Harlander-Locke MP, Lawrence PF, Lyden S, Fatima J, et al; Vascular Low-Frequency Disease Consortium. Treatment and outcomes of aortic endograft infection. *J Vasc Surg* 2016; **63:** 332–340.
909. Fukuchi K, Ishida Y, Higashi M, Tsunekawa T, Ogino H, Minatoya K, et al. Detection of aortic graft infection by fluorodeoxyglucose positron emission tomography: Comparison with computed tomographic findings. *J Vasc Surg* 2005; **42:** 919–925.
910. Shukuzawa K, Ohki T, Maeda K, Kanaoka Y. Risk factors and treatment outcomes for stent graft infection after endovascular aortic aneurysm repair. *J Vasc Surg* 2019; **70:** 181–192.
911. Oderich GS, Bower TC, Hofer J, Kalra M, Duncan AA, Wilson JW, et al. In situ rifampin-soaked grafts with omental coverage and antibiotic suppression are durable with low reinfection rates in patients with aortic graft enteric erosion or fistula. *J Vasc Surg* 2011; **53:** 99–107.
912. Kakkos SK, Bicknell CD, Tsolakis IA, Bergqvist D; Hellenic Co-operative Group on Aortic Surgery. Editor's choice - Management of secondary aorto-enteric and other abdominal arterio-enteric fistulas: A review and pooled data analysis. *Eur J Vasc Endovasc Surg* 2016; **52:** 770–786.
913. Chaer RA, Barbato JE, Lin SC, Zenati M, Kent KC, McKinsey JF. Isolated iliac artery aneurysms: A contemporary comparison of endovascular and open repair. *J Vasc Surg* 2008; **47:** 708–713.
914. Huang Y, Gloviczki P, Duncan AA, Kalra M, Hoskin TL, Oderich GS, et al. Common iliac artery aneurysm: Expansion rate and results of open surgical and endovascular repair. *J Vasc Surg* 2008; **47:** 1203–1211.
915. Buck DB, Bensley RP, Darling J, Curran T, McCallum JC, Moll FL, et al. The effect of endovascular treatment on isolated iliac artery aneurysm treatment and mortality. *J Vasc Surg* 2015; **62:** 331–335.
916. Patel NV, Long GW, Cheema ZF, Rimar K, Brown OW, Shanley CJ. Open vs. endovascular repair of isolated iliac artery aneurysms: A 12-year experience. *J Vasc Surg* 2009; **49:** 1147–1153.
917. Zhorzel S, Busch A, Trenner M, Reutersberg B, Salvermoser M, Eckstein HH, et al. Open versus endovascular repair of isolated iliac artery aneurysms. *Vasc Endovascular Surg* 2019; **53:** 12–20.
918. Mehta M, Veith FJ, Ohki T, Cynamon J, Goldstein K, Suggs WD, et al. Unilateral and bilateral hypogastric artery interruption during aortoiliac aneurysm repair in 154 patients: A relatively innocuous procedure. *J Vasc Surg* 2001; **33 Suppl:** S27–S32.
919. Eagleton MJ, Shah S, Petkosevek D, Mastracci TM, Greenberg

RK. Hypogastric and subclavian artery patency affects onset and recovery of spinal cord ischemia associated with aortic endografting. *J Vasc Surg* 2014; **59:** 89–94.
920. Taudorf M, Grønvall J, Schroeder TV, Lönn L. Endovascular aneurysm repair treatment of aortoiliac aneurysms: Can iliac branched devices prevent gluteal claudication? *J Vasc Interv Radiol* 2016; **27:** 174–180.
921. van Sterkenburg SM, Heyligers JM, van Bladel M, Verhagen HJ, Eefting D, van Sambeek MR, et al. Dutch IBE collaboration: Experience with the GORE EXCLUDER iliac branch endoprosthesis for common iliac artery aneurysms. *J Vasc Surg* 2016; **63:** 1451–1457.
922. Gloviczki P, Lawrence PF, Forbes TL. Update of the society for vascular surgery abdominal aortic aneurysm guidelines. *J Vasc Surg* 2018; **67:** 1.
923. Braithwaite B; IMPROVE Trial Investigators. Endovascular strategy or open repair for ruptured abdominal aortic aneurysm: One-year outcomes from the IMPROVE randomized trial. *Eur Heart J* 2015; **36:** 2061–2069.
924. Ulug P; IMPROVE Trial Investigators. Comparative clinical effectiveness and cost effectiveness of endovascular strategy *v* open repair for ruptured abdominal aortic aneurysm: Three year results of the IMPROVE randomised trial. *BMJ* 2017; **359:** j4859.
925. Sweeting MJ, Ulug P, Powell JT, Desgranges P, Balm R, Balm R. Ruptured aneurysm trials: The importance of longer-term outcomes and meta-analysis for 1-year mortality. *Eur J Vasc Endovasc Surg* 2015; **50:** 297–302.
926. Ersryd S, Djavani-Gidlund K, Wanhainen A, Björck M. Editor's choice - Abdominal compartment syndrome after surgery for abdominal aortic aneurysm: A nationwide population based study. *Eur J Vasc Endovasc Surg* 2016; **52:** 158–165.
927. Karkos CD, Menexes GC, Patelis N, Kalogirou TE, Giagtzidis IT, Harkin DW. A systematic review and meta-analysis of abdominal compartment syndrome after endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2014; **59:** 829–842.
928. Björck M, Wanhainen A. Management of abdominal compartment syndrome and the open abdomen. *Eur J Vasc Endovasc Surg* 2014; **47:** 279–287.
929. Khashram M, Williman JA, Hider PN, Jones GT, Roake JA. Management of modifiable vascular risk factors improves late survival following abdominal aortic aneurysm repair: A systematic review and meta-analysis. *Ann Vasc Surg* 2017; **39:** 301–311.
930. Karkos CD, Papadimitriou CT, Chatzivasileiadis TN, Kapsali NS, Kalogirou TE, Giagtzidis IT, et al. The impact of aortic occlusion balloon on mortality after endovascular repair of ruptured abdominal aortic aneurysms: A meta-analysis and meta-regression analysis. *Cardiovasc Intervent Radiol* 2015; **38:** 1425–1437.
931. Mani K, Lees T, Beiles B, Jensen LP, Venermo M, Simo G, et al. Treatment of abdominal aortic aneurysm in nine countries 2005–2009: A vascunet report. *Eur J Vasc Endovasc Surg* 2011; **42:** 598–607.
932. The Japanese Society For Vascular Surgery Database Management Committee Member, Ncd Vascular Surgery Data Analysis Team. Vascular surgery in Japan: 2011 annual report by the Japanese Society for vascular surgery. *Ann Vasc Dis* 2018; **11:** 377–397.
933. The Japanese Society For Vascular Surgery Database Management Committee Member, Ncd Vascular Surgery Data Analysis Team. Vascular surgery in Japan: 2012 annual report by the Japanese Society for vascular surgery. *Ann Vasc Dis* 2019; **12:** 260–279.
934. Japanese Society for Vascular Surgery. 血管外科手術例数アニュアルレポート2013. [in Japanese] Available at: http://www.jsvs.org/ja/enquete/aggregate_2013re3.pdf (accessed July 31, 2020).
935. Acosta S, Ogren M, Bengtsson H, Bergqvist D, Lindblad B, Zdanowski Z. Increasing incidence of ruptured abdominal aortic aneurysm: A population-based study. *J Vasc Surg* 2006; **44:** 237–243.
936. Berland TL, Veith FJ, Cayne NS, Mehta M, Mayer D, Lachat M. Technique of supraceliac balloon control of the aorta during endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2013; **57:** 272–275.
937. Powell JT, Sweeting MJ, Thompson MM, Ashleigh R, Bell R, Gomes M, et al; IMPROVE Trial Investigators. Endovascular or open repair strategy for ruptured abdominal aortic aneurysm: 30 day outcomes from IMPROVE randomised trial. *BMJ* 2014; **348:** f7661.
938. Reimerink JJ, Hoornweg LL, Vahl AC, Wisselink W, van den Broek TA, Legemate DA, et al; Amsterdam Acute Aneurysm Trial Collaborators. Endovascular repair versus open repair of ruptured abdominal aortic aneurysms: A multicenter randomized controlled trial. *Ann Surg* 2013; **258:** 248–256.
939. Desgranges P, Kobeiter H, Katsahian S, Bouffi M, Gouny P, Favre JP, et al; ECAR Investigators. Editor's choice - ECAR (Endovasculaire ou Chirurgie dans les Anévrysmes aorto-iliaques Rompus): A French randomized controlled trial of endovascular versus open surgical repair of ruptured aorto-iliac aneurysms. *Eur J Vasc Endovasc Surg* 2015; **50:** 303–310.
940. Edwards ST, Schermerhorn ML, O'Malley AJ, Bensley RP, Hurks R, Cotterill P, et al. Comparative effectiveness of endovascular versus open repair of ruptured abdominal aortic aneurysm in the medicare population. *J Vasc Surg* 2014; **59:** 575–582.
941. Zhang S, Feng J, Li H, Zhang Y, Lu Q, Jing Z. Open surgery (OS) versus endovascular aneurysm repair (EVAR) for hemodynamically stable and unstable ruptured abdominal aortic aneurysm (rAAA). *Heart Vessels* 2016; **31:** 1291–1302.
942. Mayer D, Rancic Z, Meier C, Pfammatter T, Veith FJ, Lachat M. Open abdomen treatment following endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2009; **50:** 1–7.
943. Peppelenbosch AG, Vermeulen Windsant IC, Jacobs MJ, Tordoir JH, Schurink GW. Open repair for ruptured abdominal aortic aneurysm and the risk of spinal cord ischemia: Review of the literature and risk-factor analysis. *Eur J Vasc Endovasc Surg* 2010; **40:** 589–595.
944. Ali MM, Flahive J, Schanzer A, Simons JP, Aiello FA, Doucet DR, et al. In patients stratified by preoperative risk, endovascular repair of ruptured abdominal aortic aneurysms has a lower in-hospital mortality and morbidity than open repair. *J Vasc Surg* 2015; **61:** 1399–1407.
945. Kotsikoris I, Papas TT, Papanas N, Maras D, Andrikopoulou M, Bessias N, et al. Aortocaval fistula formation due to ruptured abdominal aortic aneurysms: A 12-year series. *Vasc Endovascular Surg* 2012; **46:** 26–29.
946. Nakad G, AbiChedid G, Osman R. Endovascular treatment of major abdominal arteriovenous fistulas: A systematic review. *Vasc Endovascular Surg* 2014; **48:** 388–395.
947. Melas N, Saratzis A, Saratzis N, Lazaridis I, Kiskinis D. Inferior vena cava stent-graft placement to treat endoleak associated with an aortocaval fistula. *J Endovasc Ther* 2011; **18:** 250–254.
948. LaBarbera M, Nathanson D, Hui P. Percutaneous closure of aortocaval fistula using the amplatzer muscular VSD occluder. *J Invasive Cardiol* 2011; **23:** 343–344.
949. Busuttil SJ, Goldstone J. Diagnosis and management of aortoenteric fistulas. *Semin Vasc Surg* 2001; **14:** 302–311.
950. Armstrong PA, Back MR, Wilson JS, Shames ML, Johnson BL, Bandyk DF. Improved outcomes in the recent management of secondary aortoenteric fistula. *J Vasc Surg* 2005; **42:** 660–666.
951. Ranasinghe W, Loa J, Allaf N, Lewis K, Sebastian MG. Primary aortoenteric fistulae: The challenges in diagnosis and review of treatment. *Ann Vasc Surg* 2011; **25:** 386.e1–386.e5.
952. Busuttil RW, Rees W, Baker JD, Wilson SE. Pathogenesis of aortoduodenal fistula: Experimental and clinical correlates. *Surgery* 1979; **85:** 1–13.
953. Sweeney MS, Gadacz TR. Primary aortoduodenal fistula: Manifestation, diagnosis, and treatment. *Surgery* 1984; **96:** 492–497.
954. Ingu A, Takagi N, Izumiyama O, Fujita M, Hasegawa T, Abe T. Isolated iliac artery aneurysmocolonic fistula with pericolic abscess. *Ann Vasc Surg* 2002; **16:** 663–665.
955. Lawlor DK, DeRose G, Harris KA, Forbes TL. Primary aorto/iliac-enteric fistula-report of 6 new cases. *Vasc Endovascular Surg* 2004; **38:** 281–286.
956. Hirst AE Jr, Affeldt J. Abdominal aortic aneurysm with rupture into the duodenum; a report of eight cases. *Gastroenterology* 1951; **17:** 504–514.
957. Voorhoeve R, Moll FL, de Letter JA, Bast TJ, Wester JP, Slee PH. Primary aortoenteric fistula: Report of eight new cases and review of the literature. *Ann Vasc Surg* 1996; **10:** 40–48.
958. O'Hara PJ, Hertzer NR, Beven EG, Krajewski LP. Surgical management of infected abdominal aortic grafts: Review of a 25-year experience. *J Vasc Surg* 1986; **3:** 725–731.
959. Hallett JW, Marshall DM, Petterson TM, Gray DT, Bower TC, Cherry KJ, et al. Graft-related complications after abdominal aortic aneurysm repair: Reassurance from a 36-year population-based experience. *J Vasc Surg* 1997; **25:** 277–286.

960. Spanos K, Kouvelos G, Karathanos C, Matsagkas M, Giannoukas AD. Current status of endovascular treatment of aortoenteric fistula. *Semin Vasc Surg* 2017; **30:** 80–84.
961. Saratzis N, Saratzis A, Melas N, Ktenidis K, Kiskinis D. Aortoduodenal fistulas after endovascular stent-graft repair of abdominal aortic aneurysms: Single-center experience and review of the literature. *J Endovasc Ther* 2008; **15:** 441–448.
962. O'Connor S, Andrew P, Batt M, Becquemin JP. A systematic review and meta-analysis of treatments for aortic graft infection. *J Vasc Surg* 2006; **44:** 38–45.
963. Lemos DW, Raffetto JD, Moore TC, Menzoian JO. Primary aortoduodenal fistula: A case report and review of the literature. *J Vasc Surg* 2003; **37:** 686–689.
964. Chung J, Clagett GP. Neoaortoiliac System (NAIS) procedure for the treatment of the infected aortic graft. *Semin Vasc Surg* 2011; **24:** 220–226.
965. Pagni S, Denatale RW, Sweeney T, McLaughlin C, Ferneini AM. Primary aorto-duodenal fistula secondary to infected abdominal aortic aneurysms: The role of local debridement and extra-anatomic bypass. *J Cardiovasc Surg (Torino)* 1999; **40:** 31–35.
966. Robinson JA, Johansen K. Aortic sepsis: Is there a role for in situ graft reconstruction? *J Vasc Surg* 1991; **13:** 677–684.
967. Chiesa R, Melissano G, Marone EM, Marrocco-Trischitta MM, Kahlberg A. Aorto-oesophageal and aortobronchial fistulae following thoracic endovascular aortic repair: A national survey. *Eur J Vasc Endovasc Surg* 2010; **39:** 273–279.
968. Kakkos SK, Antoniadis PN, Klonaris CN, Papazoglou KO, Giannoukas AD, Matsagkas MI, et al. Open or endovascular repair of aortoenteric fistulas?: A multicentre comparative study. *Eur J Vasc Endovasc Surg* 2011; **41:** 625–634.
969. Kasashima S, Zen Y, Kawashima A, Endo M, Matsumoto Y, Kasashima F, et al. A clinicopathologic study of immunoglobulin G4-related sclerosing disease of the thoracic aorta. *J Vasc Surg* 2010; **52:** 1587–1595.
970. Kasashima S, Kasashima F, Kawashima A, Endo M, Matsumoto Y, Kawakami K. Clinical outcomes after endovascular repair and open surgery to treat immunoglobulin G4-related and nonrelated inflammatory abdominal aortic aneurysms. *J Endovasc Ther* 2017; **24:** 833–845.
971. Skeik N, Ostertag-Hill CA, Garberich RF, Alden PB, Alexander JQ, Cragg AH, et al. Diagnosis, management, and outcome of aortitis at a single center. *Vasc Endovascular Surg* 2017; **51:** 470–479.
972. van Bommel EF, Hendriksz TR, Huiskes AW, Zeegers AG. Brief communication: Tamoxifen therapy for nonmalignant retroperitoneal fibrosis. *Ann Intern Med* 2006; **144:** 101–106.
973. van Bommel EF, van der Veer SJ, Hendriksz TR, Bleumink GS. Persistent chronic peri-aortitis ('inflammatory aneurysm') after abdominal aortic aneurysm repair: Systematic review of the literature. *Vasc Med* 2008; **13:** 293–303.
974. Hellmann DB, Grand DJ, Freischlag JA. Inflammatory abdominal aortic aneurysm. *JAMA* 2007; **297:** 395–400.
975. Paravastu SC, Ghosh J, Murray D, Farquharson FG, Serracino-Inglott F, Walker MG. A systematic review of open versus endovascular repair of inflammatory abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2009; **38:** 291–297.
976. Stone WM, Fankhauser GT, Bower TC, Oderich GS, Oldenburg WA, Kalra M, et al. Comparison of open and endovascular repair of inflammatory aortic aneurysms. *J Vasc Surg* 2012; **56:** 951–956.
977. Walker DI, Bloor K, Williams G, Gillie I. Inflammatory aneurysms of the abdominal aorta. *Br J Surg* 1972; **59:** 609–614.
978. Kim IY, Eun YH, Jeong H, Park TK, Kim H, Lee J, et al. Clinical characteristics and outcomes of 61 patients with chronic periaortitis including IgG4-related and non-IgG4-related cases. *Int J Rheum Dis* 2017; **20:** 1751–1762.
979. Jois RN, Gaffney K, Marshall T, Scott DG. Chronic periaortitis. *Rheumatology (Oxford)* 2004; **43:** 1441–1446.
980. Sterpetti AV, Hunter WJ, Feldhaus RJ, Chasan P, McNamara M, Cisternino S, et al. Inflammatory aneurysms of the abdominal aorta: Incidence, pathologic, and etiologic considerations. *J Vasc Surg* 1989; **9:** 643–650.
981. Koch AE, Haines GK, Rizzo RJ, Radosevich JA, Pope RM, Robinson PG, et al. Human abdominal aortic aneurysms: Immunophenotypic analysis suggesting an immune-mediated response. *Am J Pathol* 1990; **137:** 1199–1213.
982. Rasmussen TE, Hallett JW, Metzger RL, Richardson DM, Harmsen WS, Goronzy JJ, et al. Genetic risk factors in inflammatory abdominal aortic aneurysms: Polymorphic residue 70 in the HLA-DR B1 gene as a key genetic element. *J Vasc Surg* 1997; **25:** 356–364.
983. Rasmussen TE, Hallett JW, Tazelaar HD, Miller VM, Schulte S, O'Fallon WM, et al. Human leukocyte antigen class II immune response genes, female gender, and cigarette smoking as risk and modulating factors in abdominal aortic aneurysms. *J Vasc Surg* 2002; **35:** 988–993.
984. Yonemitsu Y, Nakagawa K, Tanaka S, Mori R, Sugimachi K, Sueishi K. In situ detection of frequent and active infection of human cytomegalovirus in inflammatory abdominal aortic aneurysms: Possible pathogenic role in sustained chronic inflammatory reaction. *Lab Invest* 1996; **74:** 723–736.
985. Rasmussen TE, Hallett JW. Inflammatory aortic aneurysms: A clinical review with new perspectives in pathogenesis. *Ann Surg* 1997; **225:** 155–164.
986. Park MC, Lee SW, Park YB, Chung NS, Lee SK. Clinical characteristics and outcomes of Takayasu's arteritis: Analysis of 108 patients using standardized criteria for diagnosis, activity assessment, and angiographic classification. *Scand J Rheumatol* 2005; **34:** 284–292.
987. Baskerville PA, Blakeney CG, Young AE, Browse NL. The diagnosis and treatment of peri-aortic fibrosis ('inflammatory' aneurysms). *Br J Surg* 1983; **70:** 381–385.
988. Pennell RC, Hollier LH, Lie JT, Bernatz PE, Joyce JW, Pairolero PC, et al. Inflammatory abdominal aortic aneurysms: A thirty-year review. *J Vasc Surg* 1985; **2:** 859–869.
989. Savarese RP, Rosenfeld JC, DeLaurentis DA. Inflammatory abdominal aortic aneurysm. *Surg Gynecol Obstet* 1986; **162:** 405–410.
990. Hayashi T, Ikeda N, Maeda T, Watanabe T. Bilateral ureteral obstruction secondary to abdominal aortic aneurysm. [in Japanese] *Acta urologica Japonica* 1982; **28:** 203–207.
991. 尾崎俊也, 松尾汎, 増田喜一, 他. 炎症性腹部真性大動脈瘤(IAAA)の画像診断. [in Japanese] *Jpn J Med Imaging* 1991; **10:** 24–30.
992. Bianchini Massoni C, von Stein P, Schernthaner M, Gallitto E, Rengier F, Katzen BT, et al. Endovascular treatment of inflammatory infrarenal aortic aneurysms. *Vasc Endovascular Surg* 2016; **50:** 21–28.
993. Walter MA, Melzer RA, Schindler C, Müller-Brand J, Tyndall A, Nitzsche EU. The value of [^{18}F]FDG-PET in the diagnosis of large-vessel vasculitis and the assessment of activity and extent of disease. *Eur J Nucl Med Mol Imaging* 2005; **32:** 674–681.
994. Sakamoto A, Okamoto K, Ishizaka N, Tejima K, Hirata Y, Nagai R. ^{18}F-fluorodeoxyglucose positron emission tomography in a case of retroperitoneal fibrosis. *Int Heart J* 2006; **47:** 645–650.
995. Ishizaka N, Sohmiya K, Miyamura M, Umeda T, Tsuji M, Katsumata T, et al. Infected aortic aneurysm and inflammatory aortic aneurysm--in search of an optimal differential diagnosis. *J Cardiol* 2012; **59:** 123–131.
996. Bown MJ, Nicholson ML, Bell PR, Sayers RD. Cytokines and inflammatory pathways in the pathogenesis of multiple organ failure following abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg* 2001; **22:** 485–495.
997. Klontz KC. Frequency of infected aneurysms among patients in Department of Veterans Affairs hospitals, 1986–1990: The role of Salmonella. *Mil Med* 1997; **162:** 766–768.
998. Chan FY, Crawford ES, Coselli JS, Safi HJ, Williams TW. In situ prosthetic graft replacement for mycotic aneurysm of the aorta. *Ann Thorac Surg* 1989; **47:** 193–203.
999. Müller BT, Wegener OR, Grabitz K, Pillny M, Thomas L, Sandmann W. Mycotic aneurysms of the thoracic and abdominal aorta and iliac arteries: Experience with anatomic and extra-anatomic repair in 33 cases. *J Vasc Surg* 2001; **33:** 106–113.
1000. Miller DV, Oderich GS, Aubry MC, Panneton JM, Edwards WD. Surgical pathology of infected aneurysms of the descending thoracic and abdominal aorta: Clinicopathologic correlations in 29 cases (1976 to 1999). *Hum Pathol* 2004; **35:** 1112–1120.
1001. Hsu RB, Chen RJ, Wang SS, Chu SH. Infected aortic aneurysms: Clinical outcome and risk factor analysis. *J Vasc Surg* 2004; **40:** 30–35.
1002. Fichelle JM, Tabet G, Cormier P, Farkas JC, Laurian C, Gigou F, et al. Infected infrarenal aortic aneurysms: When is in situ reconstruction safe? *J Vasc Surg* 1993; **17:** 635–645.
1003. Yamanaka K, Omura A, Nomura Y, Miyahara S, Shirasaka T, Sakamoto T, et al. Surgical strategy for aorta-related infection. *Eur J Cardiothorac Surg* 2014; **46:** 974–980.
1004. Moneta GL, Taylor LM, Yeager RA, Edwards JM, Nicoloff

AD, McConnell DB, et al. Surgical treatment of infected aortic aneurysm. *Am J Surg* 1998; **175:** 396–399.
1005. Fillmore AJ, Valentine RJ. Surgical mortality in patients with infected aortic aneurysms. *J Am Coll Surg* 2003; **196:** 435–441.
1006. Hollier LH, Money SR, Creely B, Bower TC, Kazmier FJ. Direct replacement of mycotic thoracoabdominal aneurysms. *J Vasc Surg* 1993; **18:** 477–485.
1007. Vogt PR, Brunner-La Rocca HP, Carrel T, von Segesser LK, Ruef C, Debatin J, et al. Cryopreserved arterial allografts in the treatment of major vascular infection: A comparison with conventional surgical techniques. *J Thorac Cardiovasc Surg* 1998; **116:** 965–972.
1008. Lesèche G, Castier Y, Petit MD, Bertrand P, Kitzis M, Mussot S, et al. Long-term results of cryopreserved arterial allograft reconstruction in infected prosthetic grafts and mycotic aneurysms of the abdominal aorta. *J Vasc Surg* 2001; **34:** 616–622.
1009. Teebken OE, Pichlmaier MA, Brand S, Haverich A. Cryopreserved arterial allografts for *in situ* reconstruction of infected arterial vessels. *Eur J Vasc Endovasc Surg* 2004; **27:** 597–602.
1010. Bandyk DF, Novotney ML, Johnson BL, Back MR, Roth SR. Use of rifampin-soaked gelatin-sealed polyester grafts for *in situ* treatment of primary aortic and vascular prosthetic infections. *J Surg Res* 2001; **95:** 44–49.
1011. Daenens K, Fourneau I, Nevelsteen A. Ten-year experience in autogenous reconstruction with the femoral vein in the treatment of aortofemoral prosthetic infection. *Eur J Vasc Endovasc Surg* 2003; **25:** 240–245.
1012. Mathisen DJ, Grillo HC, Vlahakes GJ, Daggett WM. The omentum in the management of complicated cardiothoracic problems. *J Thorac Cardiovasc Surg* 1988; **95:** 677–684.
1013. Coselli JS, Crawford ES. Primary aortoesophageal fistula from aortic aneurysm: Successful surgical treatment by use of omental pedicle graft. *J Vasc Surg* 1990; **12:** 269–277.
1014. Berchtold C, Eibl C, Seelig MH, Jakob P, Schönleben K. Endovascular treatment and complete regression of an infected abdominal aortic aneurysm. *J Endovasc Ther* 2002; **9:** 543–548.
1015. Bell RE, Taylor PR, Aukett M, Evans GH, Reidy JF. Successful endoluminal repair of an infected thoracic pseudoaneurysm caused by methicillin-resistant *Staphylococcus aureus*. *J Endovasc Ther* 2003; **10:** 29–32.
1016. Ting AC, Cheng SW, Ho P, Poon JT. Endovascular repair for multiple Salmonella mycotic aneurysms of the thoracic aorta presenting with Cardiovocal syndrome. *Eur J Cardiothorac Surg* 2004; **26:** 221–224.
1017. González-Fajardo JA, Gutiérrez V, Martín-Pedrosa M, Del Rio L, Carrera S, Vaquero C. Endovascular repair in the presence of aortic infection. *Ann Vasc Surg* 2005; **19:** 94–98.
1018. Hornez E, Béranger F, Monchal T, Baudouin Y, Boddaert G, De Lesquen H, et al. Management specificities for abdominal, pelvic and vascular penetrating trauma. *J Visc Surg* 2017; **154 Suppl:** S43–S55.
1019. Salsamendi J, Pereira K, Rey J, Narayanan G. Endovascular coil embolization in the treatment of a rare case of post-traumatic abdominal aortic pseudoaneurysms: Brief report and review of literature. *Ann Vasc Surg* 2016; **30:** 310.e1–310.e8.
1020. Sadaghianloo N, Jean-Baptiste E, Breaud J, Declemy S, Kurzenne JY, Hassen-Khodja R. Blunt abdominal aortic trauma in paediatric patients. *Injury* 2014; **45:** 183–191.
1021. Tomic I, Dragas M, Vasin D, Loncar Z, Fatic N, Davidovic L. Seat-belt abdominal aortic injury-treatment modalities. *Ann Vasc Surg* 2018; **53:** 270.e13–270.e16.
1022. Tsai R, Raptis D, Raptis C, Mellnick VM. Traumatic abdominal aortic injury: Clinical considerations for the diagnostic radiologist. *Abdom Radiol (NY)* 2018; **43:** 1084–1093.
1023. Brenner M, Hicks C. Major abdominal trauma: Critical decisions and new frontiers in management. *Emerg Med Clin North Am* 2018; **36:** 149–160.
1024. Huh U, Lee CW, Kim SH, Park CI, Chung SW, Song S, et al. Successful treatment using a kissing stent for blunt abdominal aortic injury: A case report. *Cardiovasc Intervent Radiol* 2018; **41:** 972–975.
1025. Tsai TT, Evangelista A, Nienaber CA, Myrmel T, Meinhardt G, Cooper JV, et al; International Registry of Acute Aortic Dissection. Partial thrombosis of the false lumen in patients with acute type B aortic dissection. *N Engl J Med* 2007; **357:** 349–359.
1026. Trimarchi S, Tolenaar JL, Jonker FH, Murray B, Tsai TT, Eagle KA, et al. Importance of false lumen thrombosis in type B aortic dissection prognosis. *J Thorac Cardiovasc Surg* 2013; **145 Suppl:** S208–S212.
1027. Tolenaar JL, van Keulen JW, Trimarchi S, Jonker FH, van Herwaarden JA, Verhagen HJ, et al. Number of entry tears is associated with aortic growth in type B dissections. *Ann Thorac Surg* 2013; **96:** 39–42.
1028. Tisnado J, Cho SR, Beachley MC, Vines FS. Ulcerlike projections: A precursor angiographic sign to thoracic aortic dissection. *AJR Am J Roentgenol* 1980; **135:** 719–722.
1029. Sueyoshi E, Matsuoka Y, Sakamoto I, Uetani M, Hayashi K, Narimatsu M. Fate of intramural hematoma of the aorta: CT evaluation. *J Comput Assist Tomogr* 1997; **21:** 931–938.
1030. Song JK, Kim HS, Kang DH, Lim TH, Song MG, Park SW, et al. Different clinical features of aortic intramural hematoma versus dissection involving the ascending aorta. *J Am Coll Cardiol* 2001; **37:** 1604–1610.
1031. Kaji S, Akasaka T, Horibata Y, Nishigami K, Shono H, Katayama M, et al. Long-term prognosis of patients with type A aortic intramural hematoma. *Circulation* 2002; **106 Suppl:** I248–I252.
1032. Nishigami K, Tsuchiya T, Shono H, Horibata Y, Honda T. Disappearance of aortic intramural hematoma and its significance to the prognosis. *Circulation* 2000; **102 Suppl:** III243–III247.
1033. Krukenberg E. [Beiträge zur Frage des Aneurysma dissecans.] Contribution to the question of dissecting aneurysm. *Beitr Pathol Anat Allg Pathol* 1920; **67:** 329–351.
1034. Macura KJ, Corl FM, Fishman EK, Bluemke DA. Pathogenesis in acute aortic syndromes: Aortic dissection, intramural hematoma, and penetrating atherosclerotic aortic ulcer. *AJR Am J Roentgenol* 2003; **181:** 309–316.
1035. Kaji S, Akasaka T, Katayama M, Yamamuro A, Yamabe K, Tamita K, et al. Long-term prognosis of patients with type B aortic intramural hematoma. *Circulation* 2003; **108 Suppl:** II307–II311.
1036. Oderich GS, Kärkkäinen JM, Reed NR, Tenorio ER, Sandri GA. Penetrating aortic ulcer and intramural hematoma. *Cardiovasc Intervent Radiol* 2019; **42:** 321–334.
1037. Evangelista A, Czerny M, Nienaber C, Schepens M, Rousseau H, Cao P, et al. Interdisciplinary expert consensus on management of type B intramural haematoma and penetrating aortic ulcer. *Eur J Cardiothorac Surg* 2015; **47:** 209–217.
1038. Neschis DG, Scalea TM, Flinn WR, Griffith BP. Blunt aortic injury. *N Engl J Med* 2008; **359:** 1708–1716.
1039. Demetriades D, Velmahos GC, Scalea TM, Jurkovich GJ, Karmy-Jones R, Teixeira PG, et al. Blunt traumatic thoracic aortic injuries: Early or delayed repair--results of an American Association for the Surgery of Trauma prospective study. *J Trauma* 2009; **66:** 967–973.
1040. Fox N, Schwartz D, Salazar JH, Haut ER, Dahm P, Black JH, et al. Evaluation and management of blunt traumatic aortic injury: A practice management guideline from the Eastern Association for the Surgery of Trauma. *J Trauma Acute Care Surg* 2015; **78:** 136–146.
1041. Fabian TC, Davis KA, Gavant ML, Croce MA, Melton SM, Patton JH, et al. Prospective study of blunt aortic injury: Helical CT is diagnostic and antihypertensive therapy reduces rupture. *Ann Surg* 1998; **227:** 666–677.
1042. Fabian TC, Richardson JD, Croce MA, Smith JS, Rodman G, Kearney PA, et al. Prospective study of blunt aortic injury: Multicenter Trial of the American Association for the Surgery of Trauma. *J Trauma* 1997; **42:** 374–383.
1043. Murad MH, Rizvi AZ, Malgor R, Carey J, Alkatib AA, Erwin PJ, et al. Comparative effectiveness of the treatments for thoracic aortic transection. *J Vasc Surg* 2011; **53:** 193–199.
1044. Januzzi JL, Sabatine MS, Eagle KA, Evangelista A, Bruckman D, Fattori R, et al; International Registry of Aortic Dissection Investigators. Iatrogenic aortic dissection. *Am J Cardiol* 2002; **89:** 623–626.
1045. Gómez-Moreno S, Sabaté M, Jiménez-Quevedo P, Vázquez P, Alfonso F, Angiolillo DJ, et al. Iatrogenic dissection of the ascending aorta following heart catheterisation: Incidence, management and outcome. *EuroIntervention* 2006; **2:** 197–202.
1046. Leontyev S, Borger MA, Legare JF, Merk D, Hahn J, Seeburger J, et al. Iatrogenic type A aortic dissection during cardiac procedures: Early and late outcome in 48 patients. *Eur J Cardiothorac Surg* 2012; **41:** 641–646.
1047. von Kodolitsch Y, Schwartz AG, Nienaber CA. Clinical prediction of acute aortic dissection. *Arch Intern Med* 2000; **160:** 2977–2982.
1048. Mehta RH, Suzuki T, Hagan PG, Bossone E, Gilon D, Llovet A, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. Predicting death in patients with acute

type A aortic dissection. *Circulation* 2002; **105:** 200–206.
1049. Tittle SL, Lynch RJ, Cole PE, Singh HS, Rizzo JA, Kopf GS, et al. Midterm follow-up of penetrating ulcer and intramural hematoma of the aorta. *J Thorac Cardiovasc Surg* 2002; **123:** 1051–1059.
1050. von Kodolitsch Y, Csösz SK, Koschyk DH, Schalwat I, Loose R, Karck M, et al. Intramural hematoma of the aorta: Predictors of progression to dissection and rupture. *Circulation* 2003; **107:** 1158–1163.
1051. Uchida K, Imoto K, Takahashi M, Suzuki S, Isoda S, Sugiyama M, et al. Pathologic characteristics and surgical indications of superacute type A intramural hematoma. *Ann Thorac Surg* 2005; **79:** 1518–1521.
1052. Shimokawa T, Ozawa N, Takanashi S, Itoh T. Intermediate-term results of surgical treatment of acute intramural hematoma involving the ascending aorta. *Ann Thorac Surg* 2008; **85:** 982–986.
1053. Estrera A, Miller C, Lee TY, De Rango P, Abdullah S, Walkes JC, et al. Acute type A intramural hematoma: Analysis of current management strategy. *Circulation* 2009; **120 Suppl:** S287–S291.
1054. Moizumi Y, Komatsu T, Motoyoshi N, Tabayashi K. Management of patients with intramural hematoma involving the ascending aorta. *J Thorac Cardiovasc Surg* 2002; **124:** 918–924.
1055. Song JK, Yim JH, Ahn JM, Kim DH, Kang JW, Lee TY, et al. Outcomes of patients with acute type A aortic intramural hematoma. *Circulation* 2009; **120:** 2046–2052.
1056. Kitai T, Kaji S, Yamamuro A, Tani T, Tamita K, Kinoshita M, et al. Clinical outcomes of medical therapy and timely operation in initially diagnosed type A aortic intramural hematoma: A 20-year experience. *Circulation* 2009; **120 Suppl:** S292–S298.
1057. Pocar M, Passolunghi D, Moneta A, Donatelli F. Recovery of severe neurological dysfunction after restoration of cerebral blood flow in acute aortic dissection. *Interact Cardiovasc Thorac Surg* 2010; **10:** 839–841.
1058. Tsukube T, Hayashi T, Kawahira T, Haraguchi T, Matsukawa R, Kozawa S, et al. Neurological outcomes after immediate aortic repair for acute type A aortic dissection complicated by coma. *Circulation* 2011; **124 Suppl:** S163–S167.
1059. Bogaert J, Meyns B, Rademakers FE, Bosmans H, Verschakelen J, Flameng W, et al. Follow-up of aortic dissection: Contribution of MR angiography for evaluation of the abdominal aorta and its branches. *Eur Radiol* 1997; **7:** 695–702.
1060. Leontyev S, Borger MA, Etz CD, Moz M, Seeburger J, Bakhtiary F, et al. Experience with the conventional and frozen elephant trunk techniques: A single-centre study. *Eur J Cardiothorac Surg* 2013; **44:** 1076–1083.
1061. Tsagakis K, Pacini D, Di Bartolomeo R, Gorlitzer M, Weiss G, Grabenwoger M, et al. Multicenter early experience with extended aortic repair in acute aortic dissection: Is simultaneous descending stent grafting justified? *J Thorac Cardiovasc Surg* 2010; **140 Suppl:** S116–S120.
1062. Shrestha M, Pichlmaier M, Martens A, Hagl C, Khaladj N, Haverich A. Total aortic arch replacement with a novel four-branched frozen elephant trunk graft: First-in-man results. *Eur J Cardiothorac Surg* 2013; **43:** 406–410.
1063. Ando M, Takamoto S, Okita Y, Morota T, Matsukawa R, Kitamura S. Elephant trunk procedure for surgical treatment of aortic dissection. *Ann Thorac Surg* 1998; **66:** 82–87.
1064. Crawford ES, Kirklin JW, Naftel DC, Svensson LG, Coselli JS, Safi HJ. Surgery for acute dissection of ascending aorta: Should the arch be included? *J Thorac Cardiovasc Surg* 1992; **104:** 46–59.
1065. Uchida N. Open stent grafting for complex diseases of the thoracic aorta: Clinical utility. *Gen Thorac Cardiovasc Surg* 2013; **61:** 118–126.
1066. Kazui T, Washiyama N, Muhammad BA, Terada H, Yamashita K, Takinami M, et al. Extended total arch replacement for acute type A aortic dissection: Experience with seventy patients. *J Thorac Cardiovasc Surg* 2000; **119:** 558–565.
1067. Zierer A, Moon MR, Melby SJ, Moazami N, Lawton JS, Kouchoukos NT, et al. Impact of perfusion strategy on neurologic recovery in acute type A aortic dissection. *Ann Thorac Surg* 2007; **83:** 2122–2129.
1068. Khaladj N, Shrestha M, Peterss S, Strueber M, Karck M, Pichlmaier M, et al. Ascending aortic cannulation in acute aortic dissection type A: The Hannover experience. *Eur J Cardiothorac Surg* 2008; **34:** 792–796.
1069. Wong DR, Coselli JS, Palmero L, Bozinovski J, Carter SA, Murariu D, et al. Axillary artery cannulation in surgery for acute or subacute ascending aortic dissections. *Ann Thorac Surg* 2010; **90:** 731–737.
1070. Wada S, Yamamoto S, Honda J, Hiramoto A, Wada H, Hosoda Y. Transapical aortic cannulation for cardiopulmonary bypass in type A aortic dissection operations. *J Thorac Cardiovasc Surg* 2006; **132:** 369–372.
1071. Okita Y, Minatoya K, Tagusari O, Ando M, Nagatsuka K, Kitamura S. Prospective comparative study of brain protection in total aortic arch replacement: Deep hypothermic circulatory arrest with retrograde cerebral perfusion or selective antegrade cerebral perfusion. *Ann Thorac Surg* 2001; **72:** 72–79.
1072. Omura A, Miyahara S, Yamanaka K, Sakamoto T, Matsumori M, Okada K, et al. Early and late outcomes of repaired acute DeBakey type I aortic dissection after graft replacement. *J Thorac Cardiovasc Surg* 2016; **151:** 341–348.
1073. Yang B, Norton EL, Shih T, Farhat L, Wu X, Hornsby WE, et al. Late outcomes of strategic arch resection in acute type A aortic dissection. *J Thorac Cardiovasc Surg* 2019; **157:** 1313–1321.
1074. Rylski B, Bavaria JE, Milewski RK, Vallabhajosyula P, Moser W, Kremens E, et al. Long-term results of neomedia sinus valsalva repair in 489 patients with type A aortic dissection. *Ann Thorac Surg* 2014; **98:** 582–589.
1075. Tanaka K, Morioka K, Li W, Yamada N, Takamori A, Handa M, et al. Adventitial inversion technique without the aid of biologic glue or Teflon buttress for acute type A aortic dissection. *Eur J Cardiothorac Surg* 2005; **28:** 864–869.
1076. Bachet J, Goudot B, Dreyfus GD, Brodaty D, Dubois C, Delentdecker P, et al. Surgery for acute type A aortic dissection: The Hopital Foch experience (1977–1998). *Ann Thorac Surg* 1999; **67:** 2006–2009.
1077. Kamohara K, Koga S, Takaki J, Yoshida N, Furukawa K, Morita S. Long-term durability of preserved aortic root after repair of acute type A aortic dissection. *Gen Thorac Cardiovasc Surg* 2017; **65:** 441–448.
1078. Lai DT, Miller DC, Mitchell RS, Oyer PE, Moore KA, Robbins RC, et al. Acute type A aortic dissection complicated by aortic regurgitation: Composite valve graft versus separate valve graft versus conservative valve repair. *J Thorac Cardiovasc Surg* 2003; **126:** 1978–1986.
1079. Concistrè G, Casali G, Santaniello E, Montalto A, Fiorani B, Dell'Aquila A, et al. Reoperation after surgical correction of acute type A aortic dissection: Risk factor analysis. *Ann Thorac Surg* 2012; **93:** 450–455.
1080. Kazui T, Washiyama N, Bashar AH, Terada H, Suzuki K, Yamashita K, et al. Role of biologic glue repair of proximal aortic dissection in the development of early and midterm redissection of the aortic root. *Ann Thorac Surg* 2001; **72:** 509–514.
1081. Gott VL, Gillinov AM, Pyeritz RE, Cameron DE, Reitz BA, Greene PS, et al. Aortic root replacement: Risk factor analysis of a seventeen-year experience with 270 patients. *J Thorac Cardiovasc Surg* 1995; **109:** 536–545.
1082. David TE, Armstrong S, Ivanov J, Feindel CM, Omran A, Webb G. Results of aortic valve-sparing operations. *J Thorac Cardiovasc Surg* 2001; **122:** 39–46.
1083. Inoue Y, Minatoya K, Oda T, Itonaga T, Seike Y, Tanaka H, et al. Surgical outcomes for acute type A aortic dissection with aggressive primary entry resection. *Eur J Cardiothorac Surg* 2016; **50:** 567–573.
1084. Bachet J, Larrazet F, Goudot B, Dreyfus G, Folliguet T, Laborde F, et al. When should the aortic arch be replaced in Marfan patients? *Ann Thorac Surg* 2007; **83:** S774–S779.
1085. Kimura N, Itoh S, Yuri K, Adachi K, Matsumoto H, Yamaguchi A, et al. Reoperation for enlargement of the distal aorta after initial surgery for acute type A aortic dissection. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S91–S98.
1086. Hagl C, Pichlmaier M, Khaladj N. Elephant trunks in aortic surgery: Fresh and frozen. *J Thorac Cardiovasc Surg* 2013; **145 Suppl:** S98–S102.
1087. von Segesser LK, Killer I, Ziswiler M, Linka A, Ritter M, Jenni R, et al. Dissection of the descending thoracic aorta extending into the ascending aorta: A therapeutic challenge. *J Thorac Cardiovasc Surg* 1994; **108:** 755–761.
1088. Hanafusa Y, Ogino H, Sasaki H, Minatoya K, Ando M, Okita Y, et al. Total arch replacement with elephant trunk procedure for retrograde dissection. *Ann Thorac Surg* 2002; **74:** S1836–S1839.
1089. Inoue Y, Matsuda H, Omura A, Seike Y, Uehara K, Sasaki H, et al. Long-term outcomes of total arch replacement with the non-frozen elephant trunk technique for Stanford Type A acute

aortic dissection. *Interact Cardiovasc Thorac Surg* 2018; **27:** 455–460.
1090. Di Bartolomeo R, Di Marco L, Armaro A, Marsilli D, Leone A, Pilato E, et al. Treatment of complex disease of the thoracic aorta: The frozen elephant trunk technique with the E-vita open prosthesis. *Eur J Cardiothorac Surg* 2009; **35:** 671–676.
1091. Uchida N, Shibamura H, Katayama A, Shimada N, Sutoh M, Ishihara H. Operative strategy for acute type A aortic dissection: Ascending aortic or hemiarch versus total arch replacement with frozen elephant trunk. *Ann Thorac Surg* 2009; **87:** 773–777.
1092. Jakob H, Tsagakis K, Tossios P, Massoudy P, Thielmann M, Buck T, et al. Combining classic surgery with descending stent grafting for acute DeBakey type I dissection. *Ann Thorac Surg* 2008; **86:** 95–101.
1093. Colli A, Carrozzini M, Francescato A, Galuppo M, Comisso M, Toto F, et al. Acute DeBakey Type I aortic dissection without intimal tear in the arch: Is total arch replacement the right choice? *Interact Cardiovasc Thorac Surg* 2018; **26:** 84–90.
1094. Watanuki H, Ogino H, Minatoya K, Matsuda H, Sasaki H, Ando M, et al. Is emergency total arch replacement with a modified elephant trunk technique justified for acute type A aortic dissection? *Ann Thorac Surg* 2007; **84:** 1585–1591.
1095. Larsen M, Trimarchi S, Patel HJ, Di Eusanio M, Greason KL, Peterson MD, et al. Extended versus limited arch replacement in acute Type A aortic dissection. *Eur J Cardiothorac Surg* 2017; **52:** 1104–1110.
1096. Conzelmann LO, Weigang E, Mehlhorn U, Abugameh A, Hoffmann I, Blettner M, et al; GERAADA Investigators. Mortality in patients with acute aortic dissection type A: Analysis of pre- and intraoperative risk factors from the German Registry for Acute Aortic Dissection Type A (GERAADA). *Eur J Cardiothorac Surg* 2016; **49:** e44–e52.
1097. Poon SS, Theologou T, Harrington D, Kuduvalli M, Oo A, Field M. Hemiarch versus total aortic arch replacement in acute type A dissection: A systematic review and meta-analysis. *Ann Cardiothorac Surg* 2016; **5:** 156–173.
1098. Sultan I, McGarvey J, Vallabhajosyula P, Desai ND, Bavaria JE, Szeto WY. Routine use of hemiarch during acute type A aortic dissection repair. *Ann Cardiothorac Surg* 2016; **5:** 245–247.
1099. Li B, Ma WG, Liu YM, Sun LZ. Is extended arch replacement justified for acute type A aortic dissection? *Interact Cardiovasc Thorac Surg* 2015; **20:** 120–126.
1100. Fichadiya A, Gregory AJ, Kotha VK, Herget EJ, Smith HN, Tai E, et al. Extended-arch repair for acute type-A aortic dissection: Perioperative and mid-term results. *Eur J Cardiothorac Surg* 2019; **56:** 714–721.
1101. Svensson LG, Crawford ES, Coselli JS, Safi HJ, Hess KR. Impact of cardiovascular operation on survival in the Marfan patient. *Circulation* 1989; **80:** I233–I242.
1102. Shimizu H, Kasahara H, Nemoto A, Yamabe K, Ueda T, Yozu R. Can early aortic root surgery prevent further aortic dissection in Marfan syndrome? *Interact Cardiovasc Thorac Surg* 2012; **14:** 171–175.
1103. Miyamoto S, Hadama T, Anai H, Wada T, Iwata E, Tanaka H, et al. Simplified elephant trunk technique promotes thrombo-occlusion of the false lumen in acute type A aortic dissection. *Ann Thorac Cardiovasc Surg* 2006; **12:** 412–416.
1104. Inoue Y, Matsuda H, Omura A, Seike Y, Uehara K, Sasaki H, et al. Comparative study of the frozen elephant trunk and classical elephant trunk techniques to supplement total arch replacement for acute type A aortic dissection. *Eur J Cardiothorac Surg* 2019; **56:** 579–586.
1105. Ma WG, Zhang W, Zhu JM, Ziganshin BA, Zhi AH, Zheng J, et al. Long-term outcomes of frozen elephant trunk for type A aortic dissection in patients with Marfan syndrome. *J Thorac Cardiovasc Surg* 2017; **154:** 1175–1189.
1106. Kato M, Kuratani T, Kaneko M, Kyo S, Ohnishi K. The results of total arch graft implantation with open stent-graft placement for type A aortic dissection. *J Thorac Cardiovasc Surg* 2002; **124:** 531–540.
1107. Shimamura K, Kuratani T, Matsumiya G, Kato M, Shirakawa Y, Takano H, et al. Long-term results of the open stent-grafting technique for extended aortic arch disease. *J Thorac Cardiovasc Surg* 2008; **135:** 1261–1269.
1108. Filsoufi F, Chikwe J, Carpentier A. Rationale for remodelling annuloplasty to address functional tricuspid regurgitation during left-sided valve surgery. *Eur J Cardiothorac Surg* 2015; **47:** 1–3.
1109. Yamane Y, Uchida N, Mochizuki S, Furukawa T, Yamada K. Early- and mid-term aortic remodelling after the frozen elephant trunk technique for retrograde type A acute aortic dissection using the new Japanese J Graft open stent graft. *Interact Cardiovasc Thorac Surg* 2017; **25:** 720–726.
1110. Shrestha M, Haverich A, Martens A. Total aortic arch replacement with the frozen elephant trunk procedure in acute DeBakey type I aortic dissections. *Eur J Cardiothorac Surg* 2017; **51 suppl:** i29–i34.
1111. Shrestha M, Martens A, Kaufeld T, Beckmann E, Bertele S, Krueger H, et al. Single-centre experience with the frozen elephant trunk technique in 251 patients over 15 years. *Eur J Cardiothorac Surg* 2017; **52:** 858–866.
1112. Berger T, Kreibich M, Morlock J, Kondov S, Scheumann J, Kari FA, et al. True-lumen and false-lumen diameter changes in the downstream aorta after frozen elephant trunk implantation. *Eur J Cardiothorac Surg* 2018; **54:** 375–381.
1113. Smith HN, Boodhwani M, Ouzounian M, Saczkowski R, Gregory AJ, Herget EJ, et al. Classification and outcomes of extended arch repair for acute Type A aortic dissection: A systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg* 2017; **24:** 450–459.
1114. Jakob H, Dohle D, Benedik J, Jánosi RA, Schlosser T, Wendt D, et al. Long-term experience with the E-vita Open hybrid graft in complex thoracic aortic disease†. *Eur J Cardiothorac Surg* 2017; **51:** 329–338.
1115. Jakob H, Tsagakis K. DeBakey type I dissection: When hybrid stent-grafting is indicated? *J Cardiovasc Surg (Torino)* 2010; **51:** 633–640.
1116. Jakob H, Tsagakis K, Pacini D, Di Bartolomeo R, Mestres C, Mohr F, et al. The International E-vita Open Registry: Data sets of 274 patients. *J Cardiovasc Surg (Torino)* 2011; **52:** 717–723.
1117. Iafrancesco M, Goebel N, Mascaro J, Franke UFW, Pacini D, Di Bartolomeo R, et al; International E-vita Open Registry Group. Aortic diameter remodelling after the frozen elephant trunk technique in aortic dissection: Results from an international multicentre registry. *Eur J Cardiothorac Surg* 2017; **52:** 310–318.
1118. Goebel N, Nagib R, Salehi-Gilani S, Ahad S, Albert M, Ursulescu A, et al. One-stage hybrid aortic repair using the frozen elephant trunk in acute DeBakey type I aortic dissection. *J Thorac Dis* 2018; **10:** 4195–4203.
1119. Shrestha M, Fleissner F, Ius F, Koigeldiyev N, Kaufeld T, Beckmann E, et al. Total aortic arch replacement with frozen elephant trunk in acute type A aortic dissections: Are we pushing the limits too far? *Eur J Cardiothorac Surg* 2015; **47:** 361–366.
1120. Shrestha M, Bachet J, Bavaria J, Carrel TP, De Paulis R, Di Bartolomeo R, et al. Current status and recommendations for use of the frozen elephant trunk technique: A position paper by the Vascular Domain of EACTS. *Eur J Cardiothorac Surg* 2015; **47:** 759–769.
1121. Di Bartolomeo R, Pantaleo A, Berretta P, Murana G, Castrovinci S, Cefarelli M, et al. Frozen elephant trunk surgery in acute aortic dissection. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S105–S109.
1122. Tan L, Xiao J, Zhou X, Shen K, Li F, Luo J, et al. Untreated distal intimal tears may be associated with paraplegia after total arch replacement and frozen elephant trunk treatment of acute Stanford type A aortic dissection. *J Thorac Cardiovasc Surg* 2019; **158:** 343–350.e1.
1123. Pan XD, Li B, Ma WG, Zheng J, Liu YM, Zhu JM, et al. Endovascular repair of residual intimal tear or distal new entry after frozen elephant trunk for type A aortic dissection. *J Thorac Dis* 2017; **9:** 529–536.
1124. Morisaki A, Isomura T, Fukada Y, Yoshida M. Kinking of an open stent graft after total arch replacement with the frozen elephant technique for acute Type A aortic dissection. *Interact Cardiovasc Thorac Surg* 2018; **26:** 875–877.
1125. Uchida N, Katayama A, Kuraoka M, Katayama K, Takahashi S, Takasaki T, et al. Extended aortic repair using frozen elephant trunk technique for Marfan syndrome with acute aortic dissection. *Ann Thorac Cardiovasc Surg* 2013; **19:** 279–282.
1126. Sun L, Li M, Zhu J, Liu Y, Chang Q, Zheng J, et al. Surgery for patients with Marfan syndrome with type A dissection involving the aortic arch using total arch replacement combined with stented elephant trunk implantation: The acute versus the chronic. *J Thorac Cardiovasc Surg* 2011; **142:** e85–e91.
1127. Neri E, Toscano T, Papalia U, Frati G, Massetti M, Capannini G, et al. Proximal aortic dissection with coronary malperfusion: Presentation, management, and outcome. *J Thorac Cardiovasc Surg* 2001; **121:** 552–560.
1128. Kawahito K, Adachi H, Murata S, Yamaguchi A, Ino T.

Coronary malperfusion due to type A aortic dissection: Mechanism and surgical management. *Ann Thorac Surg* 2003; **76:** 1471–1476.
1129. Uchida K, Karube N, Kasama K, Minami T, Yasuda S, Goda M, et al. Early reperfusion strategy improves the outcomes of surgery for type A acute aortic dissection with malperfusion. *J Thorac Cardiovasc Surg* 2018; **156:** 483–489.
1130. Imoto K, Uchida K, Karube N, Yasutsune T, Cho T, Kimura K, et al. Risk analysis and improvement of strategies in patients who have acute type A aortic dissection with coronary artery dissection. *Eur J Cardiothorac Surg* 2013; **44:** 419–425.
1131. Funatsu T, Fukuda H, Takeuchi M, Masai M, Kawano S, Abe K. Progression of left coronary artery dissection during and after aortic replacement in acute type A aortic dissection: A case report. *Ann Thorac Cardiovasc Surg* 2007; **13:** 209–212.
1132. Yagdi T, Atay Y, Engin C, Mahmudov R, Tetik O, Iyem H, et al. Impact of organ malperfusion on mortality and morbidity in acute type A aortic dissections. *J Card Surg* 2006; **21:** 363–369.
1133. Shiiya N, Matsuzaki K, Kunihara T, Murashita T, Matsui Y. Management of vital organ malperfusion in acute aortic dissection: Proposal of a mechanism-specific approach. *Gen Thorac Cardiovasc Surg* 2007; **55:** 85–90.
1134. Eren E, Toker ME, Tunçer A, Keles C, Erdogan HB, Anasiz H, et al. Surgical management of coronary malperfusion due to type A aortic dissection. *J Card Surg* 2007; **22:** 2–6.
1135. Asakura T, Gojo S, Ishikawa M, Nishimura T, Imanaka K, Katogi T, et al. Coronary malperfusion due to acute type A aortic dissection; surgical strategy and results. [in Japanese] *Jpn J Thorac Surg* 2007; **60:** 297–302.
1136. Girdauskas E, Kuntze T, Borger MA, Falk V, Mohr FW. Surgical risk of preoperative malperfusion in acute type A aortic dissection. *J Thorac Cardiovasc Surg* 2009; **138:** 1363–1369.
1137. Chen YF, Chien TM, Yu CP, Ho KJ, Wen H, Li WY, et al. Acute aortic dissection type A with acute coronary involvement: A novel classification. *Int J Cardiol* 2013; **168:** 4063–4069.
1138. Czerny M, Schoenhoff F, Etz C, Englberger L, Khaladj N, Zierer A, et al. The impact of pre-operative malperfusion on outcome in acute type A aortic dissection: Results from the GERAADA registry. *J Am Coll Cardiol* 2015; **65:** 2628–2635.
1139. Tang YF, Zhang GX, Liao ZL, Han L, Xu ZY. Surgical treatment of coronary malperfusion with acute type A aortic dissection. *Chin Med J (Engl)* 2016; **129:** 1000–1002.
1140. Uchida K, Karube N, Minami T, Cho T, Matsuki Y, Nemoto H, et al. Treatment of coronary malperfusion in type A acute aortic dissection. *Gen Thorac Cardiovasc Surg* 2018; **66:** 621–625.
1141. Goldberg JB, Lansman SL, Kai M, Tang GHL, Malekan R, Spielvogel D. Malperfusion in Type A dissection: Consider reperfusion first. *Semin Thorac Cardiovasc Surg* 2016; **29:** 181–185.
1142. Hashiyama N, Goda M, Uchida K, Isomatsu Y, Suzuki S, Mo M, et al. Stanford type B aortic dissection is more frequently associated with coronary artery atherosclerosis than type A. *J Cardiothorac Surg* 2018; **13:** 80.
1143. Francone M, Bucciarelli-Ducci C, Carbone I, Canali E, Scardala R, Calabrese FA, et al. Impact of primary coronary angioplasty delay on myocardial salvage, infarct size, and microvascular damage in patients with ST-segment elevation myocardial infarction: Insight from cardiovascular magnetic resonance. *J Am Coll Cardiol* 2009; **54:** 2145–2153.
1144. Lee MS, Dahodwala MQ. Percutaneous coronary intervention for acute myocardial infarction due to unprotected left main coronary artery occlusion: status update 2014. *Catheter Cardiovasc Interv* 2015; **85:** 416–420.
1145. Barabas M, Gosselin G, Crépeau J, Petitclerc R, Cartier R, Théroux P. Left main stenting-as a bridge to surgery-for acute type A aortic dissection and anterior myocardial infarction. *Catheter Cardiovasc Interv* 2000; **51:** 74–77.
1146. Imoto K, Uchida K, Suzuki S, Isoda S, Karube N, Kimura K. Stenting of a left main coronary artery dissection and stent-graft implantation for acute type A aortic dissection. *J Endovasc Ther* 2005; **12:** 258–261.
1147. Ohara Y, Hiasa Y, Hosokawa S. Successful treatment in a case of acute aortic dissection complicated with acute myocardial infarction due to occlusion of the left main coronary artery. *J Invasive Cardiol* 2003; **15:** 660–662.
1148. Cardozo C, Riadh R, Mazen M. Acute myocardial infarction due to left main compression aortic dissection treated by direct stenting. *J Invasive Cardiol* 2004; **16:** 89–91.
1149. Masuyama S, Matsuda M, Soeda T, Yuasa S, Shimizu K. Acute type A aortic dissection combined with surgical treatment with acute myocardial infarction. [in Japanese] *Jpn J Thorac Surg* 2005; **58:** 861–864.
1150. Masuyama S, Komiya T, Tamura N, Sakaguchi G, Obata S, Kimura C, et al. Coronary malperfusion of left main trunk due to localized dissection of the ascending aorta. [in Japanese] *Jpn J Thorac Surg* 2007; **60:** 433–440.
1151. Camaro C, Wouters NT, Gin MT, Bosker HA. Acute myocardial infarction with cardiogenic shock in a patient with acute aortic dissection. *Am J Emerg Med* 2009; **27:** 899.e3–899.e6.
1152. Shimamura J, Kubota H, Tonari K, Endo H, Tsuchiya H, Takahashi Y, et al. Acute aortic dissection with left main coronary malperfusion treated with precedent stenting followed by a definitive surgery. [in Japanese] *Jpn J Thorac Surg* 2010; **63:** 537–541.
1153. Ravandi A, Penny WF. Percutaneous intervention of an acute left main coronary occlusion due to dissection of the aortic root. *JACC Cardiovasc Interv* 2011; **4:** 713–715.
1154. Saxena P, Boyle A, Shetty S, Edwards M. Left main coronary artery stenting prior to surgical repair of a type a aortic dissection. *J Card Surg* 2011; **26:** 634–635.
1155. Hamamoto M, Furukawa T. Coronary artery stenting as a bridge to surgery in a patient with Stanford type A acute aortic dissection involving left main trunk of coronary artery. [in Japanese] *Jpn J Thorac Surg* 2011; **64:** 823–827.
1156. Hanaki Y, Yumoto K, I S, Aoki H, Fukuzawa T, Watanabe T, et al. Coronary stenting with cardiogenic shock due to acute ascending aortic dissection. *World J Cardiol* 2015; **7:** 104–110.
1157. Tamaki M, Kitamura H, Koyama Y, Kimura A, Okawa Y. Left main coronary malperfusion from acute non-communicating aortic dissection. *Gen Thorac Cardiovasc Surg* 2018; **66:** 172–174.
1158. Joshi D, Bicer EI, Donmez C, Hsiung MC, Nanda NC, Sadat K, et al. Incremental value of live/real time three-dimensional transesophageal echocardiography over the two-dimensional technique in the assessment of aortic aneurysm and dissection. *Echocardiography* 2012; **29:** 620–630.
1159. Estrera AL, Garami Z, Miller CC, Porat EE, Achouh PE, Dhareshwar J, et al. Acute type A aortic dissection complicated by stroke: Can immediate repair be performed safely? *J Thorac Cardiovasc Surg* 2006; **132:** 1404–1408.
1160. Okita Y, Ikeno Y, Yokawa K, Koda Y, Henmi S, Gotake Y, et al. Direct perfusion of the carotid artery in patients with brain malperfusion secondary to acute aortic dissection. *Gen Thorac Cardiovasc Surg* 2019; **67:** 161–167.
1161. Luehr M, Etz CD, Nozdrzykowski M, Lehmkuhl L, Misfeld M, Bakhtiary F, et al. Extra-anatomic revascularization for preoperative cerebral malperfusion due to distal carotid artery occlusion in acute type A aortic dissection. *Eur J Cardiothorac Surg* 2016; **49:** 652–659.
1162. Geirsson A, Szeto WY, Pochettino A, McGarvey ML, Keane MG, Woo YJ, et al. Significance of malperfusion syndromes prior to contemporary surgical repair for acute type A dissection: Outcomes and need for additional revascularizations. *Eur J Cardiothorac Surg* 2007; **32:** 255–262.
1163. Gaul C, Dietrich W, Friedrich I, Sirch J, Erbguth FJ. Neurological symptoms in type A aortic dissections. *Stroke* 2007; **38:** 292–297.
1164. Cambria RP, Brewster DC, Gertler J, Moncure AC, Gusberg R, Tilson MD, et al. Vascular complications associated with spontaneous aortic dissection. *J Vasc Surg* 1988; **7:** 199–209.
1165. Fukuda I, Imazuru T. Intentional delay of surgery for acute type A dissection with stroke. *J Thorac Cardiovasc Surg* 2003; **126:** 290–291.
1166. Most H, Reinhard B, Gahl B, Englberger L, Kadner A, Weber A, et al. Is surgery in acute aortic dissection type A still contraindicated in the presence of preoperative neurological symptoms? *Eur J Cardiothorac Surg* 2015; **48:** 945–950.
1167. Tanaka H, Okada K, Yamashita T, Morimoto Y, Kawanishi Y, Okita Y. Surgical results of acute aortic dissection complicated with cerebral malperfusion. *Ann Thorac Surg* 2005; **80:** 72–76.
1168. Bossone E, Rampoldi V, Nienaber CA, Trimarchi S, Ballotta A, Cooper JV, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. Usefulness of pulse deficit to predict in-hospital complications and mortality in patients with acute type A aortic dissection. *Am J Cardiol* 2002; **89:** 851–855.
1169. Di Eusanio M, Patel HJ, Nienaber CA, Montgomery DM, Korach A, Sundt TM, et al. Patients with type A acute aortic dissection presenting with major brain injury: Should we operate on them? *J Thorac Cardiovasc Surg* 2013; **145 Suppl:** S213–S221.
1170. Tsukube T, Haraguchi T, Okada Y, Matsukawa R, Kozawa S,

Ogawa K, et al. Long-term outcomes after immediate aortic repair for acute type A aortic dissection complicated by coma. *J Thorac Cardiovasc Surg* 2014; **148:** 1013–1019.
1171. Pocar M, Passolunghi D, Moneta A, Mattioli R, Donatelli F. Coma might not preclude emergency operation in acute aortic dissection. *Ann Thorac Surg* 2006; **81:** 1348–1351.
1172. Morimoto N, Okada K, Okita Y. Lack of neurologic improvement after aortic repair for acute type A aortic dissection complicated by cerebral malperfusion: Predictors and association with survival. *J Thorac Cardiovasc Surg* 2011; **142:** 1540–1544.
1173. Chiu P, Rotto TJ, Goldstone AB, Whisenant JB, Woo YJ, Fischbein MP. Time-to-operation does not predict outcome in acute type A aortic dissection complicated by neurologic injury at presentation. *J Thorac Cardiovasc Surg* 2019; **158:** 665–672.
1174. Jonker FH, Patel HJ, Upchurch GR, Williams DM, Montgomery DG, Gleason TG, et al. Acute type B aortic dissection complicated by visceral ischemia. *J Thorac Cardiovasc Surg* 2015; **149:** 1081–1086.
1175. Tsagakis K, Konorza T, Dohle DS, Kottenberg E, Buck T, Thielmann M, et al. Hybrid operating room concept for combined diagnostics, intervention and surgery in acute type A dissection. *Eur J Cardiothorac Surg* 2013; **43:** 397–404.
1176. Williams DM, Lee DY, Hamilton BH, Marx MV, Narasimham DL, Kazanjian SN, et al. The dissected aorta: Percutaneous treatment of ischemic complications--principles and results. *J Vasc Interv Radiol* 1997; **8:** 605–625.
1177. Kurimoto Y, Morishita K, Fukada J, Kawaharada N, Komatsu K, Yama N, et al. A simple but useful method of screening for mesenteric ischemia secondary to acute aortic dissection. *Surgery* 2004; **136:** 42–46.
1178. Böckler D, Ockert S, Schumacher H, Allenberg JR. Images in vascular medicine: Undiagnosed fatal mesenteric ischemia in acute type B aortic dissection. *Vasc Med* 2006; **11:** 133–134.
1179. Ferlan G, Lospalluti M, Capone G, De Pasquale C. Mesenteric ischemia in a patient with an acute aortic dissection type A: One-step repair of the aortic and visceral lesions: Role of laparoscopy for timely diagnosis and treatment. *Interact Cardiovasc Thorac Surg* 2011; **12:** 835–836.
1180. Tshomba Y, Coppi G, Marone EM, Bertoglio L, Kahlberg A, Carlucci M, et al. Diagnostic laparoscopy for early detection of acute mesenteric ischaemia in patients with aortic dissection. *Eur J Vasc Endovasc Surg* 2012; **43:** 690–697.
1181. Alemanno G, Somigli R, Prosperi P, Bergamini C, Maltinti G, Giordano A, et al. Combination of diagnostic laparoscopy and intraoperative indocyanine green fluorescence angiography for the early detection of intestinal ischemia not detectable at CT scan. *Int J Surg Case Rep* 2016; **26:** 77–80.
1182. Davis CB, Kendall JL. Emergency bedside ultrasound diagnosis of superior mesenteric artery dissection complicating acute aortic dissection. *J Emerg Med* 2013; **45:** 894–896.
1183. Odagiri S, Koide S, Ariizumi K, Suzuki I, Kamabuchi K, Inamura S, et al. Successful right common iliac to superior mesenteric artery bypass for mesenteric ischemia associated with acute aortic dissection: Report of a case. *Surg Today* 1993; **23:** 1014–1017.
1184. Connell DA, Thomson KR, Gibson RN, Wall AJ. Stent placement in coeliac and superior mesenteric arteries to restore vascular perfusion following aortic dissection. *Australas Radiol* 1995; **39:** 68–70.
1185. Fabre O, Vincentelli A, Willoteaux S, Beregi JP, Prat A. Preoperative fenestration for type A acute aortic dissection with mesenteric malperfusion. *Ann Thorac Surg* 2002; **73:** 950–951.
1186. Arthurs ZM, Titus J, Bannazadeh M, Eagleton MJ, Srivastava S, Sarac TP, et al. A comparison of endovascular revascularization with traditional therapy for the treatment of acute mesenteric ischemia. *J Vasc Surg* 2011; **53:** 698–705.
1187. Estrera AL, Huynh TT, Porat EE, Miller CC, Smith JJ, Safi HJ. Is acute type A aortic dissection a true surgical emergency? *Semin Vasc Surg* 2002; **15:** 75–82.
1188. Yamashiro S, Arakaki R, Kise Y, Inafuku H, Kuniyoshi Y. Management of visceral malperfusion complicated with acute type A aortic dissection. *Interact Cardiovasc Thorac Surg* 2015; **21:** 346–351.
1189. Okada Y, Okimoto M, Katsumata M, Takeuchi S. Temporary perfusion for mesenteric ischemia with acute type A aortic dissection. *Ann Thorac Surg* 2007; **83:** 293–294.
1190. Iida Y, Obitsu Y, Shigematsu H. Use of side branch of total arch replacement graft as bypass inflow to prevent visceral ischemia with type B aortic dissection. *Gen Thorac Cardiovasc Surg* 2012; **60:** 440–442.
1191. Tanaka K, Chikazawa G, Sakaguchi T, Totsugawa T, Tamura K, Yoshitaka H. Hybrid treatment for type A acute aortic dissection with multiorgan malperfusion. *Ann Thorac Surg* 2014; **98:** 1118–1120.
1192. Suzuki T, Mehta RH, Ince H, Nagai R, Sakomura Y, Weber F, et al; International Registry of Aortic Dissection. Clinical profiles and outcomes of acute type B aortic dissection in the current era: Lessons from the International Registry of Aortic Dissection (IRAD). *Circulation* 2003; **108 Suppl:** II312–II317.
1193. Charlton-Ouw KM, Sandhu HK, Leake SS, Jeffress K, Miller CC, Durham CA, et al. Need for limb revascularization in patients with acute aortic dissection is associated with mesenteric ischemia. *Ann Vasc Surg* 2016; **36:** 112–120.
1194. Liu WP, Chen WK, Ng KC. Aortic dissection presenting as acute lower extremity ischemia: Report of a case. *Yale J Biol Med* 2002; **75:** 211–214.
1195. Tamura K, Nakajima K, Chikazawa G, Hiraoka A, Totsugawa T, Sakaguchi T, et al. Effectiveness of the use of near-infrared spectroscopy to treat acute type A aortic dissection complicated with limb ischemia: Report of a case. *Ann Vasc Dis* 2015; **8:** 249–251.
1196. Kashima I, Tsutsumi K, Okamoto M. Salvage of severe ischemic lower limb having peak creatine phosphokinase level exceeding 200,000 IU/L treated by continuous hemodiafiltration. *Ann Vasc Surg* 2014; **28:** 1795.e15–1795.e18.
1197. Song JK, Kim HS, Song JM, Kang DH, Ha JW, Rim SJ, et al. Outcomes of medically treated patients with aortic intramural hematoma. *Am J Med* 2002; **113:** 181–187.
1198. Hayashi H, Kawamata H, Kumazaki T. Thrombosed type aortic dissection showing changes in the false lumen to the patent type. [in Japanese] *J Jpn Radiol Soc* 1994; **54:** 1217–1224.
1199. Matsuo H. The thrombosed type of aortic dissection-its clinical features and diagnosis. *Int J Angiol* 1998; **7:** 329–334.
1200. Matsuo H. Recognition and management of thrombosed type of aortic dissection with long-term follow-up results. *Int J Angiol* 2000; **9:** 27–30.
1201. Shimizu H, Yoshino H, Udagawa H, Watanuki A, Yano K, Ide H, et al. Prognosis of aortic intramural hemorrhage compared with classic aortic dissection. *Am J Cardiol* 2000; **85:** 792–795.
1202. Moizumi Y, Komatsu T, Motoyoshi N, Tabayashi K. Clinical features and long-term outcome of type A and type B intramural hematoma of the aorta. *J Thorac Cardiovasc Surg* 2004; **127:** 421–427.
1203. Mohr-Kahaly S, Erbel R, Kearney P, Puth M, Meyer J. Aortic intramural hemorrhage visualized by transesophageal echocardiography: Findings and prognostic implications. *J Am Coll Cardiol* 1994; **23:** 658–664.
1204. Nienaber CA, von Kodolitsch Y, Petersen B, Loose R, Helmchen U, Haverich A, et al. Intramural hemorrhage of the thoracic aorta: Diagnostic and therapeutic implications. *Circulation* 1995; **92:** 1465–1472.
1205. Murray JG, Manisali M, Flamm SD, VanDyke CW, Lieber ML, Lytle BW, et al. Intramural hematoma of the thoracic aorta: MR image findings and their prognostic implications. *Radiology* 1997; **204:** 349–355.
1206. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *J Am Coll Cardiol* 2010; **55:** e27–e129.
1207. Song JM, Kim HS, Song JK, Kang DH, Hong MK, Kim JJ, et al. Usefulness of the initial noninvasive imaging study to predict the adverse outcomes in the medical treatment of acute type A aortic intramural hematoma. *Circulation* 2003; **108 Suppl:** II324–II328.
1208. Kaji S, Nishigami K, Akasaka T, Hozumi T, Takagi T, Kawamoto T, et al. Prediction of progression or regression of type A aortic intramural hematoma by computed tomography. *Circulation* 1999; **100 Suppl:** II281–II286.
1209. Ganaha F, Miller DC, Sugimoto K, Do YS, Minamiguchi H, Saito H, et al. Prognosis of aortic intramural hematoma with and without penetrating atherosclerotic ulcer: A clinical and radiological analysis. *Circulation* 2002; **106:** 342–348.

1210. Kitai T, Kaji S, Yamamuro A, Tani T, Kinoshita M, Ehara N, et al. Impact of new development of ulcer-like projection on clinical outcomes in patients with type B aortic dissection with closed and thrombosed false lumen. *Circulation* 2010; **122 Suppl:** S74–S80.
1211. Kaji S, Akasaka T, Katayama M, Yamamuro A, Yamabe K, Tamita K, et al. Prognosis of retrograde dissection from the descending to the ascending aorta. *Circulation* 2003; **108 Suppl:** II300–II306.
1212. Kim JB, Choo SJ, Kim WK, Kim HJ, Jung SH, Chung CH, et al. Outcomes of acute retrograde type A aortic dissection with an entry tear in descending aorta. *Circulation* 2014; **130 Suppl:** S39–S44.
1213. Sabik JF, Nemeh H, Lytle BW, Blackstone EH, Gillinov AM, Rajeswaran J, et al. Cannulation of the axillary artery with a side graft reduces morbidity. *Ann Thorac Surg* 2004; **77:** 1315–1320.
1214. Strauch JT, Spielvogel D, Lauten A, Lansman SL, McMurtry K, Bodian CA, et al. Axillary artery cannulation: Routine use in ascending aorta and aortic arch replacement. *Ann Thorac Surg* 2004; **78:** 103–108.
1215. Shiiya N, Yasuda K, Murashita T, Suto Y, Kanaoka T, Matsui Y, et al. Transapical aortic cannulation for hypothermic aortic operation through a left thoracotomy: An alternative to avoid retrograde arterial perfusion. *J Thorac Cardiovasc Surg* 1997; **113:** 1113–1114.
1216. Abe T, Terada T, Noda R, Sakurai H. Aortocarotid bypass at the time of central aortic repair for type A acute aortic dissections. *J Thorac Cardiovasc Surg* 2012; **143:** 976–978.
1217. Furukawa T, Uchida N, Takahashi S, Yamane Y, Mochizuki S, Yamada K, et al. Management of cerebral malperfusion in surgical repair of acute type A aortic dissection. *Eur J Cardiothorac Surg* 2017; **52:** 327–332.
1218. Kouchoukos NT, Masetti P, Mauney MC, Murphy MC, Castner CF. One-stage repair of extensive chronic aortic dissection using the arch-first technique and bilateral anterior thoracotomy. *Ann Thorac Surg* 2008; **86:** 1502–1509.
1219. Minale C, Splittgerber FH, Wendt G, Messmer BJ. One-stage intrathoracic repair of extended aortic aneurysms. *J Card Surg* 1994; **9:** 604–613.
1220. de la Cruz KI, Green SY, Preventza OA, Coselli JS. Aortic arch replacement in patients with chronic dissection: Special considerations. *Semin Cardiothorac Vasc Anesth* 2016; **20:** 314–321.
1221. Dong Z, Fu W, Wang Y, Wang C, Yan Z, Guo D, et al. Stent graft-induced new entry after endovascular repair for Stanford type B aortic dissection. *J Vasc Surg* 2010; **52:** 1450–1457.
1222. Ergin MA, Phillips RA, Galla JD, Lansman SL, Mendelson DS, Quintana CS, et al. Significance of distal false lumen after type A dissection repair. *Ann Thorac Surg* 1994; **57:** 820–825.
1223. Moore NR, Parry AJ, Trottman-Dickenson B, Pillai R, Westaby S. Fate of the native aorta after repair of acute type A dissection: A magnetic resonance imaging study. *Heart* 1996; **75:** 62–66.
1224. Fattori R, Bacchi-Reggiani L, Bertaccini P, Napoli G, Fusco F, Longo M, et al. Evolution of aortic dissection after surgical repair. *Am J Cardiol* 2000; **86:** 868–872.
1225. Hirotani T, Nakamichi T, Munakata M, Takeuchi S. Routine extended graft replacement for an acute type A aortic dissection and the patency of the residual false channel. *Ann Thorac Surg* 2003; **76:** 1957–1961.
1226. Yeh CH, Chen MC, Wu YC, Wang YC, Chu JJ, Lin PJ. Risk factors for descending aortic aneurysm formation in medium-term follow-up of patients with type A aortic dissection. *Chest* 2003; **124:** 989–995.
1227. Yamashita C, Okada M, Ataka K, Yoshida M, Azami T, Ozaki M, et al. Reoperation after repair of type A and B dissecting aneurysm. *J Cardiovasc Surg (Torino)* 1998; **39:** 721–727.
1228. Moriyama Y, Yotsumoto G, Masuda H, Iguro Y, Watanabe S, Hisatomi K, et al. Repair of an acute type A dissection: Fate of the remnant false lumen and preserved aortic valve. *Surg Today* 1999; **29:** 413–418.
1229. Pugliese P, Pessotto R, Santini F, Montalbano G, Luciani GB, Mazzucco A. Risk of late reoperations in patients with acute type A aortic dissection: Impact of a more radical surgical approach. *Eur J Cardiothorac Surg* 1998; **13:** 576–581.
1230. Kirsch M, Legras A, Bruzzi M, Louis N. Fate of the distal aorta after surgical repair of acute DeBakey type I aortic dissection: A review. *Arch Cardiovasc Dis* 2011; **104:** 125–130.
1231. Malvindi PG, van Putte BP, Sonker U, Heijmen RH, Schepens MA, Morshuis WJ. Reoperation after acute type A aortic dissection repair: A series of 104 patients. *Ann Thorac Surg* 2013; **95:** 922–927.
1232. Kawamoto S, Saiki Y. Redo arch replacement after ascending aortic surgery. [in Japanese] *Jpn J Thorac Surg* 2013; **66:** 655–659.
1233. Wang H, Wagner M, Benrashid E, Keenan J, Wang A, Ranney D, et al. Outcomes of reoperation after acute type A aortic dissection: Implications for index repair strategy. *J Am Heart Assoc* 2017; **6:** e006376.
1234. Raanani E, David TE, Dellgren G, Armstrong S, Ivanov J, Feindel CM. Redo aortic root replacement: Experience with 31 patients. *Ann Thorac Surg* 2001; **71:** 1460–1463.
1235. Kirsch EW, Radu NC, Mekontso-Dessap A, Hillion ML, Loisance D. Aortic root replacement after previous surgical intervention on the aortic valve, aortic root, or ascending aorta. *J Thorac Cardiovasc Surg* 2006; **131:** 601–608.
1236. David TE, Feindel CM, Ivanov J, Armstrong S. Aortic root replacement in patients with previous heart surgery. *J Card Surg* 2004; **19:** 325–328.
1237. Malvindi PG, van Putte BP, Heijmen RH, Schepens MA, Morshuis WJ. Reoperations on the aortic root: Experience in 46 patients. *Ann Thorac Surg* 2010; **89:** 81–86.
1238. Di Eusanio M, Berretta P, Cefarelli M, Di Bartolomeo R. Root graft substitution after aortic valve replacement: Sparing the valve prosthesis is a valid option. *Eur J Cardiothorac Surg* 2013; **44:** 427–430.
1239. Kazui T, Kimura N, Yamada O, Komatsu S. Total arch graft replacement in patients with acute type A aortic dissection. *Ann Thorac Surg* 1994; **58:** 1462–1468.
1240. Murayama H, Hayashida N, Matsuo K, Kito H, Asano S, Yajima N, et al. Reoperation after surgery for the thoracic aorta. [in Japanese] *Jpn J Vasc Surg* 2004; **13:** 519–525.
1241. Halstead JC, Spielvogel D, Meier DM, Rinke S, Bodian C, Malekan R, et al. Composite aortic root replacement in acute type A dissection: Time to rethink the indications? *Eur J Cardiothorac Surg* 2005; **27:** 626–632.
1242. Yang B, Norton EL, Hobbs R, Farhat L, Wu X, Hornsby WE, et al. Short- and long-term outcomes of aortic root repair and replacement in patients undergoing acute type A aortic dissection repair: Twenty-year experience. *J Thorac Cardiovasc Surg* 2019; **157:** 2125–2136.
1243. Keeling WB, Leshnower BG, Thourani VH, Kilgo PS, Chen EP. Outcomes following redo sternotomy for aortic surgery. *Interact Cardiovasc Thorac Surg* 2012; **15:** 63–68.
1244. Kato N, Shimono T, Hirano T, Ishida M, Yada I, Takeda K. Transluminal placement of endovascular stent-grafts for the treatment of type A aortic dissection with an entry tear in the descending thoracic aorta. *J Vasc Surg* 2001; **34:** 1023–1028.
1245. Zhang R, Zhou J, Feng J, Zhao Z, Liu J, Li Z, et al. Inducing false lumen thrombosis for retrograde type A aortic dissection. *J Thorac Cardiovasc Surg* 2017; **153:** 57–65.
1246. Shu C, Wang T, Li QM, Li M, Jiang XH, Luo MY, et al. Thoracic endovascular aortic repair for retrograde type A aortic dissection with an entry tear in the descending aorta. *J Vasc Interv Radiol* 2012; **23:** 453–460.
1247. Roselli EE, Hasan SM, Idrees JJ, Aftab M, Eagleton MJ, Menon V, et al. Inoperable patients with acute type A dissection: Are they candidates for endovascular repair? *Interact Cardiovasc Thorac Surg* 2017; **25:** 582–588.
1248. Kitamura T, Torii S, Horai T, Sughimoto K, Irisawa Y, Hayashi H, et al. Outcomes of patients who declined surgery for acute Stanford type A aortic dissection with patent false lumen of the ascending aorta. *Interact Cardiovasc Thorac Surg* 2017; **25:** 47–51.
1249. Fujimura N, Kawaguchi S, Obara H, Yoshitake A, Inoue M, Otsubo S, et al. Anatomic Feasibility of next-generation stent grafts for the management of type A aortic dissection in Japanese patients. *Circ J* 2017; **81:** 1388–1394.
1250. Moon MC, Greenberg RK, Morales JP, Martin Z, Lu Q, Dowdall JF, et al. Computed tomography-based anatomic characterization of proximal aortic dissection with consideration for endovascular candidacy. *J Vasc Surg* 2011; **53:** 942–949.
1251. Sobocinski J, O'Brien N, Maurel B, Bartoli M, Goueffic Y, Sassard T, et al. Endovascular approaches to acute aortic type A dissection: A CT-based feasibility study. *Eur J Vasc Endovasc Surg* 2011; **42:** 442–447.
1252. Zhang H, Li M, Jin W, Wang Z. Endoluminal and surgical treatment for the management of Stanford type A aortic dissection. *Eur J Cardiothorac Surg* 2004; **26:** 857–859.

1253. Ihnken K, Sze D, Dake MD, Fleischmann D, Van der Starre P, Robbins R. Successful treatment of a Stanford type A dissection by percutaneous placement of a covered stent graft in the ascending aorta. *J Thorac Cardiovasc Surg* 2004; **127:** 1808–1810.
1254. Zimpfer D, Czerny M, Kettenbach J, Schoder M, Wolner E, Lammer J, et al. Treatment of acute type a dissection by percutaneous endovascular stent-graft placement. *Ann Thorac Surg* 2006; **82:** 747–749.
1255. Ye C, Chang G, Li S, Hu Z, Yao C, Chen W, et al. Endovascular stent-graft treatment for Stanford type A aortic dissection. *Eur J Vasc Endovasc Surg* 2011; **42:** 787–794.
1256. Lu Q, Feng J, Zhou J, Zhao Z, Bao J, Feng R, et al. Endovascular repair of ascending aortic dissection: A novel treatment option for patients judged unfit for direct surgical repair. *J Am Coll Cardiol* 2013; **61:** 1917–1924.
1257. Ronchey S, Serrao E, Alberti V, Fazzini S, Trimarchi S, Tolenaar JL, et al. Endovascular stenting of the ascending aorta for type A aortic dissections in patients at high risk for open surgery. *Eur J Vasc Endovasc Surg* 2013; **45:** 475–480.
1258. Bernardes RC, Navarro TP, Reis FR, Lima LC, Monteiro EL, Procopio RJ, et al. Early experience with off-the-shelf endografts using a zone 0 proximal landing site to treat the ascending aorta and arch. *J Thorac Cardiovasc Surg* 2014; **148:** 105–112.
1259. Li Z, Lu Q, Feng R, Zhou J, Zhao Z, Bao J, et al. Outcomes of endovascular repair of ascending aortic dissection in patients unsuitable for direct surgical repair. *J Am Coll Cardiol* 2016; **68:** 1944–1954.
1260. Khoynezhad A, Donayre CE, Walot I, Koopmann MC, Kopchok GE, White RA. Feasibility of endovascular repair of ascending aortic pathologies as part of an FDA-approved physician-sponsored investigational device exemption. *J Vasc Surg* 2016; **63:** 1483–1495.
1261. Tsilimparis N, Debus ES, Oderich GS, Haulon S, Terp KA, Roeder B, et al. International experience with endovascular therapy of the ascending aorta with a dedicated endograft. *J Vasc Surg* 2016; **63:** 1476–1482.
1262. Nauta FJH, Kim JB, Patel HJ, Peterson MD, Eckstein HH, Khoynezhad A, et al. Early outcomes of acute retrograde dissection from the international registry of acute aortic dissection. *Semin Thorac Cardiovasc Surg* 2017; **29:** 150–159.
1263. Masuda Y, Yamada Z, Morooka N, Watanabe S, Inagaki Y. Prognosis of patients with medically treated aortic dissections. *Circulation* 1991; **84 Suppl:** III7–II13.
1264. Kaji S. Acute medical management of aortic dissection. *Gen Thorac Cardiovasc Surg* 2019; **67:** 203–207.
1265. Estrera AL, Miller CC, Safi HJ, Goodrick JS, Keyhani A, Porat EE, et al. Outcomes of medical management of acute type B aortic dissection. *Circulation* 2006; **114 Suppl:** I384–I389.
1266. Zhou JC, Zhang N, Zhang ZH, Wang TT, Zhu YF, Kang H, et al; Pressure in Acute Type B Aortic Dissection (RAID) study group. Intensive blood pressure control in patients with acute type B aortic dissection (RAID): Study protocol for randomized controlled trial. *J Thorac Dis* 2017; **9:** 1369–1374.
1267. Kaji S. Update on the therapeutic strategy of type B aortic dissection. *J Atheroscler Thromb* 2018; **25:** 203–212.
1268. Takeshita S, Sakamoto S, Kitada S, Akutsu K, Hashimoto H. Angiotensin-converting enzyme inhibitors reduce long-term aortic events in patients with acute type B aortic dissection. *Circ J* 2008; **72:** 1758–1761.
1269. Suzuki T, Isselbacher EM, Nienaber CA, Pyeritz RE, Eagle KA, Tsai TT, et al; IRAD Investigators. Type-selective benefits of medications in treatment of acute aortic dissection (from the International Registry of Acute Aortic Dissection [IRAD]). *Am J Cardiol* 2012; **109:** 122–127.
1270. Kodama K, Nishigami K, Sakamoto T, Sawamura T, Hirayama T, Misumi H, et al. Tight heart rate control reduces secondary adverse events in patients with type B acute aortic dissection. *Circulation* 2008; **118 Suppl:** S167–S170.
1271. Trimarchi S, Eagle KA, Nienaber CA, Pyeritz RE, Jonker FH, Suzuki T, et al; IRAD Investigators. Importance of refractory pain and hypertension in acute type B aortic dissection: Insights from the International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2010; **122:** 1283–1289.
1272. Moulakakis KG, Mylonas SN, Dalainas I, Kakisis J, Kotsis T, Liapis CD. Management of complicated and uncomplicated acute type B dissection: A systematic review and meta-analysis. *Ann Cardiothorac Surg* 2014; **3:** 234–246.
1273. Faure EM, Canaud L, Marty-Ané C, Becquemin JP, Alric P. Endovascular management of rupture in acute type B aortic dissections. *Eur J Vasc Endovasc Surg* 2015; **49:** 655–660.
1274. Sobocinski J, Dias NV, Hongku K, Lombardi JV, Zhou Q, Saunders AT, et al. Thoracic endovascular aortic repair with stent grafts alone or with a composite device design in patients with acute type B aortic dissection in the setting of malperfusion. *J Vasc Surg* 2020; **71:** 400–407.
1275. Ramdass M. TEVAR for symptomatic Stanford B dissection: A systematic review of 30-day mortality and morbidity. *Thorac Cardiovasc Surg* 2015; **63:** 97–112.
1276. Laas J, Heinemann M, Schaefers HJ, Daniel W, Borst HG. Management of thoracoabdominal malperfusion in aortic dissection. *Circulation* 1991; **84 Suppl:** III20–III24.
1277. Trimarchi S, Segreti S, Grassi V, Lomazzi C, Cova M, Piffaretti G, et al. Open fenestration for complicated acute aortic B dissection. *Ann Cardiothorac Surg* 2014; **3:** 418–422.
1278. Szeberin Z, Dósa E, Fehérvári M, Csobay-Novák C, Pintér N, Entz L. Early and long-term outcome after open surgical suprarenal aortic fenestration in patients with complicated acute type B aortic dissection. *Eur J Vasc Endovasc Surg* 2015; **50:** 44–50.
1279. Vendrell A, Frandon J, Rodiere M, Chavanon O, Baguet JP, Bricault I, et al. Aortic dissection with acute malperfusion syndrome: Endovascular fenestration via the funnel technique. *J Thorac Cardiovasc Surg* 2015; **150:** 108–115.
1280. Lombardi JV, Cambria RP, Nienaber CA, Chiesa R, Teebken O, Lee A, et al; STABLE investigators. Prospective multicenter clinical trial (STABLE) on the endovascular treatment of complicated type B aortic dissection using a composite device design. *J Vasc Surg* 2012; **55:** 629–640.
1281. Alfson DB, Ham SW. Type B aortic dissections: Current guidelines for treatment. *Cardiol Clin* 2017; **35:** 387–410.
1282. Charlton-Ouw KM, Sandhu HK, Leake SS, Miller CC, Afifi RO, Azizzadeh A, et al. New type A dissection after acute type B aortic dissection. *J Vasc Surg* 2018; **67:** 85–92.
1283. Wilkinson DA, Patel HJ, Williams DM, Dasika NL, Deeb GM. Early open and endovascular thoracic aortic repair for complicated type B aortic dissection. *Ann Thorac Surg* 2013; **96:** 23–30.
1284. Sobocinski J, Lombardi JV, Dias NV, Berger L, Zhou Q, Jia F, et al. Volume analysis of true and false lumens in acute complicated type B aortic dissections after thoracic endovascular aortic repair with stent grafts alone or with a composite device design. *J Vasc Surg* 2016; **63:** 1216–1224.
1285. Desai ND, Gottret JP, Szeto WY, McCarthy F, Moeller P, Menon R, et al. Impact of timing on major complications after thoracic endovascular aortic repair for acute type B aortic dissection. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S151–S156.
1286. Heijmen R; VIRTUE Registry Investigators. Mid-term outcomes and aortic remodelling after thoracic endovascular repair for acute, subacute, and chronic aortic dissection: The VIRTUE Registry. *Eur J Vasc Endovasc Surg* 2014; **48:** 363–371.
1287. Nienaber CA, Kische S, Rousseau H, Eggebrecht H, Rehders TC, Kundt G, et al; INSTEAD-XL trial. Endovascular repair of type B aortic dissection: Long-term results of the randomized investigation of stent grafts in aortic dissection trial. *Circ Cardiovasc Interv* 2013; **6:** 407–416.
1288. Tsai TT, Fattori R, Trimarchi S, Isselbacher E, Myrmel T, Evangelista A, et al; International Registry of Acute Aortic Dissection (IRAD). Long-term survival in patients presenting with type B acute aortic dissection: Insights from the International Registry of Acute Aortic Dissection. *Circulation* 2006; **114:** 2226–2231.
1289. Clough RE, Nienaber CA. Evidence for and risks of endovascular treatment of asymptomatic acute type B aortic dissection. *J Cardiovasc Surg (Torino)* 2017; **58:** 270–277.
1290. Charilaou P, Ziganshin BA, Peterss S, Rajbanshi BG, Rajakaruna C, Zaza KJ, et al. Current experience with acute type B aortic dissection: Validity of the complication-specific approach in the present era. *Ann Thorac Surg* 2016; **101:** 936–943.
1291. Li D, Ye L, He Y, Cao X, Liu J, Zhong W, et al. False lumen status in patients with acute aortic dissection: A systematic review and meta-analysis. *J Am Heart Assoc* 2016; **5:** e003172.
1292. Evangelista A, Salas A, Ribera A, Ferreira-González I, Cuellar H, Pineda V, et al. Long-term outcome of aortic dissection with patent false lumen: Predictive role of entry tear size and location. *Circulation* 2012; **125:** 3133–3141.
1293. Brunkwall J, Lammer J, Verhoeven E, Taylor P. ADSORB: A study on the efficacy of endovascular grafting in uncomplicated acute dissection of the descending aorta. *Eur J Vasc Endovasc*

Surg 2012; **44:** 31–36.
1294. Brunkwall J, Kasprzak P, Verhoeven E, Heijmen R, Taylor P, Alric P, et al; ADSORB Trialists. Endovascular repair of acute uncomplicated aortic type B dissection promotes aortic remodelling: 1 year results of the ADSORB trial. *Eur J Vasc Endovasc Surg* 2014; **48:** 285–291.
1295. Kinoshita H, Fujimoto E, Arase H, Kurobe H, Chikugo F, Sogabe H, et al. Efficacy and optimal timing of endovascular treatment for type B aortic dissection. *Ann Vasc Dis* 2015; **8:** 307–313.
1296. Qing KX, Yiu WK, Cheng SW. A morphologic study of chronic type B aortic dissections and aneurysms after thoracic endovascular stent grafting. *J Vasc Surg* 2012; **55:** 1268–1276.
1297. Akin I, Kische S, Ince H, Nienaber CA. Indication, timing and results of endovascular treatment of type B dissection. *Eur J Vasc Endovasc Surg* 2009; **37:** 289–296.
1298. Nienaber CA. Influence and critique of the INSTEAD Trial (TEVAR versus medical treatment for uncomplicated type B aortic dissection). *Semin Vasc Surg* 2011; **24:** 167–171.
1299. Matsuda H. Treatment of uncomplicated type B aortic dissection. *Gen Thorac Cardiovasc Surg* 2017; **65:** 74–79.
1300. Nienaber CA, Rousseau H, Eggebrecht H, Kische S, Fattori R, Rehders TC, et al; INSTEAD Trial. Randomized comparison of strategies for type B aortic dissection: The INvestigation of STEnt Grafts in Aortic Dissection (INSTEAD) trial. *Circulation* 2009; **120:** 2519–2528.
1301. Fanelli F, Cannavale A, O'Sullivan GJ, Gazzetti M, Cirelli C, Lucatelli P, et al. Endovascular repair of acute and chronic aortic type B dissections: Main factors affecting aortic remodeling and clinical outcome. *JACC Cardiovasc Interv* 2016; **9:** 183–191.
1302. Kim TH, Ko YG, Kwon SW, Choi D, Lee DY, Shim WH, et al. Large false lumen area is a predictor of failed false lumen volume reduction after stent-graft repair in type B aortic dissection. *J Endovasc Ther* 2014; **21:** 697–706.
1303. Kanaoka Y, Ohki T, Kurosawa K, Maeda K, Shukuzawa K, Hara M, et al. Early and midterm outcomes of endovascular treatment for chronic aneurysmal aortic dissection: A retrospective study. *Ther Adv Cardiovasc Dis* 2018; **12:** 275–287.
1304. Kölbel T, Rohlffs F, Debus ES, Tsilimparis N. Polytetrafluoroethylene excludes the false lumen: Expanding material options for the candy-plug technique. *J Endovasc Ther* 2016; **23:** 487–488.
1305. Kölbel T, Carpenter SW, Lohrenz C, Tsilimparis N, Larena-Avellaneda A, Debus ES. Addressing persistent false lumen flow in chronic aortic dissection: The knickerbocker technique. *J Endovasc Ther* 2014; **21:** 117–122.
1306. Pellenc Q, Roussel A, De Blic R, Girault A, Cerceau P, Ben Abdallah I, et al. False lumen embolization in chronic aortic dissection promotes thoracic aortic remodeling at midterm follow-up. *J Vasc Surg* 2019; **70:** 710–717.
1307. Spanos K, Kölbel T, Rohlffs F, Heidemann F, Giannoukas AD, Debus SE, et al. Intentional targeted false lumen occlusion after aortic dissection: A systematic review of the literature. *Ann Vasc Surg* 2019; **56:** 317–329.
1308. Fattori R, Tsai TT, Myrmel T, Evangelista A, Cooper JV, Trimarchi S, et al. Complicated acute type B dissection: Is surgery still the best option?: A report from the International Registry of Acute Aortic Dissection. *JACC Cardiovasc Interv* 2008; **1:** 395–402.
1309. Patel AY, Eagle KA, Vaishnava P. Acute type B aortic dissection: Insights from the International Registry of Acute Aortic Dissection. *Ann Cardiothorac Surg* 2014; **3:** 368–374.
1310. Afifi RO, Sandhu HK, Leake SS, Boutrous ML, Kumar V, Azizzadeh A, et al. Outcomes of patients with acute type B (DeBakey III) aortic dissection: A 13-year, single-center experience. *Circulation* 2015; **132:** 748–754.
1311. Zeeshan A, Woo EY, Bavaria JE, Fairman RM, Desai ND, Pochettino A, et al. Thoracic endovascular aortic repair for acute complicated type B aortic dissection: Superiority relative to conventional open surgical and medical therapy. *J Thorac Cardiovasc Surg* 2010; **140 Suppl:** S109–S115.
1312. Trimarchi S, Nienaber CA, Rampoldi V, Myrmel T, Suzuki T, Bossone E, et al; IRAD Investigators. Role and results of surgery in acute type B aortic dissection: Insights from the International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2006; **114 Suppl:** I357–I364.
1313. White RA, Miller DC, Criado FJ, Dake MD, Diethrich EB, Greenberg RK, et al; Multidisciplinary Society for Vascular Surgery Outcomes Committee. Report on the results of thoracic endovascular aortic repair for acute, complicated, type B aortic dissection at 30 days and 1 year from a multidisciplinary subcommittee of the Society for Vascular Surgery Outcomes Committee. *J Vasc Surg* 2011; **53:** 1082–1090.
1314. Hanna JM, Andersen ND, Ganapathi AM, McCann RL, Hughes GC. Five-year results for endovascular repair of acute complicated type B aortic dissection. *J Vasc Surg* 2014; **59:** 96–106.
1315. Trimarchi S, Jonker FH, Muhs BE, Grassi V, Righini P, Upchurch GR, et al. Long-term outcomes of surgical aortic fenestration for complicated acute type B aortic dissections. *J Vasc Surg* 2010; **52:** 261–266.
1316. Weiss G, Tsagakis K, Jakob H, Di Bartolomeo R, Pacini D, Barberio G, et al. The frozen elephant trunk technique for the treatment of complicated type B aortic dissection with involvement of the aortic arch: Multicentre early experience. *Eur J Cardiothorac Surg* 2015; **47:** 106–114.
1317. Lombardi JV, Hughes GC, Appoo JJ, Bavaria JE, Beck AW, Cambria RP, et al. Society for Vascular Surgery (SVS) and Society of Thoracic Surgeons (STS) reporting standards for type B aortic dissections. *Ann Thorac Surg* 2020; **109:** 959–981.
1318. Alsac JM, Girault A, El Batti S, Abou Rjeili M, Alomran F, Achouh P, et al. Experience of the Zenith Dissection Endovascular System in the emergency setting of malperfusion in acute type B dissections. *J Vasc Surg* 2014; **59:** 645–650.
1319. Hofferberth SC, Newcomb AE, Yii MY, Yap KK, Boston RC, Nixon IK, et al. Combined proximal stent grafting plus distal bare metal stenting for management of aortic dissection: Superior to standard endovascular repair? *J Thorac Cardiovasc Surg* 2012; **144:** 956–962.
1320. Sfyroeras GS, Rubio V, Pagan P, Diethrich EB, Rodriguez JA. Endovascular management of malperfusion in acute type B aortic dissections. *J Endovasc Ther* 2011; **18:** 78–86.
1321. Soler RJ, Bartoli MA, Simonet G, Amabile P, Sarlon-Bartoli G, Magnan PE. Total endovascular treatment of acute non-A-non-B dissection complicated by visceral malperfusion without primary entry tear coverage. *Ann Vasc Surg* 2017; **45:** 268.e9–268.e12.
1322. Massmann A, Kunihara T, Fries P, Schneider G, Buecker A, Schäfers HJ. Uncovered stent implantation in complicated acute aortic dissection type B. *J Thorac Cardiovasc Surg* 2014; **148:** 3003–3011.
1323. Sailer AM, van Kuijk SM, Nelemans PJ, Chin AS, Kino A, Huininga M, et al. Computed tomography imaging features in acute uncomplicated stanford type-B aortic dissection predict late adverse events. *Circ Cardiovasc Imaging* 2017; **10:** e005709.
1324. Weiss G, Wolner I, Folkmann S, Sodeck G, Schmidli J, Grabenwöger M, et al. The location of the primary entry tear in acute type B aortic dissection affects early outcome. *Eur J Cardiothorac Surg* 2012; **42:** 571–576.
1325. Loewe C, Czerny M, Sodeck GH, Ta J, Schoder M, Funovics M, et al. A new mechanism by which an acute type B aortic dissection is primarily complicated, becomes complicated, or remains uncomplicated. *Ann Thorac Surg* 2012; **93:** 1215–1222.
1326. Smedberg C, Hultgren R, Delle M, Blohmé L, Olsson C, Steuer J. Temporal and morphological patterns predict outcome of endovascular repair in acute complicated type B aortic dissection. *Eur J Vasc Endovasc Surg* 2018; **56:** 349–355.
1327. Thakkar D, Dake MD. Management of type B aortic dissections: Treatment of acute dissections and acute complications from chronic dissections. *Tech Vasc Interv Radiol* 2018; **21:** 124–130.
1328. Sherrah AG, Grieve SM, Jeremy RW, Bannon PG, Vallely MP, Puranik R. MRI in chronic aortic dissection: A systematic review and future directions. *Front Cardiovasc Med* 2015; **2:** 5.
1329. Kret MR, Azarbal AF, Mitchell EL, Liem TK, Landry GJ, Moneta GL. Compliance with long-term surveillance recommendations following endovascular aneurysm repair or type B aortic dissection. *J Vasc Surg* 2013; **58:** 25–31.
1330. Elefteriades JA, Lovoulos CJ, Coady MA, Tellides G, Kopf GS, Rizzo JA. Management of descending aortic dissection. *Ann Thorac Surg* 1999; **67:** 2002–2005.
1331. Elefteriades JA, Hartleroad J, Gusberg RJ, Salazar AM, Black HR, Kopf GS, et al. Long-term experience with descending aortic dissection: The complication-specific approach. *Ann Thorac Surg* 1992; **53:** 11–21.
1332. Dake MD, Kato N, Mitchell RS, Semba CP, Razavi MK, Shimono T, et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. *N Engl J Med* 1999; **340:** 1546–1552.
1333. Eggebrecht H, Nienaber CA, Neuhäuser M, Baumgart D, Kische S, Schmermund A, et al. Endovascular stent-graft

placement in aortic dissection: A meta-analysis. *Eur Heart J* 2006; **27:** 489–498.
1334. Leurs LJ, Bell R, Degrieck Y, Thomas S, Hobo R, Lundbom J, et al; EUROSTAR. Endovascular treatment of thoracic aortic diseases: Combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. *J Vasc Surg* 2004; **40:** 670–679.
1335. Swee W, Dake MD. Endovascular management of thoracic dissections. *Circulation* 2008; **117:** 1460–1473.
1336. Nienaber CA, Kische S, Zeller T, Rehders TC, Schneider H, Lorenzen B, et al. Provisional extension to induce complete attachment after stent-graft placement in type B aortic dissection: The PETTICOAT concept. *J Endovasc Ther* 2006; **13:** 738–746.
1337. Melissano G, Bertoglio L, Rinaldi E, Civilini E, Tshomba Y, Kahlberg A, et al. Volume changes in aortic true and false lumen after the "PETTICOAT" procedure for type B aortic dissection. *J Vasc Surg* 2012; **55:** 641–651.
1338. Eggebrecht H, Thompson M, Rousseau H, Czerny M, Lönn L, Mehta RH, et al. Retrograde ascending aortic dissection during or after thoracic aortic stent graft placement: Insight from the European registry on endovascular aortic repair complications. *Circulation* 2009; **120 Suppl:** S276–S281.
1339. Szeto WY, McGarvey M, Pochettino A, Moser GW, Hoboken A, Cornelius K, et al. Results of a new surgical paradigm: Endovascular repair for acute complicated type B aortic dissection. *Ann Thorac Surg* 2008; **86:** 87–94.
1340. Pearce BJ, Passman MA, Patterson MA, Taylor SM, Lecroy CJ, Combs BR, et al. Early outcomes of thoracic endovascular stent-graft repair for acute complicated type B dissection using the Gore TAG endoprosthesis. *Ann Vasc Surg* 2008; **22:** 742–749.
1341. Ehrlich MP, Dumfarth J, Schoder M, Gottardi R, Holfeld J, Juraszek A, et al. Midterm results after endovascular treatment of acute, complicated type B aortic dissection. *Ann Thorac Surg* 2010; **90:** 1444–1448.
1342. Steuer J, Eriksson MO, Nyman R, Björck M, Wanhainen A. Early and long-term outcome after thoracic endovascular aortic repair (TEVAR) for acute complicated type B aortic dissection. *Eur J Vasc Endovasc Surg* 2011; **41:** 318–323.
1343. Wiedemann D, Ehrlich M, Amabile P, Lovato L, Rousseau H, Evangelista-Masip A, et al. Emergency endovascular stent grafting in acute complicated type B dissection. *J Vasc Surg* 2014; **60:** 1204–1208.
1344. Leshnower BG, Duwayri YM, Chen EP, Li C, Zehner CA, Binongo JN, et al. Aortic remodeling after endovascular repair of complicated acute type B aortic dissection. *Ann Thorac Surg* 2017; **103:** 1878–1885.
1345. Cambria RP, Conrad MF, Matsumoto AH, Fillinger M, Pochettino A, Carvalho S, et al. Multicenter clinical trial of the conformable stent graft for the treatment of acute, complicated type B dissection. *J Vasc Surg* 2015; **62:** 271–278.
1346. Shimono T, Kato N, Yasuda F, Suzuki T, Yuasa U, Onoda K, et al. Transluminal stent-graft placements for the treatments of acute onset and chronic aortic dissections. *Circulation* 2002; **106 Suppl:** I241–I247.
1347. Coselli JS, Büket S, Djukanovic B. Aortic arch operation: Current treatment and results. *Ann Thorac Surg* 1995; **59:** 19–27.
1348. Kato N, Hirano T, Kawaguchi T, Ishida M, Shimono T, Yada I, et al. Aneurysmal degeneration of the aorta after stent-graft repair of acute aortic dissection. *J Vasc Surg* 2001; **34:** 513–518.
1349. Canaud L, Gandet T, Sfeir J, Ozdemir BA, Solovei L, Alric P. Risk factors for distal stent graft-induced new entry tear after endovascular repair of thoracic aortic dissection. *J Vasc Surg* 2019; **69:** 1610–1614.
1350. Sultan I, Dufendach K, Kilic A, Bianco V, Trivedi D, Althouse AD, et al. Bare metal stent use in type B aortic dissection may offer positive remodeling for the distal aorta. *Ann Thorac Surg* 2018; **106:** 1364–1370.
1351. Liu F, Ge YY, Guo W, Liu XP, Jia X, Xiong J, et al. Preoperative thoracic false lumen branches are predictors of aortic enlargement after stent grafting for DeBakey IIIb aortic dissection. *J Thorac Cardiovasc Surg* 2018; **155:** 21–29.
1352. Kische S, D'Ancona G, Belu IC, Stoeckicht Y, Agma U, Ortak J, et al. Perioperative and mid-term results of endovascular management of complicated type B aortic dissection using a proximal thoracic endoprosthesis and selective distal bare stenting. *Eur J Cardiothorac Surg* 2015; **48:** e77–e84.
1353. Lombardi JV, Cambria RP, Nienaber CA, Chiesa R, Mossop P, Haulon S, et al; STABLE investigators. Aortic remodeling after endovascular treatment of complicated type B aortic dissection with the use of a composite device design. *J Vasc Surg* 2014; **59:** 1544–1554.
1354. Kuo HN, Lai HC, Chang YW, Wang CC, Lee WL, Chan SW, et al. Axillofemoral bypass relieves visceral malperfusion in type B aortic dissection. *Ann Thorac Surg* 2013; **95:** 703–705.
1355. Chino S, Kato N, Nakajima K, Hashimoto T, Higashigawa T, Ouchi T, et al. Thoracic endovascular aortic repair for the treatment of ruptured acute type B aortic dissection. *Jpn J Radiol* 2019; **37:** 321–327.
1356. Minami T, Imoto K, Uchida K, Yasuda S, Sugiura T, Karube N, et al. Clinical outcomes of emergency surgery for acute type B aortic dissection with rupture. *Eur J Cardiothorac Surg* 2013; **44:** 360–365.
1357. Uchida N, Katayama A, Tamura K, Sutoh M, Murao N, Kuraoka M. Early entry closure for acute type B aortic dissection by open stent grafting. *Gen Thorac Cardiovasc Surg* 2011; **59:** 329–334.
1358. Fattori R, Cao P, De Rango P, Czerny M, Evangelista A, Nienaber C, et al. Interdisciplinary expert consensus document on management of type B aortic dissection. *J Am Coll Cardiol* 2013; **61:** 1661–1678.
1359. Pape LA, Awais M, Woznicki EM, Suzuki T, Trimarchi S, Evangelista A, et al. Presentation, diagnosis, and outcomes of acute aortic dissection: 17-year trends from the international registry of acute aortic dissection. *J Am Coll Cardiol* 2015; **66:** 350–358.
1360. Bossone E, Gorla R, LaBounty TM, Suzuki T, Gilon D, Strauss C, et al. Presenting systolic blood pressure and outcomes in patients with acute aortic dissection. *J Am Coll Cardiol* 2018; **71:** 1432–1440.
1361. Akutsu K, Yoshino H, Shimokawa T, Ogino H, Kunihara T, Takahashi T, et al; Tokyo CCU Network and Tokyo Acute Aortic Super Network. Is systolic blood pressure high in patients with acute aortic dissection on first medical contact before hospital transfer? *Heart Vessels* 2019; **34:** 1748–1757.
1362. Jonker FH, Trimarchi S, Muhs BE, Rampoldi V, Montgomery DG, Froehlich JB, et al; IRAD Investigators. The role of age in complicated acute type B aortic dissection. *Ann Thorac Surg* 2013; **96:** 2129–2134.
1363. Trimarchi S, Tolenaar JL, Tsai TT, Froehlich J, Pegorer M, Upchurch GR, et al. Influence of clinical presentation on the outcome of acute B aortic dissection: Evidences from IRAD. *J Cardiovasc Surg (Torino)* 2012; **53:** 161–168.
1364. Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: Results of prospectively designed overviews of randomised trials: Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet* 2000; **356:** 1955–1964.
1365. Chan KK, Lai P, Wright JM. First-line beta-blockers versus other antihypertensive medications for chronic type B aortic dissection. *Cochrane Database Syst Rev* 2014: CD010426.
1366. Arnáiz-García ME, González-Santos JM, Arnáiz-García AM, Arnáiz J. Endovascular repair or best medical treatment: What is the optimal management of uncomplicated Type-B acute aortic dissection? *J Thorac Dis* 2017; **9:** 3458–3462.
1367. Teraa M, van Herwaarden JA, Trimarchi S, Moll FL. Morphologic characteristics for treatment guidance in uncomplicated acute type B aortic dissection. *Circulation* 2014; **130:** 1723–1725.
1368. Kato M, Kuratani T. The history and current status of thoracic endovascular aneurysm repair in Japan. *J Cardiovasc Surg (Torino)* 2008; **49:** 503–510.
1369. Watanabe Y, Shimamura K, Yoshida T, Daimon T, Shirakawa Y, Torikai K, et al. Aortic remodeling as a prognostic factor for late aortic events after thoracic endovascular aortic repair in type B aortic dissection with patent false lumen. *J Endovasc Ther* 2014; **21:** 517–525.
1370. Kato M, Matsuda T, Kaneko M, Kuratani T, Mizushima T, Seo Y, et al. Outcomes of stent-graft treatment of false lumen in aortic dissection. *Circulation* 1998; **98 Suppl:** II305–II311.
1371. Nienaber CA, Kische S, Akin I, Rousseau H, Eggebrecht H, Fattori R, et al. Strategies for subacute/chronic type B aortic dissection: The Investigation Of Stent Grafts in Patients with type B Aortic Dissection (INSTEAD) trial 1-year outcome. *J Thorac Cardiovasc Surg* 2010; **140 Suppl:** S101–S108.
1372. Cooper M, Hicks C, Ratchford EV, Salameh MJ, Malas M. Diagnosis and treatment of uncomplicated type B aortic dissection. *Vasc Med* 2016; **21:** 547–552.
1373. Schwartz SI, Durham C, Clouse WD, Patel VI, Lancaster RT, Cambria RP, et al. Predictors of late aortic intervention in patients with medically treated type B aortic dissection. *J Vasc*

Surg 2018; **67:** 78–84.
1374. Ulug P, McCaslin JE, Stansby G, Powell JT. Endovascular versus conventional medical treatment for uncomplicated chronic type B aortic dissection. *Cochrane Database Syst Rev* 2012: CD006512.
1375. Omura A, Matsuda H, Fukuda T, Nomura Y, Kawasaki R, Murakami H, et al. Midterm outcomes of thoracic endovascular repair for uncomplicated type B aortic dissection with double-barrel type. *Gen Thorac Cardiovasc Surg* 2019; **67:** 1021–1029.
1376. Hughes GC. Management of acute type B aortic dissection; ADSORB trial. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S158–S162.
1377. Kamman AV, Brunkwall J, Verhoeven EL, Heijmen RH, Trimarchi S; ADSORB trialists. Predictors of aortic growth in uncomplicated type B aortic dissection from the Acute Dissection Stent Grafting or Best Medical Treatment (ADSORB) database. *J Vasc Surg* 2017; **65:** 964–971.
1378. Khoynezhad A, White RA. Pathogenesis and management of retrograde type A aortic dissection after thoracic endovascular aortic repair. *Ann Vasc Surg* 2013; **27:** 1201–1206.
1379. Ma T, Dong ZH, Fu WG, Guo DQ, Xu X, Chen B, et al. Incidence and risk factors for retrograde type A dissection and stent graft-induced new entry after thoracic endovascular aortic repair. *J Vasc Surg* 2018; **67:** 1026–1033.
1380. Canaud L, Sfeir J, Alric P, Bommart S. Factors favoring retrograde type A aortic dissection after endovascular aortic repair. *Ann Thorac Surg* 2018; **105:** 668.
1381. Shalhub S, Eagle KA, Asch FM, LeMaire SA, Milewicz DM; GenTAC Investigators for the Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) Consortium. Endovascular thoracic aortic repair in confirmed or suspected genetically triggered thoracic aortic dissection. *J Vasc Surg* 2018; **68:** 364–371.
1382. Al-Kalei AMA, Wu Z, Zhang H. Influence of primary intimal tear location in type B aortic dissection as a factor portending retrograde type A aortic dissection after endovascular repair. *J Vasc Interv Radiol* 2018; **29:** 833–840.
1383. Zhao Y, Yin H, Chen Y, Wang M, Zheng L, Li Z, et al. Restrictive bare stent prevents distal stent graft-induced new entry in endovascular repair of type B aortic dissection. *J Vasc Surg* 2018; **67:** 93–103.
1384. Burdess A, Mani K, Tegler G, Wanhainen A. Stent-graft induced new entry tears after type B aortic dissection: How to treat and how to prevent? *J Cardiovasc Surg (Torino)* 2018; **59:** 789–796.
1385. Jang H, Kim MD, Kim GM, Won JY, Ko YG, Choi D, et al. Risk factors for stent graft-induced new entry after thoracic endovascular aortic repair for Stanford type B aortic dissection. *J Vasc Surg* 2017; **65:** 676–685.
1386. Pantaleo A, Jafrancesco G, Buia F, Leone A, Lovato L, Russo V, et al. Distal stent graft-induced new entry: An emerging complication of endovascular treatment in aortic dissection. *Ann Thorac Surg* 2016; **102:** 527–532.
1387. Huang CY, Hsu HL, Chen PL, Chen IM, Hsu CP, Shih CC. The impact of distal stent graft-induced new entry on aortic remodeling of chronic type B dissection. *Ann Thorac Surg* 2018; **105:** 785–793.
1388. Cambria RP, Brewster DC, Moncure AC, Steinberg FL, Abbott WM. Spontaneous aortic dissection in the presence of coexistent or previously repaired atherosclerotic aortic aneurysm. *Ann Surg* 1988; **208:** 619–624.
1389. Glower DD, Fann JI, Speier RH, Morrison L, White WD, Smith LR, et al. Comparison of medical and surgical therapy for uncomplicated descending aortic dissection. *Circulation* 1990; **82 Suppl:** IV39–IV46.
1390. Enezate TH, Omran J, Al-Dadah AS, White C, Patel M, Mahmud E, et al. Thoracic endovascular repair versus medical management for acute uncomplicated type B aortic dissection. *Catheter Cardiovasc Interv* 2018; **91:** 1138–1143.
1391. Fattori R, Montgomery D, Lovato L, Kische S, Di Eusanio M, Ince H, et al. Survival after endovascular therapy in patients with type B aortic dissection: A report from the International Registry of Acute Aortic Dissection (IRAD). *JACC Cardiovasc Interv* 2013; **6:** 876–882.
1392. Wallin JD, Cook ME, Blanski L, Bienvenu GS, Clifton GG, Langford H, et al. Intravenous nicardipine for the treatment of severe hypertension. *Am J Med* 1988; **85:** 331–338.
1393. Kurokawa Y, Uede T, Ohta K, Honmou O. A case presenting a severe paralytic ileus during the continuous intravenous injection of nicardipine hydrochloride. [in Japanese] *Brain and Nerve* 1991; **43:** 77–80.
1394. Leung S, Gregg SR, Coopersmith CM, Layon AJ, Oropello J, Brown DR, et al; Academic Leaders in Critical Care Medicine Task Force of the Society of the Critical Care Medicine. Critical care organizations: Business of critical care and value/performance building. *Crit Care Med* 2018; **46:** 1–11.
1395. Niino T, Hata M, Sezai A, Yoshitake I, Unosawa S, Shimura K, et al. Optimal clinical pathway for the patient with type B acute aortic dissection. *Circ J* 2009; **73:** 264–268.
1396. Booher AM, Isselbacher EM, Nienaber CA, Trimarchi S, Evangelista A, Montgomery DG, et al; IRAD Investigators. The IRAD classification system for characterizing survival after aortic dissection. *Am J Med* 2013; **126:** 730.e19–730.e24.
1397. Fukumoto H, Nishimoto Y, Nishimoto M, Ibaragi T, Suzuki S, Fujiwara A. Prognosis of stanford type B acute aortic dissection and availability of early rehabilitation program in medical treatment. *Jpn J Cardiovasc Surg* 2002; **31:** 114–119.
1398. Song JM, Kim SD, Kim JH, Kim MJ, Kang DH, Seo JB, et al. Long-term predictors of descending aorta aneurysmal change in patients with aortic dissection. *J Am Coll Cardiol* 2007; **50:** 799–804.
1399. Tanaka A, Sandhu HK, Afifi RO, Miller CC 3rd, Ray A, Hassan M, et al. Outcomes of open repairs of chronic distal aortic dissection anatomically amenable to endovascular repairs. *J Thorac Cardiovasc Surg* 2019, doi:10.1016/j.jtcvs.2019.09.083.
1400. van Bogerijen GH, Patel HJ, Williams DM, Yang B, Dasika NL, Eliason JL, et al. Propensity adjusted analysis of open and endovascular thoracic aortic repair for chronic type B dissection: A twenty-year evaluation. *Ann Thorac Surg* 2015; **99:** 1260–1266.
1401. Conway AM, Qato K, Mondry LR, Stoffels GJ, Giangola G, Carroccio A. Outcomes of thoracic endovascular aortic repair for chronic aortic dissections. *J Vasc Surg* 2018; **67:** 1345–1352.
1402. Norberto EM, Gutiérrez VM, Taylor J, Vaquero C. Coil embolization of persistent false lumen after stent graft repair of type B aortic dissection. *J Vasc Surg* 2011; **54:** 201–204.
1402a. Rodriguez JA, Olsen DM, Lucas L, Wheatley G, Ramaiah V, Diethrich EB. Aortic remodeling after endografting of thoracoabdominal aortic dissection. *J Vasc Surg* 2008; **47:** 1188–1194.
1403. Zhang H, Ge YY, Lu K, Cao L, Liu P, Liu XP, et al. Coil embolization for persistent thoracic false lumen of type B aortic dissection after thoracic endovascular aortic repair. *Ann Vasc Surg* 2019; **57:** 60–68.
1404. Kölbel T, Lohrenz C, Kieback A, Diener H, Debus ES, Larena-Avellaneda A. Distal false lumen occlusion in aortic dissection with a homemade extra-large vascular plug: The candy-plug technique. *J Endovasc Ther* 2013; **20:** 484–489.
1405. Ogawa Y, Nishimaki H, Chiba K, Murakami K, Sakurai Y, Fujiwara K, et al. Candy-plug technique using an excluder aortic extender for distal occlusion of a large false lumen aneurysm in chronic aortic dissection. *J Endovasc Ther* 2016; **23:** 483–486.
1406. Rohlffs F, Tsilimparis N, Fiorucci B, Heidemann F, Debus ES, Kölbel T. The Candy-plug technique: Technical aspects and early results of a new endovascular method for false lumen occlusion in chronic aortic dissection. *J Endovasc Ther* 2017; **24:** 549–555.
1407. Okita Y, Tagusari O, Minatoya K, Ando M, Kitamura S, Nakajima N, et al. Is distal anastomosis only to the true channel in chronic type B aortic dissection justified? *Ann Thorac Surg* 1999; **68:** 1586–1591.
1408. Coselli JS, Green SY, Price MD, Zhang Q, Preventza O, de la Cruz KI, et al. Spinal cord deficit after 1114 extent II open thoracoabdominal aortic aneurysm repairs. *J Thorac Cardiovasc Surg* 2020; **159:** 1–13.
1409. Corvera J, Copeland H, Blitzer D, Hicks A, Manghelli J, Hess P, et al. Open repair of chronic thoracic and thoracoabdominal aortic dissection using deep hypothermia and circulatory arrest. *J Thorac Cardiovasc Surg* 2017; **154:** 389–395.
1410. Kouchoukos NT, Kulik A, Castner CF. Open thoracoabdominal aortic repair for chronic type B dissection. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S125–S129.
1411. Etz CD, Zoli S, Mueller CS, Bodian CA, Di Luozzo G, Lazala R, et al. Staged repair significantly reduces paraplegia rate after extensive thoracoabdominal aortic aneurysm repair. *J Thorac Cardiovasc Surg* 2010; **139:** 1464–1472.
1412. Köksoy C, LeMaire SA, Curling PE, Raskin SA, Schmittling ZC, Conklin LD, et al. Renal perfusion during thoracoabdominal aortic operations: Cold crystalloid is superior to normothermic blood. *Ann Thorac Surg* 2002; **73:** 730–738.

1413. DeBakey ME, McCollum CH, Crawford ES, Morris GC, Howell J, Noon GP, et al. Dissection and dissecting aneurysms of the aorta: Twenty-year follow-up of five hundred twenty-seven patients treated surgically. *Surgery* 1982; **92:** 1118–1134.
1414. Leach SD, Toole AL, Stern H, DeNatale RW, Tilson MD. Effect of β-adrenergic blockade on the growth rate of abdominal aortic aneurysms. *Arch Surg* 1988; **123:** 606–609.
1415. Groenink M, den Hartog AW, Franken R, Radonic T, de Waard V, Timmermans J, et al. Losartan reduces aortic dilatation rate in adults with Marfan syndrome: A randomized controlled trial. *Eur Heart J* 2013; **34:** 3491–3500.
1416. Chaddha A, Kline-Rogers E, Woznicki EM, Brook R, Housholder-Hughes S, Braverman AC, et al. Activity recommendations for postaortic dissection patients. *Circulation* 2014; **130:** e140–e142.
1417. Deleted in proof.
1418. Leontyev S, Haag F, Davierwala PM, Lehmkuhl L, Borger MA, Etz CD, et al. Postoperative changes in the distal residual aorta after surgery for acute type A aortic dissection: Impact of false lumen patency and size of descending aorta. *Thorac Cardiovasc Surg* 2017; **65:** 90–98.
1419. Heo W, Song SW, Kim TH, Lee JS, Yoo KJ, Cho BK, et al. Differential impact of intimal tear location on aortic dilation and reintervention in acute type I aortic dissection after total arch replacement. *J Thorac Cardiovasc Surg* 2019; **158:** 327–338.
1420. Diehm N, Vermassen F, van Sambeek MR, Abel D; DEFINE Investigators. Standardized definitions and clinical endpoints in trials investigating endovascular repair of aortic dissections. *Eur J Vasc Endovasc Surg* 2013; **46:** 645–650.
1421. Verscheure D, Haulon S, Tsilimparis N, Resch T, Wanhainen A, Mani K, et al. Endovascular treatment of post type A chronic aortic arch dissection with a branched endograft: Early results from a retrospective international multicenter study. *Ann Surg* 2021; **273:** 997–1003.
1422. Rylski B, Beyersdorf F, Desai ND, Euringer W, Siepe M, Kari FA, et al. Distal aortic reintervention after surgery for acute DeBakey type I or II aortic dissection: Open versus endovascular repair. *Eur J Cardiothorac Surg* 2015; **48:** 258–263.
1423. Giles KA, Beck AW, Lala S, Patterson S, Back M, Fatima J, et al. Implications of secondary aortic intervention after thoracic endovascular aortic repair for acute and chronic type B dissection. *J Vasc Surg* 2019; **69:** 1367–1378.
1424. Faure EM, Canaud L, Agostini C, Shaub R, Böge G, Marty-ané C, et al. Reintervention after thoracic endovascular aortic repair of complicated aortic dissection. *J Vasc Surg* 2014; **59:** 327–333.
1425. Aguir S, El Batti S, Achouh P, Julia P, Bel A, Fabiani JN, et al. Technical aspects of open repair for degenerative aneurysmal evolution despite early thoracic endovascular repair of type B aortic dissection. *Ann Vasc Surg* 2017; **40:** 297.e13–297.e17.
1426. Suzuki T, Asai T, Kinoshita T. Predictors for late reoperation after surgical repair of acute type A aortic dissection. *Ann Thorac Surg* 2018; **106:** 63–69.
1427. Yamauchi T, Kubota S, Ohata T, Hasegawa K, Ueda H. Enlargement of aortic arch vessels after surgical repair of type A aortic dissection. *J Vasc Surg* 2017; **65:** 669–675.
1428. Vikholm P, Astudillo R, Thelin S. Long-term survival and frequency of reinterventions after proximal aortic surgery: A retrospective study. *Eur J Cardiothorac Surg* 2019; **56:** 722–730.
1429. Gaudino M, Girardi LN, Rahouma M, Leonard JR, Di Franco A, Lau C, et al. Editor's choice - Aortic re-operation after replacement of the proximal aorta: A systematic review and meta-analysis. *Eur J Vasc Endovasc Surg* 2018; **56:** 515–523.
1430. Dohle DS, El Beyrouti H, Brendel L, Pfeiffer P, El-Mehsen M, Vahl CF. Survival and reinterventions after isolated proximal aortic repair in acute type A aortic dissection. *Interact Cardiovasc Thorac Surg* 2019; **28:** 981–988.
1431. Olsson C, Hillebrant CG, Liska J, Lockowandt U, Eriksson P, Franco-Cereceda A. Mortality and reoperations in survivors operated on for acute type A aortic dissection and implications for catheter-based or hybrid interventions. *J Vasc Surg* 2013; **58:** 333–339.
1432. Pan E, Gudbjartsson T, Ahlsson A, Fuglsang S, Geirsson A, Hansson EC, et al. Low rate of reoperations after acute type A aortic dissection repair from The Nordic Consortium Registry. *J Thorac Cardiovasc Surg* 2018; **156:** 939–948.
1433. Russo CF, Mariscalco G, Colli A, Santè P, Nicolini F, Miceli A, et al. Italian multicentre study on type A acute aortic dissection: A 33-year follow-up. *Eur J Cardiothorac Surg* 2016; **49:** 125–131.
1434. Tanaka A, Sandhu HK, Estrera AL. Descending endografts for type A dissections: Con. *Ann Cardiothorac Surg* 2016; **5:** 227–232.
1435. Settepani F, Cappai A, Basciu A, Barbone A, Citterio E, Ornaghi D, et al. Hybrid versus conventional treatment of acute type A aortic dissection. *J Card Surg* 2015; **30:** 707–713.
1436. Fleischman F, Elsayed RS, Cohen RG, Tatum JM, Kumar SR, Kazerouni K, et al. Selective aortic arch and root replacement in repair of acute type A aortic dissection. *Ann Thorac Surg* 2018; **105:** 505–512.
1437. Tolis G, Sundt TM. Contemporary insights into the management of type A aortic dissection. *Expert Rev Cardiovasc Ther* 2016; **14:** 1189–1196.
1438. Estrera AL, Sandhu H, Afifi RO, Azizzadeh A, Charlton-Ouw K, Miller CC, et al. Open repair of chronic complicated type B aortic dissection using the open distal technique. *Ann Cardiothorac Surg* 2014; **3:** 375–384.
1439. Dell'Aquila AM, Pollari F, Fattouch K, Santarpino G, Hillebrand J, Schneider S, et al. Early outcomes in re-do operation after acute type A aortic dissection: Results from the multicenter READD database. *Heart Vessels* 2017; **32:** 566–573.
1440. Luciani N, De Geest R, Lauria G, Farina P, Luciani M, Glieca F, et al. Late reoperations after acute aortic dissection repair: Single-center experience. *Asian Cardiovasc Thorac Ann* 2015; **23:** 787–794.
1441. Roselli EE, Loor G, He J, Rafael AE, Rajeswaran J, Houghtaling PL, et al. Distal aortic interventions after repair of ascending dissection: The argument for a more aggressive approach. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S117–S124.
1442. Nozdrzykowski M, Luehr M, Garbade J, Schmidt A, Leontyev S, Misfeld M, et al. Outcomes of secondary procedures after primary thoracic endovascular aortic repair. *Eur J Cardiothorac Surg* 2016; **49:** 770–777.
1443. Czerny M, Schmidli J, Adler S, van den Berg JC, Bertoglio L, Carrel T, et al. Current options and recommendations for the treatment of thoracic aortic pathologies involving the aortic arch: An expert consensus document of the European Association for Cardio-Thoracic surgery (EACTS) and the European Society for Vascular Surgery (ESVS). *Eur J Cardiothorac Surg* 2019; **55:** 133–162.
1444. Takamoto S, Okita Y, Ando M, Morota T, Handa N, Kawashima Y. Retrograde cerebral circulation for distal aortic arch surgery through a left thoracotomy. *J Card Surg* 1994; **9:** 576–583.
1445. Coselli JS, LeMaire SA, Preventza O, de la Cruz KI, Cooley DA, Price MD, et al. Outcomes of 3309 thoracoabdominal aortic aneurysm repairs. *J Thorac Cardiovasc Surg* 2016; **151:** 1323–1337.
1446. Coselli JS, Spiliotopoulos K, Preventza O, de la Cruz KI, Amarasekara H, Green SY. Open aortic surgery after thoracic endovascular aortic repair. *Gen Thorac Cardiovasc Surg* 2016; **64:** 441–449.
1447. Strauch JT, Spielvogel D, Lauten A, Galla JD, Lansman SL, McMurtry K, et al. Technical advances in total aortic arch replacement. *Ann Thorac Surg* 2004; **77:** 581–590.
1448. Keeling WB, Tian DH, Leshnower BG, Numata S, Hughes GC, Matalanis G, et al; IAASSG Investigators. Safety of moderate hypothermia with antegrade cerebral perfusion in total aortic arch replacement. *Ann Thorac Surg* 2018; **105:** 54–61.
1449. Keenan JE, Wang H, Gulack BC, Ganapathi AM, Andersen ND, Englum BR, et al. Does moderate hypothermia really carry less bleeding risk than deep hypothermia for circulatory arrest?: A propensity-matched comparison in hemiarch replacement. *J Thorac Cardiovasc Surg* 2016; **152:** 1559–1569.
1450. Yan TD, Bannon PG, Bavaria J, Coselli JS, Elefteriades JA, Griepp RB, et al. Consensus on hypothermia in aortic arch surgery. *Ann Cardiothorac Surg* 2013; **2:** 163–168.
1451. Harrington DK, Bonser M, Moss A, Heafield MT, Riddoch MJ, Bonser RS. Neuropsychometric outcome following aortic arch surgery: A prospective randomized trial of retrograde cerebral perfusion. *J Thorac Cardiovasc Surg* 2003; **126:** 638–644.
1452. Estrera AL, Sheinbaum R, Miller CC, Azizzadeh A, Walkes JC, Lee TY, et al. Cerebrospinal fluid drainage during thoracic aortic repair: Safety and current management. *Ann Thorac Surg* 2009; **88:** 9–15.
1453. Cheung AT, Weiss SJ, McGarvey ML, Stecker MM, Hogan MS, Escherich A, et al. Interventions for reversing delayed-onset postoperative paraplegia after thoracic aortic reconstruction. *Ann Thorac Surg* 2002; **74:** 413–421.
1454. Cheung AT, Pochettino A, McGarvey ML, Appoo JJ, Fairman RM, Carpenter JP, et al. Strategies to manage paraplegia risk

after endovascular stent repair of descending thoracic aortic aneurysms. *Ann Thorac Surg* 2005; **80:** 1280–1289.
1455. Matsuda H, Fukuda T, Iritani O, Nakazawa T, Tanaka H, Sasaki H, et al. Spinal cord injury is not negligible after TEVAR for lower descending aorta. *Eur J Vasc Endovasc Surg* 2010; **39:** 179–186.
1456. Afifi RO, Sandhu HK, Zaidi ST, Trinh E, Tanaka A, Miller CC, et al. Intercostal artery management in thoracoabdominal aortic surgery: To reattach or not to reattach? *J Thorac Cardiovasc Surg* 2018; **155:** 1372–1378.
1457. Safi HJ, Miller CC, Huynh TT, Estrera AL, Porat EE, Winnerkvist AN, et al. Distal aortic perfusion and cerebrospinal fluid drainage for thoracoabdominal and descending thoracic aortic repair: Ten years of organ protection. *Ann Surg* 2003; **238:** 372–381.
1458. Shiiya N, Kunihara T, Matsuzaki K, Yasuda K. Evolving strategy and results of spinal cord protection in type I and II thoracoabdominal aortic aneurysm repair. *Ann Thorac Cardiovasc Surg* 2005; **11:** 178–185.
1459. Shiiya N, Washiyama N, Tsuda K, Yamanaka K, Takahashi D, Yamashita K, et al. Japanese perspective in surgery for thoracoabdominal aortic aneurysms. *Gen Thorac Cardiovasc Surg* 2019; **67:** 187–191.
1460. Matsuda H, Ogino H, Fukuda T, Iritani O, Sato S, Iba Y, et al. Multidisciplinary approach to prevent spinal cord ischemia after thoracic endovascular aneurysm repair for distal descending aorta. *Ann Thorac Surg* 2010; **90:** 561–565.
1461. Acher CW, Wynn MM, Archibald J. Naloxone and spinal fluid drainage as adjuncts in the surgical treatment of thoracoabdominal and thoracic aneurysms. *Surgery* 1990; **108:** 755–761.
1462. Shiiya N, Yasuda K. ¥Surgical treatment of thoracoabdominal aortic aneurysm. [in Japanese] *Jpn J Thorac Surg* 1997; **50:** 133–143.
1463. Komiyama M. Functional vascular anatomy of the spine and spinal cord. [in Japanese] *Neurol Surg* 2013; **41:** 481–492.
1464. Dommisse GF. The blood supply of the spinal cord: A critical vascular zone in spinal surgery. *J Bone Joint Surg Br* 1974; **56:** 225–235.
1465. Moore WM, Hollier LH. The influence of severity of spinal cord ischemia in the etiology of delayed-onset paraplegia. *Ann Surg* 1991; **213:** 427–432.
1466. Etz CD, Homann TM, Luehr M, Kari FA, Weisz DJ, Kleinman G, et al. Spinal cord blood flow and ischemic injury after experimental sacrifice of thoracic and abdominal segmental arteries. *Eur J Cardiothorac Surg* 2008; **33:** 1030–1038.
1467. Etz CD, Luehr M, Kari FA, Bodian CA, Smego D, Plestis KA, et al. Paraplegia after extensive thoracic and thoracoabdominal aortic aneurysm repair: Does critical spinal cord ischemia occur postoperatively? *J Thorac Cardiovasc Surg* 2008; **135:** 324–330.
1468. Hollier LH, Money SR, Naslund TC, Proctor CD, Buhrman WC, Marino RJ, et al. Risk of spinal cord dysfunction in patients undergoing thoracoabdominal aortic replacement. *Am J Surg* 1992; **164:** 210–214.
1469. Safi HJ, Hess KR, Randel M, Iliopoulos DC, Baldwin JC, Mootha RK, et al. Cerebrospinal fluid drainage and distal aortic perfusion: Reducing neurologic complications in repair of thoracoabdominal aortic aneurysm types I and II. *J Vasc Surg* 1996; **23:** 223–229.
1470. Sakurai M, Hayashi T, Abe K, Sadahiro M, Tabayashi K. Delayed and selective motor neuron death after transient spinal cord ischemia: A role of apoptosis? *J Thorac Cardiovasc Surg* 1998; **115:** 1310–1315.
1471. Svensson LG, Rickards E, Coull A, Rogers G, Fimmel CJ, Hinder RA. Relationship of spinal cord blood flow to vascular anatomy during thoracic aortic cross-clamping and shunting. *J Thorac Cardiovasc Surg* 1986; **91:** 71–78.
1472. Nojiri J, Matsumoto K, Kato A, Miho T, Furukawa K, Ohtsubo S, et al. The Adamkiewicz artery: Demonstration by intra-arterial computed tomographic angiography. *Eur J Cardiothorac Surg* 2007; **31:** 249–255.
1473. Shiiya N, Wakasa S, Matsui K, Sugiki T, Shingu Y, Yamakawa T, et al. Anatomical pattern of feeding artery and mechanism of intraoperative spinal cord ischemia. *Ann Thorac Surg* 2009; **88:** 768–772.
1474. Meffert P, Bischoff MS, Brenner R, Siepe M, Beyersdorf F, Kari FA. Significance and function of different spinal collateral compartments following thoracic aortic surgery: Immediate versus long-term flow compensation. *Eur J Cardiothorac Surg* 2014; **45:** 799–804.
1475. Etz CD, Di Luozzo G, Zoli S, Lazala R, Plestis KA, Bodian CA, et al. Direct spinal cord perfusion pressure monitoring in extensive distal aortic aneurysm repair. *Ann Thorac Surg* 2009; **87:** 1764–1774.
1476. Yoshioka K, Tanaka R, Ueyama Y, Abiko A. Three-dimensional demonstration of the collateral circulation to the artery of Adamkiewicz via inferior epigastric artery with computed tomography angiography. *Eur J Cardiothorac Surg* 2015; **48:** 175.
1477. Griepp RB, Griepp EB. Spinal cord protection in surgical and endovascular repair of thoracoabdominal aortic disease. *J Thorac Cardiovasc Surg* 2015; **149 Suppl:** S86–S90.
1478. Griepp RB, Griepp EB. Spinal cord perfusion and protection during descending thoracic and thoracoabdominal aortic surgery: The collateral network concept. *Ann Thorac Surg* 2007; **83:** S865–S869.
1479. Shiiya N, Matsui Y, Murashita T, Sasaki S, Sakuma M, Yasuda K. Effects of multiple small segmental resection and hypothermia with regard to causes of spinal cord injury and selection of reconstruction methods in thoracoabdominal aortic aneurysms. [in Japanese] *Jpn J Vasc Surg* 1997; **6:** 531–536.
1480. Shiiya N, Yasuda K, Matsui Y, Sakuma M, Sasaki S. Spinal cord protection during thoracoabdominal aortic aneurysm repair: Results of selective reconstruction of the critical segmental arteries guided by evoked spinal cord potential monitoring. *J Vasc Surg* 1995; **21:** 970–975.
1481. Tanaka H, Minatoya K, Matsuda H, Sasaki H, Iba Y, Oda T, et al. Embolism is emerging as a major cause of spinal cord injury after descending and thoracoabdominal aortic repair with a contemporary approach: Magnetic resonance findings of spinal cord injury. *Interact Cardiovasc Thorac Surg* 2014; **19:** 205–210.
1482. Griepp RB, Ergin MA, Galla JD, Lansman S, Khan N, Quintana C, et al. Looking for the artery of Adamkiewicz: A quest to minimize paraplegia after operations for aneurysms of the descending thoracic and thoracoabdominal aorta. *J Thorac Cardiovasc Surg* 1996; **112:** 1202–1215.
1483. Etz CD, Halstead JC, Spielvogel D, Shahani R, Lazala R, Homann TM, et al. Thoracic and thoracoabdominal aneurysm repair: Is reimplantation of spinal cord arteries a waste of time? *Ann Thorac Surg* 2006; **82:** 1670–1677.
1484. Flores J, Kunihara T, Shiiya N, Yoshimoto K, Matsuzaki K, Yasuda K. Extensive deployment of the stented elephant trunk is associated with an increased risk of spinal cord injury. *J Thorac Cardiovasc Surg* 2006; **131:** 336–342.
1485. Yamada N, Okita Y, Minatoya K, Tagusari O, Ando M, Takamiya M, et al. Preoperative demonstration of the Adamkiewicz artery by magnetic resonance angiography in patients with descending or thoracoabdominal aortic aneurysms. *Eur J Cardiothorac Surg* 2000; **18:** 104–111.
1486. Laschinger JC, Cunningham JN, Baumann FG, Cooper MM, Krieger KH, Spencer FC. Monitoring of somatosensory evoked potentials during surgical procedures on the thoracoabdominal aorta: III. Intraoperative identification of vessels critical to spinal cord blood supply. *J Thorac Cardiovasc Surg* 1987; **94:** 271–274.
1487. Sueda T, Okada K, Orihashi K, Sugawara Y, Kouchi K, Imai K. Cold blood spinal cord plegia for prediction of spinal cord ischemia during thoracoabdominal aneurysm repair. *Ann Thorac Surg* 2002; **73:** 1155–1159.
1488. Shiiya N, Takahashi D, Tsuda K. Evoked potentials monitoring in aortic surgery. [in Japanese] *Jpn J Thorac Surg* 2014; **67:** 630–635.
1489. Crawford ES, Mizrahi EM, Hess KR, Coselli JS, Safi HJ, Patel VM. The impact of distal aortic perfusion and somatosensory evoked potential monitoring on prevention of paraplegia after aortic aneurysm operation. *J Thorac Cardiovasc Surg* 1988; **95:** 357–367.
1490. Tsuda K, Shiiya N, Takahashi D, Ohkura K, Yamashita K, Kando Y. Transoesophageal spinal cord stimulation for motor-evoked potentials monitoring: Feasibility, safety and stability. *Eur J Cardiothorac Surg* 2015; **48:** 245–251.
1491. Tsuda K, Shiiya N, Takahashi D, Ohkura K, Yamashita K, Kando Y, et al. Transesophageal versus transcranial motor evoked potentials to monitor spinal cord ischemia. *J Thorac Cardiovasc Surg* 2016; **151:** 509–517.
1492. von Aspern K, Haunschild J, Hoyer A, Luehr M, Bakhtiary F, Misfeld M, et al. Non-invasive spinal cord oxygenation monitoring: Validating collateral network near-infrared spectroscopy for thoracoabdominal aortic aneurysm repair. *Eur J Cardiothorac Surg* 2016; **50:** 675–683.

1493. von Aspern K, Haunschild J, Ziemann M, Misfeld M, Mohr FW, Borger MA, et al. Evaluation of collateral network near-infrared spectroscopy during and after segmental artery occlusion in a chronic large animal model. *J Thorac Cardiovasc Surg* 2019; **158:** 155–164.
1494. Wadouh F, Arndt CF, Oppermann E, Borst HG, Wadouh R. The mechanism of spinal cord injury after simple and double aortic cross-clamping. *J Thorac Cardiovasc Surg* 1986; **92:** 121–127.
1495. Dapunt OE, Midulla PS, Sadeghi AM, Mezrow CK, Wolfe D, Gandsas A, et al. Pathogenesis of spinal cord injury during simulated aneurysm repair in a chronic animal model. *Ann Thorac Surg* 1994; **58:** 689–697.
1496. Kawaharada N, Ito T, Koyanagi T, Harada R, Hyodoh H, Kurimoto Y, et al. Spinal cord protection with selective spinal perfusion during descending thoracic and thoracoabdominal aortic surgery. *Interact Cardiovasc Thorac Surg* 2010; **10:** 986–991.
1497. Griffiths IR, Pitts LH, Crawford RA, Trench JG. Spinal cord compression and blood flow: I. The effect of raised cerebrospinal fluid pressure on spinal cord blood flow. *Neurology* 1978; **28:** 1145–1151.
1498. Oka Y, Miyamoto T. Prevention of spinal cord injury after cross-clamping of the thoracic aorta. *Jpn J Surg* 1984; **14:** 159–162.
1499. Miyamoto K, Ueno A, Wada T, Kimoto S. A new and simple method of preventing spinal cord damage following temporary occlusion of the thoracic aorta by draining the cerebrospinal fluid. *J Cardiovasc Surg (Torino)* 1960; **1:** 188–197.
1500. Crawford ES, Svensson LG, Hess KR, Shenaq SS, Coselli JS, Safi HJ, et al. A prospective randomized study of cerebrospinal fluid drainage to prevent paraplegia after high-risk surgery on the thoracoabdominal aorta. *J Vasc Surg* 1991; **13:** 36–46.
1501. Dardik A, Perler BA, Roseborough GS, Williams GM. Subdural hematoma after thoracoabdominal aortic aneurysm repair: An underreported complication of spinal fluid drainage? *J Vasc Surg* 2002; **36:** 47–50.
1502. Vacanti FX, Ames A. Mild hypothermia and Mg^{++} protect against irreversible damage during CNS ischemia. *Stroke* 1984; **15:** 695–698.
1503. Safi HJ, Miller CC, Subramaniam MH, Campbell MP, Iliopoulos DC, O'Donnell JJ, et al. Thoracic and thoracoabdominal aortic aneurysm repair using cardiopulmonary bypass, profound hypothermia, and circulatory arrest via left side of the chest incision. *J Vasc Surg* 1998; **28:** 591–598.
1504. Wojewski PA. Spinal cord protection during thoracoabdominal aneurysm resection. *J Thorac Cardiovasc Surg* 1995; **109:** 1244–1246.
1505. Davison JK, Cambria RP, Vierra DJ, Columbia MA, Koustas G. Epidural cooling for regional spinal cord hypothermia during thoracoabdominal aneurysm repair. *J Vasc Surg* 1994; **20:** 304–310.
1506. Kunihara T, Matsuzaki K, Shiiya N, Saijo Y, Yasuda K. Naloxone lowers cerebrospinal fluid levels of excitatory amino acids after thoracoabdominal aortic surgery. *J Vasc Surg* 2004; **40:** 681–690.
1507. Coselli JS. Reflection of pioneers: Redo thoracoabdominal aortic aneurysm repair controversies in thoracic aortic aneurysm surgery. *Gen Thorac Cardiovasc Surg* 2019; **67:** 168–174.
1508. Afifi RO, Sandhu HK, Trott AE, Nguyen TC, Miller CC, Estrera AL, et al. Redo thoracoabdominal aortic aneurysm repair: A single-center experience over 25 years. *Ann Thorac Surg* 2017; **103:** 1421–1428.
1509. Antoniou A, Bashir M, Harky A, Di Salvo C. Redo proximal thoracic aortic surgery: Challenges and controversies. *Gen Thorac Cardiovasc Surg* 2019; **67:** 118–126.
1510. Dearani JA, Burkhart HM, Stulak JM, Sundt TM, Schaff HV. Management of the aortic root in adult patients with conotruncal anomalies. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu* 2009; **12:** 122–129.
1511. Stulak JM, Burkhart HM, Sundt TM, Connolly HM, Suri RM, Schaff HV, et al. Spectrum and outcome of reoperations after the Ross procedure. *Circulation* 2010; **122:** 1153–1158.
1512. Ota H, Morita Y, Saiki Y, Takase K. Coil embolization of left ventricular outflow tract pseudoaneurysms: Techniques and 5-year results. *Interact Cardiovasc Thorac Surg* 2017; **24:** 631–633.
1513. Jain V, Gruberg L, Bilfinger TV, Tassiopoulos AK, Loh SA. Coil embolization of an aortic pseudoaneurysm after open repair of type A aortic dissection. *Ann Vasc Surg* 2014; **28:** 1312.e1–1312.e5.
1514. Hosoyama K, Kawamoto S, Motoyoshi N, Saiki Y. Intraoperative vacuum-assisted closure following in situ graft replacement for an infected thoracic aortic graft. *J Thorac Cardiovasc Surg* 2015; **150:** e36–e38.
1515. Saiki Y, Kawamoto S, Sai S, Tabayashi K. An effective vacuum-assisted closure treatment for mediastinitis with aortic arch replacement. *Interact Cardiovasc Thorac Surg* 2008; **7:** 712–714.
1516. Dobell AR, Jain AK. Catastrophic hemorrhage during redo sternotomy. *Ann Thorac Surg* 1984; **37:** 273–278.
1517. Luciani N, De Geest R, Anselmi A, Glieca F, De Paulis S, Possati G. Results of reoperation on the aortic root and the ascending aorta. *Ann Thorac Surg* 2011; **92:** 898–903.
1518. Coselli JS, Rosu C, Amarasekara HS, Green SY, Zhang Q, Price MD, et al. Reoperative surgery on the thoracoabdominal aorta. *J Thorac Cardiovasc Surg* 2018; **155:** 474–485.
1519. Davidovic LB, Ducic SM, Vujcic AD. Is late open conversion after TEVAR more risky than primary open repair of descending thoracic aneurysms? *J Cardiovasc Surg (Torino)* 2019; **60:** 147–148.
1520. Roselli EE, Abdel-Halim M, Johnston DR, Soltesz EG, Greenberg RK, Svensson LG, et al. Open aortic repair after prior thoracic endovascular aortic repair. *Ann Thorac Surg* 2014; **97:** 750–756.
1521. Lima B, Roselli EE, Soltesz EG, Johnston DR, Pujara AC, Idrees J, et al. Modified and "reverse" frozen elephant trunk repairs for extensive disease and complications after stent grafting. *Ann Thorac Surg* 2012; **93:** 103–109.
1522. Melissano G, Tshomba Y, Mascia D, Baccellieri D, Kahlberg A, Bertoglio L, et al. Late open conversion after TEVAR. *J Cardiovasc Surg (Torino)* 2016; **57:** 491–497.
1523. Marques de Marino P, Oikonomou K, Verhoeven EL, Katsargyris A. Techniques and outcomes of secondary endovascular repair for postdissection TAA/TAAA. *J Cardiovasc Surg (Torino)* 2018; **59:** 767–774.
1524. Nienaber CA, Fattori R, Mehta RH, Richartz BM, Evangelista A, Petzsch M, et al; International Registry of Acute Aortic Dissection. Gender-related differences in acute aortic dissection. *Circulation* 2004; **109:** 3014–3021.
1525. Akutsu K, Morisaki H, Okajima T, Yoshimuta T, Tsutsumi Y, Takeshita S, et al. Genetic analysis of young adult patients with aortic disease not fulfilling the diagnostic criteria for Marfan syndrome. *Circ J* 2010; **74:** 990–997.
1526. Loeys BL, Dietz HC, Braverman AC, Callewaert BL, De Backer J, Devereux RB, et al. The revised Ghent nosology for the Marfan syndrome. *J Med Genet* 2010; **47:** 476–485.
1527. Halushka MK, Angelini A, Bartoloni G, Basso C, Batoroeva L, Bruneval P, et al. Consensus statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology: II. Noninflammatory degenerative diseases - nomenclature and diagnostic criteria. *Cardiovasc Pathol* 2016; **25:** 247–257.
1528. Marfan AB. Un cas de deformation congenitale des quatre membres, plue prononcee aux extremities, caracterisee par l'allongement des os avec un certain degre d'amincissement. *Bul Sco Chir Paris* 1896; **13:** 220–225.
1529. Baer RW, Taussig HB, Oppenheimer EH. Congenital aneurysmal dilatation of the aorta associated with arachnodactyly. *Bull Johns Hopkins Hosp* 1943; **72:** 309–331.
1530. Dietz HC, Cutting GR, Pyeritz RE, Maslen CL, Sakai LY, Corson GM, et al. Marfan syndrome caused by a recurrent *de novo* missense mutation in the fibrillin gene. *Nature* 1991; **352:** 337–339.
1531. Milewicz DM, Pyeritz RE, Crawford ES, Byers PH. Marfan syndrome: Defective synthesis, secretion, and extracellular matrix formation of fibrillin by cultured dermal fibroblasts. *J Clin Invest* 1992; **89:** 79–86.
1532. Robinson PN, Arteaga-Solis E, Baldock C, Collod-Béroud G, Booms P, De Paepe A, et al. The molecular genetics of Marfan syndrome and related disorders. *J Med Genet* 2006; **43:** 769–787.
1533. Roman MJ, Devereux RB, Kramer-Fox R, O'Loughlin J. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. *Am J Cardiol* 1989; **64:** 507–512.
1534. Pettersen MD, Du W, Skeens ME, Humes RA. Regression equations for calculation of z scores of cardiac structures in a large cohort of healthy infants, children, and adolescents: An echocardiographic study. *J Am Soc Echocardiogr* 2008; **21:** 922–934.
1535. Marfan Foundation. Z-score Calculattion. Available at: https://

www.marfan.org/dx/zscore (accessed July 31, 2020).
1536. Pope FM, Nicholls AC, Jones PM, Wells RS, Lawrence D. EDS IV (acrogeria): New autosomal dominant and recessive types. *J R Soc Med* 1980; **73:** 180–186.
1537. Malfait F, Francomano C, Byers P, Belmont J, Berglund B, Black J, et al. The 2017 international classification of the Ehlers-Danlos syndromes. *Am J Med Genet C Semin Med Genet* 2017; **175:** 8–26.
1538. Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, et al. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in *TGFBR1* or *TGFBR2*. *Nat Genet* 2005; **37:** 275–281.
1539. Loeys BL, Schwarze U, Holm T, Callewaert BL, Thomas GH, Pannu H, et al. Aneurysm syndromes caused by mutations in the TGF-β receptor. *N Engl J Med* 2006; **355:** 788–798.
1540. Mizuguchi T, Collod-Beroud G, Akiyama T, Abifadel M, Harada N, Morisaki T, et al. Heterozygous *TGFBR2* mutations in Marfan syndrome. *Nat Genet* 2004; **36:** 855–860.
1541. Mátyás G, Arnold E, Carrel T, Baumgartner D, Boileau C, Berger W, et al. Identification and in silico analyses of novel *TGFBR1* and *TGFBR2* mutations in Marfan syndrome-related disorders. *Hum Mutat* 2006; **27:** 760–769.
1542. van de Laar IM, Oldenburg RA, Pals G, Roos-Hesselink JW, de Graaf BM, Verhagen JM, et al. Mutations in *SMAD3* cause a syndromic form of aortic aneurysms and dissections with early-onset osteoarthritis. *Nat Genet* 2011; **43:** 121–126.
1543. Boileau C, Guo DC, Hanna N, Regalado ES, Detaint D, Gong L, et al; National Heart, Lung, and Blood Institute (NHLBI) Go Exome Sequencing Project. *TGFB2* mutations cause familial thoracic aortic aneurysms and dissections associated with mild systemic features of Marfan syndrome. *Nat Genet* 2012; **44:** 916–921.
1544. Bertoli-Avella AM, Gillis E, Morisaki H, Verhagen JMA, de Graaf BM, van de Beek G, et al. Mutations in a TGF-β ligand, *TGFB3*, cause syndromic aortic aneurysms and dissections. *J Am Coll Cardiol* 2015; **65:** 1324–1336.
1545. Tran-Fadulu V, Pannu H, Kim DH, Vick GW, Lonsford CM, Lafont AL, et al. Analysis of multigenerational families with thoracic aortic aneurysms and dissections due to *TGFBR1* or *TGFBR2* mutations. *J Med Genet* 2009; **46:** 607–613.
1546. Franceschini P, Guala A, Licata D, Di Cara G, Franceschini D. Arterial tortuosity syndrome. *Am J Med Genet* 2000; **91:** 141–143.
1547. Coucke PJ, Willaert A, Wessels MW, Callewaert B, Zoppi N, De Backer J, et al. Mutations in the facilitative glucose transporter GLUT10 alter angiogenesis and cause arterial tortuosity syndrome. *Nat Genet* 2006; **38:** 452–457.
1548. Meester JA, Vandeweyer G, Pintelon I, Lammens M, Van Hoorick L, De Belder S, et al. Loss-of-function mutations in the X-linked biglycan gene cause a severe syndromic form of thoracic aortic aneurysms and dissections. *Genet Med* 2017; **19:** 386–395.
1549. Ziganshin BA, Bailey AE, Coons C, Dykas D, Charilaou P, Tanriverdi LH, et al. Routine genetic testing for thoracic aortic aneurysm and dissection in a clinical setting. *Ann Thorac Surg* 2015; **100:** 1604–1611.
1550. Morisaki T, Morisaki H. Genetics of hereditary large vessel diseases. *J Hum Genet* 2016; **61:** 21–26.
1551. Matura LA, Ho VB, Rosing DR, Bondy CA. Aortic dilatation and dissection in Turner syndrome. *Circulation* 2007; **116:** 1663–1670.
1552. Guo DC, Pannu H, Tran-Fadulu V, Papke CL, Yu RK, Avidan N, et al. Mutations in smooth muscle α-actin (*ACTA2*) lead to thoracic aortic aneurysms and dissections. *Nat Genet* 2007; **39:** 1488–1493.
1553. Zhu L, Vranckx R, Khau Van Kien P, Lalande A, Boisset N, Mathieu F, et al. Mutations in myosin heavy chain 11 cause a syndrome associating thoracic aortic aneurysm/aortic dissection and patent ductus arteriosus. *Nat Genet* 2006; **38:** 343–349.
1554. Wang L, Guo DC, Cao J, Gong L, Kamm KE, Regalado E, et al. Mutations in myosin light chain kinase cause familial aortic dissections. *Am J Hum Genet* 2010; **87:** 701–707.
1555. Guo DC, Papke CL, Tran-Fadulu V, Regalado ES, Avidan N, Johnson RJ, et al. Mutations in smooth muscle alpha-actin (*ACTA2*) cause coronary artery disease, stroke, and Moyamoya disease, along with thoracic aortic disease. *Am J Hum Genet* 2009; **84:** 617–627.
1556. Guo DC, Regalado E, Casteel DE, Santos-Cortez RL, Gong L, Kim JJ, et al; GenTAC Registry Consortium. Recurrent gain-of-function mutation in *PRKG1* causes thoracic aortic aneurysms and acute aortic dissections. *Am J Hum Genet* 2013; **93:** 398–404.
1557. Morisaki H, Akutsu K, Ogino H, Kondo N, Yamanaka I, Tsutsumi Y, et al. Mutation of *ACTA2* gene as an important cause of familial and nonfamilial nonsyndromatic thoracic aortic aneurysm and/or dissection (TAAD). *Hum Mutat* 2009; **30:** 1406–1411.
1558. Tutar E, Ekici F, Atalay S, Nacar N. The prevalence of bicuspid aortic valve in newborns by echocardiographic screening. *Am Heart J* 2005; **150:** 513–515.
1559. McBride KL, Riley MF, Zender GA, Fitzgerald-Butt SM, Towbin JA, Belmont JW, et al. *NOTCH1* mutations in individuals with left ventricular outflow tract malformations reduce ligand-induced signaling. *Hum Mol Genet* 2008; **17:** 2886–2893.
1560. Sandford RM, Bown MJ, London NJ, Sayers RD. The genetic basis of abdominal aortic aneurysms: A review. *Eur J Vasc Endovasc Surg* 2007; **33:** 381–390.
1561. Ogata T, Shibamura H, Tromp G, Sinha M, Goddard KA, Sakalihasan N, et al. Genetic analysis of polymorphisms in biologically relevant candidate genes in patients with abdominal aortic aneurysms. *J Vasc Surg* 2005; **41:** 1036–1042.
1562. Renard M, Francis C, Ghosh R, Scott AF, Witmer PD, Adès LC, et al. Clinical validity of genes for heritable thoracic aortic aneurysm and dissection. *J Am Coll Cardiol* 2018; **72:** 605–615.
1563. Franken R, Teixido-Tura G, Brion M, Forteza A, Rodriguez-Palomares J, Gutierrez L, et al. Relationship between fibrillin-1 genotype and severity of cardiovascular involvement in Marfan syndrome. *Heart* 2017; **103:** 1795–1799.
1564. Faivre L, Collod-Beroud G, Loeys BL, Child A, Binquet C, Gautier E, et al. Effect of mutation type and location on clinical outcome in 1,013 probands with Marfan syndrome or related phenotypes and *FBN1* mutations: An international study. *Am J Hum Genet* 2007; **81:** 454–466.
1565. Tsipouras P, Byers PH, Schwartz RC, Chu ML, Weil D, Pepe G, et al. Ehlers-Danlos syndrome type IV: Cosegregation of the phenotype to a COL3A1 allele of type III procollagen. *Hum Genet* 1986; **74:** 41–46.
1566. Pepin MG, Schwarze U, Rice KM, Liu M, Leistritz D, Byers PH. Survival is affected by mutation type and molecular mechanism in vascular Ehlers-Danlos syndrome (EDS type IV). *Genet Med* 2014; **16:** 881–888.
1567. Judge DP, Dietz HC. Marfan's syndrome. *Lancet* 2005; **366:** 1965–1976.
1568. Meijboom LJ, Vos FE, Timmermans J, Boers GH, Zwinderman AH, Mulder BJ. Pregnancy and aortic root growth in the Marfan syndrome: A prospective study. *Eur Heart J* 2005; **26:** 914–920.
1569. Roman MJ, Pugh NL, Hendershot TP, Devereux RB, Dietz H, Holmes K, et al; GenTAC Investigators. Aortic complications associated with pregnancy in Marfan syndrome: The NHLBI National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC). *J Am Heart Assoc* 2016; **5:** e004052.
1570. Renard M, Muiño-Mosquera L, Manalo EC, Tufa S, Carlson EJ, Keene DR, et al. Sex, pregnancy and aortic disease in Marfan syndrome. *PLoS One* 2017; **12:** e0181166.
1571. Donnelly RT, Pinto NM, Kocolas I, Yetman AT. The immediate and long-term impact of pregnancy on aortic growth rate and mortality in women with Marfan syndrome. *J Am Coll Cardiol* 2012; **60:** 224–229.
1572. Keschenau PR, Kotelis D, Bisschop J, Barbati ME, Grommes J, Mees B, et al. Editor's choice: Open thoracic and thoraco-abdominal aortic repair in patients with connective tissue disease. *Eur J Vasc Endovasc Surg* 2017; **54:** 588–596.
1573. David TE, David CM, Manlhiot C, Colman J, Crean AM, Bradley T. Outcomes of aortic valve-sparing operations in Marfan syndrome. *J Am Coll Cardiol* 2015; **66:** 1445–1453.
1574. Svensson LG, Blackstone EH, Alsalihi M, Batizy LH, Roselli EE, McCullough R, et al. Midterm results of David reimplantation in patients with connective tissue disorder. *Ann Thorac Surg* 2013; **95:** 555–562.
1575. Ando M, Yamauchi H, Morota T, Taketani T, Shimada S, Nawata K, et al. Long-term outcome after the original and simple modified technique of valve-sparing aortic root reimplantation in Marfan-based population, David V University of Tokyo modification. *J Cardiol* 2016; **67:** 86–91.
1576. Benedetto U, Melina G, Takkenberg JJ, Roscitano A, Angeloni E, Sinatra R. Surgical management of aortic root disease in Marfan syndrome: A systematic review and meta-analysis. *Heart* 2011; **97:** 955–958.
1577. Price J, Magruder JT, Young A, Grimm JC, Patel ND, Alejo D,

et al. Long-term outcomes of aortic root operations for Marfan syndrome: A comparison of Bentall versus aortic valve-sparing procedures. *J Thorac Cardiovasc Surg* 2016; **151:** 330–336.
1578. Schoenhoff FS, Langhammer B, Wustmann K, Reineke D, Kadner A, Carrel T. Decision-making in aortic root surgery in Marfan syndrome: Bleeding, thromboembolism and risk of reintervention after valve-sparing or mechanical aortic root replacement. *Eur J Cardiothorac Surg* 2015; **48:** 931–936.
1579. Coselli JS, Volguina IV, LeMaire SA, Sundt TM, Connolly HM, Stephens EH, et al; Aortic Valve Operative Outcomes in Marfan Patients Study Group. Early and 1-year outcomes of aortic root surgery in patients with Marfan syndrome: A prospective, multicenter, comparative study. *J Thorac Cardiovasc Surg* 2014; **147:** 1758–1767.
1580. Burgstaller JM, Held U, Mosbahi S, Stak D, Steurer J, Eckstein F, et al. A systemic review and meta-analysis: Long-term results of the Bentall versus the David procedure in patients with Marfan syndrome. *Eur J Cardiothorac Surg* 2018; **54:** 411–419.
1581. de Beaufort HWL, Trimarchi S, Korach A, Di Eusanio M, Gilon D, Montgomery DG, et al. Aortic dissection in patients with Marfan syndrome based on the IRAD data. *Ann Cardiothorac Surg* 2017; **6:** 633–641.
1582. Roselli EE, Idrees JJ, Lowry AM, Masabni K, Soltesz EG, Johnston DR, et al. Beyond the aortic root: Staged open and endovascular repair of arch and descending aorta in patients with connective tissue disorders. *Ann Thorac Surg* 2016; **101:** 906–912.
1583. Rylski B, Bavaria JE, Beyersdorf F, Branchetti E, Desai ND, Milewski RK, et al. Type A aortic dissection in Marfan syndrome: Extent of initial surgery determines long-term outcome. *Circulation* 2014; **129:** 1381–1386.
1584. Schoenhoff FS, Kadner A, Czerny M, Jungi S, Meszaros K, Schmidli J, et al. Should aortic arch replacement be performed during initial surgery for aortic root aneurysm in patients with Marfan syndrome? *Eur J Cardiothorac Surg* 2013; **44:** 346–351.
1585. Chen Y, Ma WG, Zhi AH, Lu L, Zheng J, Zhang W, et al. Fate of distal aorta after frozen elephant trunk and total arch replacement for type A aortic dissection in Marfan syndrome. *J Thorac Cardiovasc Surg* 2019; **157:** 835–849.
1586. Eid-Lidt G, Gaspar J, Meléndez-Ramírez G, Cervantes S J, González-Pacheco H, Dámas de Los Santos F, et al. Endovascular treatment of type B dissection in patients with Marfan syndrome: Mid-term outcomes and aortic remodeling. *Catheter Cardiovasc Interv* 2013; **82:** E898–E905.
1587. Kouchoukos NT. Endovascular surgery in Marfan syndrome: CON. *Ann Cardiothorac Surg* 2017; **6:** 677–681.
1588. Patel ND, Arnaoutakis GJ, George TJ, Allen JG, Alejo DE, Dietz HC, et al. Valve-sparing aortic root replacement in Loeys-Dietz syndrome. *Ann Thorac Surg* 2011; **92:** 556–561.
1589. Aftab M, Cikach FS, Zhu Y, Idrees JJ, Rigelsky CM, Kalahasti V, et al. Loeys-Dietz syndrome: Intermediate-term outcomes of medically and surgically managed patients. *J Thorac Cardiovasc Surg* 2019; **157:** 439–450.
1590. Schoenhoff FS, Mueller C, Czerny M, Matyas G, Kadner A, Schmidli J, et al. Outcome of aortic surgery in patients with Loeys-Dietz syndrome primarily treated as having Marfan syndrome. *Eur J Cardiothorac Surg* 2014; **46:** 444–449.
1591. Oderich GS, Panneton JM, Bower TC, Lindor NM, Cherry KJ, Noel AA, et al. The spectrum, management and clinical outcome of Ehlers-Danlos syndrome type IV: A 30-year experience. *J Vasc Surg* 2005; **42:** 98–106.
1592. Holscher CM, Dakour Aridi H, Locham SS, Hicks CW, Canner JK, Malas M, et al. Aortic surgery outcomes of Marfan syndrome and Ehlers-Danlos syndrome patients at teaching and nonteaching hospitals. *Ann Vasc Surg* 2019; **55:** 175–181.
1593. Salim MA, Alpert BS, Ward JC, Pyeritz RE. Effect of beta-adrenergic blockade on aortic root rate of dilation in the Marfan syndrome. *Am J Cardiol* 1994; **74:** 629–633.
1594. Gao L, Mao Q, Wen D, Zhang L, Zhou X, Hui R. The effect of beta-blocker therapy on progressive aortic dilatation in children and adolescents with Marfan's syndrome: A meta-analysis. *Acta Paediatr* 2011; **100:** e101–e105.
1595. Lacro RV, Dietz HC, Sleeper LA, Yetman AT, Bradley TJ, Colan SD, et al; Pediatric Heart Network Investigators. Atenolol versus losartan in children and young adults with Marfan's syndrome. *N Engl J Med* 2014; **371:** 2061–2071.
1596. Forteza A, Evangelista A, Sánchez V, Teixidó-Turà G, Sanz P, Gutiérrez L, et al. Efficacy of losartan vs. atenolol for the prevention of aortic dilation in Marfan syndrome: A randomized clinical trial. *Eur Heart J* 2016; **37:** 978–985.
1597. Teixido-Tura G, Forteza A, Rodríguez-Palomares J, González Mirelis J, Gutiérrez L, Sánchez V, et al. Losartan versus atenolol for prevention of aortic dilation in patients with Marfan syndrome. *J Am Coll Cardiol* 2018; **72:** 1613–1618.
1598. Kang YN, Chi SC, Wu MH, Chiu HH. The effects of losartan versus beta-blockers on cardiovascular protection in marfan syndrome: A systematic review and meta-analysis. *J Formos Med Assoc* 2020; **119:** 182–190.
1599. Milleron O, Arnoult F, Ropers J, Aegerter P, Detaint D, Delorme G, et al. Marfan Sartan: A randomized, double-blind, placebo-controlled trial. *Eur Heart J* 2015; **36:** 2160–2166.
1600. Ong KT, Perdu J, De Backer J, Bozec E, Collignon P, Emmerich J, et al. Effect of celiprolol on prevention of cardiovascular events in vascular Ehlers-Danlos syndrome: A prospective randomised, open, blinded-endpoints trial. *Lancet* 2010; **376:** 1476–1484.
1601. Di Eusanio M, Berretta P, Folesani G, Di Bartolomeo R. Aortic disease in Marfan syndrome: Current role of surgery and thoracic endovascular aortic repair. [Article in Italian] *G Ital Cardiol (Rome)* 2013; **14:** 538–547.
1602. Tinelli G, Ferraresi M, Watkins AC, Hertault A, Soler R, Azzaoui R, et al. Aortic treatment in connective tissue disease. *J Cardiovasc Surg (Torino)* 2019; **60:** 518–525.
1603. Preventza O, Mohammed S, Cheong BY, Gonzalez L, Ouzounian M, Livesay JJ, et al. Endovascular therapy in patients with genetically triggered thoracic aortic disease: Applications and short- and mid-term outcomes. *Eur J Cardiothorac Surg* 2014; **46:** 248–253.
1604. Nordon IM, Hinchliffe RJ, Holt PJ, Morgan R, Jahangiri M, Loftus IM, et al. Endovascular management of chronic aortic dissection in patients with Marfan syndrome. *J Vasc Surg* 2009; **50:** 987–991.
1605. Faure EM, El Batti S, Abou Rjeili M, Ben Abdallah I, Julia P, Alsac JM. Stent-assisted, balloon-induced intimal disruption and relamination of aortic dissection in patients with Marfan syndrome: Midterm outcomes and aortic remodeling. *J Thorac Cardiovasc Surg* 2018; **156:** 1787–1793.
1606. Clough RE, Martin-Gonzalez T, Van Calster K, Hertault A, Spear R, Azzaoui R, et al. Endovascular repair of thoracoabdominal and arch aneurysms in patients with connective tissue disease using branched and fenestrated devices. *Ann Vasc Surg* 2017; **44:** 158–163.
1607. van de Luijtgaarden KM, Bastos Gonçalves F, Hoeks SE, Blankensteijn JD, Böckler D, Stolker RJ, et al. Higher 30 day mortality in patients with familial abdominal aortic aneurysm after EVAR. *Eur J Vasc Endovasc Surg* 2017; **54:** 142–149.
1608. Ryer EJ, Garvin RP, Zhou Y, Sun H, Pham A, Orlova K, et al. Outcomes of familial abdominal aortic aneurysm repair in the Vascular Quality Initiative. *J Vasc Surg* 2019; **69:** 717–727.
1609. Schoenhoff FS, Carrel TP. Re-interventions on the thoracic and thoracoabdominal aorta in patients with Marfan syndrome. *Ann Cardiothorac Surg* 2017; **6:** 662–671.
1610. Chen Y, Ma WG, Li JR, Zheng J, Li Q, Liu YM, et al. Can frozen elephant trunk cure type I dissection confined to thoracic aorta in Marfan Syndrome? *Ann Thorac Surg* 2020; **109:** 1174–1182.
1611. Glebova NO, Cameron DE, Black JH. Treatment of thoracoabdominal aortic disease in patients with connective tissue disorders. *J Vasc Surg* 2018; **68:** 1257–1267.
1612. Parisi R, Secco GG, Di Eusanio M, Fattori R. Endovascular repair of aortic dissection in Marfan syndrome: Current status and future perspectives. *Diseases* 2015; **3:** 159–166.
1613. Böckler D, Meisenbacher K, Peters AS, Grond-Ginsbach C, Bischoff MS. Endovaskuläre treatment of genetically linked aortic diseases. *Gefasschirurgie* 2017; **22 Suppl:** 1–7.
1614. Yammine H, Briggs CS, Stanley GA, Ballast JK, Anderson WE, Nussbaum T, et al. Retrograde type A dissection after thoracic endovascular aortic repair for type B aortic dissection. *J Vasc Surg* 2019; **69:** 24–33.
1615. Waterman AL, Feezor RJ, Lee WA, Hess PJ, Beaver TM, Martin TD, et al. Endovascular treatment of acute and chronic aortic pathology in patients with Marfan syndrome. *J Vasc Surg* 2012; **55:** 1234–1241.
1616. Miyahara S, Okita Y. Overview of current surgical strategies for aortic disease in patients with Marfan syndrome. *Surg Today* 2016; **46:** 1006–1018.
1617. Masri A, Kalahasti V, Alkharabsheh S, Svensson LG, Sabik JF, Roselli EE, et al. Characteristics and long-term outcomes of contemporary patients with bicuspid aortic valves. *J Thorac Cardiovasc Surg* 2016; **151:** 1650–1659.

1618. Girdauskas E, Borger MA, Secknus MA, Girdauskas G, Kuntze T. Is aortopathy in bicuspid aortic valve disease a congenital defect or a result of abnormal hemodynamics?: A critical reappraisal of a one-sided argument. *Eur J Cardiothorac Surg* 2011; **39:** 809–814.
1619. Sievers HH, Schmidtke C. A classification system for the bicuspid aortic valve from 304 surgical specimens. *J Thorac Cardiovasc Surg* 2007; **133:** 1226–1233.
1620. Fazel SS, Mallidi HR, Lee RS, Sheehan MP, Liang D, Fleischman D, et al. The aortopathy of bicuspid aortic valve disease has distinctive patterns and usually involves the transverse aortic arch. *J Thorac Cardiovasc Surg* 2008; **135:** 901–907.
1621. Schaefer BM, Lewin MB, Stout KK, Gill E, Prueitt A, Byers PH, et al. The bicuspid aortic valve: An integrated phenotypic classification of leaflet morphology and aortic root shape. *Heart* 2008; **94:** 1634–1638.
1622. Fernandes SM, Sanders SP, Khairy P, Jenkins KJ, Gauvreau K, Lang P, et al. Morphology of bicuspid aortic valve in children and adolescents. *J Am Coll Cardiol* 2004; **44:** 1648–1651.
1623. Januzzi JL, Isselbacher EM, Fattori R, Cooper JV, Smith DE, Fang J, et al; International Registry of Aortic Dissection (IRAD). Characterizing the young patient with aortic dissection: Results from the International Registry of Aortic Dissection (IRAD). *J Am Coll Cardiol* 2004; **43:** 665–669.
1624. Detaint D, Michelena HI, Nkomo VT, Vahanian A, Jondeau G, Sarano ME. Aortic dilatation patterns and rates in adults with bicuspid aortic valves: A comparative study with Marfan syndrome and degenerative aortopathy. *Heart* 2014; **100:** 126–134.
1625. Itagaki S, Chikwe JP, Chiang YP, Egorova NN, Adams DH. Long-term risk for aortic complications after aortic valve replacement in patients with bicuspid aortic valve versus Marfan syndrome. *J Am Coll Cardiol* 2015; **65:** 2363–2369.
1626. Sherrah AG, Andvik S, van der Linde D, Davies L, Bannon PG, Padang R, et al. Nonsyndromic thoracic aortic aneurysm and dissection: Outcomes with marfan syndrome versus bicuspid aortic valve aneurysm. *J Am Coll Cardiol* 2016; **67:** 618–626.
1627. Grewal N, Franken R, Mulder BJ, Goumans MJ, Lindeman JH, Jongbloed MR, et al. Histopathology of aortic complications in bicuspid aortic valve versus Marfan syndrome: Relevance for therapy? *Heart Vessels* 2016; **31:** 795–806.
1628. Garg V, Muth AN, Ransom JF, Schluterman MK, Barnes R, King IN, et al. Mutations in *NOTCH1* cause aortic valve disease. *Nature* 2005; **437:** 270–274.
1629. Kent KC, Crenshaw ML, Goh DL, Dietz HC. Genotype-phenotype correlation in patients with bicuspid aortic valve and aneurysm. *J Thorac Cardiovasc Surg* 2013; **146:** 158–165.
1630. Bissell MM, Hess AT, Biasiolli L, Glaze SJ, Loudon M, Pitcher A, et al. Aortic dilation in bicuspid aortic valve disease: Flow pattern is a major contributor and differs with valve fusion type. *Circ Cardiovasc Imaging* 2013; **6:** 499–507.
1631. Guzzardi DG, Barker AJ, van Ooij P, Malaisrie SC, Puthumana JJ, Belke DD, et al. Valve-related hemodynamics mediate human bicuspid aortopathy: Insights from wall shear stress mapping. *J Am Coll Cardiol* 2015; **66:** 892–900.
1632. Rodríguez-Palomares JF, Dux-Santoy L, Guala A, Kale R, Maldonado G, Teixidó-Turà G, et al. Aortic flow patterns and wall shear stress maps by 4D-flow cardiovascular magnetic resonance in the assessment of aortic dilatation in bicuspid aortic valve disease. *J Cardiovasc Magn Reson* 2018; **20:** 28.
1633. Michelena HI, Khanna AD, Mahoney D, Margaryan E, Topilsky Y, Suri RM, et al. Incidence of aortic complications in patients with bicuspid aortic valves. *JAMA* 2011; **306:** 1104–1112.
1634. Etz CD, Zoli S, Brenner R, Roder F, Bischoff M, Bodian CA, et al. When to operate on the bicuspid valve patient with a modestly dilated ascending aorta. *Ann Thorac Surg* 2010; **90:** 1884–1892.
1635. Boodhwani M, Andelfinger G, Leipsic J, Lindsay T, McMurtry MS, Therrien J, et al; Canadian Cardiovascular Society. Canadian Cardiovascular Society position statement on the management of thoracic aortic disease. *Can J Cardiol* 2014; **30:** 577–589.
1636. Carlson M, Airhart N, Lopez L, Silberbach M. Moderate aortic enlargement and bicuspid aortic valve are associated with aortic dissection in Turner syndrome: Report of the international turner syndrome aortic dissection registry. *Circulation* 2012; **126:** 2220–2226.
1637. Hui SK, Fan CS, Christie S, Feindel CM, David TE, Ouzounian M. The aortic root does not dilate over time after replacement of the aortic valve and ascending aorta in patients with bicuspid or tricuspid aortic valves. *J Thorac Cardiovasc Surg* 2018; **156:** 5–13.
1638. Wojnarski CM, Svensson LG, Roselli EE, Idrees JJ, Lowry AM, Ehrlinger J, et al. Aortic dissection in patients with bicuspid aortic valve-associated aneurysms. *Ann Thorac Surg* 2015; **100:** 1666–1674.
1639. Hiratzka LF, Creager MA, Isselbacher EM, Svensson LG, Nishimura RA, Bonow RO, et al. Surgery for aortic dilatation in patients with bicuspid aortic valves: A statement of clarification from the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Thorac Cardiovasc Surg* 2016; **151:** 959–966.
1640. Borger MA, Fedak PWM, Stephens EH, Gleason TG, Girdauskas E, Ikonomidis JS, et al. The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve-related aortopathy: Full online-only version. *J Thorac Cardiovasc Surg* 2018; **156:** e41–e74.
1641. Saric M, Kronzon I. Aortic atherosclerosis and embolic events. *Curr Cardiol Rep* 2012; **14:** 342–349.
1642. Oyama N, Gona P, Salton CJ, Chuang ML, Jhaveri RR, Blease SJ, et al. Differential impact of age, sex, and hypertension on aortic atherosclerosis: The Framingham Heart Study. *Arterioscler Thromb Vasc Biol* 2008; **28:** 155–159.
1643. Amarenco P, Duyckaerts C, Tzourio C, Hénin D, Bousser MG, Hauw JJ. The prevalence of ulcerated plaques in the aortic arch in patients with stroke. *N Engl J Med* 1992; **326:** 221–225.
1644. Amarenco P, Cohen A, Tzourio C, Bertrand B, Hommel M, Besson G, et al. Atherosclerotic disease of the aortic arch and the risk of ischemic stroke. *N Engl J Med* 1994; **331:** 1474–1479.
1645. Davila-Roman VG, Barzilai B, Wareing TH, Murphy SF, Kouchoukos NT. Intraoperative ultrasonographic evaluation of the ascending aorta in 100 consecutive patients undergoing cardiac surgery. *Circulation* 1991; **84 Suppl:** III47–III53.
1646. Dávila-Román VG, Barzilai B, Wareing TH, Murphy SF, Schechtman KB, Kouchoukos NT. Atherosclerosis of the ascending aorta: Prevalence and role as an independent predictor of cerebrovascular events in cardiac patients. *Stroke* 1994; **25:** 2010–2016.
1647. The Stroke Prevention in Atrial Fibrillation Investigators Committee on Echocardiography. Transesophageal echocardiographic correlates of thromboembolism in high-risk patients with nonvalvular atrial fibrillation. *Ann Intern Med* 1998; **128:** 639–647.
1648. French Study of Aortic Plaques in Stroke Group. Atherosclerotic disease of the aortic arch as a risk factor for recurrent ischemic stroke. *N Engl J Med* 1996; **334:** 1216–1221.
1649. Moolenaar W, Lamers CB. Cholesterol crystal embolization in the Netherlands. *Arch Intern Med* 1996; **156:** 653–657.
1650. Rhodes JM. Cholesterol crystal embolism: An important "new" diagnosis for the general physician. *Lancet* 1996; **347:** 1641.
1651. Moolenaar W, Lamers CB. Gastrointestinal blood loss due to cholesterol crystal embolization. *J Clin Gastroenterol* 1995; **21:** 220–223.
1652. Blauth CI, Cosgrove DM, Webb BW, Ratliff NB, Boylan M, Piedmonte MR, et al. Atheroembolism from the ascending aorta: An emerging problem in cardiac surgery. *J Thorac Cardiovasc Surg* 1992; **103:** 1104–1112.
1653. Ramirez G, O'Neill WM, Lambert R, Bloomer HA. Cholesterol embolization: A complication of angiography. *Arch Intern Med* 1978; **138:** 1430–1432.
1654. van der Linden J, Hadjinikolaou L, Bergman P, Lindblom D. Postoperative stroke in cardiac surgery is related to the location and extent of atherosclerotic disease in the ascending aorta. *J Am Coll Cardiol* 2001; **38:** 131–135.
1655. Jolly SS, Amlani S, Hamon M, Yusuf S, Mehta SR. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: A systematic review and meta-analysis of randomized trials. *Am Heart J* 2009; **157:** 132–140.
1656. Eggebrecht H, Schmermund A, Voigtländer T, Kahlert P, Erbel R, Mehta RH. Risk of stroke after transcatheter aortic valve implantation (TAVI): A meta-analysis of 10,037 published patients. *EuroIntervention* 2012; **8:** 129–138.
1657. Lin PH, Bush RL, Conklin BS, Chen C, Weiss VJ, Chaikof EL, et al. Late complication of aortoiliac stent placement- atheroembolization of the lower extremities. *J Surg Res* 2002; **103:** 153–159.
1658. Toogood GJ, Torrie EP, Magee TR, Galland RB. Early experience with stenting for iliac occlusive disease. *Eur J Vasc Endovasc Surg* 1998; **15:** 165–168.

1659. Ballard JL, Bergan JJ, Singh P, Yonemoto H, Killeen JD. Aortoiliac stent deployment versus surgical reconstruction: Analysis of outcome and cost. *J Vasc Surg* 1998; **28:** 94–103.
1660. Sharma PV, Babu SC, Shah PM, Nassoura ZE. Changing patterns of atheroembolism. *Cardiovasc Surg* 1996; **4:** 573–579.
1661. Ferrari E, Vidal R, Chevallier T, Baudouy M. Atherosclerosis of the thoracic aorta and aortic debris as a marker of poor prognosis: Benefit of oral anticoagulants. *J Am Coll Cardiol* 1999; **33:** 1317–1322.
1662. Dressler FA, Craig WR, Castello R, Labovitz AJ. Mobile aortic atheroma and systemic emboli: Efficacy of anticoagulation and influence of plaque morphology on recurrent stroke. *J Am Coll Cardiol* 1998; **31:** 134–138.
1663. Blackshear JL, Zabalgoitia M, Pennock G, Fenster P, Strauss R, Halperin J, et al. *Warfarin* safety and efficacy in patients with thoracic aortic plaque and atrial fibrillation. *Am J Cardiol* 1999; **83:** 453–455.
1664. Tunick PA, Nayar AC, Goodkin GM, Mirchandani S, Francescone S, Rosenzweig BP, et al; NYU Atheroma Group. Effect of treatment on the incidence of stroke and other emboli in 519 patients with severe thoracic aortic plaque. *Am J Cardiol* 2002; **90:** 1320–1325.
1665. Di Tullio MR, Russo C, Jin Z, Sacco RL, Mohr JP, Homma S; Patent Foramen Ovale in Cryptogenic Stroke Study Investigators. Aortic arch plaques and risk of recurrent stroke and death. *Circulation* 2009; **119:** 2376–2382.
1666. Hyman BT, Landas SK, Ashman RF, Schelper RL, Robinson RA. Warfarin-related purple toes syndrome and cholesterol microembolization. *Am J Med* 1987; **82:** 1233–1237.
1667. Hitti WA, Wali RK, Weinman EJ, Weiman EJ, Drachenberg C, Briglia A. Cholesterol embolization syndrome induced by thrombolytic therapy. *Am J Cardiovasc Drugs* 2008; **8:** 27–34.
1668. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomised placebo-controlled trial. *Lancet* 2002; **360:** 7–22.
1669. Pitsavos CE, Aggeli KI, Barbetseas JD, Skoumas IN, Lambrou SG, Frogoudaki AA, et al. Effects of *pravastatin* on thoracic aortic atherosclerosis in patients with heterozygous familial hypercholesterolemia. *Am J Cardiol* 1998; **82:** 1484–1488.
1670. Lima JA, Desai MY, Steen H, Warren WP, Gautam S, Lai S. Statin-induced cholesterol lowering and plaque regression after 6 months of magnetic resonance imaging-monitored therapy. *Circulation* 2004; **110:** 2336–2341.
1671. Tahara N, Kai H, Ishibashi M, Nakaura H, Kaida H, Baba K, et al. Simvastatin attenuates plaque inflammation: Evaluation by fluorodeoxyglucose positron emission tomography. *J Am Coll Cardiol* 2006; **48:** 1825–1831.
1672. Keen RR, McCarthy WJ, Shireman PK, Feinglass J, Pearce WH, Durham JR, et al. Surgical management of atheroembolization. *J Vasc Surg* 1995; **21:** 773–781.
1673. Baumann DS, McGraw D, Rubin BG, Allen BT, Anderson CB, Sicard GA. An institutional experience with arterial atheroembolism. *Ann Vasc Surg* 1994; **8:** 258–265.
1674. Bojar RM, Payne DD, Murphy RE, Schwartz SL, Belden JR, Caplan LR, et al. Surgical treatment of systemic atheroembolism from the thoracic aorta. *Ann Thorac Surg* 1996; **61:** 1389–1393.
1675. Stern A, Tunick PA, Culliford AT, Lachmann J, Baumann FG, Kanchuger MS, et al. Protruding aortic arch atheromas: Risk of stroke during heart surgery with and without aortic arch endarterectomy. *Am Heart J* 1999; **138:** 746–752.
1676. Wolf PS, Burman HE, Starnes BW. Endovascular treatment of massive thoracic aortic thrombus and associated ruptured atheroma. *Ann Vasc Surg* 2010; **24:** 416.e9–416.e12.
1677. Siani A, Accrocca F, De Vivo G, Mounayergi F, Marcucci G. Endovascular treatment of symptomatic thrombus of the descending thoracic aorta. *Ann Vasc Surg* 2016; **36:** 295.e13–295.e16.
1678. Laperche T, Laurian C, Roudaut R, Steg PG; The Filiale Echocardiographie de la Société Française de Cardiologie. Mobile thromboses of the aortic arch without aortic debris: A transesophageal echocardiographic finding associated with unexplained arterial embolism. *Circulation* 1997; **96:** 288–294.
1679. Pagni S, Trivedi J, Ganzel BL, Williams M, Kapoor N, Ross C, et al. Thoracic aortic mobile thrombus: Is there a role for early surgical intervention? *Ann Thorac Surg* 2011; **91:** 1875–1881.
1680. Avegliano G, Evangelista A, Elorz C, González-Alujas T, García del Castillo H, Soler-Soler J. Acute peripheral arterial ischemia and suspected aortic dissection: Usefulness of transesophageal echocardiography in differential diagnosis with aortic thrombosis. *Am J Cardiol* 2002; **90:** 674–677.
1681. Criado E, Wall P, Lucas P, Gasparis A, Proffit T, Ricotta J. Transesophageal echo-guided endovascular exclusion of thoracic aortic mobile thrombi. *J Vasc Surg* 2004; **39:** 238–242.
1682. Gouëffic Y, Chaillou P, Pillet JC, Duveau D, Patra P. Surgical treatment of nonaneurysmal aortic arch lesions in patients with systemic embolization. *J Vasc Surg* 2002; **36:** 1186–1193.
1683. Arima T, Muroya K, Kawamoto K, Koba Y, Omura T. Aortic thrombosis in a patient with malignant disease: A literature review and case presentation. *Vasc Endovascular Surg* 2019; **53:** 139–144.
1684. Apiyasawat S, Wongpraparut N, Jacobson L, Berkowitz H, Jacobs LE, Kotler MN. Cisplatin induced localized aortic thrombus. *Echocardiography* 2003; **20:** 199–200.
1685. Robaldo A, Pagliari S, Colotto P. Acute ascending thrombosis of abdominal and suprarenal aorta. *Case Rep Surg* 2014; **2014:** 348064.
1686. Ding X, Liu Y, Su Q, Hu S, Jiang J. Diagnosis and treatment of aortic saddle embolism. *Ann Vasc Surg* 2019; **56:** 124–131.
1687. Psacharopulo D, Ferrero E, Ferri M, Viazzo A, Singh Bahia S, Trucco A, et al. Increasing efficacy of endovascular recanalization with covered stent graft for TransAtlantic Inter-Society Consensus II D aortoiliac complex occlusion. *J Vasc Surg* 2015; **62:** 1219–1226.
1688. Bastos Gonçalves F, Voûte MT, Hoeks SE, Chonchol MB, Boersma EE, Stolker RJ, et al. Calcification of the abdominal aorta as an independent predictor of cardiovascular events: A meta-analysis. *Heart* 2012; **98:** 988–994.
1689. Sagban AT, Grotemeyer D, Rehbein H, Sandmann W, Duran M, Balzer KM, et al. Occlusive aortic disease as coral reef aorta: Experience in 80 cases. [Article in German] *Zentralbl Chir* 2010; **135:** 438–444.
1690. Grotemeyer D, Pourhassan S, Rehbein H, Voiculescu A, Reinecke P, Sandmann W. The coral reef aorta: A single centre experience in 70 patients. *Int J Angiol* 2007; **16:** 98–105.
1691. Gaggiano A, Kasemi H, Monti A, Laurito A, Maselli M, Manzo P, et al. Extra-anatomic revascularization of extensive coral reef aorta. *Ann Vasc Surg* 2017; **44:** 422.e1–422.e7.
1692. Holfeld J, Gottardi R, Zimpfer D, Dorfmeister M, Dumfarth J, Funovics M, et al. Treatment of symptomatic coral reef aorta by endovascular stent-graft placement. *Ann Thorac Surg* 2008; **85:** 1817–1819.
1693. Anderson JL, Antman EM, Harold JG, Jessup M, O'Gara PT, Pinto FJ, et al. Clinical practice guidelines on perioperative cardiovascular evaluation: Collaborative efforts among the ACC, AHA, and ESC. *Circulation* 2014; **130:** 2213–2214.
1694. Grimme FA, Goverde PC, Verbruggen PJ, Zeebregts CJ, Reijnen MM. Editor's choice--First results of the Covered Endovascular Reconstruction of the Aortic Bifurcation (CERAB) technique for aortoiliac occlusive disease. *Eur J Vasc Endovasc Surg* 2015; **50:** 638–647.
1695. Hollier LH, Kazmier FJ, Ochsner J, Bowen JC, Procter CD. "Shaggy" aorta syndrome with atheromatous embolization to visceral vessels. *Ann Vasc Surg* 1991; **5:** 439–444.
1696. Kazmier FJ. Shaggy aorta syndrome and disseminated atheromatous embolization. *In:* Bergan JJ, Yao JST, editors. Aortic Surgery. W.B. Saunders, 1989; 189–194.
1697. Fukuda I, Daitoku K, Minakawa M, Fukuda W. Shaggy and calcified aorta: Surgical implications. *Gen Thorac Cardiovasc Surg* 2013; **61:** 301–313.
1698. Nemoto M, Hoshina K, Takayama T, Miura S, Nakazawa T, Kato M, et al. Statins reduce extensive aortic atheromas in patients with abdominal aortic aneurysms. *Ann Vasc Dis* 2013; **6:** 711–717.
1699. Corti R, Fuster V, Fayad ZA, Worthley SG, Helft G, Smith D, et al. Lipid lowering by simvastatin induces regression of human atherosclerotic lesions: Two years' follow-up by high-resolution noninvasive magnetic resonance imaging. *Circulation* 2002; **106:** 2884–2887.
1700. Hoshina K, Nemoto M, Hashimoto T, Miura S, Urabe G, Nakazawa T, et al; Study Design of PROCEDURE Study. A randomized comparison of the dose-dependent effects of pitavastatin in patients with abdominal aortic aneurysm with massive aortic atheroma: Prevention of Cholesterol Embolization during Endovascular and Open Aneurysm Repair with Pitavastatin (PROCEDURE) Study. *Ann Vasc Dis* 2013; **6:** 62–66.
1701. Kwon H, Han Y, Noh M, Gwon JG, Cho YP, Kwon TW. Impact of shaggy aorta in patients with abdominal aortic aneurysm following open or endovascular aneurysm repair. *Eur*

J Vasc Endovasc Surg 2016; **52:** 613–619.
1702. Yokawa K, Ikeno Y, Henmi S, Yamanaka K, Okada K, Okita Y. Impact of shaggy aorta on outcomes of open thoracoabdominal aortic aneurysm repair. *J Thorac Cardiovasc Surg* 2020; **160:** 889–897.
1703. Okada K, Omura A, Kano H, Inoue T, Oka T, Minami H, et al. Effect of atherothrombotic aorta on outcomes of total aortic arch replacement. *J Thorac Cardiovasc Surg* 2013; **145:** 984–991.
1704. Maeda K, Ohki T, Kanaoka Y, Shukuzawa K, Baba T, Momose M. A novel shaggy aorta scoring system to predict embolic complications following thoracic endovascular aneurysm repair. *Eur J Vasc Endovasc Surg* 2020; **60:** 57–66.
1705. Shiiya N, Kunihara T, Kamikubo Y, Yasuda K. Isolation technique for stroke prevention in patients with a mobile atheroma. *Ann Thorac Surg* 2001; **72:** 1401–1402.
1706. Wada T, Anai H, Shuto T, Sakaguchi T, Hongo T, Shuto R, et al. A new method for protection from shower embolism during TEVAR on a shaggy aorta. *Gen Thorac Cardiovasc Surg* 2015; **63:** 105–108.
1707. Takano T, Takase S, Kagoshima A, Yokoyama H. Prevention of embolization in concomitant endovascular therapy for thoracic and abdominal aneurysms with severely atheromatous aorta. *Ann Vasc Dis* 2016; **9:** 345–348.
1708. Kulik A, Castner CF, Kouchoukos NT. Outcomes after thoracoabdominal aortic aneurysm repair with hypothermic circulatory arrest. *J Thorac Cardiovasc Surg* 2011; **141:** 953–960.
1709. Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, Gross WL, et al. Nomenclature of systemic vasculitides: Proposal of an international consensus conference. *Arthritis Rheum* 1994; **37:** 187–192.
1710. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013; **65:** 1–11.
1711. Isobe M, Amano K, Arimura Y, Ishizu A, Ito S, Kaname S, et al; JCS Joint Working Group. JCS 2017 Guideline on Management of Vasculitis Syndrome: Digest Version. *Circ J* 2020; **84:** 299–359.
1712. Stone JR, Bruneval P, Angelini A, Bartoloni G, Basso C, Batoroeva L, et al. Consensus statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology: I. Inflammatory diseases. *Cardiovasc Pathol* 2015; **24:** 267–278.
1713. Ishibashi-Ueda H, Ohta-Ogo K, Matsuyama TA, Takayasu, Ikeda Y, Ogino H. Arteritis and aortic valve regurgitation: The histology of aortic valve of Takayasu arteritis at the time of valve replacement. *Virchows Arch* 2013; **463:** 200.
1714. Miller DV, Isotalo PA, Weyand CM, Edwards WD, Aubry MC, Tazelaar HD. Surgical pathology of noninfectious ascending aortitis: A study of 45 cases with emphasis on an isolated variant. *Am J Surg Pathol* 2006; **30:** 1150–1158.
1715. James TGI. Uremia due to aneurysm of the abdominal aorta. *Br J Urol* 1935; **7:** 157.
1716. Research Committee to establish diagnostic criteria and development of treatment for systemic IgG4-related sclerosing disease. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011: Research Program of Intractable Disease provided by the Ministry of Health, Labor, and Welfare of Japan. [in Japanese] *J Jpn Soc Intern Med* 2012; **101:** 795–804.
1717. Maeda H, Handa N, Matsumoto M, Hougaku H, Ogawa S, Oku N, et al. Carotid lesions detected by B-mode ultrasonography in Takayasu's arteritis: "Macaroni sign" as an indicator of the disease. *Ultrasound Med Biol* 1991; **17:** 695–701.
1718. Choe YH, Han BK, Koh EM, Kim DK, Do YS, Lee WR. Takayasu's arteritis: Assessment of disease activity with contrast-enhanced MR imaging. *AJR Am J Roentgenol* 2000; **175:** 505–511.
1719. Soussan M, Nicolas P, Schramm C, Katsahian S, Pop G, Fain O, et al. Management of large-vessel vasculitis with FDG-PET: A systematic literature review and meta-analysis. *Medicine (Baltimore)* 2015; **94:** e622.
1720. Matsunaga N, Hayashi K, Sakamoto I, Ogawa Y, Matsumoto T. Takayasu arteritis: Protean radiologic manifestations and diagnosis. *Radiographics* 1997; **17:** 579–594.
1721. Hayashi H, Katayama N, Takagi R, Ichikawa T, Kumazaki T, Ebata K. CT analysis of vascular wall during the active phase of Takayasu's aortitis. *Eur Radiol* 1991; **1 Suppl:** S239.
1722. Ueno A, Awane Y, Wakabayashi A, Shimizu K. Successfully operated obliterative brachiocephalic arteritis (Takayasu) associated with the elongated coarctation. *Jpn Heart J* 1967; **8:** 538–544.
1723. Qureshi MA, Martin Z, Greenberg RK. Endovascular management of patients with Takayasu arteritis: Stents versus stent grafts. *Semin Vasc Surg* 2011; **24:** 44–52.
1724. Lee GY, Jeon P, Do YS, Sung K, Kim DI, Kim YW, et al. Comparison of outcomes between endovascular treatment and bypass surgery in Takayasu arteritis. *Scand J Rheumatol* 2014; **43:** 153–161.
1725. Baril DT, Carroccio A, Palchik E, Ellozy SH, Jacobs TS, Teodorescu V, et al. Endovascular treatment of complicated aortic aneurysms in patients with underlying arteriopathies. *Ann Vasc Surg* 2006; **20:** 464–471.
1726. Ohigashi H, Haraguchi G, Konishi M, Tezuka D, Kamiishi T, Ishihara T, et al. Improved prognosis of Takayasu arteritis over the past decade--comprehensive analysis of 106 patients. *Circ J* 2012; **76:** 1004–1011.
1727. Nakaoka Y, Isobe M, Takei S, Tanaka Y, Ishii T, Yokota S, et al. Efficacy and safety of tocilizumab in patients with refractory Takayasu arteritis: Results from a randomised, double-blind, placebo-controlled, phase 3 trial in Japan (the TAKT study). *Ann Rheum Dis* 2018; **77:** 348–354.
1728. Mazlumzadeh M, Hunder GG, Easley KA, Calamia KT, Matteson EL, Griffing WL, et al. Treatment of giant cell arteritis using induction therapy with high-dose glucocorticoids: A double-blind, placebo-controlled, randomized prospective clinical trial. *Arthritis Rheum* 2006; **54:** 3310–3318.
1729. Villiger PM, Adler S, Kuchen S, Wermelinger F, Dan D, Fiege V, et al. Tocilizumab for induction and maintenance of remission in giant cell arteritis: A phase 2, randomised, double-blind, placebo-controlled trial. *Lancet* 2016; **387:** 1921–1927.
1730. 日本循環器学会・IgG4 関連疾患研究班合同ワーキンググループ報告. Diagnostic Guidelines for IgG4-related periaortitis/periarteritis and retroperitoneal fibrosis. [in Japanese] Available at: http://www.j-circ.or.jp/topics/IgG4_doc.pdf (accessed July 31, 2020).
1731. Vaglio A, Palmisano A, Alberici F, Maggiore U, Ferretti S, Cobelli R, et al. Prednisone versus tamoxifen in patients with idiopathic retroperitoneal fibrosis: An open-label randomised controlled trial. *Lancet* 2011; **378:** 338–346.
1732. 厚生労働科学研究難治性疾患克服研究事業 ベーチェット病に関する調査研究班. 血管型ベーチェット病診療ガイドライン ステートメント案. [in Japanese] 2014.
1733. Ito I. Medical treatment of Takayasu arteritis. *Heart Vessels Suppl* 1992; **7:** 133–137.
1734. Watanabe Y, Miyata T, Tanemoto K. Current clinical features of new patients with Takayasu arteritis observed from cross-country research in Japan: Age and sex specificity. *Circulation* 2015; **132:** 1701–1709.
1735. Fields CE, Bower TC, Cooper LT, Hoskin T, Noel AA, Panneton JM, et al. Takayasu's arteritis: Operative results and influence of disease activity. *J Vasc Surg* 2006; **43:** 64–71.
1736. Reilly JM, Savage EB, Brophy CM, Tilson MD. Hydrocortisone rapidly induces aortic rupture in a genetically susceptible mouse. *Arch Surg* 1990; **125:** 707–709.
1737. Tajima Y, Goto H, Ohara M, Hashimoto M, Akamatsu D, Shimizu T, et al. Oral steroid use and abdominal aortic aneurysm expansion: Positive Association. *Circ J* 2017; **81:** 1774–1782.
1738. Takagi A, Kajiura N, Tada Y, Ueno A. Surgical treatment of non-specific inflammatory arterial aneurysms. *J Cardiovasc Surg (Torino)* 1986; **27:** 117–124.
1739. Burke A, Tavora FR, Maleszewski JJ, et al. Tumors of the great vessels. *In:* Atlas of Tumor Pathology, 4th Series, Fascicle 22 - Tumors of the heart and great vessels. AFIP, 2015; 391–411.
1740. Alexander JJ, Moawad J, Cai D. Primary intimal sarcoma of the aorta associated with a dacron graft and resulting in arterial rupture. *Vasc Endovascular Surg* 2006; **40:** 509–515.
1741. Nakajima H, Kobayashi J, Matsuda H, Ishibashi-Ueda H. A primary angiosarcoma in the aorta. *Interact Cardiovasc Thorac Surg* 2007; **6:** 832–833.
1742. Sebenik M, Ricci A, DiPasquale B, Mody K, Pytel P, Jee KJ, et al. Undifferentiated intimal sarcoma of large systemic blood vessels: Report of 14 cases with immunohistochemical profile and review of the literature. *Am J Surg Pathol* 2005; **29:** 1184–1193.
1743. Dehqanzada ZA, Menezes G, Mukherjee D. Epithelioid angiosarcoma of the aorta in a 47-year-old man: A case report and literature review. *J Surg Educ* 2007; **64:** 165–170.
1744. Rusthoven CG, Liu AK, Bui MM, Schefter TE, Elias AD, Lu X, et al. Sarcomas of the aorta: A systematic review and pooled analysis of published reports. *Ann Vasc Surg* 2014; **28:** 515–525.
1745. Bendel EC, Maleszewski JJ, Araoz PA. Imaging sarcomas of

the great vessels and heart. *Semin Ultrasound CT MR* 2011; **32:** 377–404.
1746. Restrepo CS, Betancourt SL, Martinez-Jimenez S, Gutierrez FR. Aortic tumors. *Semin Ultrasound CT MR* 2012; **33:** 265–272.
1747. Ugurlucan M, Barburoglu M, Sayin OA, Beyaz MO, Ekiz F, Acunas B, et al. Endovascular treatment for primary aortic angiosarcoma to relieve thoracic aortic stenosis. *Ann Vasc Surg* 2014; **28:** 1799.e5–1799.e8.
1748. Richens D, Kotidis K, Neale M, Oakley C, Fails A. Rupture of the aorta following road traffic accidents in the United Kingdom 1992–1999: The results of the co-operative crash injury study. *Eur J Cardiothorac Surg* 2003; **23:** 143–148.
1749. Azizzadeh A, Keyhani K, Miller CC, Coogan SM, Safi HJ, Estrera AL. Blunt traumatic aortic injury: Initial experience with endovascular repair. *J Vasc Surg* 2009; **49:** 1403–1408.
1750. Canaud L, Alric P, Branchereau P, Joyeux F, Hireche K, Berthet JP, et al. Open versus endovascular repair for patients with acute traumatic rupture of the thoracic aorta. *J Thorac Cardiovasc Surg* 2011; **142:** 1032–1037.
1751. Rabin J, DuBose J, Sliker CW, O'Connor JV, Scalea TM, Griffith BP. Parameters for successful nonoperative management of traumatic aortic injury. *J Thorac Cardiovasc Surg* 2014; **147:** 143–149.
1752. Katz NM, Blackstone EH, Kirklin JW, Karp RB. Incremental risk factors for spinal cord injury following operation for acute traumatic aortic transection. *J Thorac Cardiovasc Surg* 1981; **81:** 669–674.
1753. Pate JW, Fabian TC, Walker WA. Acute traumatic rupture of the aortic isthmus: Repair with cardiopulmonary bypass. *Ann Thorac Surg* 1995; **59:** 90–99.
1754. Demetriades D, Velmahos GC, Scalea TM, Jurkovich GJ, Karmy-Jones R, Teixeira PG, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: Results of an American Association for the Surgery of Trauma Multicenter Study. *J Trauma* 2008; **64:** 561–571.
1755. Lettinga-van de Poll T, Schurink GW, De Haan MW, Verbruggen JP, Jacobs MJ. Endovascular treatment of traumatic rupture of the thoracic aorta. *Br J Surg* 2007; **94:** 525–533.
1756. Neschis DG, Moaine S, Gutta R, Charles K, Scalea TM, Flinn WR, et al. Twenty consecutive cases of endograft repair of traumatic aortic disruption: Lessons learned. *J Vasc Surg* 2007; **45:** 487–492.
1757. Marcheix B, Dambrin C, Bolduc JP, Arnaud C, Hollington L, Cron C, et al. Endovascular repair of traumatic rupture of the aortic isthmus: Midterm results. *J Thorac Cardiovasc Surg* 2006; **132:** 1037–1041.
1758. Kato N, Dake MD, Miller DC, Semba CP, Mitchell RS, Razavi MK, et al. Traumatic thoracic aortic aneurysm: Treatment with endovascular stent-grafts. *Radiology* 1997; **205:** 657–662.
1759. Harris DG, Rabin J, Starnes BW, Khoynezhad A, Conway RG, Taylor BS, et al. Evolution of lesion-specific management of blunt thoracic aortic injury. *J Vasc Surg* 2016; **64:** 500–505.
1760. Lee WA, Matsumura JS, Mitchell RS, Farber MA, Greenberg RK, Azizzadeh A, et al. Endovascular repair of traumatic thoracic aortic injury: Clinical practice guidelines of the Society for Vascular Surgery. *J Vasc Surg* 2011; **53:** 187–192.
1761. Starnes BW, Lundgren RS, Gunn M, Quade S, Hatsukami TS, Tran NT, et al. A new classification scheme for treating blunt aortic injury. *J Vasc Surg* 2012; **55:** 47–54.
1762. Lamarche Y, Berger FH, Nicolaou S, Bilawich AM, Louis L, Inacio JR, et al. Vancouver simplified grading system with computed tomographic angiography for blunt aortic injury. *J Thorac Cardiovasc Surg* 2012; **144:** 347–354.
1763. Caffarelli AD, Mallidi HR, Maggio PM, Spain DA, Miller DC, Mitchell RS. Early outcomes of deliberate nonoperative management for blunt thoracic aortic injury in trauma. *J Thorac Cardiovasc Surg* 2010; **140:** 598–605.
1764. Kommerell B. Verlagerung des Ösophagus durch eine abnorm verlaufende arteria subclavia dextra (arteria lusoria). *Fortschr Geb Roentgenstrahlen* 1936; **54:** 590–595.
1765. Molz G, Burri B. Aberrant subclavian artery (arteria lusoria): Sex differences in the prevalence of various forms of the malformation: Evaluation of 1378 observations. *Virchows Arch A Pathol Anat Histol* 1978; **380:** 303–315.
1766. Idrees J, Keshavamurthy S, Subramanian S, Clair DG, Svensson LG, Roselli EE. Hybrid repair of kommerell diverticulum. *J Thorac Cardiovasc Surg* 2014; **147:** 973–976.
1767. Backer CL, Mavroudis C, Rigsby CK, Holinger LD. Trends in vascular ring surgery. *J Thorac Cardiovasc Surg* 2005; **129:** 1339–1347.
1768. Ikeno Y, Koda Y, Yokawa K, Gotake Y, Henmi S, Nakai H, et al. Graft replacement of kommerell diverticulum and in situ aberrant subclavian artery reconstruction. *Ann Thorac Surg* 2019; **107:** 770–779.
1769. Campbell M. Natural history of coarctation of the aorta. *Br Heart J* 1970; **32:** 633–640.
1770. Heinemann MK, Ziemer G, Wahlers T, Köhler A, Borst HG. Extraanatomic thoracic aortic bypass grafts: Indications, techniques, and results. *Eur J Cardiothorac Surg* 1997; **11:** 169–175.
1771. Erben Y, Oderich GS, Verhagen HJM, Witsenburg M, van den Hoven AT, Debus ES, et al. Multicenter experience with endovascular treatment of aortic coarctation in adults. *J Vasc Surg* 2019; **69:** 671–679.
1772. Souders CR, Pearson CM, Adams HD. An aortic deformity simulating mediastinal tumor: A subclinical form of coarctation. *Dis Chest* 1951; **20:** 35–45.
1773. Gay WA, Young WG. Pseudocoarctation of the aorta: A reappraisal. *J Thorac Cardiovasc Surg* 1969; **58:** 739–745.
1774. Mullins CE, Gillette PC, McNamara DG. The complex of cervical aortic arch. *Pediatrics* 1973; **51:** 210–215.
1775. Haughton VM, Fellows KE, Rosenbaum AE. The cervical aortic arches. *Radiology* 1975; **114:** 675–681.
1776. Gomibuchi T, Seto T, Yamamoto T, Nakahara K, Ohashi N, Ohtsu Y, et al. Surgical repair of cervical aortic arch with brain circulation anomaly through clamshell incision. *Ann Thorac Surg* 2017; **104:** e235–e237.
1777. Zientara A, Schwegler I, Attigah N, Genoni M, Dzemali O. Anomaly of Haughton type D left cervical aortic arch in combination with type B dissection: Case report and literature review. *J Cardiothorac Surg* 2018; **13:** 79.
1778. Czerny M, Eggebrecht H, Sodeck G, Weigang E, Livi U, Verzini F, et al. New insights regarding the incidence, presentation and treatment options of aorto-oesophageal fistulation after thoracic endovascular aortic repair: The European registry of endovascular aortic repair complications. *Eur J Cardiothorac Surg* 2014; **45:** 452–457.
1779. Kubota S, Shiiya N, Shingu Y, Wakasa S, Ooka T, Tachibana T, et al. Surgical strategy for aortoesophageal fistula in the endovascular era. *Gen Thorac Cardiovasc Surg* 2013; **61:** 560–564.
1780. Hollander JE, Quick G. Aortoesophageal fistula: A comprehensive review of the literature. *Am J Med* 1991; **91:** 279–287.
1781. Canaud L, Alric P, Gandet T, Ozdemir BA, Albat B, Marty-Ane C. Open surgical secondary procedures after thoracic endovascular aortic repair. *Eur J Vasc Endovasc Surg* 2013; **46:** 667–674.
1782. Luehr M, Etz CD, Nozdrzykowski M, Garbade J, Lehmkuhl L, Schmidt A, et al. Emergency open surgery for aorto-oesophageal and aorto-bronchial fistulae after thoracic endovascular aortic repair: A single-centre experience. *Eur J Cardiothorac Surg* 2015; **47:** 374–383.
1783. Kan CD, Lee HL, Yang YJ. Outcome after endovascular stent graft treatment for mycotic aortic aneurysm: A systematic review. *J Vasc Surg* 2007; **46:** 906–912.
1784. Dubrueil JM. Observation sur la perforation de l'oesophage et de l'aorte thoracique par une potion d'os avale: Avec des reflexions. *J Univ Sci Med* 1818; **9:** 357–365.
1785. Chiari H. Under fremdkoreverletzung des oesophagus mit aortenperforation. *Ber Klin Wochenschr* 1914; **51:** 7–9.
1786. Ctercteko G, Mok CK. Aorta-esophageal fistula induced by a foreign body: The first recorded survival. *J Thorac Cardiovasc Surg* 1980; **80:** 233–235.
1787. Snyder DM, Crawford ES. Successful treatment of primary aorta-esophageal fistula resulting from aortic aneurysm. *J Thorac Cardiovasc Surg* 1983; **85:** 457–463.
1788. Xi EP, Zhu J, Zhu SB, Zhang Y. Secondary aortoesophageal fistula after thoracic aortic aneurysm endovascular repair: Literature review and new insights regarding the hypothesized mechanisms. *Int J Clin Exp Med* 2014; **7:** 3244–3252.
1789. Marcelo FB. Aorto-esophageal fistula: An unusual cause of massive hematemesis and melena. *Acta Med Philipp* 1965; **2:** 27–34.
1790. Kahlberg A, Grandi A, Loschi D, Vermassen F, Moreels N, Chakfé N, et al. A systematic review of infected descending thoracic aortic grafts and endografts. *J Vasc Surg* 2019; **69:** 1941–1951.
1791. Yamanaka K, Nonaka M, Iwakura A, Asao Y. Repair of aortoesophageal fistula after total aortic arch grafting. *Interact Cardiovasc Thorac Surg* 2011; **12:** 655–656.
1792. Valtonen EJ, Koivuniemi A. Aortoesophageal fistula complicating

carcinoma of the esophagus: Report of observations in two cases. *J Thorac Cardiovasc Surg* 1967; **53:** 448–452.
1793. Yonago RH, Iben AB, Mark JB. Aortic bypass in the management of aortoesophageal fistula. *Ann Thorac Surg* 1969; **7:** 235–237.
1794. Vogt PR, von Segesser LK, Goffin Y, Pasic M, Turina MI. Cryopreserved arterial homografts for in situ reconstruction of mycotic aneurysms and prosthetic graft infection. *Eur J Cardiothorac Surg* 1995; **9:** 502–506.
1795. Saito A, Motomura N, Hattori O, Kinoshita O, Shimada S, Saiki Y, et al. Outcome of surgical repair of aorto-eosophageal fistulas with cryopreserved aortic allografts. *Interact Cardiovasc Thorac Surg* 2012; **14:** 532–537.
1796. Perlroth J, Kuo M, Tan J, Bayer AS, Miller LG. Adjunctive use of rifampin for the treatment of *Staphylococcus aureus* infections: A systematic review of the literature. *Arch Intern Med* 2008; **168:** 805–819.
1797. Inoue T, Nishino T, Peng YF, Saga T. Successful one-stage operation of aortoesophageal fistula from thoracic aneurysm using a rifampicin-soaked synthetic graft. *Interact Cardiovasc Thorac Surg* 2008; **7:** 322–324.
1798. Hardman S, Cope A, Swann A, Bell PR, Naylor AR, Hayes PD. An in vitro model to compare the antimicrobial activity of silver-coated versus rifampicin-soaked vascular grafts. *Ann Vasc Surg* 2004; **18:** 308–313.
1799. Girardet A. Doppelte perforation eines tuberkelknotens in die aorta und di bifurcation der traqchea. *Dtsch Med Wochenschr* 1914; **40:** 1425–1428.
1800. von Segesser LK, Tkebuchava T, Niederhäuser U, Künzli A, Lachat M, Genoni M, et al. Aortobronchial and aortoesophageal fistulae as risk factors in surgery of descending thoracic aortic aneurysms. *Eur J Cardiothorac Surg* 1997; **12:** 195–201.
1801. Ishikawa N, Maruta K, Oi M, Iizuka H, Kawaura H, Omoto T. Thoracic endovascular repair for aorto-esophageal fistula in patients with esophageal carcinoma: Report of 3 cases. *Vasc Endovascular Surg* 2013; **47:** 65–69.
1802. Liang H, Chen C, Liu W, Yu F. Definitive treatment for aortoesophageal fistula by endovascular stent graft. *Indian J Surg* 2016; **78:** 151–154.
1803. Okita Y, Yamanaka K, Okada K, Matsumori M, Inoue T, Fukase K, et al. Strategies for the treatment of aorto-oesophageal fistula. *Eur J Cardiothorac Surg* 2014; **46:** 894–900.
1804. Yamatsuji T, Naomoto Y, Shirakawa Y, Gunduz M, Hiraki T, Yasui K, et al. Intra-aortic stent graft in oesophageal carcinoma invading the aorta: Prophylaxis for fatal haemorrhage. *Int J Clin Pract* 2006; **60:** 1600–1603.
1805. Matono S, Fujita H, Tanaka T, Nagano T, Nishimura K, Murata K, et al. Thoracic endovascular aortic repair for aortic complications after esophagectomy for cancer: Report of three cases. *Dis Esophagus* 2011; **24:** E36–E40.
1806. Sasaki A, Egashira H, Tokoro S, Ichita C, Takizawa S, Tsukiyama T, et al. Thoracic endovascular aortic repair of esophageal cancer-associated aortoesophageal fistula: A case report and literature review. *Case Rep Oncol Med* 2018; **2018:** 9851397.
1807. Ferrero E, Viazzo A, Ferri M, Rocca R, Pecchio A, Piazza S, et al. Acute management of aortoesophageal fistula and tracheo-esophageal fistula treated by thoracic endovascular aortic repair and esophageal endoprosthesis: A case misdiagnosed as esophageal cancer. *Ann Vasc Surg* 2011; **25:** 1142.e1–1142.e5.
1808. Sato S, Nakamura A, Shimizu Y, Goto T, Kitahara A, Koike T, et al. Early and mid-term outcomes of simultaneous thoracic endovascular stent grafting and combined resection of thoracic malignancies and the aortic wall. *Gen Thorac Cardiovasc Surg* 2019; **67:** 227–233.
1809. Ito K, Oguri T, Nakano A, Fukumitsu K, Fukuda S, Kanemitsu Y, et al. Aortoesophageal fistula occurring during lung cancer treatment: A case treated by thoracic endovascular aortic repair. *Intern Med* 2019; **58:** 3025–3028.
1810. Islam S, Williams DM, Teitelbaum DH. Aortobronchial fistula from invasive *Aspergillus* infection of the lung: An endovascular approach to repair. *J Pediatr Surg* 2005; **40:** e19–e22.
1811. Alric P, Berthet JP, Branchereau P, Veerapen R, Marty-Ané CH. Endovascular repair for acute rupture of the descending thoracic aorta. *J Endovasc Ther* 2002; **9 Suppl:** II51–II59.
1812. Yoo JH, Lee CT, Shim YS, Chung JW, Ahn H, Kim KW. Aortobronchial fistula presenting as recurrent hemoptysis and successfully treated with an endovascular stent graft. *Respiration* 2001; **68:** 537–539.
1813. Picichè M, De Paulis R, Fabbri A, Chiariello L. Postoperative aortic fistulas into the airways: Etiology, pathogenesis, presentation, diagnosis, and management. *Ann Thorac Surg* 2003; **75:** 1998–2006.
1814. MacIntosh EL, Parrott JC, Unruh HW. Fistulas between the aorta and tracheobronchial tree. *Ann Thorac Surg* 1991; **51:** 515–519.
1815. Jonker FH, Heijmen R, Trimarchi S, Verhagen HJ, Moll FL, Muhs BE. Acute management of aortobronchial and aorto-esophageal fistulas using thoracic endovascular aortic repair. *J Vasc Surg* 2009; **50:** 999–1004.
1816. Dorweiler B, Weigang E, Duenschede F, Pitton MB, Dueber C, Vahl CF. Strategies for endovascular aortic repair in aorto-bronchial and aortoesophageal fistulas. *Thorac Cardiovasc Surg* 2013; **61:** 575–580.
1817. Chiesa R, Melissano G, Marone EM, Kahlberg A, Marrocco-Trischitta MM, Tshomba Y. Endovascular treatment of aorto-esophageal and aortobronchial fistulae. *J Vasc Surg* 2010; **51:** 1195–1202.
1818. 西上和宏, 荻野均, 井上寛治, 他. 急性期における解離性大動脈瘤の具体的な医療手順に関する調査研究. 平成14年度総括研究報告書：効果的医療技術の確立推進臨床研究事業. 2003.
1819. Nishigami K, Honda T, Shono H, Ohdo T, Horibata Y. Usefulness and safety of the early rehabilitation program for patients with acute aortic dissection. [in Japanese] *J Cardiol* 1999; **34:** 19–24.
1820. Ad Hoc Committee for Early Rehabilitation, The Japanese Society of Intensive Care Medicine. Evidence based expert consensus for early rehabilitation in the intensive care unit. [in Japanese] *J Jpn Soc Intensive Care Med* 2017; **24:** 255–303.
1821. Adler J, Malone D. Early mobilization in the intensive care unit: A systematic review. *Cardiopulm Phys Ther J* 2012; **23:** 5–13.
1822. Crawford ES. The diagnosis and management of aortic dissection. *JAMA* 1990; **264:** 2537–2541.
1823. Chaddha A, Eagle KA, Braverman AC, Kline-Rogers E, Hirsch AT, Brook R, et al. Exercise and physical activity for the post-aortic dissection patient: The clinician's conundrum. *Clin Cardiol* 2015; **38:** 647–651.
1824. Spanos K, Tsilimparis N, Kölbel T. Exercise after Aortic Dissection: To run or not to run. *Eur J Vasc Endovasc Surg* 2018; **55:** 755–756.
1825. Fuglsang S, Heiberg J, Hjortdal VE, Laustsen S. Exercise-based cardiac rehabilitation in surgically treated type-A aortic dissection patients. *Scand Cardiovasc J* 2017; **51:** 99–105.
1826. Myers JN, White JJ, Narasimhan B, Dalman RL. Effects of exercise training in patients with abdominal aortic aneurysm: Preliminary results from a randomized trial. *J Cardiopulm Rehabil Prev* 2010; **30:** 374–383.
1827. Pouwels S, Willigendael EM, van Sambeek MR, Nienhuijs SW, Cuypers PW, Teijink JA. Beneficial effects of pre-operative exercise therapy in patients with an abdominal aortic aneurysm: A systematic review. *Eur J Vasc Endovasc Surg* 2015; **49:** 66–76.
1828. Kato M, Kubo A, Green FN, Takagi H. Meta-analysis of randomized controlled trials on safety and efficacy of exercise training in patients with abdominal aortic aneurysm. *J Vasc Surg* 2019; **69:** 933–943.
1829. Barakat HM, Shahin Y, Khan JA, McCollum PT, Chetter IC. Preoperative supervised exercise improves outcomes after elective abdominal aortic aneurysm repair: A randomized controlled trial. *Ann Surg* 2016; **264:** 47–53.
1830. Bekker A, Lee C, de Santi S, Pirraglia E, Zaslavsky A, Farber S, et al. Does mild cognitive impairment increase the risk of developing postoperative cognitive dysfunction? *Am J Surg* 2010; **199:** 782–788.
1831. Wu CY, Su TW, Huang KY, Ko PJ, Yu SY, Kao TC, et al. Pleural Empyema and Aortic Aneurysm: A Retrospective National Population-Based Cohort Study. *Medicine (Baltimore)* 2015; **94:** e2142.
1832. Tajiri M, Kawayama T, Nakamura S, Matsuyama M, Nishimura S, Kato M, et al. Chronic obstructive pulmonary disease as a risk factor of post-operative lung complications in the patients with unruptured aortic aneurysm. [in Japanese] *J Jp Soc Resp Care Rehab* 2013; **23:** 293–299.
1833. Hayashi K, Hirashiki A, Kodama A, Kobayashi K, Yasukawa Y, Shimizu M, et al. Impact of preoperative regular physical activity on postoperative course after open abdominal aortic aneurysm surgery. *Heart Vessels* 2016; **31:** 578–583.
1834. Lima RM, Vainshelboim B, Ganatra R, Dalman R, Chan K, Myers J. Exercise training improves ventilatory efficiency in patients with a small abdominal aortic aneurysm: A RANDOMIZED CONTROLLED STUDY. *J Cardiopulm Rehabil Prev* 2018; **38:** 239–245.

1835. Kendall F, Oliveira J, Peleteiro B, Pinho P, Bastos PT. Inspiratory muscle training is effective to reduce postoperative pulmonary complications and length of hospital stay: A systematic review and meta-analysis. *Disabil Rehabil* 2018; **40:** 864–882.
1836. Katsura M, Kuriyama A, Takeshima T, Fukuhara S, Furukawa TA. Preoperative inspiratory muscle training for postoperative pulmonary complications in adults undergoing cardiac and major abdominal surgery. *Cochrane Database Syst Rev* 2015: CD010356.
1837. Mans CM, Reeve JC, Elkins MR. Postoperative outcomes following preoperative inspiratory muscle training in patients undergoing cardiothoracic or upper abdominal surgery: A systematic review and meta analysis. *Clin Rehabil* 2015; **29:** 426–438.
1838. Vagvolgyi A, Rozgonyi Z, Kerti M, Agathou G, Vadasz P, Varga J. Effectiveness of pulmonary rehabilitation and correlations in between functional parameters, extent of thoracic surgery and severity of post-operative complications: Randomized clinical trial. *J Thorac Dis* 2018; **10:** 3519–3531.
1839. Boden I, Skinner EH, Browning L, Reeve J, Anderson L, Hill C, et al. Preoperative physiotherapy for the prevention of respiratory complications after upper abdominal surgery: Pragmatic, double blinded, multicentre randomised controlled trial. *BMJ* 2018; **360:** j5916.
1840. Gomes Neto M, Martinez BP, Reis HF, Carvalho VO. Pre- and postoperative inspiratory muscle training in patients undergoing cardiac surgery: Systematic review and meta-analysis. *Clin Rehabil* 2017; **31:** 454–464.
1841. do Nascimento Junior P, Módolo NS, Andrade S, Guimarães MM, Braz LG, El Dib R. Incentive spirometry for prevention of postoperative pulmonary complications in upper abdominal surgery. *Cochrane Database Syst Rev* 2014: CD006058.
1842. Vagvolgyi A, Rozgonyi Z, Kerti M, Vadasz P, Varga J. Effectiveness of perioperative pulmonary rehabilitation in thoracic surgery. *J Thorac Dis* 2017; **9:** 1584–1591.
1843. Myers J, Powell A, Smith K, Fonda H, Dalman RL; Stanford AAA SCCOR Investigators. Cardiopulmonary exercise testing in small abdominal aortic aneurysm: Profile, safety, and mortality estimates. *Eur J Cardiovasc Prev Rehabil* 2011; **18:** 459–466.
1844. Barakat HM, Shahin Y, Barnes R, Gohil R, Souroullas P, Khan J, et al. Supervised exercise program improves aerobic fitness in patients awaiting abdominal aortic aneurysm repair. *Ann Vasc Surg* 2014; **28:** 74–79.
1845. Nakayama A, Morita H, Nagayama M, Hoshina K, Uemura Y, Tomoike H, et al. Cardiac rehabilitation protects against the expansion of abdominal aortic aneurysm. *J Am Heart Assoc* 2018; **7:** e004246.
1846. Fick DM, Agostini JV, Inouye SK. Delirium superimposed on dementia: A systematic review. *J Am Geriatr Soc* 2002; **50:** 1723–1732.
1847. Aykut K, Albayrak G, Guzeloglu M, Baysak A, Hazan E. Preoperative mild cognitive dysfunction predicts pulmonary complications after coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth* 2013; **27:** 1267–1270.
1848. Harrington MB, Kraft M, Grande LJ, Rudolph JL. Independent association between preoperative cognitive status and discharge location after cardiac surgery. *Am J Crit Care* 2011; **20:** 129–137.
1849. Watanabe S, Izawa K, Kobayashi T, Kobayashi T, Yokoyama H, Kondo M, et al. The inhibiting factors of physical therapy in aortic dissection repair. [in Japanese] *Physical Therapy Japan* 2005; **32:** 72–76.
1850. Adachi Y, Kamisaka K, Tahara M, Oura K, Shibukawa T, Hanafusa Y, et al. Difference in in-hospital postoperative rehabilitation outcome in patients with thoracic and thoracoabdominal aortic aneurysms. [in Japanese] *Physical Therapy Japan* 2015; **42:** 503–510.
1851. Brustia P, Renghi A, Aronici M, Gramaglia L, Porta C, Musiani A, et al. Fast-track in abdominal aortic surgery: Experience in over 1,000 patients. *Ann Vasc Surg* 2015; **29:** 1151–1159.
1852. Feo CV, Portinari M, Tsolaki E, Romagnoni G, Verri M, Camerani S, et al. The effect of an Enhanced Recovery Program in elective retroperitoneal abdominal aortic aneurysm repair. *J Vasc Surg* 2016; **63:** 888–894.
1853. Tatsuishi W, Kohri T, Kodera K, Asano R, Kataoka G, Kubota S, et al. Usefulness of an enhanced recovery after surgery protocol for perioperative management following open repair of an abdominal aortic aneurysm. *Surg Today* 2012; **42:** 1195–1200.
1854. Pasin L, Nardelli P, Landoni G, Beretta L, Piras D, Baccellieri D, et al. Enhanced recovery after surgery program in elective infrarenal abdominal aortic aneurysm repair. *J Cardiovasc Surg (Torino)* 2019; **60:** 369–374.
1855. Corone S, Iliou MC, Pierre B, Feige JM, Odjinkem D, Farrokhi T, et al; Cardiac Rehabilitation working Group of the French Society of Cardiology. French registry of cases of type I acute aortic dissection admitted to a cardiac rehabilitation center after surgery. *Eur J Cardiovasc Prev Rehabil* 2009; **16:** 91–95.
1856. Wakabayashi H, Takahashi R, Murakami T. The prevalence and prognosis of sarcopenic dysphagia in patients who require dysphagia rehabilitation. *J Nutr Health Aging* 2019; **23:** 84–88.
1857. Wakabayashi H, Takahashi R, Watanabe N, Oritsu H, Shimizu Y. Prevalence of skeletal muscle mass loss and its association with swallowing function after cardiovascular surgery. *Nutrition* 2017; **38:** 70–73.
1858. Bowles BJ, Puntil-Sheltman J. Is dysphagia after cardiac operations a "preexisting condition"? *Ann Thorac Surg* 2016; **101:** 1450–1453.
1859. Kagaya H, Okada S, Shigeta R, Ogata N, Ota K, Shibata S, et al. Dysphagia associated with unilateral vocal cord immobility after cardiovascular surgery. *Am J Phys Med Rehabil* 2011; **90:** 901–907.
1860. Japanese Physical Therapy Association. Japanese guidelines for the physical therapy (2011). [in Japanese] Available at: http://jspt.japanpt.or.jp/guideline/1st/ (accessed July 31, 2020).
1861. 尾本正, 石川昇, 福隅正臣, 他. Rehabilitation program after operation for a thoracic aorta aneurysm [in Japanese]. 呼吸と循環 2008; **56:** 1173–1176.
1862. Howard DP, Banerjee A, Fairhead JF, Perkins J, Silver LE, Rothwell PM. Population-based study of incidence and outcome of acute aortic dissection and premorbid risk factor control: 10-year results from the Oxford Vascular Study. *Circulation* 2013; **127:** 2031–2037.
1863. Davies RR, Gallo A, Coady MA, Tellides G, Botta DM, Burke B, et al. Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. *Ann Thorac Surg* 2006; **81:** 169–177.
1864. Elefteriades JA, Farkas EA. Thoracic aortic aneurysm clinically pertinent controversies and uncertainties. *J Am Coll Cardiol* 2010; **55:** 841–857.
1865. Pape LA, Tsai TT, Isselbacher EM, Oh JK, O'gara PT, Evangelista A, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. Aortic diameter ≥5.5 cm is not a good predictor of type A aortic dissection: Observations from the International Registry of Acute Aortic Dissection (IRAD). *Circulation* 2007; **116:** 1120–1127.
1866. Parish LM, Gorman JH, Kahn S, Plappert T, St John-Sutton MG, Bavaria JE, et al. Aortic size in acute type A dissection: Implications for preventive ascending aortic replacement. *Eur J Cardiothorac Surg* 2009; **35:** 941–946.
1867. de Virgilio C, Nelson RJ, Milliken J, Snyder R, Chiang F, MacDonald WD, et al. Ascending aortic dissection in weight lifters with cystic medial degeneration. *Ann Thorac Surg* 1990; **49:** 638–642.
1868. Elefteriades JA, Hatzaras I, Tranquilli MA, Elefteriades AJ, Stout R, Shaw RK, et al. Weight lifting and rupture of silent aortic aneurysms. *JAMA* 2003; **290:** 2803.
1869. Elefteriades JA. Beating a sudden killer. *Sci Am* 2005; **293:** 64–71.
1870. Hatzaras I, Tranquilli M, Coady M, Barrett PM, Bible J, Elefteriades JA. Weight lifting and aortic dissection: More evidence for a connection. *Cardiology* 2007; **107:** 103–106.
1871. Toresdahl BG, Asif IM, Rodeo SA, Ling DI, Chang CJ. Cardiovascular screening of Olympic athletes reported by chief medical officers of the Rio 2016 Olympic Games. *Br J Sports Med* 2018; **52:** 1097–1100.
1872. Hatzaras IS, Bible JE, Koullias GJ, Tranquilli M, Singh M, Elefteriades JA. Role of exertion or emotion as inciting events for acute aortic dissection. *Am J Cardiol* 2007; **100:** 1470–1472.
1873. Landenhed M, Engström G, Gottsäter A, Caulfield MP, Hedblad B, Newton-Cheh C, et al. Risk profiles for aortic dissection and ruptured or surgically treated aneurysms: A prospective cohort study. *J Am Heart Assoc* 2015; **4:** e001513.
1874. Seguchi M, Wada H, Sakakura K, Nakagawa T, Ibe T, Ikeda N, et al. Circadian variation of acute aortic dissection. *Int Heart J* 2015; **56:** 324–328.
1875. Manfredini R, Fabbian F, Manfredini F, Salmi R, Gallerani M, Bossone E. Chronobiology in aortic diseases: "Is this really a random phenomenon?". *Prog Cardiovasc Dis* 2013; **56:** 116–124.
1876. John TG, Stonebridge PA. Seasonal variation in operations for

ruptured abdominal aortic aneurysm and acute lower limb ischaemia. *J R Coll Surg Edinb* 1993; **38:** 161–162.
1877. Benouaich V, Soler P, Gourraud PA, Lopez S, Rousseau H, Marcheix B. Impact of meteorological conditions on the occurrence of acute type A aortic dissections. *Interact Cardiovasc Thorac Surg* 2010; **10:** 403–406.
1878. Upshur RE, Mamdani MM, Knight K. Are there seasonal patterns to ruptured aortic aneurysms and dissections of the aorta? *Eur J Vasc Endovasc Surg* 2000; **20:** 173–176.
1879. Mehta RH, Manfredini R, Bossone E, Fattori R, Evagelista A, Boari B, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. The winter peak in the occurrence of acute aortic dissection is independent of climate. *Chronobiol Int* 2005; **22:** 723–729.
1880. Rabus MB, Eren E, Erkanli K, Alp M, Yakut C. Does acute aortic dissection display seasonal variation? *Heart Surg Forum* 2009; **12:** E238–E240.
1881. Li Y, Ji C, Zhang J, Han Y. The effect of ambient temperature on the onset of acute Stanford type B aortic dissection. *Vasa* 2016; **45:** 395–401.
1882. Lasica RM, Perunicic J, Mrdovic I, Tesic BV, Stojanovic R, Milic N, et al. Temporal variations at the onset of spontaneous acute aortic dissection. *Int Heart J* 2006; **47:** 585–595.
1883. Kumar N, Pandey A, Venkatraman A, Garg N. Seasonality in acute aortic dissection related hospitalizations and mortality in the United States: A nationwide analysis from 2004–2011. *Int J Cardiol* 2015; **179:** 321–322.
1884. Ishikawa K, Niwa M, Tanaka T. Difference of intensity and disparity in impact of climate on several vascular diseases. *Heart Vessels* 2012; **27:** 1–9.
1885. Majd P, Madershahian N, Sabashnikov A, Weber C, Ahmad W, Weymann A, et al. Impact of meteorological conditions on the incidence of acute aortic dissection. *Ther Adv Cardiovasc Dis* 2018; **12:** 321–326.
1886. Repanos C, Chadha NK. Is there a relationship between weather conditions and aortic dissection? *BMC Surg* 2005; **5:** 21.
1887. Manfredini R, Boari B, Salmi R, Gallerani M, Manfredini F, Gasbarro V, et al. Day-of-week variability in the occurrence and outcome of aortic diseases: Does it exist? *Am J Emerg Med* 2008; **26:** 363–366.
1888. Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001; **345:** 663–668.
1889. Gallerani M, Imberti D, Bossone E, Eagle KA, Manfredini R. Higher mortality in patients hospitalized for acute aortic rupture or dissection during weekends. *J Vasc Surg* 2012; **55:** 1247–1254.
1890. Manfredini R, Portaluppi F, Zamboni P, Salmi R, Gallerani M. Circadian variation in spontaneous rupture of abdominal aorta. *Lancet* 1999; **353:** 643–644.
1891. Gallerani M, Portaluppi F, Grandi E, Manfredini R. Circadian rhythmicity in the occurrence of spontaneous acute dissection and rupture of thoracic aorta. *J Thorac Cardiovasc Surg* 1997; **113:** 603–604.
1892. Killeen S, Neary P, O'Sullivan M, Redmond HP, Fulton G. Daily diurnal variation in admissions for ruptured abdominal aortic aneurysms. *World J Surg* 2007; **31:** 1869–1871.
1893. Muller JE, Stone PH, Turi ZG, Rutherford JD, Czeisler CA, Parker C, et al. Circadian variation in the frequency of onset of acute myocardial infarction. *N Engl J Med* 1985; **313:** 1315–1322.
1894. Cohen MC, Rohtla KM, Lavery CE, Muller JE, Mittleman MA. Meta-analysis of the morning excess of acute myocardial infarction and sudden cardiac death. *Am J Cardiol* 1997; **79:** 1512–1516.
1895. Manfredini R, Boari B, Bressan S, Gallerani M, Salmi R, Portaluppi F, et al. Influence of circadian rhythm on mortality after myocardial infarction: Data from a prospective cohort of emergency calls. *Am J Emerg Med* 2004; **22:** 555–559.
1896. Marler JR, Price TR, Clark GL, Muller JE, Robertson T, Mohr JP, et al. Morning increase in onset of ischemic stroke. *Stroke* 1989; **20:** 473–476.
1897. Marsh EE, Biller J, Adams HP, Marler JR, Hulbert JR, Love BB, et al. Circadian variation in onset of acute ischemic stroke. *Arch Neurol* 1990; **47:** 1178–1180.
1898. Portaluppi F, Manfredini R, Fersini C. From a static to a dynamic concept of risk: The circadian epidemiology of cardiovascular events. *Chronobiol Int* 1999; **16:** 33–49.
1899. Hata M, Yoshitake I, Wakui S, Unosawa S, Takahashi K, Kimura H, et al. Sleep disorders and aortic dissection in a working population. *Surg Today* 2012; **42:** 403–405.
1900. Suka M, Yoshida K, Sugimori H. Persistent insomnia is a predictor of hypertension in Japanese male workers. *J Occup Health* 2003; **45:** 344–350.
1901. King CR, Knutson KL, Rathouz PJ, Sidney S, Liu K, Lauderdale DS. Short sleep duration and incident coronary artery calcification. *JAMA* 2008; **300:** 2859–2866.
1902. Ikehara S, Iso H, Date C, Kikuchi S, Watanabe Y, Wada Y, et al; JACC Study Group. Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: The JACC study. *Sleep* 2009; **32:** 295–301.
1903. Delsart P, Juthier F, Clough RE, Sobocinski J, Azzaoui R, Ramstein J, et al. Prognostic significance of sleep apnea syndrome on false lumen aortic expansion in post-acute aortic syndrome. *Ann Thorac Surg* 2016; **102:** 1558–1564.
1904. Onitsuka S, Akashi H, Tayama K, Okazaki T, Ishihara K, Hiromatsu S, et al. Long-term outcome and prognostic predictors of medically treated acute type B aortic dissections. *Ann Thorac Surg* 2004; **78:** 1268–1273.
1905. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, et al. Editor's choice: 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2018; **55:** 305–368.
1906. Eldrup N, Budtz-Lilly J, Laustsen J, Bibby BM, Paaske WP. Long-term incidence of myocardial infarct, stroke, and mortality in patients operated on for abdominal aortic aneurysms. *J Vasc Surg* 2012; **55:** 311–317.
1907. Heart Protection Study Collaborative Group. Randomized trial of the effects of cholesterol-lowering with simvastatin on peripheral vascular and other major vascular outcomes in 20,536 people with peripheral arterial disease and other high-risk conditions. *J Vasc Surg* 2007; **45:** 645–654.
1908. Kertai MD, Boersma E, Westerhout CM, van Domburg R, Klein J, Bax JJ, et al. Association between long-term statin use and mortality after successful abdominal aortic aneurysm surgery. *Am J Med* 2004; **116:** 96–103.
1909. Parmar GM, Lowman B, Combs BR, Taylor SM, Patterson MA, Passman MA, et al. Effect of lipid-modifying drug therapy on survival after abdominal aortic aneurysm repair. *J Vasc Surg* 2013; **58:** 355–363.
1910. Robertson L, Atallah E, Stansby G. Pharmacological treatment of vascular risk factors for reducing mortality and cardiovascular events in patients with abdominal aortic aneurysm. *Cochrane Database Syst Rev* 2017; **1:** CD010447.
1911. Zhang W, Liu Z, Liu C. Effect of lipid-modifying therapy on long-term mortality after abdominal aortic aneurysm repair: A systemic review and meta-analysis. *World J Surg* 2015; **39:** 794–801.
1912. Bahia SS, Vidal-Diez A, Seshasai SR, Shpitser I, Brownrigg JR, Patterson BO, et al. Cardiovascular risk prevention and all-cause mortality in primary care patients with an abdominal aortic aneurysm. *Br J Surg* 2016; **103:** 1626–1633.
1913. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, et al. European guidelines on cardiovascular disease prevention in clinical practice: Executive summary: Fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (Constituted by representatives of nine societies and by invited experts). *Eur Heart J* 2007; **28:** 2375–2414.
1914. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016; **37:** 2315–2381.
1915. Wemmelund H, Høgh A, Hundborg HH, Thomsen RW, Johnsen SP, Lindholt JS. Statin use and rupture of abdominal aortic aneurysm. *Br J Surg* 2014; **101:** 966–975.
1916. Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, et al. Variability in measurement of abdominal aortic aneurysms. *J Vasc Surg* 1995; **21:** 945–952.
1917. Lindholt JS, Vammen S, Juul S, Henneberg EW, Fasting H. The validity of ultrasonographic scanning as screening method for abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 1999; **17:** 472–475.
1918. Long A, Rouet L, Lindholt JS, Allaire E. Measuring the

maximum diameter of native abdominal aortic aneurysms: Review and critical analysis. *Eur J Vasc Endovasc Surg* 2012; **43:** 515–524.
1919. Wilmink AB, Forshaw M, Quick CR, Hubbard CS, Day NE. Accuracy of serial screening for abdominal aortic aneurysms by ultrasound. *J Med Screen* 2002; **9:** 125–127.
1920. Roy J, Labruto F, Beckman MO, Danielson J, Johansson G, Swedenborg J. Bleeding into the intraluminal thrombus in abdominal aortic aneurysms is associated with rupture. *J Vasc Surg* 2008; **48:** 1108–1113.
1921. Bastos Gonçalves F, Baderkhan H, Verhagen HJ, Wanhainen A, Björck M, Stolker RJ, et al. Early sac shrinkage predicts a low risk of late complications after endovascular aortic aneurysm repair. *Br J Surg* 2014; **101:** 802–810.
1922. Bastos Gonçalves F, van de Luijtgaarden KM, Hoeks SE, Hendriks JM, ten Raa S, Rouwet EV, et al. Adequate seal and no endoleak on the first postoperative computed tomography angiography as criteria for no additional imaging up to 5 years after endovascular aneurysm repair. *J Vasc Surg* 2013; **57:** 1503–1511.
1923. Brown LC, Greenhalgh RM, Powell JT, Thompson SG. EVAR Trial Participants. Use of baseline factors to predict complications and reinterventions after endovascular repair of abdominal aortic aneurysm. *Br J Surg* 2010; **97:** 1207–1217.
1924. Nathan DP, Boonn W, Lai E, Wang GJ, Desai N, Woo EY, et al. Presentation, complications, and natural history of penetrating atherosclerotic ulcer disease. *J Vasc Surg* 2012; **55:** 10–15.
1925. Parodi J, Berguer R, Carrascosa P, Khanafer K, Capunay C, Wizauer E. Sources of error in the measurement of aortic diameter in computed tomography scans. *J Vasc Surg* 2014; **59:** 74–79.
1926. Wicky S, Wintermark M, Schnyder P, Capasso P, Denys A. Imaging of blunt chest trauma. *Eur Radiol* 2000; **10:** 1524–1538.
1927. Parmer SS, Carpenter JP, Stavropoulos SW, Fairman RM, Pochettino A, Woo EY, et al. Endoleaks after endovascular repair of thoracic aortic aneurysms. *J Vasc Surg* 2006; **44:** 447–452.
1928. Eggebrecht H, Schmermund A, von Birgelen C, Naber CK, Bartel T, Wenzel RR, et al. Resistant hypertension in patients with chronic aortic dissection. *J Hum Hypertens* 2005; **19:** 227–231.
1929. Grabenwöger M, Alfonso F, Bachet J, Bonser R, Czerny M, Eggebrecht H, et al. Thoracic Endovascular Aortic Repair (TEVAR) for the treatment of aortic diseases: A position statement from the European Association for Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J* 2012; **33:** 1558–1563.
1930. Eggebrecht H, Zenge M, Ladd ME, Erbel R, Quick HH. In vitro evaluation of current thoracic aortic stent-grafts for real-time MR-guided placement. *J Endovasc Ther* 2006; **13:** 62–71.
1931. Karthikesalingam A, Bahia SS, Patterson BO, Peach G, Vidal-Diez A, Ray KK, et al. The shortfall in long-term survival of patients with repaired thoracic or abdominal aortic aneurysms: Retrospective case-control analysis of hospital episode statistics. *Eur J Vasc Endovasc Surg* 2013; **46:** 533–541.
1932. Bartee S, Shrestha S, Ramos B, Bilbrey T, Carbone P, Schussler JM, et al. Specificity of testing in a cardiac rehabilitation setting resulting in a patient's return to high-intensity outdoor activity following aortic dissection repair. *Proc (Bayl Univ Med Cent)* 2016; **29:** 151–153.
1933. Einstein AJ, Weiner SD, Bernheim A, Kulon M, Bokhari S, Johnson LL, et al. Multiple testing, cumulative radiation dose, and clinical indications in patients undergoing myocardial perfusion imaging. *JAMA* 2010; **304:** 2137–2144.
1934. 医療放射線防護連絡協議会, 日本医学物理学会, 日本医学放射線学会, 他. 最新の国内実態調査結果に基づく診断参考レベルの設定 (平成27年6月7日). [in Japanese] Available at: http://www.radher.jp/J-RIME/report/DRLhoukokusyo.pdf (accessed July 31, 2020).
1935. Davenport MS, Khalatbari S, Cohan RH, Dillman JR, Myles JD, Ellis JH. Contrast material-induced nephrotoxicity and intravenous low-osmolality iodinated contrast material: Risk stratification by using estimated glomerular filtration rate. *Radiology* 2013; **268:** 719–728.
1936. McDonald JS, McDonald RJ, Carter RE, Katzberg RW, Kallmes DF, Williamson EE. Risk of intravenous contrast material-mediated acute kidney injury: A propensity score-matched study stratified by baseline-estimated glomerular filtration rate. *Radiology* 2014; **271:** 65–73.
1937. 総論：5 造影剤の安全性—造影剤腎症とNSF—. [in Japanese] Japan Radiological Society. 画像診断ガイドライン 2016年版. Kanehara-Shuppan, 2016; 37–41.

Appendix 1. Details of Members

Chair:
- Hitoshi Ogino, Department of Cardiovascular Surgery, Tokyo Medical University

Vice-Chairman:
- Osamu Iida, Cardiovascular Center, Kansai Rosai Hospital

Members:
- Koichi Akutsu, Cardiovascular Medicine, Nippon Medical School Hospital
- Yoshiro Chiba, Department of Cardiology, Mito Saiseikai General Hospital
- Hiromitsu Hayashi, Department of Radiology, Nippon Medical School
- Hatsue Ishibashi-Ueda, Department of Pathology, National Cerebral and Cardiovascular Center
- Shuichiro Kaji, Department of Cardiovascular Medicine, Kansai Electric Power Hospital
- Masaaki Kato, Department of Cardiovascular Surgery, Morinomiya Hospital
- Kimihiro Komori, Division of Vascular and Endovascular Surgery, Department of Surgery, Nagoya University Graduate School of Medicine
- Hitoshi Matsuda, Department of Cardiovascular Surgery, National Cerebral and Cardiovascular Center
- Kenji Minatoya, Department of Cardiovascular Surgery, Graduate School of Medicine, Kyoto University
- Hiroko Morisaki, Department of Medical Genetics, Sakakibara Heart Institute
- Takao Ohki, Division of Vascular Surgery, Department of Surgery, The Jikei University School of Medicine
- Yoshikatsu Saiki, Division of Cardiovascular Surgery, Graduate School of Medicine, Tohoku University
- Kunihiro Shigematsu, Department of Vascular Surgery, International University of Health and Welfare Mita Hospital
- Norihiko Shiiya, First Department of Surgery, Hamamatsu University School of Medicine
- Hideyuki Shimizu, Department of Cardiovascular Surgery, Keio University

Collaborators:
- Nobuyoshi Azuma, Department of Vascular Surgery, Asahikawa Medical University
- Hirooki Higami, Department of Cardiology, Japanese Red Cross Otsu Hospital
- Shigeo Ichihashi, Department of Radiology, Nara Medical University
- Toru Iwahashi, Department of Cardiovascular Surgery, Tokyo Medical University
- Kentaro Kamiya, Department of Cardiovascular Surgery, Tokyo Medical University
- Takahiro Katsumata, Department of Thoracic and Cardiovascular Surgery, Osaka Medical College
- Nobuyoshi Kawaharada, Department of Cardiovascular Surgery, Sapporo Medical University School of Medicine
- Yoshihisa Kinoshita, Department of Cardiology, Toyohashi Heart Center
- Takuya Matsumoto, Department of Vascular Surgery, International University of Health and Welfare
- Shinji Miyamoto, Department of Cardiovascular Surgery, Oita University
- Takayuki Morisaki, Department of General Medicine, IMSUT

Hospital, the Institute of Medical Science, the University of Tokyo
- Tetsuro Morota, Department of Cardiovascular Surgery, Nippon Medical School Hospital
- Kiyonori Nanto, Department of Cardiology, Kansai Rosai Hospital
- Toshiya Nishibe, Department of Cardiovascular Surgery, Tokyo Medical University
- Kenji Okada, Department of Surgery, Division of Cardiovascular Surgery, Kobe University Graduate School of Medicine
- Kazumasa Orihashi, Department of Surgery II, Kochi Medical School
- Junichi Tazaki, Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University
- Masanao Toma, Department of Cardiology, Hyogo Prefectural Amagasaki General Medical Center
- Takuro Tsukube, Department of Cardiovascular Surgery, Japanese Red Cross Kobe Hospital
- Keiji Uchida, Cardiovascular Center, Yokohama City University Medical Center
- Tatsuo Ueda, Department of Radiology, Nippon Medical School
- Akihiko Usui, Department of Cardiac Surgery, Nagoya University Graduate School of Medicine
- Kazuo Yamanaka, Cardiovascular Center, Nara Prefecture General Medical Center
- Haruo Yamauchi, Department of Cardiac Surgery, The University of Tokyo Hospital
- Kunihiro Yoshioka, Department of Radiology, Iwate Medical University

Independent Assessment Committee:
- Takeshi Kimura, Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University
- Tetsuro Miyata, Vascular Center, Sanno Medical Center
- Yutaka Okita, Department of Surgery, Division of Cardiovascular Surgery, Kobe University Graduate School of Medicine
- Minoru Ono, Department of Cardiac Surgery, Graduate School of Medicine, The University of Tokyo
- Yuichi Ueda, Nara Prefecture General Medical Center

(Members are listed in alphabetical order, and affiliations are as of June 2021)

Appendix 2. Disclosure of Potential Conflicts of Interest (COI): JCS/JSCVS/JATS/JSVS 2020 Guideline on Diagnosis and Treatment of Aortic Aneurysm and Aortic Dissection (2017/1/1–2019/12/31)

Author	Member's own declaration items									COI of the marital partner, first-degree family members, or those who share income and property			COI of the head of the organization/department to which the member belongs (if the member is in a position to collaborate with the head of the organization/department)	
	Employer/leadership position (private company)	Stakeholder	Patent royalty	Honorarium	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Employer/leadership position (private company)	Stakeholder	Patent royalty	Research grant	Scholarship (educational) grant
Chair: Hitoshi Ogino	TERUMO CORPORATION JCT Co., Ltd.													
Vice-Chairman: Osamu Iida				Cardinal Health Japan TERUMO CORPORATION Boston Scientific Corporation W. L. Gore & Associates G.K. Medtronic Japan Co., Ltd.										
Members: Hiromitsu Hayashi							Daiichi Sankyo Company, Limited							
Members: Kimihiro Komori				Daiichi Sankyo Company, Limited			Sanofi K.K. Daiichi Sankyo Company, Limited W. L. Gore & Associates G.K.							
Members: Hitoshi Matsuda							Medtronic Japan Co., Ltd.							
Members: Kenji Minatoya				Japan Lifeline Co.,Ltd. TERUMO CORPORATION		Sumitomo Bakelite Co., Ltd. Akita Sumitomo Bakelite Co., Ltd.	Edwards Lifesciences Corporation SENKO MEDICAL INSTRUMENT Mfg. Co., Ltd.							
Members: Takao Ohki	Endovascular Japan W. L. Gore & Associates					Cardinal Health Japan								
Members: Yoshikatsu Saiki				Asahi Kasei Pharma Corp.			SENKO MEDICAL INSTRUMENT Mfg. Co., Ltd. Century Medical, Inc. Eisai Co., Ltd. Japan Blood Products Organization Edwards Lifesciences Corporation Asahi Kasei Pharma Corp. W. L. Gore & Associates G.K. TERUMO CORPORATION JMS Co., Ltd.							

Author	Member's own declaration items									COI of the marital partner, first-degree family members, or those who share income and property			COI of the head of the organization/department to which the member belongs (if the member is in a position to collaborate with the head of the organization/department)	
	Employer/leadership position (private company)	Stakeholder	Patent royalty	Honorarium	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Employer/leadership position (private company)	Stakeholder	Patent royalty	Research grant	Scholarship (educational) grant
Members: Hideyuki Shimizu							AST Co., Ltd. Edwards Lifesciences Corporation St. Jude Medical Japan Co., Ltd. TERUMO CORPORATION Ono Pharmaceutical Co., Ltd. SENKO MEDICAL INSTRUMENT Mfg. Co., Ltd. Daiichi Sankyo Company, Limited Teijin Pharma Limited Medtronic Japan Co., Ltd. Japan Lifeline Co.,Ltd. Takeda Pharmaceutical Company Limited							
Collaborators: Nobuyoshi Azuma							Hokkaido Welfare Federation of Agricultural Cooperatives							
Collaborators: Shigeo Ichihashi						W. L. Gore & Associates								
Collaborators: Nobuyoshi Kawaharada							Edwards Lifesciences Corporation							
Collaborators: Yoshihisa Kinoshita				TERUMO CORPORATION ASAHI INTECC CO., LTD.										
Collaborators: Shinji Miyamoto							Edwards Lifesciences Corporation Japan Lifeline Co.,Ltd. Oita Oka Hospital							
Collaborators: Toshiya Nishibe				Daiichi Sankyo Company, Limited										
Collaborators: Kenji Okada							NeXT Abbott Japan LLC Edwards Lifesciences Corporation Sanofi K.K. MEDICON INC. Aizawa Hospital SENKO MEDICAL INSTRUMENT Mfg. Co., Ltd. Medtronic Japan Co., Ltd.							
Collaborators: Junichi Tazaki				Daiichi Sankyo Company, Limited			Daiichi Sankyo Company, Limited	Sugita Genpaku Memorial Obama Municipal Hospital					EP-CRSU Co., Ltd.	Daiichi Sankyo Company, Limited Mitsubishi Tanabe Pharma Corporation Takeda Pharmaceutical Company Limited
Collaborators: Akihiko Usui				TERUMO CORPORATION Japan Blood Products Organization			iCorNet Laboratory Edwards Lifesciences Corporation TERUMO CORPORATION Trestech Co.,Ltd. Pfizer Japan Inc. SENKO MEDICAL INSTRUMENT Mfg. Co., Ltd. Daiichi Sankyo Company, Limited Mitsubishi Tanabe Pharma Corporation Medtronic Japan Co., Ltd. Japan Lifeline Co.,Ltd.							
Collaborators: Kazuo Yamanaka	Japan Lifeline Co.,Ltd.													
Collaborators: Kunihiro Yoshioka				Bayer Yakuhin, Ltd.		CANON MEDICAL SYSTEMS CORPORATION	Nihon Medi-Physics Co.,Ltd. GE Healthcare Eisai Co., Ltd. Bayer Yakuhin, Ltd. AMIN Co., Ltd. Nemoto Kyorindo co., Ltd.							

Author	Member's own declaration items									COI of the marital partner, first-degree family members, or those who share income and property			COI of the head of the organization/department to which the member belongs (if the member is in a position to collaborate with the head of the organization/department)	
	Employer/leadership position (private company)	Stakeholder	Patent royalty	Honorarium	Payment for manuscripts	Research grant	Scholarship (educational) grant	Endowed chair	Other rewards	Employer/ leadership position (private company)	Stakeholder	Patent royalty	Research grant	Scholarship (educational) grant
Independent Assessment Committee: Takeshi Kimura				Amgen Astellas BioPharma K.K. Abbott Vascular Japan Co., Ltd. Sanofi K.K. Bristol-Myers Squibb Boston Scientific Corporation Kowa Pharmaceutical Co., Ltd. Daiichi Sankyo Company, Limited Nippon Boehringer Ingelheim Co., Ltd.		Nipro Corporation EP-CRSU Co., Ltd. Edwards Lifesciences Corporation Daiichi Sankyo Company, Limited Pfizer Japan Inc.	Astellas Pharma Inc. Otsuka Pharmaceutical Co., Ltd. Daiichi Sankyo Company, Limited Mitsubishi Tanabe Pharma Corporation Nippon Boehringer Ingelheim Co., Ltd. Takeda Pharmaceutical Company Limited							
Independent Assessment Committee: Tetsuro Miyata				Daiichi Sankyo Company, Limited Bayer Yakuhin, Ltd. AnGes, Inc.		Bayer Yakuhin, Ltd.	Daiichi Sankyo Company, Limited							
Independent Assessment Committee: Yutaka Okita							Medtronic plc Edwards Lifesciences Corporation Japan Lifeline Co.,Ltd. TERUMO CORPORATION Abbott Japan LLC SENKO MEDICAL INSTRUMENT Mfg. Co., Ltd. JMS Co., Ltd.							
Independent Assessment Committee: Yuichi Ueda				Edwards Lifesciences Corporation										

No relevant COIs for the following members.
Members: Koichi Akutsu
Members: Yoshiro Chiba
Members: Hatsue Ishibashi-Ueda
Members: Shuichiro Kaji
Members: Masaaki Kato
Members: Hiroko Morisaki
Members: Kunihiro Shigematsu
Members: Norihiko Shiiya
Collaborators: Hirooki Higami
Collaborators: Toru Iwahashi
Collaborators: Kentaro Kamiya
Collaborators: Takahiro Katsumata
Collaborators: Takuya Matsumoto
Collaborators: Takayuki Morisaki
Collaborators: Tetsuro Morota
Collaborators: Kiyonori Nanto
Collaborators: Kazumasa Orihashi
Collaborators: Masanao Toma
Collaborators: Takuro Tsukube
Collaborators: Keiji Uchida
Collaborators: Tatsuo Ueda
Collaborators: Haruo Yamauchi
Independent Assessment Committee: Minoru Ono