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KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE

National Kidney Foundation

KDOQI CLINICAL PRACTICE GUIDELINE FOR VASCULAR ACCESS: 2019 UPDATE

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Abstract

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) has provided evidence-based guidelines for hemodialysis vascular access since 1996. Since the last update in 2006, there has been a great accumulation of new evidence and sophistication in the guidelines process. The 2019 update to the KDOQI Clinical Practice Guideline for Vascular Access is a comprehensive document intended to assist multidisciplinary practitioners care for chronic kidney disease patients and their vascular access. New topics include the end-stage kidney disease "Life-Plan" and related concepts, guidance on vascular access choice, new targets for arteriovenous access (fistulas and grafts) and central venous catheters, management of specific complications, and renewed approaches to some older topics. Appraisal of the quality of the evidence was independently conducted by using a Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, and interpretation and application followed the GRADE Evidence to Decision frameworks. As applicable, each guideline statement is accompanied by rationale/background information, a detailed justification, monitoring and evaluation guidance, implementation considerations, special discussions, and recommendations for future research.

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As they are designed to reflect the views and recommendations of the responsible KDOQI Work Group, based on data from an independent evidence review team, and because they undergo both internal and public review, KDOQI guidelines are not peer reviewed by *AJKD*.

Disclaimer

SECTION I: USE OF THE CLINICAL PRACTICE GUIDELINE

This Clinical Practice Guideline document is based on the best information available as of October 2016. It is designed to provide information and assist decision making. It is not intended to define a standard of care and should not be construed as one, nor should it be interpreted as prescribing an exclusive course of management. Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health care professional making use of these recommendations is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation. The recommendations for research contained in this document are general and do not imply a specific protocol.

SECTION II: DISCLOSURE

All reported information is provided in the "Biographical and Disclosure" section of this journal supplement and is on file at the National Kidney Foundation (NKF).

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Abbreviations and Acronyms

2D	2-dimensional
ACPP	Access circuit primary patency
AEC	Allogenic endothelial cells
AKI	Acute kidney injury
AV	Arteriovenous
AV access	Arteriovenous access: Refers to both a hemodialysis arteriovenous fistula and arteriovenous graft
AVF	Arteriovenous fistula
AVG	Arteriovenous graft
BAM	Balloon-assisted maturation
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CFD	Computational fluid dynamics
CFU	Colony-forming unit
CI	Confidence interval
CKD	Chronic kidney disease
CRBSI	Catheter-related bloodstream infection
CRI	Catheter-related infection
CT	Computed tomography
CVC	Central venous catheter; in the guidelines will refer to hemodialysis catheter, and assume tunneled, cuffed central venous catheter unless otherwise stated
CVS	Central vein stenosis
DVP	Dynamic venous pressure
eGFR	Estimated glomerular filtration rate
FDA	US Food and Drug Administration
GFR	Glomerular filtration rate
HD	Hemodialysis
HR	Hazard ratio
IDSA	Infectious Diseases Society of America
IJ	Internal jugular vein
INR	International normalized ratio
JAS	Juxta-anastomotic stenosis
KDOQI	Kidney Disease Outcomes Quality Initiative
KRT	Kidney replacement therapy
MRI	Magnetic resonance imaging
NKF	National Kidney Foundation
NS	Not significant
NT-CVC	Nontunneled, noncuffed central venous catheter
OR	Odds ratio
PCB	Paclitaxel drug-coated balloon
PD	Peritoneal dialysis
PET	Positron emission tomography
PICC	Peripherally inserted central catheter
PTA	Percutaneous balloon angioplasty
PTFE	Polytetrafluoroethylene
Qa	Access blood flow
Qa/CO	The ratio of access blood flow (mL/min) to cardiac output (mL/min)
Qb	Blood pump flow delivered to the dialyzer
QOL	Quality of life
RCT	Randomized controlled trial
RR	Relative risk
SVC	Superior vena cava
SVP	Static venous pressure
TAPP	Treatment area primary patency
TMP-SMX	Trimethhoprim/sulfamethoxazole or cotrimoxazole
TPA	Tissue plasminogen activator
UDM	Ultrasound dilution method
URR	Urea reduction ratio
USRDS	United States Renal Data System
VA	Vascular access
VAC	Vascular access coordinator
VAT	Vascular access team

Glossary

Acronecrosis: Gangrene occurring in the distal part of the extremities, usually the fingertips and toes.

Anastomosis: A communication between an artery and a vein by surgical or endovascular techniques.

Aneurysm: An abnormal dilation of the blood vessel or part of the vessel wall; in the case of vascular access, it may result from disease or trauma of the vessel wall.

Antibiotic lock: Interdialytic instillation and dwelling ("locking") of an antibiotic containing solution into the lumen of a dialysis catheter.

Antimicrobial: Any agent capable of destroying or inhibiting the growth of microorganisms.

Antimicrobial lock: Interdialytic instillation and dwelling ("locking") of an antimicrobial solution into the lumen of a dialysis catheter.

Antiseptic: Any agent capable of preventing infection by inhibiting the growth of microorganisms.

AV (arteriovenous) access abandonment: When a vascular access can no longer be used for prescribed 1 or 2 needle dialysis because it is unable to provide adequate flows and/or is deemed unsafe for the patient, and the associated problem cannot be corrected by any intervention, including medical, surgical, or radiologic interventions or rest.[1] A checklist can be used to confirm abandonment as follows:

Checklist for when an AV access can be considered abandoned:	Yes	No
The fistula/graft does not have a pulsation (even with augmentation) at the anastomosis or the access body		
The fistula/graft does not have a palpable thrill at the anastomosis or the access body		
The fistula/graft does not have an audible bruit anywhere along the anastomosis or body (up to 10 cm from the anastomosis)		
An endovascular intervention such as angioplasty, thrombolysis, stenting, embolization or other will not salvage the access to be useable		
A surgical revision will not salvage the access to be useable. Note: A revision means that it is a revision of the current access and not a surgical procedure that will effectively create new access		
A reasonable effort has been made to improve the condition of the access in order for it to be used but the access remains suboptimal, nonusable and/or patient refuses; for example, adequate management and time for rest of an infiltrated fistula		
The fistula/graft is viable but there are complications that require the abandonment of the access, eg, high cardiac output failure or severe steal syndrome		
For documentation: If other reason not stated above, indicate: _____		
I confirm that the fistula or graft is officially abandoned for further use and is not safely salvageable: _____[signature of assessor]_____		

AV access creation: The connection of an artery and vein for the purposes of establishing hemodialysis access.

Cannulation: The insertion of cannulate (a needle with a lumen) or angiocaths into a vascular vessel. The main forms of cannulation are as follows:

- **Buttonhole technique cannulation:** The cannulation into the exact same puncture site and needle track tunnel developed by repeated cannulation at the same location, angle, and depth between the skin and access vein. The scar tissue tunnel track allows the needle to pass through to the outflow vein or conduit of the AV access following the same path with each cannulation time. Typically used in autogenous arteriovenous fistula and may be acceptable in grafts made of nonautogenous biologic material such as bovine. This type of cannulation should not be used for accessing arteriovenous graft made of synthetic material such as polytetrafluoroethylene (PTFE).

- **Constant-site technique cannulation:** Another term for *buttonhole cannulation*. This should NOT be confused with *general area cannulation*. General area cannulation is neither rope ladder nor buttonhole cannulation, whereby new arterial and venous needle insertions are chronically inserted within close proximity (eg, millimeters) of prior insertions each time, that is, always in the same general areas. This poor technique leads to AV access aneurysms and damage and should be avoided.
- **Rope-ladder (also known as step-ladder) cannulation:** The cannulation needle sites for both arterial and venous needles are rotated along the length of the AV access each dialysis to reduce vessel damage.

Catheter: A device providing access to the central veins or right atrium, permitting high-volume flow rates.

Clinically significant lesion: One that contributes to clinical signs and symptoms (see AV Access Monitoring Table 13.2) without other cause, with or without a sustained change in surveillance measurements (eg, change in blood flow [Qa] or venous pressures) in the dialysis access circuit. Such a lesion is found during monitoring of vascular access (surveillance findings are supplementary) and shows >50% narrowing relative to adjacent normal vein diameter by angiography or ultrasound.

Clinical monitoring: Monitoring refers to the examination and evaluation of the access by means of physical examination or check to detect clinical signs that suggest the presence of AV access flow dysfunction, other dysfunction, or pathology. These abnormal clinical signs may include arm swelling, changes in the access bruit or thrill, or prolonged bleeding after dialysis (Tables 13.1 and 13.2). The patient's physical examination can be supplemented with concurrent dialysis measures such as those indicating recirculation (when needle placement is correctly spaced and placed) or other measures of reduced dialysis adequacy (eg, urea reduction ratio or Kt/V), in the absence of other contributing factors.

Complications:

- **Thrombotic flow–related complications or dysfunction:** Complications specifically related to the risk of or occurrence of thrombosis that leads to a clinically important reduction in intra-access flow that threatens the required access patency to achieve prescribed dialysis and/or results in clinical signs and symptoms (eg, stenosis or thrombosis).
- **Non–thrombotic flow–related complications or dysfunction:** Such complications may or may not threaten flow or patency but are associated with clinical signs and symptoms, eg, AV access aneurysms, steal syndrome.
- **Infectious complications or dysfunction:** Any infection involving the vascular access (intraluminal/access, extraluminal/access, peri-access, ie, cannulation or entry site) that results in clinically important infectious signs and symptoms.

Contingency plan: The plan of remedial measures for the anticipated problems the chosen vascular access might have. The contingency plan should be considered even before the vascular access is created or inserted.

Cumulative patency: A duration of time measuring intra-access patency that starts from the date of vascular access creation (AV access) or insertion (central venous catheter) to the date of vascular access abandonment.

Diagnostic testing: Specialized testing that is prompted by some abnormality or other medical indication and that is undertaken to diagnose the cause of the vascular access problem.

Dialysis usability: A dialysis access that can reliably and safely provide prescribed dialysis, per definition of mature fistula or graft.

Distal revascularization and interval ligation: A surgical procedure to reduce ischemia to the hand caused by steal syndrome.

Dysfunction: *AV access* or *vascular access dysfunction* has been replaced by 3 terms:

- Thrombotic flow–related complications or dysfunction
- Non–thrombotic flow–related complications or dysfunction
- Infectious complications or dysfunction

Note: Access dysfunction *is a very general term that is not specific in its terminology with regard to etiology of dysfunction. For this reason, it has been replaced with these three terms (see definition of complications).*

ESKD (End-Stage Kidney Disease) Life-Plan: The individualized set of kidney replacement modalities (hemodialysis, peritoneal dialysis, transplantation) required to sustain the life of a patient with ESKD that considers the patient's current and anticipated medical and life circumstances and preferences. The Life-Plan should be regularly re-evaluated given expected changes in a patient's life circumstances. See Rationale/Background section of Guideline 1 for further explanation and discussion about its special relevance for dialysis access.

Exit site: The location on the skin through which the catheter exits the skin surface. See also *insertion site*.

Failure to mature: An AV access that, despite radiologic or surgical intervention (ie, endovascular or open procedural management), cannot be used successfully for dialysis by 6 months after its creation.[1]

Fistula (plural, fistulae or fistulas): Autologous arteriovenous fistula, also referred to as *native fistula*.

- **Brescia-Cimino (radiocephalic) fistula:** An autologous fistula constructed between the radial artery and the cephalic vein at the wrist.
- **Endovascular fistula (or endoAVF):** An autologous fistula created by endovascular techniques, originally described by anastomosis of the proximal ulnar artery and proximal ulnar vein.
- **Gracz fistula:** An autologous fistula constructed between the proximal radial artery and a perforating branch of the cephalic or median cubital vein below the elbow.
- **Snuff-box fistula:** An autologous fistula constructed between a branch of the radial artery and an adjacent vein in the anatomic snuff box of the hand.

Fistula maturation: The process by which a fistula becomes suitable for providing prescribed dialysis.

- **Unassisted fistula (or unassisted AVF):** An arteriovenous fistula that matures and is usable for dialysis without the need for endovascular or surgical interventions, such as angioplasty. A preplanned vessel superficialization is acceptable and not considered an additional intervention.

Flow: The amount of blood flowing through a system.

- **Qa:** Intra-access blood flow
- **Qb:** Blood pump flow delivered to the dialyzer

Functional cumulative patency: Duration of time from mature fistula or graft to AV access abandonment (ie, from the first date the AV access is able to provide prescribed dialysis consistently with 2 needles for more than two thirds of dialysis sessions within 4 consecutive weeks to the date of AV access abandonment).

Functional primary patency: The duration of time from mature fistula or graft to one of the following events (whichever comes first): thrombosis or any intervention to facilitate, maintain, or re-establish patency (eg, angioplasty) (ie, from the first date the AV access is able to provide prescribed dialysis consistently with 2 needles for more than two thirds of the dialysis sessions within 4 consecutive weeks to the date of one of the following events [whichever comes first]: thrombosis or any intervention to facilitate, maintain, or re-establish patency [eg, angioplasty]).

Graft: A conduit of synthetic or biological material connecting artery to vein.

- **Synthetic:** Made of plastic polymers, such as polytetrafluoroethylene (PTFE) or polyurethane.
- **Biological:** Made of biological materials, such as bovine carotid artery, cryopreserved human femoral veins, biologically engineered vessels, etc.
- **Tapered:** Grafts for which internal diameter varies from the arterial to the venous end.
- **Untapered:** Grafts with a uniform diameter, usually 6 mm.

Infiltration injury: Infiltration injury is vessel injury related to cannulation or the dialysis procedure and can be categorized as follows:

- **Minor cannulation injury:** An injury that may result in bleeding infiltration and swelling that may be treated with conservative measures such as ice and rest for 1 to 2 days; cannulation can be reattempted for the next dialysis session. The access should be successfully recannulated with 2 needles in ≤7 days.[2] Even a minor cannulation injury may require the use of a temporary catheter.
- **Major cannulation injury:** An injury that results in significant bleeding infiltration and swelling that requires recovery for >7 days.[3]
- **Severe cannulation injury:** An injury that results in significant bleeding complications that requires one of the following: blood transfusion, emergency department visit, hospitalization, or endovascular or surgical intervention.

Insertion site: The location at which the catheter enters the vein (eg, "The right internal jugular vein is the preferred insertion site"). See also *exit site*.

Lesion, clinically significant: One that contributes to clinical signs and symptoms (see AV Access Monitoring Table 13.2) without other cause, with or without a sustained change in measurements (eg, change in access flow [Qa] or venous pressures) in the dialysis access circuit. Such a lesion is found during monitoring of vascular access (surveillance findings are supplementary).

Magnetic resonance angiography (MRA): A technique to visualize the arterial and venous systems using a radiologic contrast material, usually gadolinium, as the imaging agent.

Mature fistula: A mature fistula can be defined as physiologically mature or functionally mature.[3-5] In these guidelines, a *mature fistula* is one that can provide prescribed dialysis consistently with 2 needles for more than two thirds of dialysis sessions within 4 consecutive weeks. The criterion of two thirds is used to include studies referenced in these guidelines; however, it must be emphasized that truly mature AV access should provide reliable prescribed dialysis most times, given expert cannulation and lack of cannulation or other technical complications.

Mature graft: In these guidelines, a mature graft is one that can provide prescribed dialysis consistently with 2 needles for more than two thirds of dialysis sessions within 4 consecutive weeks.[1] The criterion of two thirds is used to include studies referenced in these guidelines; however, it must be emphasized that truly mature AV access should provide reliable prescribed dialysis most times, given expert cannulation and lack of cannulation or other technical complications.

Monitoring: See *clinical monitoring*.

Neointimal hyperplasia: The myoendothelial proliferation of cells and matrix that produces stenosis in AV accesses.

Operator: An operator can be a surgeon, nephrologist, radiologist, or other properly trained and skilled healthcare provider. An operator is the individual who creates, revises, or removes the AV access or inserts, manipulates, or removes the central venous catheter.

Operator discretion: When the operator carefully considers both the patient's individual circumstances and the operator's own clinical experience, skills, and expertise (ie, reasonable capabilities and limitations).

Patency: See *cumulative patency*, *functional cumulative patency*, *functional primary patency*, *primary patency*. *Secondary patency* can be a confusing term and has the same definition as Cumulative Patency. KDOQI suggests using the term *cumulative patency* to help standardize vascular access terminology.

Percutaneous transluminal angioplasty: The endoluminal repair of a lesion, usually with a balloon that can be inflated to pressures up to 30 atmospheres.

Physical examination (of the vascular access): Inspection, palpation, and auscultation of the vascular access.

Primary failure: The terms *primary failure*, *failure to mature*, *early failure*, *late failure*, and *mature fistula* have been inconsistently defined in the literature.[1] These guidelines have attempted to avoid discussion of *primary failure* due to these inconsistencies; however, when they appear, they are defined by the original study from which they are discussed.

Primary patency: A duration of time measuring intra-access patency that starts from the date of vascular access creation (AV access) or insertion (central venous catheter) to the date of one of the following events (whichever one comes first): thrombosis or any intervention to facilitate, maintain, or re-establish patency (eg, angioplasty).

Pseudoaneurysm: A collection of blood outside the vessel (walled off by surrounding tissue), communicating with the fistula or prosthetic graft through a defect (eg, needle hole) in the wall.

Recirculation: The return of dialyzed blood to the systemic circulation without full equilibration.

- **Cardiopulmonary recirculation:** Resulting from the return of dialyzed blood without full equilibration with all systemic venous return.
- **Access recirculation:** Resulting from the admixture of dialyzed blood with arterial access blood without equilibration with the systemic arterial circulation. Occurs under conditions in which blood pump flow is greater than intra-access flow.

Steal syndrome: Compromised perfusion and ischemia of tissue after construction of an AV access due to diversion of arterial blood flow into the AV access away from the peripheral system, leading to a range of signs and symptoms, such as mild numbness to severe motor impairment or skin ulceration to gangrene necessitating major amputation.

Stenosis: A constriction or narrowing of a duct or passage; a stricture.

- **Cephalic arch stenosis:** A common site for stenosis of the cephalic vein; the location of narrowing occurs in the cephalic vein as it arches over the shoulder in the region of the deltopectoral groove before the vein junction with the axillary vein.

Succession plan: The thoughtful planning for the next dialysis access (what it should be, location, appropriate timing of when it should be created/inserted, by whom, etc) before the current vascular access is even created. The succession plan should be re-evaluated when there are changes in the patient's medical or life circumstances and revisited before the current vascular access fails. All such considerations take into account the patient's ESKD Life-Plan, individual circumstances, and preferences.

Surveillance: The periodic evaluation of the vascular access by using device-based methods or tests that involve special instrumentation beyond clinical examination and for which an abnormal test result suggests the presence of thrombotic flow–related complications/dysfunction (defined under *dysfunction*). One example is attempting to detect stenosis by measurement of access blood flow. Access blood flow (Qa) can be measured by a number of different techniques including estimation of flow by Doppler ultrasound, dilution techniques such as ultrasound dilution, differential conductivity, glucose infusion, ionic dialysance, and timed

ultrafiltration methods or by magnetic resonance angiography (MRA). Other surveillance methods include static venous pressure. (Dynamic venous pressure is considered monitoring, not surveillance.)

Tissue plasminogen activator (TPA): A natural (endogenous) lytic used to dissolve fibrin or nonorganized thrombus. rTPA is the exogenous recombinant form used for vascular access intervention.

Transposition: The movement of a vein from its normal position by elevation and/or by lateral movement to bring the vein closer to the skin to permit improved maturation and/or easier cannulation or use for dialysis.

Ultrasound: The use of ultrasonic waves for diagnostic or therapeutic purposes, specifically to image an internal body structure.

- **Doppler ultrasound (DU):** Ultrasound that uses the Doppler effect to measure movement or flow in the body, especially blood flow.
- **Duplex Doppler ultrasound:** Combines Doppler and B-mode (grayscale) imaging to provide quantitative color velocity assessment (AV access flow) as well as anatomic visualization of stenosis/abnormality.

Systolic velocity ratio (SVR): The ratio of velocity in an abnormal vessel relative to a normal vessel.

Urokinase: A natural lytic used to dissolve fibrin or nonorganized thrombus.

Vascular access coordinator (VAC): An individual knowledgeable in dialysis access who coordinates vascular access care of the patient. This is achieved by patient and vascular access assessment, facilitating communication between the vascular access team (VAT) members, organizing/managing required vascular access tests, treatments, and required follow-up vascular access–related appointments. Often responsible for managing vascular access database and has a role in associated inputs, analysis, interpretation, and outputs. Usually critically involved in quality improvement projects.

Vascular access team (VAT): Patient and group of professionals involved in management of vascular access (includes caregivers who construct, cannulate, monitor, detect problems in, and repair vascular accesses). Caregivers include nephrologist, nephrology nurse, patient care technician, nurse practitioner, physician assistant, interventionalist, surgeons, and vascular access coordinator (VAC).

Prognosis of Chronic Kidney Disease by Glomerular Filtration Rate and Albuminuria Categories

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m^2) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no chronic kidney disease [CKD]); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.
Figure reproduced from Inker et al[6] based on the original image published in the Improving Global Outcomes KDIGO CKD guideline[7]; original image © 2012 KDIGO and is reproduced with permission of KDIGO.

FOREWORD

This third update of the KDOQI Clinical Practice Guideline for Vascular Access represents a complete revamping of the Vascular Access Guideline update that was released in 2006. This comprehensive update was performed due to the significant growth in the evidentiary database for vascular access, which was thoroughly surveyed by the evidence review team based at the University of Minnesota in Minneapolis, Minnesota. A number of important randomized clinical trials addressing vascular access for maintenance hemodialysis have been performed since the publication of the 2006 KDOQI clinical practice guideline for vascular access. More than 4,600 articles were reviewed to develop this guideline, for which 286 articles were included in the evidence tables used to develop the 26 guideline sections, their statements, and the research recommendations.

Hemodialysis access issues are managed by a number of different medical professionals. Thus, the Work Group that wrote this guideline is multidisciplinary, with members representing not only clinic-based nephrologists but also interventional nephrologists, radiologists, surgeons, and vascular access nurses, including the past presidents of both the American Society of Diagnostic and Interventional Nephrology and the Vascular Access Society of the Americas.

An important new concept introduced in this Vascular Access Guideline update is the End-Stage Kidney Disease (ESKD) Life-Plan. This individualized and comprehensive map for dialysis modalities and vascular access for the lifetime of the patient is documented in this guideline and will be supplemented by implementation tools that will be developed by the NKF.

This document is the culmination of thousands of hours of volunteer time by the guideline Work Group members as well as by those health care professionals and patients who participated in the internal and external reviewers of this guideline. The NKF extends its deepest appreciation to all of those volunteers who contributed their time and effort in developing this guideline. Special gratitude is expressed to Dr Charmaine E. Lok of the University of Toronto, the Work Group chair, for her tireless efforts to bring this document to fruition, as well as to the 2 guideline scope vice-chairs, Dr Surendra Shenoy of the Washington University School of Medicine and Dr Alexander S. Yevzlin of the University of Michigan, and to the 2 editorial committee members, Dr Thomas S. Huber of the University of Florida and Dr Timmy Lee of the University of Alabama. It is their commitment and dedication to the KDOQI process that has made this guideline document possible.

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INTRODUCTION

Rationale

Hemodialysis continues to be the single most prevalent modality of kidney replacement therapy in the United States.[8] Longevity on dialysis is directly proportional to the quality of dialysis, and that quality in turn depends on the reliability and integrity of the access to the patient's vascular system. This crucial connection is known as the *hemodialysis vascular access*. The ideal hemodialysis vascular access is one that provides reliable, complication-free access to deliver prescribed dialysis and that is also concurrently suitable for a given patient's needs. The last revision of the NKF KDOQI Clinical Practice Guidelines for Vascular Access was completed in 2006. Since then, improvements in the care of patients with ESKD, changes in patient demographics, and increasing patient longevity have resulted in a renewed interest in vascular access management. There is a need to readdress some of the practices previously considered to be best practices that have evolved as a result of updated data derived from clinical research and changing ESKD care delivery patterns.

The 2019 Guideline represents a fresh approach to vascular access care. Although the guideline statements are grounded in rigorous and sophisticated evaluation and integration of data accumulated over the last several decades, the resulting guidance statements reflect the Work Group's thoughtful and practical application to support multidisciplinary care providers in meeting the dialysis access needs of individual patients. These guideline statements emphasize a more patient-focused approach and recommend development of an ESKD Life-Plan, taking each patient's needs and preferences into consideration when choosing an access and planning up front for the likely complications and remediations of the current access, along with the transition plan to the next access. Thus, the focus moves away from the prior Fistula First approach and urges providers to think not only about what access is first, but "what's next" during the planning of the first access. Indeed, the first access may be a peritoneal dialysis (PD) catheter access, so the ESKD Life-Plan encourages a comprehensive evaluation of the patient's lifetime with ESKD and kidney replacement therapy options. This will have many benefits, including to help preserve vessels needed for successful future AV access creation and use and to avoid unnecessary procedures and complications. To summarize, KDOQI has refocused on a P-L-A-N for each patient: **P**atient **L**ife-Plan first, followed by his or her corresponding **A**ccess **N**eeds (Figs 1.1-1.6).

Moreover, we did not update the previous guideline statements number for number but, rather, used the new and existing evidence to reframe our approach to the topic. New or more rigorous evidence has reshaped some prior recommendations. For example, there is a de-emphasis on the need for AV access surveillance but a greater emphasis on the need for improved training and application of vascular access monitoring. We address the preparation for and creation of vascular accesses, the care and management of each type of vascular access, and the prevention and treatment of complications.

These guideline statements are less prescriptive in targeting the fine details within each of these areas, recognizing differences in practice patterns but still emphasizing the need for high-quality standards. As a result, we present only 3 primary targets for use in tracking performance. One target reinforces the idea that each patient has a regularly updated Life-Plan designed with his/her goals in mind to achieve the most suitable dialysis access type and considers changes in circumstances. Other chosen targets for each access type aim to limit the major known complications associated with that access type (eg, an infection rate target for central venous catheters). We chose to limit the number of targets to reasonably enable and encourage achievement. Our focus is on supporting the actions that will lead to the ideal vascular access as defined earlier, such as "reliable," "complication-free . . . to deliver prescribed dialysis," and "concurrently suitable for a given patient's needs."

Finally, we recognize the gaps in knowledge and evidence in vascular access care and provide suggestions for future research. We highlight the need for continual reevaluation within each area of care and corresponding section of the guideline, making room for new evidence and innovations in dialysis access and its affiliated activities and therapies.

This guideline is the result of 3 years of work, consisting of a substantial literature review, months of evidence analysis and discussion, and multidisciplinary integration of the resulting data into practical guidance for chronic kidney disease (CKD) and end-stage kidney disease (ESKD) care providers. We see this guideline as a recalibration and evolution of the previous recommendations. We hope that it will be valuable to our colleagues, helpful for policy makers, and influential in improving the lives of those living with CKD/ESKD.

Methods

The KDOQI guideline development process began with selection of the topic and refinement of the Guideline Scope, followed by a comprehensive literature review of the available evidence. The Guideline Scope was led by the Chair and Vice Chairs of the Guideline Scope Committee with refinement after input from the entire multidisciplinary Work Group. The literature review and evidence analysis for this update were independently carried out by the University of Minnesota Evidence-Based Practice Center, at the Minneapolis VA Center for Chronic Disease Outcomes Research. Members of a multidisciplinary Work

Group were chosen by the Guideline Chair and Guideline Scope Vice Chairs based on their content and methodology expertise and representation of fields including nephrology (adult and pediatric), nursing, vascular surgery, interventional nephrology, interventional radiology, epidemiology, and biostatistics. The analysis and quality of evidence provided by the independent evidence review team (ERT) was reviewed and discussed by this Work Group using a formal GRADE Evidence to Decision format.[9,10] The Work Group, through use of standardized work sheets, a series of regular conference calls, email correspondence, and 2 in-person meetings, developed guideline statements and accompanying strength of recommendations. After statements were agreed upon, guideline sections were drafted by individual members of the Work Group. Once all sections were drafted, they were re-reviewed by the entire multidisciplinary team via weekly-monthly teleconferences until consensus was achieved. If none was achieved, the statement went to a vote, with majority vote being the resulting statement; these have been identified in the guideline document. The guideline Chair and 2 editorial committee members (TH and TL) made editorial revisions to the text for flow and comprehensiveness.

Literature Review and Evidence Analysis

Data Sources and Searches

The ERT searched bibliographic databases, including MEDLINE and Embase via Ovid, and the Cochrane Library to identify studies published from January 2000 through October 2016. Search strategies are available in Supplement 1. They supplemented bibliographic database searches with citation searching of identified studies.

Study Selection

The ERT included trials and prospective observational studies with parallel groups that compared vascular access interventions and reported outcomes preselected for their review. Relevant interventions included those related to different vascular access types. They excluded studies enrolling predominately (<75%) pediatric or acute kidney injury participants, studies enrolling predominately (<75%) participants with vascular accesses created before 2000, studies not reporting outcomes relevant to their review, and studies not published in English.

Two investigators independently reviewed titles and abstracts of search results to identify potentially eligible references. Two investigators independently screened the full text of those references to determine if they met inclusion criteria. A third investigator resolved discrepancies.

Data Extraction and Quality Assessment

One reviewer extracted population and comparison characteristics from all eligible studies. Risk of bias was independently assessed for each eligible study by 2 investigators using methods outlined by the Agency for Healthcare Research and Quality.[11] Risk of bias was assessed as low, medium, or high based on selection of the exposed and unexposed populations, similarity of surveillance for the outcome, measurement of and adjustment for prognostic imbalance, and attrition. Studies assessed as low or medium risk of bias were included in their analyses.

Members of the ERT extracted data in a hierarchical manner to efficiently capture the most relevant data and avoid duplication of samples (when more than 1 study used the same data set). If there was a randomized controlled trial (RCT) for a comparison, they did not extract data from observational studies, unless the observational study reported a unique outcome. When a comparison was addressed only with observational studies, they identified and extracted data from large registry studies first. If there were multiple studies using the same database, such as the US Renal Data System (USRDS) or same patient population and reporting the same outcomes, they extracted only the study with the most recent data. If studies reported data that were included in the registry studies, they extracted data from these studies only if they reported a different outcome from registry studies. They did not extract data from studies if their contribution to the total population analyzed for that comparison was less than 3%. When studies used multivariate analysis, they extracted the most fully adjusted models and listed confounders adjusted for in the evidence table.

Data Synthesis and Analysis

The ERT grouped studies by comparison and independently analyzed statistical significance of the results. Heterogeneity in study populations and methods prevented data pooling. They assessed quality of evidence using GRADE.[12] Evidence quality was rated high, moderate, low, or very low.

Development of Guideline Statements

The Work Group drafted clinical practice guideline statements based on the evidence amassed by the ERT. Some statements are similar to those of the previous guidelines published in 2006[13] but have been re-emphasized or reinterpreted in light of new data. For each of the guideline statements, the quality of the evidence and the strength of the recommendations were graded separately using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach criteria.[9,14] The Work Group used an adapted version of these scales using *high* to *very low* for quality of the evidence and *strong* or *conditional* for the strength of the recommendation. Recommendation strength includes assessment of the statement's potential clinical impact (Tables A and B). The guideline statements were based on a consensus within the Work Group that the strength of the evidence amassed by the ERT was sufficient to make

definitive statements about appropriate clinical practice. When the strength of the evidence was not sufficient to make graded statements but the subject or intervention was deemed important for inclusion, the Work Group identified the statement as "There is inadequate evidence for KDOQI to make a recommendation . . .", and then identified the important issue. It was believed important to communicate to the community that the issue has been identified but that further research is required. Finally, there were many important topics that were excluded by the ERT because they did not make the ERT search criteria or criteria for analysis. Because of their importance, the Work Group offered guideline statements based on the best available evidence, independent of the ERT. Such statements begin with "KDOQI considers it reasonable" and are labeled *Expert Opinion*. Expert Opinion statements are the consensus opinion of the Work Group based on best available evidence and are ungraded. Phrasing and definitions presented were also decided on by a formal, full group process. The statements and definitions that required voting included the classification and working definition of vascular access complications, the wording of Guideline 3.1, B on vascular access location order, the wording of the Guideline 7 statement on routine preoperative ultrasound, and strength of recommendation of the Guideline 11 statement on AV access cannulation technique.

Regarding all of the guideline statements, clinicians should be aware that each patient and his/her circumstances are unique and require careful thought and individualization; thus, best clinical judgment must be used with careful application of a guideline statement, which may infrequently stray from the recommendations of the Work Group to allow for optimal patient outcomes.

This guideline and supplementary files were put through formal internal and external review processes. Internal review took place in March 2019 and included feedback from 14 individuals and groups, including the NKF Scientific Advisory Board, American Society of Diagnostic and Interventional Nephrology, and Vascular Access Society of the Americas. Reviewers were asked to read each recommendation and its supporting text; indicate whether they agreed, disagreed, or partially agreed with each; and provide comment if desired.

A public review period (May 2019) followed the same format and received 50 responses. A link to all documents was emailed to individuals who registered to receive it, and NKF publicized the review through email and social media channels. Changes and edits were made to the manuscript following each review.

Internal Review

The NKF KDOQI process for internal and external reviews is as follows:

- Once the guideline text is signed off by the Work Group Chairs, recommendations are formatted and circulated to KDOQI Leadership and the NKF Scientific Advisory Board for review. Reviewers are asked to use an online form that presents each recommendation, along with a box to check *agree*, *partially agree*, or *disagree* and space for comment.
- At the discretion of the KDOQI Chair, select outside experts and organizations may also be invited to comment at this stage.
- Reviewer comments are collated by KDOQI staff and sent to the Work Group for discussion and possible edits.
- Individual Work Group members are assigned various guideline sections and are asked to address reviewer comments; to ensure a range of perspectives, each guideline section is reviewed by a number of group members. The entire Work Group then meets and discusses the suggested edits or additions and comes to a consensus.
- After Work Group edits, the guideline document is distributed for public review.

External (Public) Review

- Throughout the later stages of guideline development, a link to register for public review is posted to the NKF guidelines web page.
- The document is sent to registered reviewers and publicized to other individuals and groups with an interest in the topic.
- Public reviewers are provided with a link to the online form that presents each recommendation along with a box to check *agree*, *partially agree*, or *disagree* and space for comment.
- Reviewer comments are collated by KDOQI staff and sent to the Work Group for discussion and possible edits.
- Individual Work Group members are assigned various guideline sections and are asked to address reviewer comments; to ensure a range of perspectives, each guideline section is reviewed by a number of group members. The entire Work Group then meets and discusses the suggested edits or additions and came to a consensus.
- The Work Group Chairs coordinate the final rewriting of the guideline document based on the public review comments, after which the final manuscript is submitted for publication in the *American Journal of Kidney Diseases*.

Box 1. Grade for Strength of Recommendation

Evidence Base	Grade	Implications		
		Patients	**Clinicians**	**Policy**
ERT derived	Strong recommendation: "We recommend"	Most people in your situation would want the recommended course of action, and only a small proportion would not.	Most patients should receive the recommended course of action.	The recommendation can be adopted as policy in most situations.
ERT derived	Conditional recommendation/ suggestion: "We suggest"	The majority of people in your situation would want the recommended course of action, but many would not.	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.
ERT derived	There is inadequate evidence	The quality of the evidence was insufficient to make a suggestion or recommendation (to support or not to support the intervention or topic) but important enough to acknowledge as an area for future study		
Work Group derived	Ungraded "KDOQI considers it reasonable"	Ungraded recommendations are based on Work Group consensus and the literature[a] not found through the formal ERT literature review.		

Note: When a statement indicates, "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT. The word "recommendation" is used for simplicity and encompasses both "recommendations" and "suggestions" (in either direction). Also, expert opinion statements that allow for the use of "the clinician's discretion and best clinical judgment" means that there is currently no rigorous evidence to recommend a therapy, device, or strategy over another. The Work Group expects that ERT-derived evidence-based statements will ultimately replace expert opinion-based statements once such rigorous evidence becomes available.
Abbreviations: ERT, evidence review team; KDOQI, Kidney Disease Outcomes Quality Initiative.
Adapted from Uhlig et al[14] with permission of Elsevier; original version of table © 2006 International Society of Nephrology.
[a]Many important topics, such as vein preservation, did not have accompanying studies that met the strict ERT search, retrieval, and analysis criteria (above). However, if the Work Group believed the topic was important enough to be included in the Clinical Practice Guideline, statements were made on these important topics with the Work Group's best attempts to support the statements with the most relevant evidence available through August 2018.

Box 2. Grade for Quality of Evidence

High quality of evidence. We are confident that the true effect lies close to that of the estimate of the effect.
Moderate quality of evidence. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality of evidence. The true effect may be substantially different from the estimate of the effect.
Very low quality of evidence. The estimate of effect is very uncertain and often will be far from the truth.

SUMMARY OF GUIDELINE STATEMENTS

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Note: Expert opinion statements that allow for the use of "the clinician's discretion and best clinical judgment" mean that there is currently no rigorous evidence to recommend a therapy, device, or strategy over another. The Work Group expects ERT-derived evidence-based statements will ultimately replace expert opinion–based statements once such rigorous evidence becomes available. The clinician's discretion carefully considers both the patient's individual circumstances and the clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations).

Guideline 1. Patient First: ESKD Life-Plan

Statements: ESKD Life-Plan and Vascular Access Choice

1.1 KDOQI considers it reasonable that each patient with progressive CKD and/or with an eGFR 15-20 mL/min/1.73 m^2 or already on kidney replacement therapy should have an individualized ESKD Life-Plan that is regularly reviewed, updated, and documented on their medical record. *(Expert Opinion)*

1.2 KDOQI considers it reasonable to conduct an annual review and update of each patient's individualized ESKD Life-Plan, together with their health care team. *(Expert Opinion)*

1.3 KDOQI considers it reasonable that, in addition to regular monitoring, a minimum quarterly overall review and update of each patient's vascular access functionality, complication risks, and potential future dialysis access options be done together with their health care team. *(Expert Opinion)*

Guideline 2. Vascular Access Types

Statements: AV Access: Indications for Use

2.1 KDOQI considers it reasonable to have an AV access (AVF or AVG) in a patient requiring HD, when consistent with their ESKD Life-Plan and overall goals of care. *(Expert Opinion)*

Note: See specific sections on incident and prevalent patients and the choice of AV access type and their appropriate locations.

Statements: Central Venous Catheters (CVC): Indications for Use

2.2 KDOQI considers it reasonable in valid clinical circumstances to use tunneled CVCs for short-term or long-term durations for incident patients, as follows *(Expert Opinion)*:

Short-term duration:

- **AVF or AVG created but not ready for use and dialysis is required**
- **Acute transplant rejection or other complications requiring dialysis**
- **PD patient with complications that require time-limited peritoneal rest or resolution of complication (eg, pleural leak)**
- **Patient has a living donor transplant confirmed with an operation date in the near future (eg, < 90 days) but requires dialysis**
- **AVF or AVG complication such as major infiltration injury or cellulitis that results in temporary nonuse until problem is resolved**

Note: In special, limited circumstances where temporary CVC is required to manage a vascular access complication (eg, <2 weeks), it may be acceptable to use a nontunneled CVC.

Long-term or indefinite duration:

- **Multiple prior failed AV accesses with no available options (see anatomic restrictions below)**
- **Valid patient preference whereby use of an AV access would severely limit QOL or achievement of life goals and after the patient has been properly informed of patient-specific risks and benefits of other potential and reasonable access options for that patient (if available)**
- **Limited life expectancy**
- **Absence of AV access creation options due to a combination of inflow artery and outflow vein problems (eg, severe arterial occlusive disease, noncorrectable central venous outflow occlusion) or in infants/children with prohibitively diminutive vessels**
- **Special medical circumstances**

Statements: Vascular Access for Incident Patients

The statements below are in the context of the ESKD Life-Plan and associated Access Algorithms and their considerations, such as patient comorbidities, circumstances, etc.

2.3 KDOQI suggests an AV access (AVF or AVG) in preference to a CVC in most incident and prevalent HD patients due to the lower infection risk associated with AV access use. *(Conditional Recommendation, Low Quality of Evidence)*

2.4 KDOQI considers it reasonable that the choice of AV access (AVF or AVG) be based on the operator's/clinician's best clinical judgment that considers the vessel characteristics, patient comorbidities, health circumstances, and patient preference. *(Expert Opinion)*

2.5 KDOQI suggests that if sufficient time and patient circumstances are favorable for a mature, usable AVF, such a functioning AVF is preferred to an AVG in incident HD patients due to fewer long-term vascular access events (eg, thrombosis, loss of primary patency, interventions) associated with unassisted AVF use. *(Conditional Recommendation, Low Quality of Evidence)*

Note: Patient circumstances refer to vessel characteristics, patient comorbidities, health circumstances, and patient preference.

Note: Unassisted AVF use refers to an AVF that matures and is used without the need for endovascular or surgical interventions, such as angioplasty. A preplanned vessel superficialization is acceptable and not considered an additional intervention.

2.6 KDOQI suggests that most incident HD patients starting dialysis with a CVC should convert to either an AVF or AVG, if possible, to reduce their risk of infection/bacteremia, infection-related hospitalizations, and adverse consequences. *(Conditional Recommendation, Very Low–Moderate Quality of Evidence)*

2.7 There is inadequate evidence for KDOQI to make recommendations on choice of incident vascular access type based on associations with all-cause hospitalizations or mortality.

2.8 There is inadequate evidence for KDOQI to make a recommendation on choice of AVF vs AVG for incident vascular access based on associations with infections, all-cause hospitalizations, or patient mortality.

2.9 There is inadequate evidence for KDOQI to make a recommendation for incident HD patients using a CVC on converting to an AV access (AVF or AVG) within the first year of dialysis initiation, solely to reduce their risk of mortality.

2.10 KDOQI considers it reasonable to use tunneled CVC in preference to nontunneled CVC due to the lower infection risk with tunneled CVC. *(Expert Opinion)*

2.11 KDOQI considers it reasonable to use nontunneled internal jugular CVC only for temporary purposes for a limited time period (<2 weeks or per individual facility policy) to limit infection risk. *(Expert Opinion)*

Statements: Vascular Access in Prevalent HD Patients

2.12 There is inadequate evidence for KDOQI to make a recommendation on the type of vascular access preferred in prevalent HD patients based on vascular access outcomes, patient hospitalizations, or mortality.

2.13 KDOQI considers it reasonable that prevalent HD patients use an AV access (AVF or AVG) in preference to a CVC, if possible, due to the association with lower vascular access–related events (eg, infection, thrombotic, and nonthrombotic complications). *(Expert Opinion)*

2.14 KDOQI considers it reasonable that if clinical circumstances are favorable for a mature, usable AVF, such a functioning AVF is preferred to AVG in prevalent HD patients. *(Expert Opinion)*

Note: Clinical circumstances refer to patient's vessel characteristics, comorbidities, health circumstances, potential exposure time to CVC use, and patient preference.

2.15 KDOQI considers it reasonable in valid clinical circumstances to use tunneled CVCs for short-term or long-term durations for prevalent patients, as follows *(Expert Opinion)*:

Short-term duration:

- **AVF or AVG created but not ready for use and dialysis is required**
- **Acute transplant rejection or other complications requiring dialysis**
- **PD patient with complications that require time-limited peritoneal rest or resolution of complication (eg, pleural leak)**
- **Patient has a living donor transplant confirmed with an operation date in the near future (eg, <90 days) but requires dialysis**
- **AVF or AVG complication such as major infiltration injury or cellulitis that results in temporary nonuse until problem is resolved**

Note: In special, limited circumstances where temporary CVC is required to manage a vascular access complication (eg, <2 weeks), it may be acceptable to use a nontunneled CVC.

Long-term or indefinite duration:

- **Multiple prior failed AV accesses with no available options (see anatomic restrictions below)**
- **Valid patient preference whereby use of an AV access would severely limit QOL or achievement of life goals and after the patient has been properly informed of patient-specific risks and benefits of other potential and reasonable access options for that patient (if available)**
- **Limited life expectancy**
- **Absence of AV access creation options due to a combination of inflow artery and outflow vein problems (eg, severe arterial occlusive disease, noncorrectable central venous outflow occlusion) or in infants/children with prohibitively diminutive vessels**
- **Special medical circumstances**

Guideline 3. Vascular Access Locations

Statements: AV Access Locations

The statements below are in the context of the ESKD Life-Plan and associated Access Algorithms and their considerations (eg, feasible anatomy, etc).

Note: See Guideline Statements 2.2 and 3.2 for CVC use and location; this section refers to AVF or AVG.

3.1 KDOQI considers it reasonable to choose the site (location) of the AV access (AVF or AVG) after careful consideration of the patient's ESKD Life-Plan (Figs 1.1-1.6), potentially following the below paths. *(Expert Opinion)* See Guideline Statement 3.2 for CVC locations:

A) A patient's ESKD Life-Plan includes an anticipated *long duration* (eg, >1 year on HD):

- **Forearm AVF (snuffbox or distal radiocephalic or transposed radiobasilic)**

- **Forearm loop AVG or proximal forearm AVF (eg, proximal radiocephalic, proximal vessel, and perforator combinations) or brachiocephalic, per operator discretion**
- **Brachiobasilic AVF or upper arm AVG, per operator discretion**

B) A patient's ESKD Life-Plan includes an anticipated *limited duration* (eg, <1 year) on HD:
- **Forearm loop AVG or brachiocephalic AVF (with high likelihood of unassisted maturation)**
- **Upper arm AVG**

C) A patient urgently starts HD without prior sufficient time to plan for and/or create an AV access and has an anticipated *limited duration* (eg, <1 year) on HD:
- **Early or standard cannulation loop AVG (forearm or upper arm location), or CVC, *per operator discretion and patient's clinical needs***

Note: The choice of upper extremity location of an AVG should be based on the operator's discretion and best clinical judgment considering the patient's ESKD Life-Plan, due to inadequate evidence to demonstrate a difference between forearm versus upper arm AVG patency or complication outcomes (including infections, hospitalizations, and mortality).

D) A patient urgently starts HD without prior sufficient time to plan for and/or create an AV access and has an anticipated long duration (eg, >1 year) on HD:
- **PD catheter, and follow above algorithm (A) if PD not a long-term option *or***
- **Forearm early cannulation loop graft; when AVG fails, follow above algorithm (A) *or***
- **CVC if high likelihood of rapid AVF maturation and usability success, then follow above algorithm (A)**

E) All AV access options in the upper extremity have been exhausted and patient's ESKD Life-Plan includes a *long duration* (eg, >1 year) on HD, the following may be considered based on individual patient circumstances and operator's best clinical judgment and expertise:
- **Lower extremity AVF or AVG or HeRO Graft (Merit Medical)**

While a suggested stepwise approach to AV access site selection is provided (Figs 1.1-1.6), *modification of the approach is encouraged as necessary to consider the individual's ESKD Life-Plan and circumstances*, and follow the below key principles, given available suitable vessels:

- Distal first to proximal next approach
- Always preserve the integrity of vessels for future vascular access options
- Nondominant extremity in preference to dominant, *only if choices are equivalent*

Statements: CVC Locations

3.2 KDOQI considers it reasonable to choose the site (location) of the CVC after careful consideration of the patient's ESKD Life-Plan as follows (*Expert Opinion*):
- **Upper extremity before lower extremity, only if choices are equivalent**
- **There are valid reasons for CVC use (Guideline Statement 2.2) and its duration of use is expected to be limited (eg, <3 months):**
  - **AV access is likely to be ready for use in near future—consider preferential use of tunneled cuffed CVC in opposite extremity to anticipated AV access**
  - **Transplant is anticipated in near future (ie, preserve iliac vessels)—consider preferential use of tunneled cuffed right IJ catheter**

  Note: See below guidance for more details on CVC location.

- **Some experts support that in urgent dialysis start situations, under limited use circumstances (eg, <1 month) and transplant is not an option, use of a tunneled, cuffed femoral CVC is acceptable (unless contraindicated) until the AV access or PD catheter can be quickly created and used. Use of the femoral vein preserves the upper extremity vessels for future AV access creation.**

  Note: Contraindications to femoral vein CVC include femoral or iliac vessel pathology or prior surgery/reconstruction; hygienic reasons (eg, chronic unresolved diarrhea), morbid obesity (BMI > 35 kg/m^2), or other difficult vein access.

- **When there are valid reasons for CVC use (Guideline Statement 2.2) and duration of use is expected to be prolonged (eg, >3 months) *without* anticipated use of AV access, CVC may be placed in the following locations in order of preference:**
  - **Internal jugular**
  - **External jugular**
  - **Femoral**
  - **Subclavian**
  - **Lumbar**

  Note: In the absence of contraindications, prior pathology (eg, central stenosis) or intervention (eg, pacemaker) CVC insertion on the right side is preferable to the left side due to more direct anatomy. If one side has pathology that limits AV access creation but allows for CVC insertion, this side should be used for the CVC to preserve the other side for AV access creation.

Guideline 4. AV Access Types and Materials

Statements: Novel AV Access Types and Materials

4.1 KDOQI suggests that the choice of material for an AVG should be based on the nephrologist's or operator's discretion and best clinical judgment since the current evidence does not demonstrate that one graft material or modification thereof is

associated with improved outcomes in terms of patency or complications. *(Conditional Recommendation, Low Quality of Evidence)*

4.2 KDOQI considers it reasonable to use early cannulation grafts as a CVC-sparing strategy in appropriate patients, considering their ESKD Life-Plan. *(Expert Opinion)*

Guideline 5. CVC Configuration and Materials

Statement: CVC Configuration and Materials

5.1 KDOQI suggests that the choice of tunneled HD CVC *type and design* be based on the clinician's discretion and best clinical judgment. *(Conditional Recommendation, Low Quality of Evidence)*

Guideline 6. Timing, Preparation, and Planning for Creation/Insertion of Dialysis Access

Statements: Education on ESKD Modalities and Dialysis Access

6.1 KDOQI considers it reasonable for adult and pediatric patients with an eGFR ≤30 mL/min/1.73 m^2 (CKD G4) with *progressive* decline in kidney function to be *educated* on all *modalities of kidney replacement therapy (KRT)* options, including transplantation, so that timely referral can be made for the appropriate modality and creation of a functional dialysis access, if necessary. *(Expert Opinion)*

Note: For pediatric patients, calculate eGFR by Schwartz formula.

6.2 KDOQI considers it reasonable for adult and pediatric patients with a *kidney transplant* with an eGFR ≤ 30 mL/min/1.73 m^2 (CKD G4) with *progressive* decline in kidney function, to be *educated* on all *modalities of KRT* options, including potential re-transplantation, so that timely referral can be made for the appropriate modality and creation of a functional dialysis access, if necessary. A re-review of the patient's ESKD Life-Plan should occur. *(Expert Opinion)*

Note: For pediatric patients, calculate eGFR by Schwartz formula.

6.3 KDOQI considers it reasonable for *PD patients* with complications refractory to therapy and/or with circumstances that make PD less conducive than HD to be educated on all kidney transplant and HD options, so that timely referral can be made for the appropriate modality preparation and creation of a functional dialysis access, if necessary. A re-review of the patient's ESKD Life-Plan should occur. *(Expert Opinion)*

Note: See Special Discussions.

6.4 KDOQI considers it reasonable and important to ensure that the predetermined dialysis access is usable to provide the prescribed dialysis when the patient is ready to initiate the planned dialysis (eg, an AV access is mature and ready for cannulation for HD). *(Expert Opinion)*

6.5 KDOQI considers it reasonable that in patients who have unplanned or urgent dialysis starts with a CVC, the ESKD Life-Plan is established with a dialysis access plan within 30 days of dialysis start. *(Expert Opinion)*

Statements: Referral for AV Access

In some facilities, referral of the patient for assessment by the vascular access team/surgeon for appropriate dialysis access is a different process than referral for the actual creation/insertion. However, for simplicity, the Guideline recommendations have been combined, keeping in mind variable timeframes between assessment for and creation of vascular access.

Nondialysis CKD Patients

6.6 KDOQI considers it reasonable that in nondialysis CKD patients with *progressive* decline in kidney function, referral for dialysis access assessment and subsequent creation should occur when eGFR is 15-20 mL/min/1.73 m^2. Earlier referral should occur in patients with unstable and/or rapid rates of eGFR decline (eg, >10 mL/min/year). *(Expert Opinion)*

Note: Nondialysis CKD patients include those with a failing transplant.

Hemodialysis Patients

6.7 KDOQI considers it reasonable that in HD patients with recurrent vascular access problems, prompt referral for assessment and creation of a new AV access should be made to allow adequate time for specialist consult and follow-up, as well as possible AV access failure and correction, and should consider individual patient circumstances and competing risk of death. *(Expert Opinion)*

Note: Recurrent vascular access problems include recurrent need for CVC use and/or ≥3 corrective interventions/6 months.

When PD Is the Modality of Choice:

6.8 KDOQI considers it reasonable and ideal to place a PD catheter at least 2 weeks before the anticipated need of the PD treatments. *(Expert Opinion)*

6.9 KDOQI considers it reasonable for an urgent PD catheter to be placed for immediate PD as necessary under the direction and care of experienced personnel in conducive environments. *(Expert Opinion)*

Statement: Vessel Preservation

6.10 KDOQI considers it reasonable to protect all central and peripheral arteries and veins from damage whenever possible, including the avoidance of peripherally inserted catheters and unnecessary venipunctures, for patients on dialysis or with CKD where dialysis access is expected in the future (CKD G3-G5). *(Expert Opinion)*

Note: Other scenarios where vessel (artery or vein) damage may occur that should be avoided include (1) radial artery access for coronary interventions and (2) venous cardiovascular implantable electronic devices; alternatives such as epicardial/leadless pacing should be considered whenever possible.

Statements: Multidisciplinary Team Approach

6.11 KDOQI considers it reasonable to educate on, coordinate, and manage all aspects of dialysis access using a multidisciplinary team within the resource capacities and feasibilities of each facility. *(Expert Opinion)*

6.12 There is inadequate evidence for KDOQI to make a recommendation on the use of a multidisciplinary team to reduce the rate of CVC use or increase the use of AVF.

Guideline 7. Patient and Vessel Examinations: Prepratory Considerations

Statements: Patient Clinical Examination

7.1 KDOQI recommends that a physical examination focused on vascular anatomy be the basis for the initial assessment and planning of vascular access creation. *(Conditional Recommendation, Very Low Quality of Evidence)*

7.2 KDOQI considers it reasonable to have greater emphasis on and more training in preoperative clinical examination to assess patients and their vessels to determine the type and location of their vascular access. *(Expert Opinion)*

Statements: Vessel Mapping for Vascular Access

7.3 KDOQI suggests selective preoperative ultrasound in patients at high risk of AV access failure (Table 7.2) rather than routine vascular mapping in all patients. *(Conditional Recommendation, Low Quality of Evidence)*

7.4 KDOQI considers it reasonable to use various imaging studies as needed to evaluate the suitability of vessels for AV access creation, such as ultrasonography for peripheral vessels (including intraoperative ultrasound) and venography for suspected central vein occlusion, while considering the patient's clinical circumstances and residual kidney function. *(Expert Opinion)*

Statements: Optimal Vessel Size for Artery and Vein of AV Access Creation

7.5 KDOQI considers it reasonable that while there is no minimum-diameter threshold to create an AVF, arteries and veins of <2 mm in diameter should undergo careful evaluation for feasibility and quality to create a functioning AVF. *(Expert Opinion)*

7.6 KDOQI considers it reasonable to evaluate multiple characteristics of vessel quality for AVF creation (size, distensibility, flow, etc). *(Expert Opinion)*

Guideline 8. AV Access Creation

Statements: Pre-Creation Infection Prevention

8.1 KDOQI considers it reasonable to conduct a careful history and physical exam by the operator and managing team prior to AV access creation to identify infection risks that should first be managed before proceeding with AV access creation (eg, dental infection, osteomyelitis, etc). *(Expert Opinion)*

8.2 KDOQI suggests that the choice of anesthesia for AVF creation should be based on the operator's discretion and best clinical judgment, as current evidence shows no difference between regional block or local anesthesia in terms of AVF usability, patency, interventions, or patient experience. *(Conditional Recommendation, Low-Moderate Level of Evidence)*

Statement: AV Access Anastomotic Configuration and Apposition Methods

8.3 KDOQI considers it reasonable that the choice of anastomotic configuration and apposition method (eg, vascular clips, sutures) for AVF creation be based on the operator's discretion and best clinical judgment, as there is insufficient evidence to prefer one configuration or apposition method over another. *(Expert Opinion)*

Statement: AV Access Anastomotic Suture Technique

8.4 KDOQI considers it reasonable that the choice of suture technique for AV access creation should be based on the operator's discretion and best clinical judgment, as there is insufficient evidence that any anastomotic suture technique is advantageous in terms of AV access patency or complications. *(Expert Opinion)*

Statements: Use of Operator-Assisted Maneuvers for AV Access Maturation

8.5 KDOQI does not suggest the use of allogenic endothelial implants to improve AVF maturation, patency, or clinical usability or to improve AVG graft patency or reduce thrombosis. *(Conditional Recommendation, Very Low Quality of Evidence)*

8.6 KDOQI does not suggest the use of pancreatic elastase to improve the patency and clinical use of AVF or AVG. *(Conditional Recommendation, Moderate Quality of Evidence)*

8.7 KDOQI considers it reasonable to have a careful individualized approach to operator-enhanced (surgical or endovascular) maneuvers during AV access creation to facilitate AV access maturation, based on the operator's best clinical judgment and expertise. *(Expert Opinion)*

Guideline 9. CVC Insertion

Statements: Techniques and Other Considerations for Placement

9.1 KDOQI recommends the use of image-guided CVC insertions to improve success of insertions. *(Conditional Recommendation, Moderate Quality of Evidence)*

9.2 KDOQI considers it reasonable that if fluoroscopy is not used to insert a tunnelled CVC, alternative imaging is used to ensure that the CVC tip has been correctly placed. *(Expert Opinion)*

Guideline 10. Post–AV Access Creation/CVC Insertion Considerations

Statement: AV Access Early Postoperative Considerations (0-30 Days)—Early AV Access Complications

10.1 KDOQI considers it reasonable for AV access (AVF and AVG) to be evaluated by a surgeon/operator for postoperative complications within 2 weeks and for an appropriate member of the vascular access team to evaluate for AVF maturation by 4-6 weeks after AV access creation and refer for further investigation if not maturing as expected. *(Expert Opinion)*

Note: Ideally, the surgeon/operator evaluating for complications would be the same individual who created the AV access.

Statements: Postoperative AV Access Maturation

Patient Enhanced

10.2 There is inadequate evidence for KDOQI to make a recommendation on the use of upper extremity exercise to facilitate postoperative AVF maturation.

10.3 KDOQI recommends the use of whole arm rather than finger exercise, if exercise is used to facilitate AVF maturation. *(Conditional Recommendation, Moderate-High Quality of Evidence)*

Pharmacologic Intervention

10.4 KDOQI does not suggest the use of heparin as an adjuvant therapy in the perioperative period to improve primary patency or initial use of AV access (AVF or AVG). *(Conditional Recommendation, Low Quality of Evidence).*

10.5 KDOQI does not suggest the use of adjuvant clopidogrel monotherapy initiation in the perioperative period to improve AVF maturation and reduce the likelihood of primary failure. *(Conditional Recommendation, Low Quality of Evidence)*

10.6 KDOQI does not suggest the use of glyceryl-trinitrate to enhance AVF maturation. *(Conditional Recommendation, Low Quality of Evidence)*

10.7 KDOQI does not suggest the use of cholecalciferol to enhance AVF maturation. *(Conditional Recommendation, Moderate Quality of Evidence)*

10.8 There is inadequate evidence for KDOQI to make a recommendation on the use of clopidogrel-prostacyclin (iloprost) for AVF usability or patency.

Endovascular and Surgical Intervention

10.9 There is inadequate evidence for KDOQI to make a recommendation on the preferred use of surgical or endovascular techniques for postoperative maturation. It is reasonable to consider a careful individualized approach to using either surgical techniques or endovascular techniques when needing to intervene on an AV access to enhance maturation postoperatively.

Statements: Timing of CVC Removal

Noncuffed, Nontunneled Catheters (NT-CVC)

10.10 KDOQI considers it reasonable to limit the use of temporary, noncuffed, nontunneled dialysis catheters to a maximum of 2 weeks due to increased risk of infection, and this should be considered only in patients in need of emergent access. *(Expert Opinion)*

Cuffed, Tunneled CVC

10.11 KDOQI considers it reasonable that in HD patients for whom a cuffed, tunneled CVC is the most appropriate permanent dialysis access, there is no maximum time limit to CVC use, but regular evaluation is required to determine if the CVC remains the most appropriate dialysis access. *(Expert Opinion)*

Note: Appropriate uses of a cuffed, tunneled CVC for chronic hemodialysis include the following:

(1) *All other AV access options have been exhausted (after thorough multidisciplinary evaluation)*
(2) *Temporary switch from another modality (eg, PD, due to PD-related complications such as pleural leak, transplant–acute rejection, etc), but the patient is expected to return to that modality after the complication is adequately resolved*
(3) *Awaiting live-donor kidney transplant with established surgical date (<90 days)*
(4) *Very limited life expectancy (eg, <6-12 months)*
(5) *Clinical conditions that would worsen with AV access (eg, HF with EF <15%, nontreatable skin lesions where cannulation/scratching significantly increases infection or rupture risk, etc)*
(6) *Patient choice after proper informed consent (eg, competent, >85-year-old elderly woman with high risk of AV access failure, needle phobia, and unknown life expectancy)*

Note: The above points regarding appropriate use of CVC are discussed in Guideline Statement 2.2

Guideline 11. Vascular Access Use

Statement: Vascular Access General Monitoring

11.1 KDOQI considers it reasonable to assess or check the vascular access and surrounding area by physical exam prior to every cannulation (if AV access) or connection (if CVC) for potential complications. *(Expert Opinion)*

Statements: AV Access Cannulation

Please review Guideline Statement 11.1.

11.2 KDOQI recommends rope ladder cannulation as the preferred cannulation technique for AVFs. *(Conditional Recommendation, Moderate Quality of Evidence)*

11.3 KDOQI considers it reasonable to limit AV access buttonhole cannulation only to special circumstances given the associated increased risks of infection and related adverse consequences. *(Expert Opinion)*

11.4 KDOQI considers it reasonable to avoid buttonhole cannulation in synthetic PTFE grafts due to potential serious consequences. *(Expert Opinion)*

11.5 KDOQI suggests that when select buttonhole cannulation is performed, the use of buttonhole cannulation devices to facilitate cannulation should be at the discretion and expertise of the cannulator. *(Conditional Recommendation, Low Quality of Evidence)*

11.6 KDOQI considers it reasonable to use skilled cannulators with established high rates of cannulation success to perform initial AV access cannulations on patients to help avoid primary infiltration injury of the AV access. *(Expert Opinion)*

11.7 KDOQI considers it reasonable to have structured training and supervision of dialysis technicians and nurses before and during their initial cannulation attempts, and regular training updates to maintain cannulation competency. *(Expert Opinion)*

11.8 KDOQI considers it reasonable to support and educate eligible patients on self-cannulation of their AV access (AVF or AVG). *(Expert Opinion)*

Note: To be clear, any consideration of buttonhole cannulation refers only to AVF and certain AVG materials. AVG made of PTFE should not be accessed by buttonhole cannulation, due to risks of "one-siteitis" and its serious consequences.

Note: See Guideline Statement 12.2 for use of ultrasound for AV access cannulation.

Statements: CVC System Connect and Disconnect Procedure Considerations

Please review Guideline Statement 11.1.

11.9 KDOQI suggests the use of a catheter care protocol for exit site and hub care to reduce catheter-related bloodstream infections and treatment of catheter dysfunction. *(Strong Recommendation, Moderate Quality of Evidence)*

11.10 KDOQI considers it reasonable, in addition to correct hand hygiene/washing, to use aseptic technique and masks for patients and staff performing catheter connection and disconnection procedures. *(Expert Opinion)*

11.11 KDOQI considers it reasonable to cleanse the catheter hub when connecting and disconnecting the catheter with a chlorhexidine based solution. If chlorhexidine is contraindicated (eg, sensitivity, allergy), povidone-iodine solution (preferably with alcohol) is a reasonable substitute and should be used. *(Expert Opinion)*

11.12 KDOQI considers it reasonable at the time of catheter dressing change to cleanse the skin surrounding the catheter exit site with a chlorhexidine based solution. If chlorhexidine is contraindicated (eg, sensitivity, allergy), povidone-iodine solution (preferably with alcohol) is a reasonable substitute and should be used. *(Expert Opinion)*

11.13 There is inadequate evidence for KDOQI to make a recommendation on the specific chlorhexidine formulation to use for infection prophylaxis, and this should be based on the clinician's best clinical judgment and local practical considerations.

11.14 There is inadequate evidence to demonstrate a difference in catheter-related infections with the use of transparent film dressing compared with nontransparent dressing; thus, the choice of catheter dressing material should be based on the clinician's discretion that considers the patient's circumstances and uses best clinical judgment.

11.15 KDOQI considers it reasonable to use a topical antiseptic or antibiotic barrier at the catheter exit site in addition to cleansing until the exit site is healed to reduce the risk of catheter-related infection. *(Expert Opinion)*

11.16 There is inadequate evidence to demonstrate a difference in catheter-related infections between the use of various antiseptic or antibiotic topical exit site barriers; thus, the choice of topical exit site barrier should be based on the clinician's discretion and best clinical judgment.

11.17 KDOQI considers it reasonable to follow these catheter care practices *(Expert Opinion)*:

- **The frequency of catheter dressing change should be based on the clinician's discretion and best clinical judgment, with a minimum of once weekly**
- **Catheter dressings should be protected against wet and dirty environments, particularly when the exit site is not yet fully healed (eg, avoid swimming and showering)**

Note: See Guideline Statements 21.2 and 21.3 for statements on CVC connectors to prevent CVC dysfunction or bacteremia and Guideline Statements 24.3-24.5 for statements on intraluminal strategies for the prophylaxis of CVC-related infections.

Guideline 12. AV Access Cannulation Complications

Statements: AV Access Cannulation Complications

12.1 KDOQI considers the following therapeutic interventions for cannulation injury reasonable to follow:

- **Any size infiltration: apply ice for a minimum of 10 minutes and refrain from maximizing the blood pump speed. *(Expert Opinion)***
- **If the infiltration is moderate, the needle should be withdrawn and manual pressure held over the infiltration site. *(Expert Opinion)***
- **If the infiltration is significantly large, in addition to the above, a decision on the necessity for dialysis that day is required—if dialysis is required, a site proximal to the infiltration injury should be cannulated; if this is not possible, reattempt at the area of injury should not proceed until manual pressure and ice is applied for 30 minutes. *(Expert Opinion)***

- **If a hematoma develops, close assessment of the site, the AV access, and the adjacent extremity should be made, including measurement of swelling, assessment of the presence of flow in the AV access both proximal and distal to the hematoma, and circulation to the associated extremity. *(Expert Opinion)***

12.2 KDOQI considers it reasonable to use ultrasound to help determine direction of flow and proper needle placement in the AV access of select patients as needed and performed by trained operators, to prevent cannulation complications. *(Expert Opinion)*

Guideline 13. AV Access Flow Dysfunction—Monitoring/Surveillance

Note: "AV access flow dysfunction" refers to clinically significant abnormalities in AV access (AVF or AVG) flow or patency due to underlying stenosis, thrombosis, or related pathology. This is in distinction to other types of AV access complications.

Statements: Appropriate Use of Monitoring/Surveillance for AV Access Flow Dysfunction

Physical Examination (Monitoring)

13.1 KDOQI recommends regular physical examination or check of the AVF, by a knowledgeable and experienced health practitioner, to detect clinical indicators of flow dysfunction of the AVF. *(Conditional/Strong Recommendation, Moderate Quality of Evidence)*

See Table 13.2 for clinical indicators.

13.2 KDOQI recommends regular physical examination or check of the AVG, by a knowledgeable and experienced health practitioner, to detect clinical indicators of flow dysfunction of the AVG. *(Conditional/Strong Recommendation, Moderate Quality of Evidence)*

See Table 13.2 for clinical indicators.

13.3 KDOQI considers it reasonable for nephrology trainees and health practitioners involved with clinical HD patient care to be properly trained in physical examination of the AV access to monitor for and detect AV access flow dysfunction. *(Expert Opinion)*

Surveillance to Facilitate Patency

13.4 There is inadequate evidence for KDOQI to make a recommendation on routine AVF surveillance by measuring access blood flow, pressure monitoring, or imaging for stenosis, that is additional to routine clinical monitoring, to improve access patency.

Note: In other words, monitoring of vascular access is primary, while surveillance findings are supplementary, and action should not be based solely on surveillance findings.

13.5 KDOQI does not suggest routine AVG surveillance by measuring access blood flow, pressure monitoring, or imaging for stenosis, that is additional to regular clinical monitoring, to improve AVG patency. *(Conditional Recommendation, Low Quality of Evidence)*

Note: In other words, monitoring of vascular access is primary, while surveillance findings are supplementary, and action should not be based solely on surveillance findings.

Investigation of Abnormalities Detected by Clinical Monitoring

Please refer to Guideline Statements 15.1-15.3.

Statements: Surveillance and Pre-emptive Intervention for AV Access Stenosis Not Associated With Clinical Indicators

Endovascular Intervention to Improve Patency

13.6 KDOQI does not recommend pre-emptive angioplasty of AVFs with stenosis, not associated with clinical indicators, to improve access patency. *(Conditional Recommendation, Moderate Quality of Evidence)*

13.7 KDOQI does not recommend pre-emptive angioplasty of AVGs with stenosis, not associated with clinical indicators, to improve access patency. *(Conditional Recommendation, Moderate Quality of Evidence)*

Surgical Intervention to Improve Patency

13.8 There is inadequate evidence for KDOQI to make a recommendation on pre-emptive surgical interventions in AVFs with stenosis, not associated with clinical indicators, to improve access patency.

Statement: Pre-emptive Intervention for AV Access Stenosis Associated With Clinical Indicators

13.9 KDOQI considers it reasonable for patients with consistently persistent clinical indicators and underlying AV access stenosis to undergo pre-emptive angioplasty of their AV access to reduce the risk of thrombosis and AV access loss. *(Expert Opinion)*

Guideline 14. AV Access Flow Dysfunction—Prevention

Statements: Noninvasive Primary and Secondary Prevention of AV Access Flow Dysfunction

Note: "AV access flow dysfunction" refers to clinically significant abnormalities in AV access (AVF or AVG) flow or patency due to underlying stenosis, thrombosis, or related pathology. This is in distinction to other types of AV access complications.

Fistulas

14.1 KDOQI suggests that the use of adjuvant far-infrared therapy to improve AVF primary patency be based on individual circumstances, feasibility, and the clinician's best judgment and expertise. *(Conditional Recommendation, Moderate Quality of Evidence)*

14.2 KDOQI does not suggest the routine use of fish oil or aspirin to prevent AVF flow dysfunction. *(Conditional Recommendation, Low-Moderate Quality of Evidence)*

14.3 There is inadequate evidence for KDOQI to make a recommendation on the use of simvastatin and ezetimibe to reduce AVF interventions or thrombosis.

14.4 There is inadequate evidence for KDOQI to make a recommendation on the use of clopidogrel-prostacyclin to improve AVF primary failure.

Grafts

14.5 KDOQI suggests careful consideration of potential individual patient benefits, risks, and circumstances prior to the use of combination dipyridamole (200 mg) and aspirin (25 mg) twice daily to improve AVG primary unassisted patency. *(Conditional Recommendation, High Quality of Evidence)*

14.6 KDOQI suggests the use of oral fish oil supplementation, in patients with newly created AV grafts, to reduce patient morbidity (ie, reduce frequency of thrombosis and related corrective interventions). *(Conditional Recommendation, Moderate Quality of Evidence)*

14.7 There is inadequate evidence for KDOQI to make a recommendation on the use of oral fish oil supplementation to prolong AVG cumulative patency.

14.8 There is inadequate evidence for KDOQI to make a recommendation on the use of simvastatin and ezetimibe for reducing AVG interventions and thrombosis.

Guideline 15. AV Access Flow Dysfunction—Confirmation and Treatment

Statements: Radiographic Confirmation of Clinically Significant AV Access Lesion

15.1 KDOQI considers it reasonable that when clinical monitoring suspects clinically significant AV access lesion (eg, stenosis), further timely and confirmatory evaluation should proceed, including imaging of the dialysis access circuit. *(Expert Opinion)*

Notes:

- *A clinically significant lesion is one that contributes to clinical signs and symptoms (see AV Access Monitoring, Table 13.2) without other cause (with or without a change in surveillance measurements, such as change in blood flow [Qa] or venous pressures).*
- *Dialysis access circuit is defined as the continuum from the heart and the arterial inflow through the AV access to the venous outflow back to the heart.*
- *The timeframe, choice, and extent of imaging studies for further evaluation are dependent on local resources and the severity of findings on clinical monitoring; a timeframe of less than 2 weeks was deemed reasonable by the KDOQI Work Group.*

15.2 KDOQI considers it reasonable to use the smallest volume of iodinated contrast or non-iodinated contrast agents (eg, CO_2 gas) by operators knowledgeable in their uses, contraindications, and risks to obtain the best possible image in all patients with CKD to preserve residual kidney function. *(Expert Opinion)*

15.3 KDOQI considers it reasonable that when further confirmatory imaging studies reveal a culprit lesion responsible for clinical signs and symptoms, the clinically significant lesion is promptly treated. *(Expert Opinion)*

Note: A clinically significant lesion is one that contributes to clinical signs and symptoms (see AV Access Monitoring, Table 13.2) without other cause (with or without a change in surveillance measurements, such as change in blood flow [Qa] or venous pressures).

Statement: General Treatment of Clinically Significant Stenosis or Thrombosed AV Access

15.4 KDOQI considers it reasonable to use a careful individualized approach to the treatment of failing or thrombosed AVF and AVG (surgical or endovascular), based on the operator's best clinical judgment and expertise and considering the patient's ESKD Life-Plan. *(Expert Opinion)*

Note: Consider both the patient's individual circumstances and the operator's clinical experience and expertise (ie, reasonable capabilities and limitations); preferably discussed and agreed on by the team managing the patient's vascular access, including but not limited to the patient and one or more of the following: nephrologist, interventionalist, surgeon, vascular access coordinator, cannulators (nurse or technician).

Statements: Treatment of Clinically Significant AV Access Stenosis

Angioplasty

15.5 KDOQI considers it reasonable to use balloon angioplasty (with high pressure as needed) as primary treatment of AVF and AVG stenotic lesions that are both clinically and angiographically significant. *(Expert Opinion)*

Note: Angiographically present stenosis without accompanying clinical signs and symptoms is inadequate to treat/intervene upon.

15.6 There is inadequate evidence for KDOQI to make a recommendation regarding the use of specialized balloons (drug-coated or cutting) versus standard high-pressure balloons in the primary treatment of AVF and AVG stenosis.

15.7 There is inadequate evidence for KDOQI to make a recommendation regarding the optimal duration of balloon inflation time during angioplasty to improve intervention primary patency in the treatment of AVF or AVG stenosis.

15.8 KDOQI considers it reasonable that a careful patient-individualized approach to the choice of balloon type for angioplasty of clinically significant AVF and AVG stenosis be based on the operator's best clinical judgment and expertise. *(Expert Opinion)*

Stents

15.9 KDOQI suggests the appropriate use of self-expanding stent-grafts in preference to angioplasty alone to treat clinically significant graft-vein anastomotic stenosis in AVG when the goal is overall better 6-month postintervention outcomes after carefully considering the patient's ESKD Life-Plan. *(Conditional Recommendation, Moderate Quality of Evidence)*

Note: Appropriate use avoids cannulation segments.

Note: Overall better 6-month outcomes refer to reduced recurrent AVG restenosis ± improved patency.

15.10 KDOQI considers it reasonable to *first consider the consequences of placement of a stent-graft on future AV access options* according to the patient's ESKD Life-Plan, with consultation with the vascular access team if necessary, prior to its placement. *(Expert Opinion)*

15.11 KDOQI suggests that the use of an appropriately placed stent-graft is preferred to angioplasty alone for the treatment of in-stent restenosis in AVG and AVF for overall better 6-month postintervention outcomes. *(Conditional Recommendation, Moderate Quality of Evidence)*

Note: Appropriate use avoids cannulation segments.

Note: Overall better 6-month outcomes refer to reduced recurrent AVG and AVF restenosis ± improved patency.

15.12 KDOQI considers it reasonable to avoid the use of bare metal stents for the treatment of clinically and/or angiographically significant AVG and AVF stenotic lesions. *(Expert Opinion)*

Statements: Treatment of Thrombosed AV Access

15.13 KDOQI considers it reasonable that management of each episode of AV access thrombosis is at the operator's/clinician's best judgement and discretion, and involves the consideration of the patient's dialysis access Succession Plan that is consistent with the ESKD Life-Plan, given the compromised AV access patency after either endovascular or surgical treatment. *(Expert Opinion)*

Note: Operator's/clinician's discretion carefully considers both the patient's individual circumstances and the operator's/clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations). The Succession Plan is a critical component of the P-L-A-N (see Monitoring and Evaluation discussion in Guideline Statement 1).

15.14 KDOQI considers it reasonable to surgically treat a failing AV access in the following circumstances: (1) endovascular treatment failures, (2) clinically significant lesions not amenable to endovascular treatment, and (3) situations in which the surgical outcomes are deemed markedly better. *(Expert Opinion)*

Note: Situations when surgical outcomes are anticipated to be better than alternative options should be first discussed and agreed upon by the team managing the patient's vascular access, including but not limited to the patient and one or more of the following: nephrologist, interventionalist, surgeon, vascular access coordinator, and cannulation expert, if possible.

Guideline 16. AV Access Infection

Statements: AV Access Infections

Monitoring and Prevention

16.1 KDOQI considers it reasonable to educate the patient on washing the access arm using antiseptic to clean the skin prior to every cannulation. *(Expert Opinion)*

16.2 KDOQI considers it reasonable to check the vascular access and surrounding area prior to every cannulation for signs and symptoms of infection. *(Expert Opinion)*

Note: This check should be done by patient and cannulator (if patient does not self-cannulate).

Special considerations from Guideline Statements 11.2, 11.3, and 11.7 are relevant to this section.

Diagnosis

16.3 KDOQI considers it reasonable to use radiologic imaging to help confirm the diagnosis of AV access infection; however, physical examination remains the hallmark for assessing for infection. *(Expert Opinion)*

Note: Radiologic imaging includes duplex ultrasound, ± CT scan, PET, and nuclear medicine scans (eg, indium scan).

Note: Signs of infection include erythema, skin breakdown, purulent discharge, and presence of exposed graft.

16.4 KDOQI considers it reasonable to investigate and closely monitor for metastatic complications (eg, endocarditis, spinal abscesses, septic arthritis) in patients with buttonhole infection from particularly dangerous organisms such as *S aureus*, Gram-negative bacteria, and fungal organisms. *(Expert Opinion)*

Note: Investigations include 2D echocardiography, MRI, joint aspirate, and other, as appropriate.

Treatment

16.5 KDOQI considers it reasonable to obtain cultures and sensitivities of the blood and any available infected AV access vessel/material, surrounding tissue, or drainage prior to initiating antibiotic therapy. *(Expert Opinion)*

16.6 KDOQI considers it reasonable for infected AV access the rapid initiation of empiric broad-spectrum antibiotics and timely referral to a surgeon knowledgeable in the management of vascular access complications. *(Expert Opinion)*

16.7 KDOQI considers it reasonable to have strict follow-up of culture results with the appropriate change in antibiotics based on organism sensitivities, with antibiotic duration according to extent of vascular access infection and surgical intervention. *(Expert Opinion)*

16.8 KDOQI considers it reasonable that the specific surgical treatment for AV access infections (with concurrent antibiotics) should be based on the patient's individual circumstances considering the extent of infection, offending organism, and future vascular access options. *(Expert Opinion)*

Guideline 17. AV Access Aneurysms

Statements: AV Access Aneurysms

Recognition and Diagnosis

17.1 KDOQI considers it reasonable to check AV access for aneurysm/pseudoaneurysms at each dialysis session by knowledgeable care providers, including but not limited to dialysis technicians, nurses, nephrologists, and vascular access coordinator. *(Expert Opinion)*

17.2 KDOQI considers it is reasonable to proactively educate patients on emergency procedures for aneurysm rupture and to obtain proactive surgical assessment when clinical findings suggest an AV access aneurysm/pseudoaneurysm to be at risk of complications. *(Expert Opinion)*

Note: An aneurysm/pseudoaneurysm that is considered at risk of complications is one with evidence of associated symptoms or skin breakdown.

17.3 KDOQI considers it is reasonable to obtain emergent surgical assessment and treatment for AV access aneurysm/pseudoaneurysm complications such as erosion or hemorrhage. *(Expert Opinion)*

17.4 KDOQI considers it reasonable to use duplex ultrasound to corroborate the physical examination suggesting an AV access aneurysm/pseudoaneurysm and to obtain information on the size, presence of stenosis/thrombus, and impact on the AV access (including flow rate [Qa] and status of the arterial inflow and the venous outflow). *(Expert Opinion)*

Management

17.5 KDOQI considers it reasonable that the presence of an aneurysm/pseudoaneurysm alone in the absence of symptoms (ie, asymptomatic) is not an indication for definitive treatment. *(Expert Opinion)*

17.6 KDOQI considers it reasonable to avoid cannulating the access segment(s) that involve the aneurysm/pseudoaneurysm if there are alternative sites. In the rare scenario where there are absolutely no suitable alternative cannulation sites, the sides (base) of the aneurysm/pseudoaneurysm should be cannulated (ie, avoid the top). *(Expert Opinion)*

17.7 KDOQI considers it reasonable to obtain appropriate imaging of the arterial inflow and venous outflow to assess volume flow or stenotic problems that may need correction prior to or during definitive treatment of symptomatic aneurysm/pseudoaneurysm. *(Expert Opinion)*

17.8 KDOQI considers it reasonable that surgical management is the preferred treatment for patients with symptomatic, large, or rapidly expanding AV access aneurysm/pseudoaneurysm (see "Treatment–Definitive" below). *(Expert Opinion)*

17.9 KDOQI considers it reasonable that a definitive surgical treatment is usually required for anastomotic aneurysms/pseudoaneurysms. *(Expert Opinion)*

Treatment–Definitive

17.10 KDOQI considers it reasonable that open surgical treatment should be deemed the definitive treatment for AV access aneurysms/pseudoaneurysms with the specific approach determined based on the local expertise. *(Expert Opinion)*

Note: This approach may include a plan for staged repair of multiple aneurysms to avoid bridging CVCs in the perioperative period.

17.11 KDOQI considers it reasonable to use covered intraluminal stents (stent grafts) as an alternative to open surgical repair of AV access aneurysms/pseudoaneurysms, only in special circumstances such as specific patient contraindication to surgery or lack of surgical option, due to the associated risk of infection in this scenario. *(Expert Opinion)*

17.12 KDOQI considers it reasonable that, should a stent graft be used to treat AV access aneurysms/pseudoaneurysm, cannulation over the stent graft segment be avoided when possible. *(Expert Opinion)*

Note: The use of stent grafts to manage aneurysms/pseudoaneurysms is not an FDA-approved indication.

Prevention

17.13 KDOQI considers it reasonable that appropriate cannulation techniques should be implemented to reduce the occurrence of AV access aneurysms/pseudoaneurysms (see Guideline Statement 11). *(Expert Opinion)*

Guideline 18. AV Access Steal

Statements: AV Access Steal

18.1 KDOQI considers it reasonable that strategies to both prevent and treat AV access steal should be developed and implemented before AV access creation, to reduce the risk of AV access steal and related morbidity, respectively. *(Expert Opinion)*

18.2 KDOQI considers it reasonable that post AV access creation, patients should be monitored closely for signs and symptoms associated with AV access steal and managed appropriately with consideration of individual circumstances as follows *(Expert Opinion)*:

- **Mild to moderate signs and symptoms require close monitoring for progression of ischemia and worsening of signs and symptoms**
- **Moderate to severe signs and symptoms often require urgent treatment to correct the hemodynamic changes and prevent any longer-term disability**

18.3 KDOQI considers it reasonable that patients with signs and symptoms consistent with AV access steal should be referred urgently to a surgeon/interventionist familiar with the diagnosis and options for the definitive treatment of AV access complications, particularly AV access steal. *(Expert Opinion)*

18.4 KDOQI considers it reasonable that the optimal treatment of AV access steal should be determined based on the patient's clinical presentation, local expertise, and resources. *(Expert Opinion)*

Guideline 19. Other AV Access Complications

Statement: Management of AVG Seroma

19.1 KDOQI considers it reasonable to carefully monitor for complications of AVG seroma and manage based on the patient's individual circumstances and the clinician's best judgment and discretion. *(Expert Opinion)*

Note: Operator's/clinician's discretion carefully considers both the patient's individual circumstances and the operator's/clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations).

Statement: Management of High-Flow AV Access

19.2 KDOQI considers it reasonable to closely monitor and prophylactically manage AV access with high flows to avoid serious or irreversible complications (eg, high output cardiac failure), based on the patient's individual circumstances and the clinician's best judgment and discretion. *(Expert Opinion)*

Note: Operator's/clinician's discretion carefully considers both the patient's individual circumstances and the operatot's/clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations).

Note: Close monitoring refers to physical examination and history on routine dialysis rounds and determination of Qa/CO every 6-12 months, or more frequently as needed.

Guideline 20. Treatment and Prevention of CVC Complications

Statement: Monitoring/Surveillance of CVC Complications

20.1 KDOQI considers it reasonable to perform a basic medical history focused on signs and symptoms of CVC-related complications (eg, dysfunction, infection) and physical examination or check of the dialysis catheter, exit site, tunnel, and surrounding area at each catheter dressing change or dialysis session. *(Expert Opinion)*

Guideline 21. Catheter Dysfunction

Statement: Definition of CVC Dysfunction

21.1 KDOQI considers it reasonable to assess for CVC dysfunction during each HD session using the following updated definition of CVC dysfunction: failure to maintain the prescribed extracorporeal blood flow required for adequate hemodialysis without lengthening the prescribed HD treatment. *(Expert Opinion)*

Statements: Pharmacologic Prevention of CVC Dysfunction

CVC Connectors to Prevent CVC Dysfunction or Bacteremia

21.2 KDOQI considers it reasonable to have an individualized approach to use special CVC connectors based on the clinician's discretion and best clinical judgment. *(Expert Opinion)*

21.3 KDOQI considers it reasonable to use an antimicrobial barrier cap to help reduce CRBSI in high-risk patients or facilities; the choice of connector should be based on clinician's discretion and best clinical judgment. *(Expert Opinion)*

Intraluminal Agents to Prevent CVC Dysfunction

21.4 KDOQI considers it reasonable that the choice to use citrate or heparin as a CVC locking solution be based on the clinician's discretion and best clinical judgment, as there is inadequate evidence to demonstrate a difference in CVC survival or complications between these locking solutions. *(Expert Opinion)*

21.5 KDOQI suggests the use of low-concentration citrate (<5%) CVC locking solution, if feasible, to help prevent CRBSI and CVC dysfunction. *(Conditional Recommendation, Low Quality of Evidence)*

21.6 KDOQI suggests that TPA may be prophylactically used as a CVC locking solution once per week to help reduce CVC dysfunction. *(Conditional Recommendation, Low Quality of Evidence)*

21.7 There is inadequate evidence for KDOQI to make a recommendation on the comparative use of the following CVC locking agents for CVC dysfunction or infection prophylaxis: tinzaparin versus unfractionated heparin, taurolidine/citrate versus heparin with or without gentamicin, neutral valve connector (Tego [ICU Medical]) versus citrate (46.7%) locking solution.

Systemic Agents to Prevent CVC Dysfunction

21.8 KDOQI recommends against the routine use of prophylactic systemic anticoagulants (eg, warfarin) for the sole purpose of maintaining or improving CVC patency, as there is inadequate evidence of benefit for CVC patency but suggestion of increased risk of harm. *(Conditional/Strong Recommendation, Low Quality of Evidence)*

21.9 KDOQI suggests that low-dose aspirin may be used to maintain tunneled CVC patency in patients with low bleeding risk. *(Conditional Recommendation, Low Quality of Evidence)*

Note: CVC refers to tunneled hemodialysis CVCs unless otherwise specified.

Guideline 22. Treatment and Management of CVC Dysfunction

Statements: Medical Management of CVC Dysfunction

Conservative Maneuvers

22.1 KDOQI considers it reasonable for a conservative bedside approach to managing CVC dysfunction prior to other medical or mechanical interventions. *(Expert Opinion)*

Pharmacologic Maneuvers

22.2 KDOQI recommends intraluminal administration of a thrombolytic agent in each CVC port to restore function of dysfunctional CVCs due to thrombosis. *(Conditional Recommendation, Moderate Quality of Evidence)*

22.3 KDOQI recommends the use of alteplase or urokinase plus citrate 4% per limb for restoring intraluminal CVC blood flow in an occluded CVC. *(Conditional Recommendation, Moderate Quality of Evidence)*

22.4 KDOQI suggests intraluminal administration of alteplase 2 mg in preference to alteplase 1 mg in each CVC port to restore function of dysfunctional CVCs due to thrombosis. *(Conditional Recommendation, Moderate Quality of Evidence)*

22.5 KDOQI suggests administering alteplase by the dwell or push method to treat CVC dysfunction. *(Conditional Recommendation, Low Quality of Evidence)*

Statements: Mechanical Management of CVC Dysfunction

22.6 KDOQI considers it reasonable that the decision to perform fibrin sheath disruption during CVC exchange for CVC dysfunction be based on the operator's discretion and best clinical judgment. *(Expert Opinion)*

22.7 There is inadequate evidence for KDOQI to make a recommendation on the efficacy of or method of fibrin sheath disruption based on CVC patency outcomes.

22.8 KDOQI considers it reasonable that CVC removal followed by replacement at a different site should be the last resort after conservative, medical, and other mechanical (eg, angioplasty, CVC exchange) strategies have all failed to treat CVC dysfunction. *(Expert Opinion)*

Guideline 23. Catheter-Related Infection

Statements: Definitions of Catheter-Related Infections

23.1 KDOQI considers it reasonable to consistently use standardized definitions for CVC-related infections to allow for comparisons across programs/jurisdictions. *(Expert Opinion)*

23.2 KDOQI considers it reasonable to use the KDOQI VA-2019 definitions of CVC-related infections (Tables 23.1 and 23.2), which consider the unique circumstances of a hemodialysis patient. *(Expert Opinion)*

Note: In order to harmonize definitions, the KDOQI VA-2019 definitions encompass those of other organizations.

Guideline 24. Prevention of CVC-Related Infection

Statement: General Prevention of CVC Infection and Use of Infection Surveillance Programs and Infection Control Teams

24.1 KDOQ considers it reasonable for an infection control program to include an infection surveillance team to monitor, track (in an electronic database), help prevent, and evaluate outcomes of vascular access infections and, in particular, CVC-related infections. *(Expert Opinion)*

Specific Prevention of CVC Infection

Routine monitoring per Guideline 20.1 is required for the prevention of CVC complications, including CVC-related infections.

Statement: Surveillance of CVC Colonization and Preemptive CRBSI Management

24.2 There is inadequate evidence for KDOQI to support routine CVC surveillance cultures for colonization and subsequent preemptive antibiotic lock installation if culture is positive.

Statements: Methods to Prevent CRBSI

Extraluminal Strategies

See Guidelines 11, 21, and 24 on "CVC System Connect and Disconnect Procedure Considerations" and section on "Prevention of CVC Dysfunction."

Intraluminal Strategies

24.3 KDOQI suggests that the selective use of specific prophylactic antibiotic locks can be considered in patients in need of long-term CVC who are at high risk of CRSBI (eg, multiple prior CRSBI), especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). *(Conditional Recommendation, Low-Moderate Level of Evidence)*

Note: Under these circumstances and given the current data, KDOQI considers it reasonable for prophylactic use of specific antibiotics: cefotaxime, gentamicin, or cotrimoxazole (TMP-SMX). KDOQI cannot support the routine prophylactic use of antibiotic locks with very low supporting evidence (Table 24.1).

24.4 KDOQI suggests that the selective use of specific prophylactic antimicrobial locks can be considered in patients in need of long-term CVC who are at high risk of CRSBI, especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). *(Conditional Recommendation, Low-Moderate Quality of Evidence)*

Note: Under these circumstances and given the current data, KDOQI can support the prophylactic use of methylene blue. KDOQI cannot support the routine prophylactic use of antimicrobial locks with very low supporting evidence (Table 24.1).

24.5 KDOQI suggests that the selective use of once weekly prophylactic CVC locking with thrombolytic agent (recombinant TPA) can be considered in patients in need of long-term CVC who are at high risk of CRSBI, especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). *(Conditional Recommendation, Moderate Quality of Evidence)*

Note: Under these circumstances and given the current data, KDOQI can support the prophylactic use of recombinant TPA.

Note: High-risk patients refers to those with prior multiple CRSBI, S aureus nasal carriers.

Guideline 25. Treatment of CVC-Related Infection

Statement: Management of the Patient With a CVC-Related Infection

25.1 KDOQI considers it reasonable and necessary to obtain appropriate cultures prior to initiating empiric antibiotics for the treatment of suspected CVC-related infection, with a change in antibiotics according to culture sensitivities. *(Expert Opinion)*

Statement: Management of the CVC in a Patient With a CVC-Related Infection

25.2 KDOQI considers it reasonable to have an individualized approach to the management of an infected catheter based on the patient's health, dialysis, and vascular access circumstances and should follow the detailed guidance. Options include CVC exchange via guidewire, CVC removal and reinsertion, CVC salvage, and concurrent antibiotic lock (particularly if the CVC is deemed to be the patient's final access). *(Expert Opinion)*

Note: See Detailed Justification section for detailed guidance.

Guideline 26. Other Vascular Access-Related Complications

Statement: Treatment and Intervention of Asymptomatic Central Venous Stenosis Without Clinical Indicators

26.1 KDOQI considers it reasonable that if *asymptomatic* central venous stenosis (without clinical indicators) is identified and/or associated with the prior or current presence of a CVC, it should not be treated. *(Expert Opinion)*

See Table 26.1 for clinical indicators of central venous stenosis.

Statement: Investigation and Treatment of Symptomatic Central Venous Stenosis With Clinical Indicators

26.2 Same as guidelines for "AV Access Flow Dysfunction–Confirmation And Treatment"

See Guideline 15. See Table 26.1 for clinical indicators of central venous stenosis.

Statement: Management of CVC Fibrin Sheath Associated With Clinical Problems

26.3 KDOQI considers it reasonable that when a CVC fibrin sheath is associated with adverse clinical manifestations (CVC dysfunction and/or infection), a CVC exchange with or without balloon disruption of the fibrin sheath should be performed. *(Expert Opinion)*

KDOQI CLINICAL PRACTICE GUIDELINE FOR VASCULAR ACCESS

Guideline 1. Patient First: ESKD Life-Plan

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Note: Expert opinion statements that allow for the use of "the clinician's discretion and best clinical judgment" mean that there is currently no rigorous evidence to recommend a therapy, device, or strategy over another. The Work Group expects ERT-derived evidence-based statements will ultimately replace expert opinion–based statements once such rigorous evidence becomes available. The clinician's discretion carefully considers both the patient's individual circumstances and the clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations).

Statements: ESKD Life-Plan and Vascular Access Choice

1.1 **KDOQI considers it reasonable that each patient with progressive CKD and/or with an eGFR 15-20 mL/min/1.73 m^2 or already on kidney replacement therapy should have an individualized ESKD Life-Plan that is regularly reviewed, updated, and documented on their medical record. (Expert Opinion)**

1.2 **KDOQI considers it reasonable to conduct an annual review and update of each patient's individualized ESKD Life-Plan, together with their health care team. (Expert Opinion)**

1.3 **KDOQI considers it reasonable that, in addition to regular monitoring, a minimum quarterly overall review and update of each patient's vascular access functionality, complication risks, and potential future dialysis access options be done together with their health care team. (Expert Opinion)**

Rationale/Background

Who Needs Consideration for Hemodialysis Vascular Access?

Patients with chronic kidney disease (CKD) who are either preparing to initiate hemodialysis (predialysis), transitioning from another kidney replacement modality (peritoneal dialysis [PD] or failing/failed kidney transplant), or are already on hemodialysis with a failing arteriovenous (AV) access or hemodialysis catheter (CVC) will need consideration for hemodialysis vascular access.

However, the actual need for hemodialysis vascular access (vs a peritoneal dialysis access or preparation for kidney transplantation) depends on the patient's current individualized End-Stage Kidney Disease (ESKD) Life-Plan and the corresponding kidney replacement therapy (KRT) modality choice and dialysis access (below). ***No decision about a single vascular access creation or placement should be made in isolation or independent of the patient's overall ESKD Life-Plan.***[15]

What Is the ESKD Life-Plan?

The ESKD Life-Plan is a strategy for living with ESKD, ideally made together by the patient and a coordinated CKD management team. For the purposes of dialysis access, this team should include but is not limited to the following professionals and supportive members: nephrologist, surgeon, radiologist, nurse, patient family member, or other supporter. The ESKD Life-Plan is a strategy that should start in the predialysis period and encompasses a continuum-of-care model for CKD to ESKD. It aims to maximize ESKD modality choices and utilization for a specific patient's foreseeable lifespan and specifically considers the patient's current medical situation, current and future life goals, preferences, social support, functional status, and logistics and other practical feasibilities.[16]

The ESKD Life-Plan maps out an individualized plan for ESKD modalities for a patient; in doing so, the dialysis access strategy is concurrently considered (Fig 1.1). It is an iterative process because events occur in one's life that may change the patient's medical, social, and other life circumstances and goals, with corresponding alterations in the patient's ESKD Life-Plan.

Detailed Justification

Prior guidelines and initiatives have emphasized a "fistula-first" approach to vascular access choice due to the AV fistula's (AVF's) associations with superior patency and lower complications compared with other vascular access types.[13,17] However, more recent data have challenged these associations because of the high complication rates of AVF maturation failure requiring interventions and, therefore, have prompted a re-evaluation of this Fistula First approach.[18-23] A patient-centered approach to hemodialysis vascular access that considers multiple aspects of a patient's needs and dialysis access eligibility has been emphasized.[20,24-27] Vascular access remains a significant challenge for patients with ESKD—we need to be creative in not only thinking about how to prepare for, create, and preserve durable long-term access but *equally important, be proactive in planning for the protection, creation, and preservation of the NEXT vascular access, long before the current one fails*. This chain of careful, continual consideration of modalities and dialysis access lifelines as it pertains to the individual patient's circumstances, needs, and preferences is the essence of the ESKD Life-Plan.

Special Discussions

This concept of the ESKD Life-Plan relies on clear, timely, and effective communication between the patient and their

family/personal supporters and key team members. As such, a kidney replacement modality and dialysis access short- and long-term plan (ESKD Life-Plan) should be updated on a regular basis. The frequency of re-evaluation depends on the patient's circumstances, but a minimum annual basis is expected.

Implementation Considerations

Choice of Dialysis Access

Because the dialysis access strategy reflects the ESKD Life-Plan, whereby the appropriate dialysis access aligns with the modality for kidney replacement therapy (dialysis or transplant), it must be individualized to help each patient achieve his or her life goals safely.

For example, a young active predialysis patient with residual kidney function might best initiate peritoneal dialysis with a PD catheter, in anticipation of a living donor kidney transplant; because that transplant eventually fails, this patient will receive a native AVF in view of starting home hemodialysis, and so on. In contrast, an older, more medically complex but functionally active patient may have started hemodialysis urgently with a central venous catheter, with plans to have a native AVF created, with a back-up plan of a synthetic arteriovenous graft (AVG) if the AVF fails to mature in a timely fashion, to avoid prolonged CVC dependence. Finally, a palliative patient may best be served with an early cannulation graft or CVC for shorter-term hemodialysis.

Guidance is provided by Figs 1.1 through 1.6.

Another supportive tool to help guide the choice of vascular access based on patient and vessel characteristics/circumstances is available at www.myvascularaccess.com.

Monitoring and Evaluation

Attainment of the "right access, in the right patient, at the right time, for the right reasons" is a more patient-centered approach to care, where population measures, such as percentage with AVF created or used, or the percentage with hemodialysis CVC *may be unhelpful* and *counterproductive* for patient-centered goals.

How does one achieve "the right access, in the right patient, at the right time, for the right reasons"? The Work Group suggests considering (1) the patient first, followed by (2) dialysis access needs—this is done by creating their individual P-L-A-N. See Fig 1.1.

Concurrently, there must always be a Vessel Preservation Plan, to ensure viability for future access. Therefore, for each vascular access, the Access Needs must include 4 plans: the Vessel Preservation, Insertion/Creation, Contingency, and Succession plans. This comprehensive plan for a patient's access needs can be remembered as *ViP ACCeS plans*: **V**essel **i**mportant **P**reservation, **A**ccess **C**reation, **C**ontingency, and **E**SKD access **S**uccession plans.

A number of measures can be used to monitor a dialysis facility, including the percentage of patients with a **P-L-A-N** on record.

Specific measures for each vascular access type can be found in Goals and Targets section of this document.

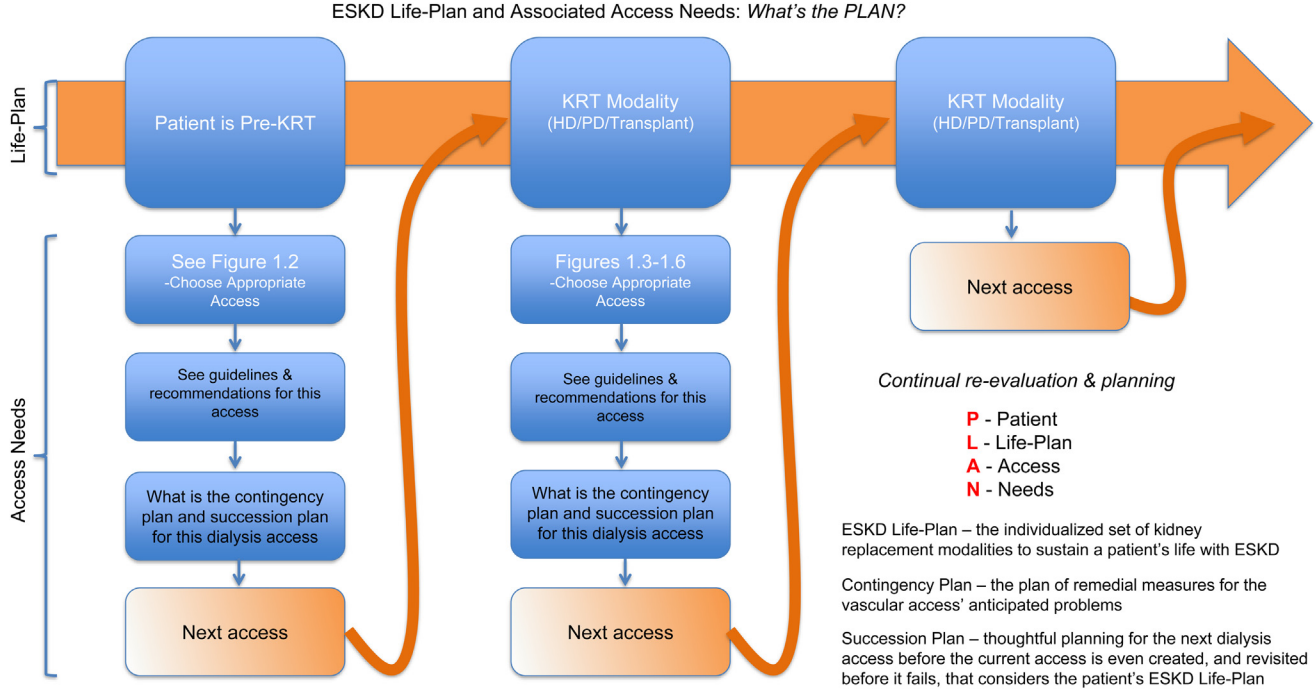


Figure 1.1. ESKD and Dialysis Access Life Plan: *What's the P-L-A-N?* Abbreviations: HD, hemodialysis; PD, peritoneal dialysis; KRT, kidney replacement therapy.

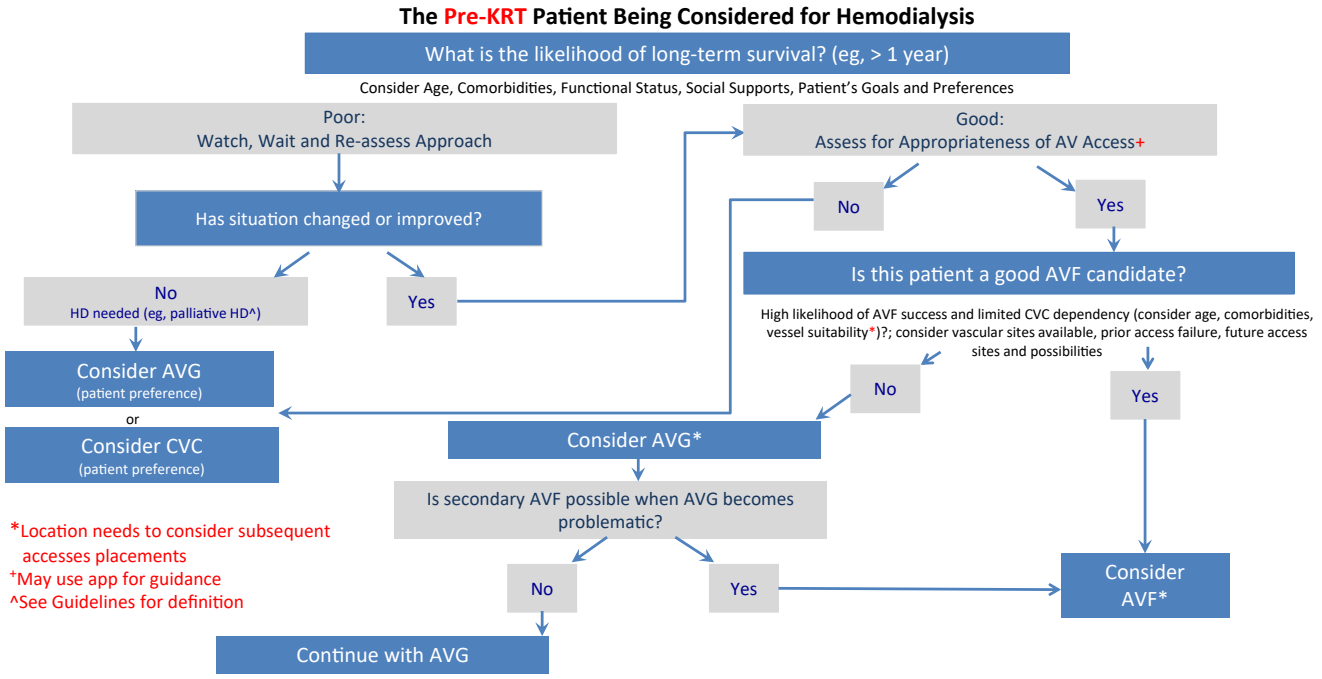


Figure 1.2. The pre-KRT patient being considered for hemodialysis. Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; CVC, central venous catheter; HD, hemodialysis; KRT, kidney renal replacement therapy; PD, peritoneal dialysis.

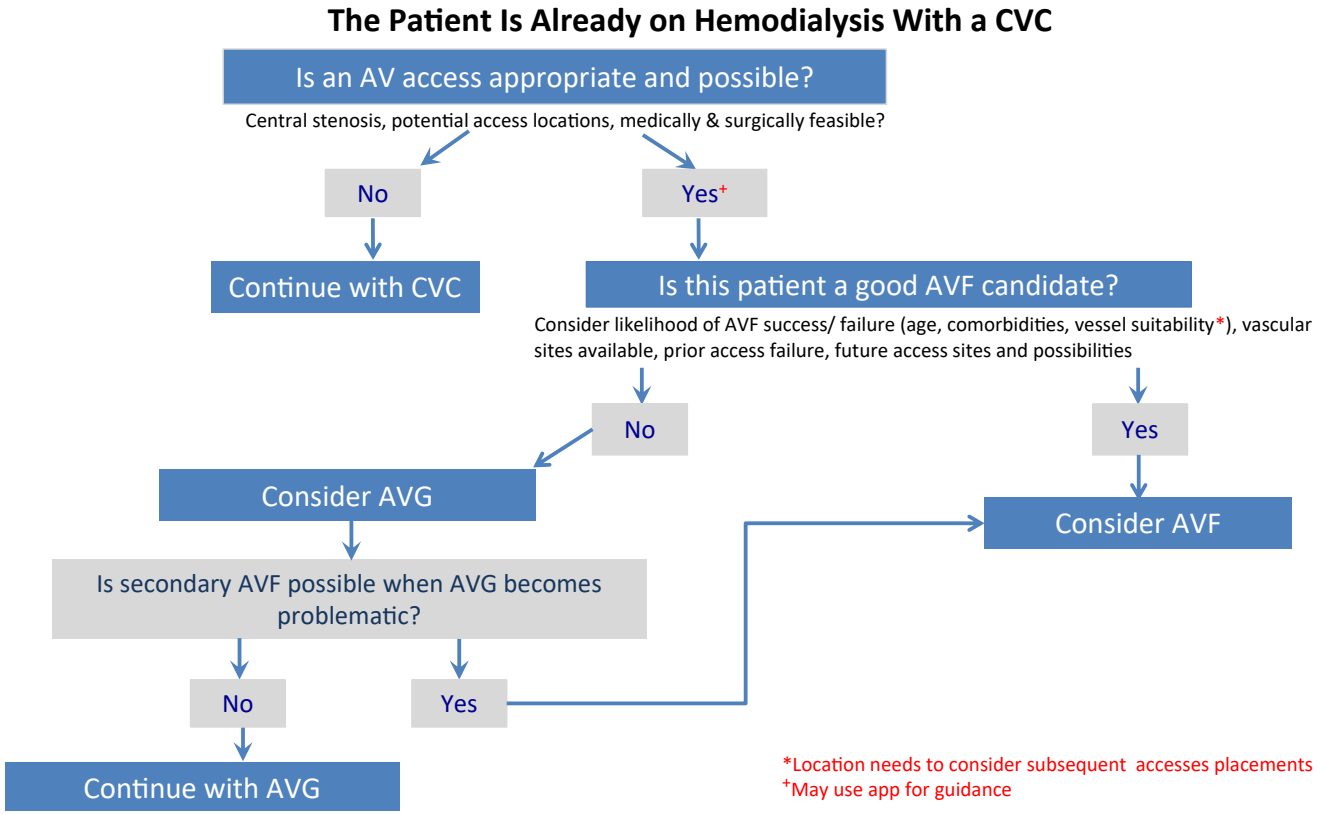


Figure 1.3. The patient is already on hemodialysis with a CVC. Abbreviations: AV, arteriovenous; CVC, central venous catheter.

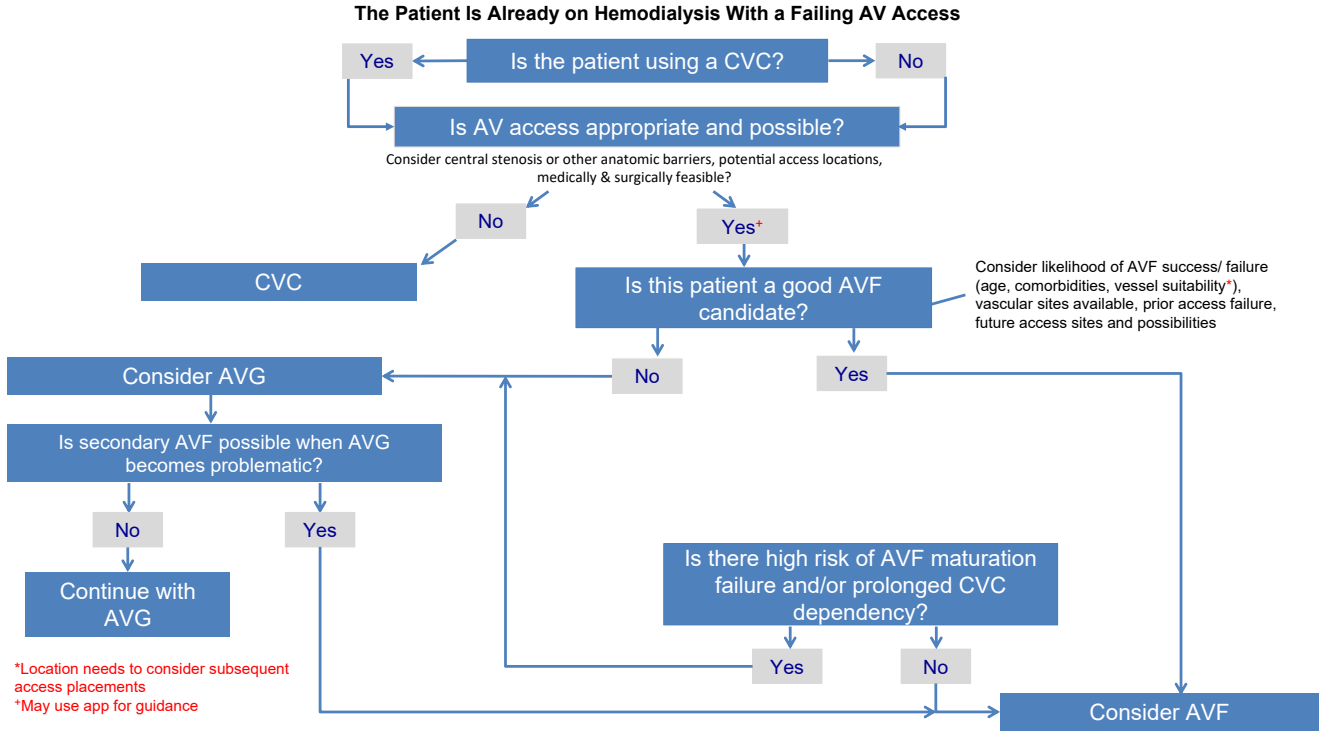


Figure 1.4. The patient is already on hemodialysis with a failing AV access. Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; CVC, central venous catheter.

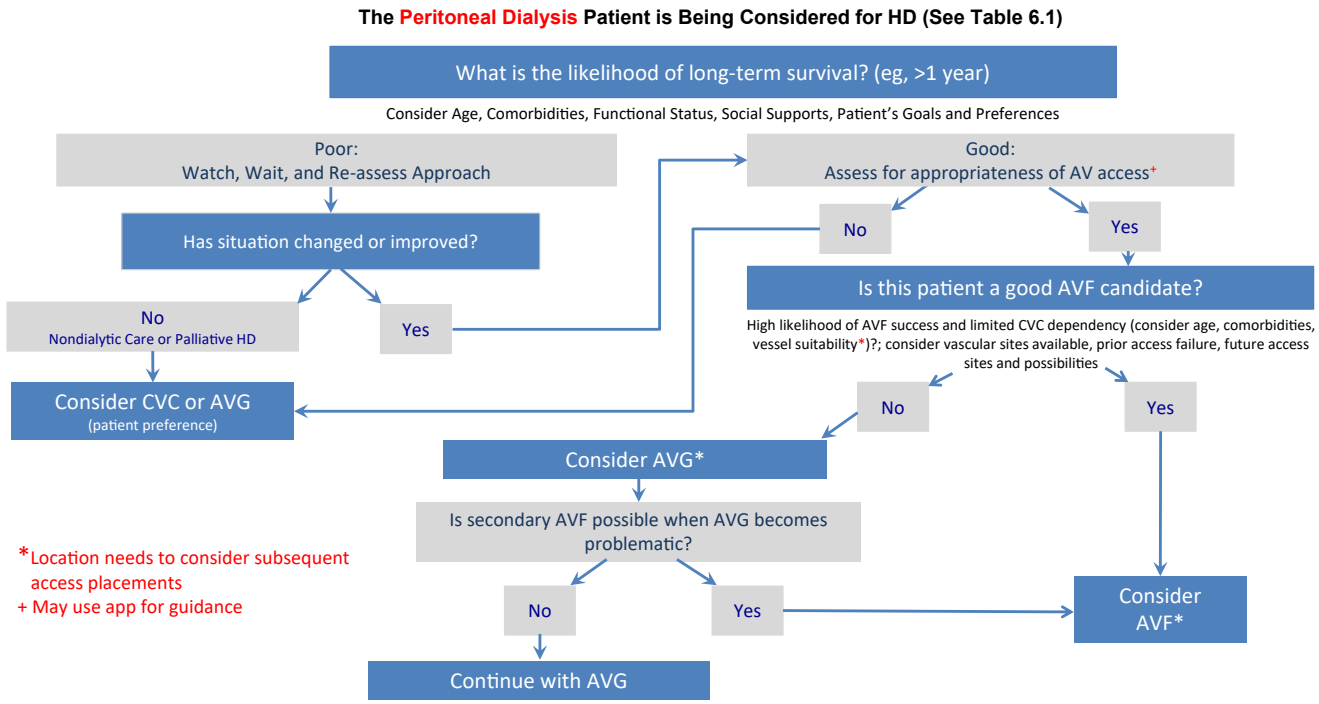


Figure 1.5. The peritoneal dialysis patient is being considered for HD. Abbreviations: AV, Arteriovenous; AVF, Arteriovenous fistula; CVC, Central venous catheter; HD, hemodialysis.

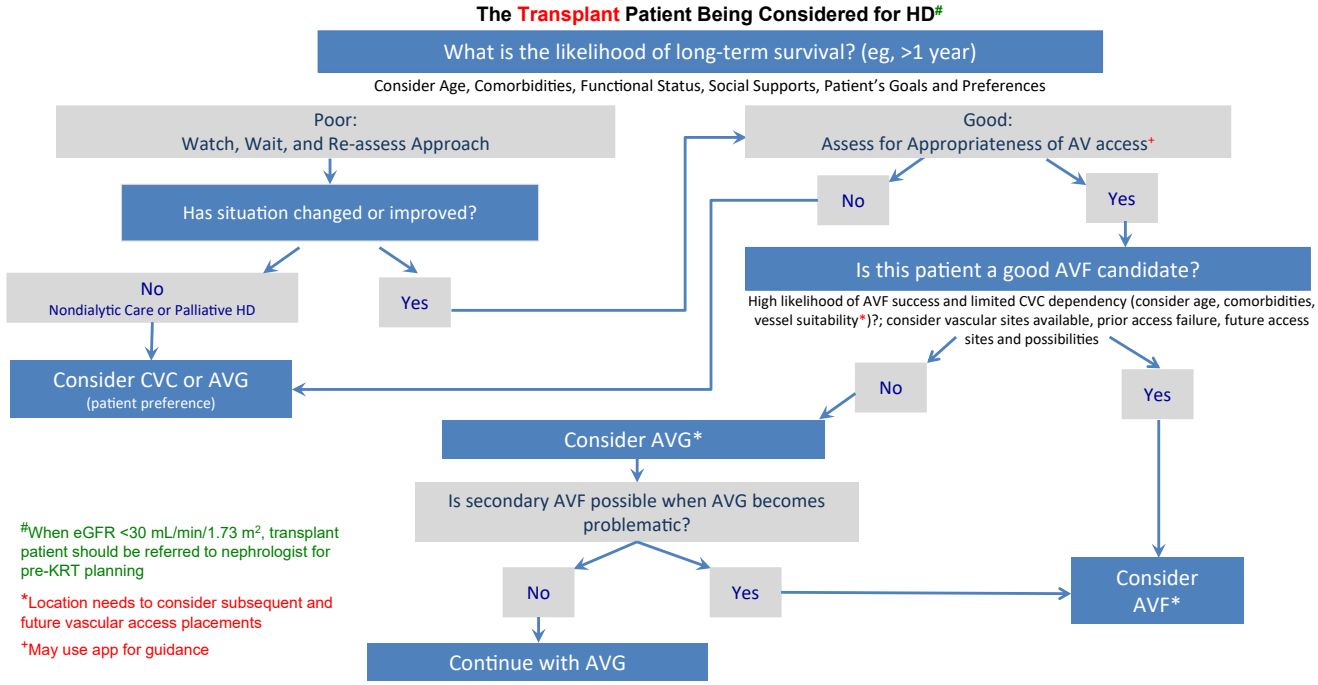


Figure 1.6. The transplant patient is being considered for HD. Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; CVC, central venous catheter; eGFR, estimated glomerular filtration rate; HD, hemodialysis; RRT, renal replacement therapy.

Who Should Update the ESKD Life-Plan and Associated Dialysis Accesses?

Ideally, the ESKD Life-Plan should be discussed with the patient within a multidisciplinary team framework (nephrologist, surgeon, interventionalist). If not feasible, the nephrologist should discuss modality options with the patient, with referral to surgeon/interventionalist for input on the appropriate dialysis access that corresponds to the chosen KRT modality.

Who Should Document the ESKD Life-Plan and Associated Access Changes?

The documentation of the ESKD Life-Plan should be the responsibility of the nephrologist and accompany the patient's medical record/chart.

A sample template can be found in **Supplement 2: ESKD Life Plan—Patient-Physician Shared Documentation.**

Future Research

The use of the ESKD Life-Plan strategy must be evaluated. Key outcomes should include

- Patient satisfaction with the dialysis access, using a validated instrument
- Rate of unnecessary dialysis access creations/placements
- Rate of vascular access procedures
- Rate of vascular access infections
- Rate of vascular access–related hospitalizations
- Patient burden, which may include all of the above components

Guideline 2. Vascular Access Types

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: AV Access: Indications for Use

2.1 **KDOQI considers it reasonable to have an AV access (AVF or AVG) in a patient requiring HD, when consistent with their ESKD Life-Plan and overall goals of care. (Expert Opinion)**

Note: See specific sections on incident and prevalent patients and the choice of AV access type and their appropriate locations

Statements: Central Venous Catheters (CVC): Indications for Use

2.2 **KDOQI considers it reasonable in valid clinical circumstances to use tunneled CVCs for short-term or long-term durations for incident patients, as follows (Expert Opinion):**

Short-term duration:

- **AVF or AVG created but not ready for use and dialysis is required**
- **Acute transplant rejection or other complications requiring dialysis**

- **PD patient with complications that require time-limited peritoneal rest or resolution of complication (eg, pleural leak)**
- **Patient has a living donor transplant confirmed with an operation date in the near future (eg, <90 days) but requires dialysis**
- **AVF or AVG complication such as major infiltration injury or cellulitis that results in temporary nonuse until problem is resolved**

Note: In special, limited circumstances where temporary CVC is required to manage a vascular access complication (eg, <2 weeks), it may be acceptable to use a nontunneled CVC.

Long-term or indefinite duration:

- **Multiple prior failed AV accesses with no available options (see anatomic restrictions below)**
- **Valid patient preference whereby use of an AV access would severely limit QOL or achievement of life goals and after the patient has been properly informed of patient-specific risks and benefits of other potential and reasonable access options for that patient (if available)**
- **Limited life expectancy**
- **Absence of AV access creation options due to a combination of inflow artery and outflow vein problems (eg, severe arterial occlusive disease, noncorrectable central venous outflow occlusion) or in infants/children with prohibitively diminutive vessels**
- **Special medical circumstances**

Statements: Vascular Access for Incident Patients

The statements below are in the context of the ESKD Life-Plan and associated Access Algorithms and their considerations, such as patient comorbidities, circumstances, etc (Figs 1.1-1.6).

2.3 **KDOQI suggests an AV access (AVF or AVG) in preference to a CVC in most incident and prevalent HD patients due to the lower infection risk associated with AV access use. (*Conditional Recommendation, Low Quality of Evidence*)**

2.4 **KDOQI considers it reasonable that the choice of AV access (AVF or AVG) be based on the operator's/clinician's best clinical judgment that considers the vessel characteristics, patient comorbidities, health circumstances, and patient preference. (*Expert Opinion*)**

2.5 **KDOQI suggests that if sufficient time and patient circumstances are favorable for a mature, usable AVF, such a functioning AVF is preferred to an AVG in incident HD patients due to fewer long-term vascular access events (eg, thrombosis, loss of primary patency, interventions) associated with unassisted AVF use. (*Conditional Recommendation, Low Quality of Evidence*)**

Note: Patient circumstances refer to vessel characteristics, patient comorbidities, health circumstances, and patient preference.

Note: Unassisted AVF use refers to an AVF that matures and is used without the need for endovascular or surgical interventions, such as angioplasty. A preplanned vessel superficialization is acceptable and not considered an additional intervention.

2.6 **KDOQI suggests that most incident HD patients starting dialysis with a CVC should convert to either an AVF or AVG, if possible, to reduce their risk of infection/bacteremia, infection-related hospitalizations, and adverse consequences. (*Conditional Recommendation, Very Low-Moderate Quality of Evidence*)**

2.7 **There is inadequate evidence for KDOQI to make recommendations on choice of incident vascular access type based on associations with all-cause hospitalizations or mortality.**

2.8 **There is inadequate evidence for KDOQI to make a recommendation on choice of AVF vs AVG for incident vascular access based on associations with infections, all-cause hospitalizations, or patient mortality.**

2.9 **There is inadequate evidence for KDOQI to make a recommendation for incident HD patients using a CVC on converting to an AV access (AVF or AVG) within the first year of dialysis initiation, solely to reduce their risk of mortality.**

2.10 **KDOQI considers it reasonable to use tunneled CVC in preference to nontunneled CVC due to the lower infection risk with tunneled CVC. (*Expert Opinion*)**

2.11 **KDOQI considers it reasonable to use nontunneled internal jugular CVC only for temporary purposes for a limited time period (<2 weeks or per individual facility policy) to limit infection risk. (*Expert Opinion*)**

Statements: Vascular Access in Prevalent HD Patients

2.12 **There is inadequate evidence for KDOQI to make a recommendation on the type of vascular access preferred in prevalent HD patients based on vascular access outcomes, patient hospitalizations, or mortality.**

2.13 **KDOQI considers it reasonable that prevalent HD patients use an AV access (AVF or AVG) in preference to a CVC, if possible, due to the association with lower vascular access–related events (eg, infection, thrombotic, and nonthrombotic complications). (*Expert Opinion*)**

2.14 **KDOQI considers it reasonable that if clinical circumstances are favorable for a mature, usable**

AVF, such a functioning AVF is preferred to AVG in prevalent HD patients. (Expert Opinion)

Note: Clinical circumstances refer to patient's vessel characteristics, comorbidities, health circumstances, potential exposure time to CVC use, and patient preference.

2.15 **KDOQI considers it reasonable in valid clinical circumstances to use tunneled CVCs for short-term or long-term durations in prevalent dialysis patients, as follows (Expert Opinion):**

Short-term duration:

- **AVF or AVG created but not ready for use and dialysis is required**
- **Acute transplant rejection or other complications requiring dialysis**
- **PD patient with complications that require time-limited peritoneal rest or resolution of complication (eg, pleural leak)**
- **Patient has a living donor transplant confirmed with an operation date in the near future (eg, <90 days) but requires dialysis**
- **AVF or AVG complication such as major infiltration injury or cellulitis that results in temporary nonuse until problem is resolved**

Note: In special, limited circumstances where temporary CVC is required to manage a vascular access complication (eg, <2 weeks), it may be acceptable to use a nontunneled CVC.

Long-term or indefinite duration:

- **Multiple prior failed AV accesses with no available options (see anatomic restrictions below)**
- **Valid patient preference whereby use of an AV access would severely limit QOL or achievement of life goals and after the patient has been properly informed of patient-specific risks and benefits of other potential and reasonable access options for that patient (if available)**
- **Limited life expectancy**
- **Absence of AV access creation options due to a combination of inflow artery and outflow vein problems (eg, severe arterial occlusive disease, noncorrectable central venous outflow occlusion) or in infants/children with prohibitively diminutive vessels**
- **Special medical circumstances**

Rationale/Background

Incident Patients

Ideally, a CKD patient will have been properly educated about KRT modalities and will have made an informed choice in a timely manner to allow for planned HD start with the appropriate dialysis access—*to achieve the right access, in the right patient, at the right time, for the right reasons*. However, prior to executing the plan to create or insert the chosen vascular access, the "contingency access plan and succession strategy" for the chosen dialysis access must be considered that incorporates the patient's various ESKD Life-Plan options (Guideline 1). The contingency plan is a plan to remediate a problematic or failing dialysis access, and the succession strategy is the preparation and planning of the next dialysis access so that it can be used when the current one fails, to ensure continual functioning dialysis access throughout the patient's life.

Incident dialysis patients are often overwhelmed by dialysis initiation and the lifestyle changes required. If the dialysis initiation is urgent or emergent, the patient may not have had a choice of vascular access and initiated with a CVC. However, once circumstances are stabilized, long-term vascular access must be carefully considered and pursued. The long-term choice of vascular access should consider the patient's current and future ESKD Life-Plan (Guideline 1).

Given these considerations, we recognize that prior guidelines generally supported the notion that the AVF was associated with improved outcomes (superior patency, lower complications, lowest cost)[13] compared with an AVG or CVC. The previous guideline statements were based on older evidence and analytic concepts. We now recognize the significant biases associated with the prior data, given newer data and analytic considerations. As an example, prior patency comparisons of AVFs versus AVGs evaluated only AVFs that were successfully used and excluded AVFs that had primary failure or were abandoned without use.[28,29,30] The impact of concluding AVF "superiority" led to the creation of many AVFs that were not usable for dialysis[31-33]. Any vascular access not usable for dialysis should be considered a complication attributable to that vascular access. Thus, this bias in analysis affects the findings of superiority of both AVF patency and complication rate. Additionally, multiple biases exist in comparisons of CVC with either an AVF or AVG.[34-36] The most apparent is the selection bias found in patients who have significant comorbidity and poor vessels who may not be eligible for an AV access or for whom their social, functional, or other circumstances are so poor that an emergent dialysis start with CVC is necessary—these confounding factors may be the very factors responsible for poor outcomes and not necessarily the use of the CVC per se. The repercussions of such biases are many, including the potentially misleading association of mortality and VA type, with CVC associated with the worse mortality. Although, indeed, each VA type has unique advantages and disadvantages—and the disadvantages of CVC may contribute to poor patient outcomes—the true magnitude of this effect is not certain in view of the selection bias and confounding effects inherent in the observational data that informed the previous guidelines.

The past decade has brought insight regarding the effect of changing patient characteristics; health care environments; processes, measurements and definitions surrounding dialysis delivery; and data analytic techniques—all of which influence hemodialysis vascular access choice and management. This Guideline attempts to consider these insights and bring a fresh slate to revisit vascular access choice and management.

Table 2.1. Access Type Comparison Studies Reviewed

Comparison	Number of Studies	References
AVF or AVG vs CVC	19	37-39,41-44,46,49,50,55,56,60-63,65,66
AVF vs AVG	8	18,21,30,40,41,45,53,54,59
AVG (thigh) to CVC	1	58
AVF (upper extremity) vs AVG (lower extremity)	1	47
No change in access type vs change in access type	4	51,52,57,64

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; CVC, central venous catheter.

Guideline 3 will discuss the location or site of vascular access creation/insertion after the type of vascular access is chosen.

Studies Evaluated for Incident and Prevalent Patients

These guidelines reviewed 33 reports of 32 observational studies evaluating different vascular access types in incident and prevalent patients using prospectively collected data from clinical or administrative databases or registries; however, no RCTs met predefined search criteria relevant to this Guideline (Supplement 3, Table S1).[18,21,30,37-66] The references to these studies are summarized in Table 2.1.

In addition, 4 studies were superseded by other studies using a more recent series of the same cohort and reporting the same outcomes[38,41,44,62]; 7 studies contributed less than 3% to the total population for a specific comparison[37,40,45,46,49,54,63]; and 6 studies had high risk of bias.[21,30,43,47,58,64] Data from those studies were not extracted or used in analysis. Thus, data from 16 studies were extracted and analyzed (Supplement 3, Tables S2 and S4). Although the ERT attempted to pool data for analysis to provide information to make recommendations, it may not have been possible due to differences in outcome definitions. For example, in comparisons between AV access types, there was variation in the start time for time-to-event analysis (eg, patency calculation) such that some analyses started ($t = 0$) when the vascular access was successfully cannulated and used but others started ($t = 0$) at the time of creation. As discussed, such methodologic differences are important to consider when interpreting the data.

Detailed Justification

Vascular Access in Incident Patients

Four studies[48,55,56,65] (total n = 570,003 incident HD patients) reported on the associations of vascular access type and bloodstream infection or mortality. Bloodstream infections were significantly lower among patients starting HD with an AVF (6.4%) versus a CVC (15%) (hazard ratio [HR], 0.28; 95% confidence interval [CI], not reported; $P < 0.001$; unadjusted relative risk [RR], 0.43; 95% CI, 0.38-0.48) or an AVG (7.5%) versus a CVC (15%) (HR, not reported; $P < 0.001$; unadjusted RR, 0.50; 95% CI, 0.41-0.60).[65]

Although AVF or AVG was associated with lower mortality compared with CVC (Fig 2.1), the evidence quality was low with moderate risk of bias; thus, choice of vascular access type should not be based on mortality risk associations alone.

This caution holds true even when considering age as an effect modifier. Three studies examined 127,389 incident HD patients, focusing on mortality outcomes among older patients.[42,61,66] Mortality was significantly lower with an AVF or AVG versus a CVC among patients <80 years old; findings were inconsistent in analysis of patients >80 years old.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S1-S7.

Vascular Access in Prevalent Patients

Three studies enrolled a total of 82,657 prevalent HD patients with at least 12 months of follow-up from the United States, Spain, and Scotland.[39,50,60] The quality of evidence was insufficient to determine associations between vascular access type and hospitalizations or mortality. Only 1 study reported primary patency,[60] which was described as "first vascular access event": 86% for AVF, 51% for AVG, and 56% for CVC at 1 year ($P < 0.001$).[60] However, the reporting of vascular access events was rated as having moderate risk of bias. Furthermore, there were no details on whether vascular accesses were first or subsequent accesses and practice patterns have since changed (prevalent cohort began treatment 1999-2001 in the study by Portoles et al[60]). Thus, the Work Group decided against making KDOQI recommendations based on these data. Recent studies have highlighted concerns of selection bias and its potential impact on outcomes.[19,34,35,67-69]

In specific comparisons of AVF versus AVG, vascular access events (thrombosis, AVG repair, or hospitalization for a vascular access problem [unadjusted RR, 0.27; 95% CI, 0.20-0.36] in Portoles et al[60] or for any cause [HR, 0.81; 95% CI, 0.79-0.83] in Lacson et al,[50] were lower with an AVF than an AVG. Mortality was also lower with an AVF than an AVG (HR, 0.89; 85% CI, 0.84-0.93) in Lacson et al.[50] Again, due to the poor quality of the evidence, the Work Group decided against making KDOQI recommendations based on these data.

Tables of studies, evidence quality, and bias are provided in Supplement 3, Tables S1-S4 and S10.

The quality concerns noted by the ERT are further supported by recent studies highlighting the considerable biases in prior studies comparing vascular access types, vascular access complications, and patient outcomes.[34-36,67-69] The uncertainty generated by the observational data informed the Work Group in reframing the previous 2006 KDOQI guideline and is reflected by the following:

1) The differences in AVF and AVG patency are uncertain and depend on the starting time of analysis, as originally noted in early observations of AVF patency.[70]

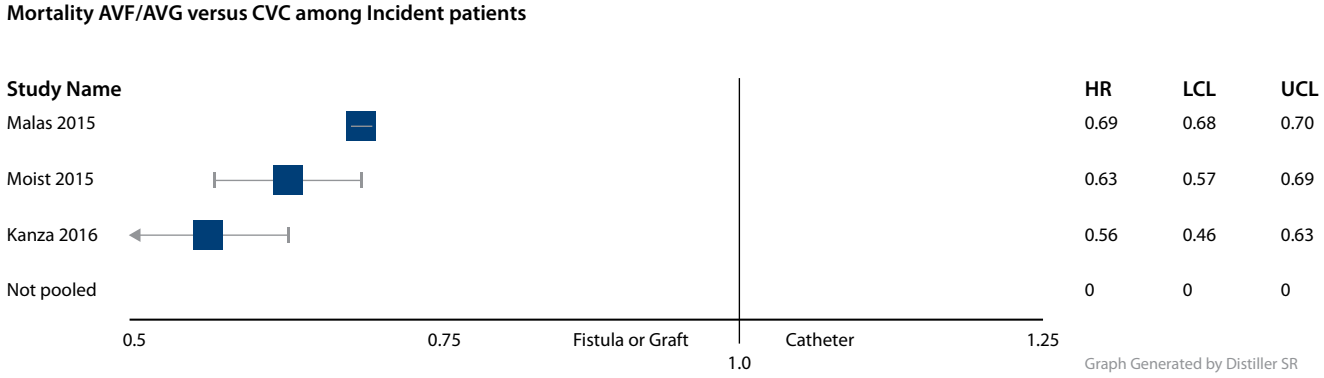


Figure 2.1. Hazard ratio for mortality with AVF or AVG versus catheter among incident HD patients. When HRs were reported as catheter versus AVF/AVG, ratios were inverted for consistency within display. Data were not pooled but are presented here for display only. Plot was made using DistillerSR Forest Plot Generator from Evidence Partners. Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; HR, hazard ratio; LCL, lower confidence limit; UCL, upper confidence limit.

Subsequent studies have demonstrated equivalency of AVF and AVG patency.[30,71-73]

2) There are few RCTs informing the comparisons of AVF versus AVG; those that have been done in fact demonstrate that there may be benefit of AVG, including in patients with poor vessels and greater comorbidity than in those with AVF.[74,75]
3) The statement that AVFs may have fewer complications compared with AVGs may not be generalizable to all AVFs and AVGs and may further depend on what constitutes a complication. The increase in AVF creation has identified a significant and variably high rate of AVF failure to mature or nonusability for dialysis (20%-60%).[14,17,24,30,33,76,77] This nonusability for dialysis should be considered a complication, particularly because it requires interventions (eg, angioplasty, balloon-assisted maturation [BAM], ligations, etc) to facilitate its use and/or CVC insertion if dialysis is needed. Any need for an unintended intervention, including CVC insertion, should be considered a complication. This is well known for AVG thrombosis and the required corrective interventions (angioplasty, thrombectomy, or surgical revision). In general, complications occur early in AVFs and later in AVGs—the total rate of complications for AVFs or AVGs has not been compared. This is particularly important when considering the required lifespan of an AV access to serve the patient, according to their ESKD Life-Plan. See case examples.

Special Discussions

When analyzing vascular access outcomes, it is important to clarify the "incident/prevalent" designation. In some studies, the "incident/prevalent" status refers to the *patient's* status—*not* the vascular access status. The vascular access used in an incident dialysis patient may not necessarily mean it was the patient's first access. For example, an incident patient starting dialysis with a CVC may have had a prior failed AVF. Similarly, an incident HD patient using an AVF may have had a prior failed AVF; the behavior of a first versus a subsequent access and the impact on the patient may differ.

Clearly, the implications of both the patient status (as incident or prevalent on dialysis) and of the vascular access (as first or subsequent) are related; however, their relative contributions to the outcome of interest are unclear and likely to depend on clinical circumstances. For example, at time of analysis, a prevalent hemodialysis patient who has a successful functioning AVF as the "first" vascular access is different than a prevalent dialysis patient who has had multiple failed AVFs and is now analyzed with a CVC as the "prevalent" (or "subsequent") vascular access—both patient and vascular access outcomes would likely differ, even though they are both considered "prevalent." These analyses do not provide information in that regard, and the associative findings should be considered in that light.

To further complicate matters, the definitions of important vascular access outcomes (such as "patency") have been highly inconsistent, making it challenging, if not impossible, to make valid comparisons between vascular access types and between studies.[1,78] For example, as discussed under vascular access for incident patients, prior patency comparisons of AVFs versus AVGs evaluated only AVFs that were successfully used and excluded AVFs that had primary failure or were abandoned without use.[29,33] The impact of concluding AVF superiority on this premise led to the creation of many AVFs that were not usable for dialysis.[30,33,76] Any vascular access not usable for dialysis should be considered a complication attributable to that vascular access. Thus, this bias in analysis affects the findings of both AVF patency superiority and complication rate.

The current KDOQI Guidelines on the choice of vascular access in prevalent patients reflect the prior inconsistencies in definitions and biases in analyses and interpretation in the existing literature. Future research is recommended to provide the necessary data required to make recommendations on type of vascular access for incident and prevalent patients in need of first or subsequent accesses. Please see the Research Recommendations section.

Implementation Considerations

See Fig 2.2.

It is important to emphasize that the primary goal of vascular access creation and planning is to create a functional vascular access that can provide reliable prescribed dialysis, with minimal interventions and complications.[15,79]

Please see the section on "KDOQI Vascular Access Guidelines Goals and Targets." The outcomes of AV accesses that have required interventions before use may have a different natural history than those not needing interventions (unassisted matured AV accesses). Further comparative study is required; until such time, caution should be made in generalizing the outcomes of AVF and AVG noted in prior literature that have not taken this into consideration.[1]

Special Populations: Pediatrics

The choice of vascular access for pediatric HD patients must take a number of factors into account. For incident patients with an unplanned dialysis initiation and who desire HD for KRT, a CVC will be necessary irrespective of age, body habitus, venous anatomy, or comorbidities.

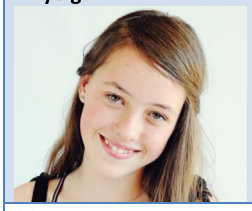
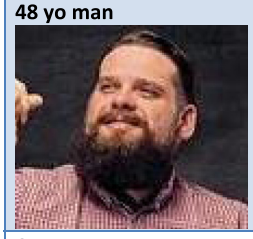
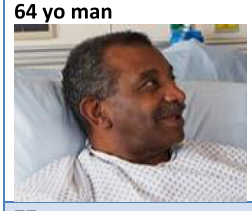
Case	Description	ESKD Life-Plan Modality Choice	Dialysis Access	Comments
14 yo girl 	Congenital cause of kidney damage, CKD nondialysis (eGFR 22 mL/min) has living donor for transplant, active – wants to be a teacher, right handed	1. Living donor transplant 2. PD 3. Home NHD	1. Transplant - NA 2. PD catheter 3. RC-AVF (left)	• Follow closely, long life anticipated • Flexibility required - Life-Plan may change • Life-Plan must consider multiple modalities and optimize dialysis access
26 yo woman 	GN, on HD; failed PD with temporary CVC, has potential living donors, actively working during day, R hand dominant	1. Home NHD 2. Transplant	1. RC-AVF (left) 2. BC-AVF (left)	Anticipating patient will get transplant – reassess annually for change in Life-Plan and AV access needs
48 yo man 	DM, HTN, AFib, obese. Copes poorly and non-adherent to medical management and presented needing to urgently start HD, works in outdoor maintenance, L handed	1. IC-HD 2. Transplant wait list 3. PD may be possible later	1. Early cannulation forearm loop graft (right) 2. BC-AVF 3. PD catheter	IC-HD most appropriate; poor self care makes patient poor home PD or HD candidate – may change over time – reassessment necessary
64 yo man 	HTN, PCKD; ESKD on HD x7 years; R handed; Jehovah witness; sudden loss of RC-AVF (left)	1. IC-HD 2. PD may be possible	1. CVC (left, IJ) 2. BC-AVF (R) 3. PD catheter	Transplant not an option due to personal reasons; continue to preserve site for future HD access; patient reluctant to consider PD due to poor home situation
77 yo woman 	Frail, DM, CAD, PVD, urgently started dialysis, with CVC, lives alone, R handed	1. IC-HD 2. PD may be possible	1. BC-AVF (left) 2. Upper arm graft (left) 3. PD catheter	Patient likely has limited life expectancy; focus on AV access and limiting CVC dependency vs preserving sites for future access
88 yo man 	Palliative patient and very frail but still enjoys time with family	1. IC-HD	1. CVC (right IJ)	Patient preference for CVC vs graft for palliative patients

Figure 2.2. ESKD Life-Plan case examples. Abbreviation: ESKD, end-stage kidney disease.

Placement of CVC may be required in patients with small or diminutive vessels that are not suitable for an AVF or AVG, but this should be considered a "bridge" or midterm solution until the vessel, sizes are adequate. There is no specific size cutoff in terms of weight or vessel diameter in this setting, and, thus, the timing for access creation (AVF or AVG) should be based on patient circumstances and local expertise. The use of CVC is associated with higher risk of bloodstream infections, greater hospitalization rates and antibiotic use with potential nephrotoxic effects on residual kidney function, and damage to central vessels making future AV access creation difficult. As such, pediatric dialysis centers must be committed to insightful best care for their patients—this current year and next as an integral part of their ESKD Life-Plan, which will include HD, transplant, and PD. The choice of AVF is preferred over AVG but may be dictated by available vascular anatomy, other clinical factors, and local surgical expertise for AV access creation and interventional radiology expertise for maintaining AV access function. The benefit margin of AVF over CVC in pediatrics has been well documented.[79-80] However, evidence demonstrating the superiority of AVF over AVG, is less available in the pediatric hemodialysis patient.[81]

The best first strategy is CVC avoidance followed by CVC minimization. Furthermore, for patients/families who are eligible and desire PD (even if needed acutely), urgent placement of a PD catheter is recommended to avoid the risks and long-term morbidities associated with CVC placement, even if used only for a few weeks to months.[83]

Future Research

- Studies evaluating first versus subsequent accesses
- RCT of various types—this is critical but challenging and may be impossible
- Consider complication rate as an outcome (define what is viewed as a complication— eg, for AVFs that fail to mature, use of a CVC may be deemed a complication, etc)
- Validation of standardized definitions for patency and complications

Guideline 3. Vascular Access Locations

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: AV Access Locations

The statements below are in the context of the ESKD Life-Plan and associated Access Algorithms and their considerations (eg, feasible anatomy, etc).

Note: See Guideline Statements 2.2 and 3.2 for CVC use and location; this section refers to AVF or AVG.

3.1 **KDOQI considers it reasonable to choose the site (location) of the AV access (AVF or AVG) after careful consideration of the patient's ESKD Life-Plan (Figs 1.1-1.6), potentially following the below paths (Expert Opinion). *See Guideline Statement 3.2 for CVC locations*:**

A) **A patient's ESKD Life-Plan includes an anticipated *long duration* (eg, >1 year on HD):**
- **Forearm AVF (snuffbox or distal radiocephalic or transposed radiobasilic)**
- **Forearm loop AVG or proximal forearm AVF (eg, proximal radiocephalic, proximal vessel, and perforator combinations) or brachiocephalic, per operator discretion**
- **Brachiobasilic AVF or upper arm AVG, per operator discretion**

B) **A patient's ESKD Life-Plan includes an anticipated *limited duration* (eg, <1 year) on HD:**
- **Forearm loop AVG or brachiocephalic AVF (with high likelihood of unassisted maturation)**
- **Upper arm AVG**

C) **A patient urgently starts HD without prior sufficient time to plan for and/or create an AV access and has an anticipated *limited duration* (eg, <1 year) on HD:**
- **Early or standard cannulation loop AVG (forearm or upper arm location), or CVC, *per operator discretion and patient's clinical needs***

Note: The choice of upper extremity location of an AVG should be based on the operator's discretion and best clinical judgment considering the patient's ESKD Life-Plan, due to inadequate evidence to demonstrate a difference between forearm versus upper arm AVG patency or complication outcomes (including infections, hospitalizations, and mortality).

D) **A patient urgently starts HD without prior sufficient time to plan for and/or create an AV access and has an anticipated long duration (eg, >1 year) on HD:**
- **PD catheter, and follow above algorithm (A) if PD not a long-term option or**
- **Forearm early cannulation loop graft; when AVG fails, follow above algorithm (A) or**
- **CVC if high likelihood of rapid AVF maturation and usability success, then follow above algorithm (A)**

E) **All AV access options in the upper extremity have been exhausted and patient's ESKD Life-Plan includes a *long duration* (eg, >1 year) on HD, the following may be considered based on individual patient circumstances and operator's best clinical judgment and expertise:**

- **Lower extremity AVF or AVG or HeRO Graft**

While a suggested stepwise approach to AV access site selection is provided (Figs 1.1-1.6), modification of the approach is encouraged as necessary to consider the individual's ESKD Life-Plan and circumstances, and follow the below key principles, given available suitable vessels:

- *Distal first to proximal next approach*
- *Always preserve the integrity of vessels for future vascular access options*
- *Nondominant extremity in preference to dominant, only if choices are equivalent*

Statements: CVC Locations

3.2 **KDOQI considers it reasonable to choose the site (location) of the CVC after careful consideration of the patient's ESKD Life-Plan as follows (*Expert Opinion*):**

- **Upper extremity before lower extremity, only if choices are equivalent**
- **There are valid reasons for CVC use (Guideline Statement 2.2) and its duration of use is expected to be limited (eg, <3 months):**
  - **AV access is likely to be ready for use in near future—consider preferential use of tunneled cuffed CVC in opposite extremity to anticipated AV access**
  - **Transplant is anticipated in near future (ie, preserve iliac vessels) —consider preferential use of tunneled cuffed right IJ catheter**

Note: See below guidance for more details on CVC location.

- **Some experts support that in urgent dialysis start situations, under limited use circumstances (eg, <1 month) and transplant is not an option, use of a tunneled, cuffed femoral CVC is acceptable (unless contraindicated) until the AV access or PD catheter can be quickly created and used. Use of the femoral vein preserves the upper extremity vessels for future AV access creation.**

Note: Contraindications to femoral vein CVC include femoral or iliac vessel pathology or prior surgery/reconstruction; hygienic reasons (eg, chronic unresolved diarrhea), morbid obesity (BMI>35 kg/m^2), or other difficult vein access.

- **When there are valid reasons for CVC use (Guideline Statement 2.2) and duration of use is expected to be prolonged (eg, >3 months) without anticipated use of AV access, CVC may be placed in the following locations in order of preference:**
  - **Internal jugular**
  - **External jugular**
  - **Femoral**
  - **Subclavian**
  - **Lumbar**

Note: In the absence of contraindications, prior pathology (eg, central stenosis) or intervention (eg, pacemaker) CVC insertion on the right side is preferable to the left side due to more direct anatomy. If one side has pathology that limits AV access creation but allows for CVC insertion, this side should be used for the CVC to preserve the other side for AV access creation.

Rationale/Background

Patients with CKD/ESKD are surviving longer with variable ESKD Life-Plans,[83] made possible by optimizing the use of all modality options. High rates of AVF maturation failure, recurrent thrombosis of AVGs, and CVC-related infections and central stenosis have made the planning of vascular access and preservation of vascular access sites a top priority for ESKD care.

Hemodialysis vascular access planning must consider both the *type* and *location* of the vascular access, keeping in mind both the current needs and the future needs of the patient. Each selection of vascular access (type and location) should provide the patient with a functional vascular access that is reliably usable for dialysis with minimal complications and interventions to allow the patient to achieve his/her dialysis goals. The vascular access contingency plan is the plan for vascular access remediation when the vascular access becomes problematic. The vascular access succession plan is the thoughtful planning and preservation for future dialysis access choice(s) when the current vascular access fails, and it considers the patient's ESKD Life-Plan.

For patients expected to have prolonged durations on HD, a distal-to-proximal approach to AVF creation (if they are deemed suitable) preferentially using the superficial veins or consideration of a forearm graft (if deemed not suitable for a forearm AVF) before upper arm AV access provides the best opportunity to preserve vessels for future vascular access sites (Table 3.1). It allows for a sequential vascular access plan for a prolonged ESKD Life-Plan on HD. However, it has been recently observed that an unintended consequence of the enthusiasm for a fistula-first approach to vascular access has led to an increasing number of upper arm AV accesses in the United States,[84] perhaps with the sole goal of reaching "fistula targets," which may inadvertently and negatively affect a patient's future vascular access options. For example, younger individuals who are expected to have long survival with ESKD might be disadvantaged by the decision to create bilateral upper arm

Table 3.1. Vessel Location by Distal to Proximal Sites

Vessel Location/ Cannulation Location	AVF	AVG
Forearm/ forearm	Snuffbox or distal radiocephalic forearm radial or ulnar basilic	Forearm loop
Forearm/upper arm	Proximal radiocephalic, antecubital vessel-perforator combinations	
Upper arm/ upper arm	Brachiocephalic	Upper arm straight
	Brachiobasilic	Upper arm loop
	Other brachial or basilic combinations	

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft.

AVF—especially basilic vein transposition—as the first (failed) and then second options for vascular access. Doing so would significantly limit their future vascular access possibilities, leaving them with suboptimal options for the remainder of their life on HD. Furthermore, failed AV access or urgent HD starts that require CVC insertion may later negatively affect vascular access options if the placed CVC contributes to the limiting effect of central stenosis. Careful consideration of the site of CVC insertion in such situations is required. Thus, this KDOQI Work Group has proposed a sequence of site selections that considers the patient's ESKD Life-Plan with a view to individualizing and optimizing access options.

Much of this KDOQI's guidance aligns with the previous KDOQI Guidelines (2.1) that recommended evaluation of the distal forearm for radiocephalic AVF followed by brachiocephalic AVF before considering brachiobasilic transposition AVF or AVG. It considered an AVG as a bridge to an AVF. The current Guideline promotes consideration of other variables such as preparation time available, expected time on dialysis, current and future modality options (eg, transplant), likelihood of AVF success, and vascular access contingency and succession plans for each vascular access type and location selected.

Detailed Justification

One RCT[85] and 8 observational studies evaluated different vascular access locations.[86-94] The RCT compared a brachiobasilic AVF to a brachiocephalic AVF among patients in whom a previous forearm AVF had failed or a forearm AVF was not feasible.[86] Primary patencies were not significantly different with a brachiobasilic AVF versus a brachiocephalic AVF at 1 year (RR, 0.98; 95% CI, 0.84-1.34) or 3 years (RR, 0.90; 95% CI, 0.73-1.11) (Supplement 3, Table S11).[85] Similarly, secondary patency was not significantly different with a brachiobasilic AVF versus a brachiocephalic AVF at 1 year (RR, 1.02; 95% CI, 0.88-1.19) or 3 years (RR, 1.02; 95% CI, 0.80-1.32; P = 0.8) in Koksoy et al[85] (Supplement 3, Table S11). Given these data, the Work Group supports a philosophy to create the most optimal AVF that would preserve future sites and allow greatest patient ease and comfort for cannulation and dialysis.

One observational study compared AVFs placed ipsilateral to a prior CVC versus contralateral to a prior CVC.[93] Secondary patency was significantly lower with an AVF ipsilateral to a prior CVC versus contralateral to a prior CVC (Supplement 3, Table S12), leading to the suggestion to insert a CVC contralateral to the planned AV access, should a CVC be required. Seven of the observational studies compared various AVF locations, including radiocephalic, brachiocephalic, brachiobasilic, or unspecified upper arm or forearm. Three studies[86,87,91] had high risk of bias (Supplement 3, Table S13)[86,87,91] and were not extracted or used in analysis. The studies used are in Supplement 3, Table S14.[85,88,89,92-94] Due to the poor quality and inconsistent evidence, we were unable to place it into clinical context to recommend a stepwise approach to vascular access creation, leading to suggestions to consider vascular access type and location that would provide the patient with functional use, preserving future sites at the discretion of the clinician after considering the patient's circumstances, available suitable vessels, and ESKD Life-Plan.

AVG Locations

If an AVG is the most appropriate type of vascular access, the evidence does not strongly support a preference of location. Dixon et al[96] compared forearm AVG with upper arm AVG in a subgroup analysis of an RCT that evaluated the effect of dipyridamole plus aspirin on AVG patency (n = 508) (Supplement 3, Table S15). Both primary and cumulative patencies did not differ by location at 1-year follow-up (Supplement 3, Table S16a). Primary patency was 70% in the forearm AVG group and 78% in the upper arm AVG group. Cumulative graft failure was 33% and 36% for the forearm AVG and upper arm AVG groups, respectively (adjusted HR, 1.36; 95% CI, 0.94-1.97). No other studies met the criteria for inclusion by the ERT.

CVC Locations

As noted, inferior AVF outcomes have been observed if a prior ipsilateral CVC has been placed.[94] However, there are lower complication risks with right internal jugular CVC insertion compared with the left side, so this must be considered in light of the patient's ESKD Life-Plan and current and future vascular access needs. One observational study compared right- versus left-sided catheter placement[98] (409 participants and 532 catheters). Catheter-related infection requiring removal was significantly higher with left-sided approaches compared with right-sided approaches (0.33 vs 0.24 per 100 catheter-days; P = 0.012) (Supplement 3, Table S16b). Decreased blood flow requiring CVC exchange (ie, CVC dysfunction) was also nonsignificantly higher with left-sided approaches (0.13 vs 0.08 per 100 catheter-days; P = 0.08) (Supplement 3, Table S16b). *However, these outcomes were modified based on the positioning of the CVC tip.* For CVC tips placed in the superior vena cava or pericavoatrial junction, CVC dysfunction and infection were higher for left-sided approaches

compared with right-sided approaches, as noted earlier. However, for CVC tips placed in the mid- to deep right atrium, CVC dysfunction and infection were similar for left- compared with right-sided approaches. This highlights the need for proper CVC placement and confirmatory imaging (Guideline 9).

Tables of studies, evidence quality, and bias are provided in Supplement 3, Tables S16b and c.

Special Discussions

Surgeons and Other Operators: Practical Considerations of Choice of Vessels

Where appropriate, consider the use of superficial veins before deep veins. Recall that venous drainage in the extremity is from superficial (veins superficial to deep fascia) to deep venous system (veins deep to deep fascia). Deep veins tend to converge in a single vein as it approaches the heart.[99] Obliteration or stenoses in the deep veins impair the availability of more distal access sites. Thus, evaluation of potential vascular access sites could consider first using the superficial veins for the outflow. Forearm and upper arm cephalic and forearm basilic veins are considered superficial veins.[100] The Work Group believed that it is reasonable to consider a forearm loop graft in the sequence as a bridge to future AVF when the superficial vein–based options are exhausted. Importantly, the AVF location should consider the maturation of the outflow vein, facilitating future cannulation. An adequate cannulation vein segment should be long enough to accommodate (1) needle separation of at least 1 inch (2.54 cm) or 2 finger widths and (2) rotation of cannulation sites to avoid aneurysm development. Furthermore, it should be easily and comfortably accessible for the patient. Having segments on the underside of the arm can be uncomfortable or very painful. Segments that are too deep may be challenging to cannulate without ultrasound guidance, which may not be readily available and/or may lead to patient and nursing/technician frustration. Although superficialization of such deep AVF may be possible, it is important to note that AVF use for dialysis is typically delayed due to the need for a planned secondary procedure. See also the commentary in Guideline 8.

Special Considerations for Internal Jugular and Femoral Vein Catheterization

Operators and clinicians should be aware of the possibility of persistent left superior vena cava anomalies and its entailments when choosing the internal jugular veins for catheterization.

In *select patients* and *limited circumstances*, tunneled cuffed femoral vein catheterization may be reasonable. For example, in situations where patients urgently start dialysis and are not transplant candidates but are in clinical environments that are conducive to quick dialysis access creation/insertion (ie, within 1 month), tunneled cuffed femoral CVC may serve several beneficial purposes. First, it will preserve central veins to ensure that AV access is feasible (assuming central veins not previously damaged or stenosed by other processes). Second, use of femoral vein CVC reminds patients and providers that CVC is only for temporary purposes. This strategy is effective only if the facility can coordinate rapid AV access creation for patients destined for HD (eg, early cannulation AVG or AVF in a patient with high likelihood of maturation success) or PD catheter insertion for patients who have chosen PD. Issues such as proper placement of the exit site to ensure patient comfort and dignity must be considered (Fig 3.1). Of note, RCTs, metanalyses, and systematic reviews have demonstrated equivalent or superior outcomes with regard to CVC thrombosis and infection, using tunneled femoral vein CVC. However, precaution with femoral CVC use, as with any CVC use, must be taken (Guidelines 20-25).[101-103]

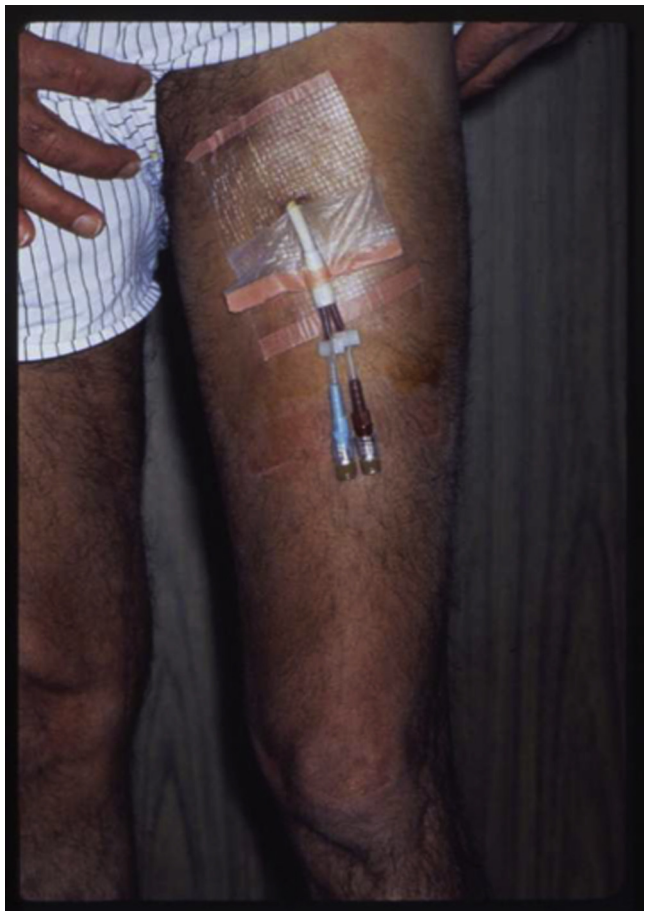


Figure 3.1. Placement of femoral vein central venous catheter.

Implementation Considerations

It is important to reiterate that the *primary goal* of vascular access creation and planning is to create a *functional vascular access* that can provide *reliable prescribed dialysis*, with *minimal interventions and complications*.[15,79]

The planning must consider contingency plans for remediation when the vascular access becomes problematic and a succession plan for future dialysis access options

when the vascular access eventually fails. This applies to all populations in need of dialysis access, including CKD patients with a failing transplant, PD patients who require transition to HD, pediatric CKD patients, other established CKD patients, or patients needing an urgent start to dialysis. A proactive approach to the pediatric CKD patient with failing eGFR is imperative to avoid CVC placement for HD initiation. This means allowing adequate maturation time to enable the AV access to be usable on the day of HD initiation—typically several months of lead time for AVF creation and a few weeks for an AVG placement. CVC avoidance for elective HD is achievable with adherence to the ESKD Life-Plan. It is imperative that health care providers communicate the ESKD Life-Plan and vascular access creation, contingency, and succession plans to provide continuity in KRT and dialysis access care.

Future Research

- It is known that medium-sized peripheral arteries (radial and ulnar) of >2 mm can develop AVF to support adequate dialysis.[104] Future research can inform on the impact of both larger and smaller vessels used for AV access creation. For example, for larger arteries, identify what characteristics are associated with a greater risk of high flow–associated problems. For smaller vessels, determine what characteristics allow for adequate AVF maturation and use.
- Weigh the potential options for vascular access type and location, as discussed; to determine and study more accurate patient-specific estimates of the predicted duration of HD and predicted probability of AVF maturation and consider the results when choosing access type and location.
- More prospective research to determine whether endoAVF creation can result in a clinically durable and cost-effective AV access compared with traditional surgical AV access creation and maintenance.

Guideline 4. AV Access Types and Materials

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Novel AV Access Types and Materials

4.1 **KDOQI suggests that the choice of material for an AVG should be based on the nephrologist's or operator's discretion and best clinical judgment since the current evidence does not demonstrate that one graft material or modification thereof is associated with improved outcomes in terms of patency or complications. (*Conditional Recommendation, Low Quality of Evidence*)**

4.2 **KDOQI considers it reasonable to use early cannulation grafts as a CVC-sparing strategy in appropriate patients, considering their ESKD Life-Plan. (*Expert Opinion*)**

Rationale/Background

Effective hemodialysis requires a suitable access for the withdrawal and return of blood. The ideal hemodialysis access should provide adequate flow rates to sustain prescribed dialysis; be easy to access/cannulate, cost effective, and acceptable to patients; and be associated with excellent long-term patency and minimal complications. A mature, functional autogenous AV access or AVF may be the most ideal access, although not all patients have suitable veins for an AVF, and not all of the veins mature sufficiently for cannulation, thereby negating their potential advantages. Furthermore, in the culture of patient-centered care, an AVF may not always be the appropriate access, given individual circumstances. Acceptable AV access can be created by using a variety of AVGs, including prosthetic, biologic, and autogenous materials. Expanded polytetrafluoroethylene (PTFE) has been the most commonly used graft material since its original description and has served as the comparator or criterion standard for numerous randomized trials. A variety of other prosthetic graft materials are commercially available, although none have proven to be superior to PTFE in terms of the patency or complications. Similarly, a variety of graft modifications have been made to improve AVG performance, including changes in wall thickness, surface modifications, diameter changes, and external support, but none have proven superior to the standard wall 6-mm PTFE graft. The use of autogenous and biological grafts had largely been abandoned with the introduction of PTFE, although some limited recent evidence suggests that nonautogenous saphenous vein and bovine carotid artery biological grafts may be associated with fewer infectious complications and improved patency, respectively. The current KDOQI statements on this topic are consistent with the previous 2006 KDOQI guideline.

Detailed Justification

PTFE has been the most widely used prosthetic material for AVGs since its introduction more than 40 years ago.[105] There have been a variety of RCTs and observational studies (Supplement 3, Table S17) evaluating various AVG materials and configurations. For example, there have been comparisons of tetrafluoroethylene (Dacron, Dupont)[106,107] or polyurethane[108,109] to PTFE, although none have proven superior in terms of patency or complication rates. Similarly, the brand of PTFE does not appear to make a difference in terms of outcome.[110,111]

There have been numerous modifications of the prosthetic AVGs, predominantly PTFE, to improve patency and reduce complications, although none of these modifications have been proven in RCTs to be consistently superior to the standard wall 6-mm PTFE AVG. These modifications have included the thickness of the AVG material (ie, thin-wall PTFE),[112] the elasticity of the AVG material (ie, stretch PTFE),[113] external reinforcement (eg, external rings), tapered AVG diameter (ie, 4- to 7-mm taper PTFE, 6- to 8-mm taper PTFE),[114,115] addition of a cuff to the venous end of the AVG,[116,117] surface modification with heparin,[118] and modification of the external surface.[119] Notably, Polo et al[115] reported that the 6- to 8-mm tapered PTFE upper arm AVGs had better primary and primary-assisted patency rates than the 6-mm grafts without an increased incidence of AV access steal, although the patient population was limited to nondiabetic patients aged <71 years. Dammers et al[114] reported no difference in the patency or incidence of steal symptoms between the 4- to 7-mm tapered and 6-mm PTFE AVGs. The 4- to 7-mm tapered grafts may theoretically reduce the incidence of steal symptoms due to the smaller diameter and resultant lower flow rates; however, the flow rates through the tapered grafts in their study were actually greater than the nontapered ones. The RCTs examining the benefit of a venous outflow cuff have been contradictory, with Sorom et al[117] reporting improved patency and increased flow rates for the cuffed AVGs. Of note, none of the cuffed AVGs failed as a result of a venous outflow stenosis. Data from a more recent study by Ko et al[116] found that primary patency was not significantly different with cuffed versus noncuffed graft at 1 or 2 years (63% vs 50% at 1 year; RR, 1.23; 95% CI, 0.71-2.13; 45% vs 32% at 2 years; RR, 1.56; 95% CI, 0.39-6.19) (Supplement 3, Table S18).

Surface treatment of AVG with heparin affords a theoretical advantage in terms of thrombosis and patency, although the available evidence failed to demonstrate any significant differences.[118] Specifically, the patency (1-year primary patency with heparin-bonded [14%] vs standard AVG [12%] at 1 year [RR, 1.10; 95% CI, 0.50-2.44]; 2-year secondary patency with heparin-bonded AVG [83%] vs standard AVG [73%] at 2 years [RR, 1.14; 95% CI, 0.96-1.34]), and complications rates were comparable between groups.

In terms of timing of graft cannulation, Aitken et al[120] reported that early cannulation PTFE grafts (ie, modification of the middle layer) were associated with reduced bacteremia and mortality when compared with tunneled dialysis CVC. A systematic review by Al Shakarchi et al[121] suggested that the newer-generation early cannulation grafts can be safely cannulated without detriment and were associated with comparable patency and complications with standard-wall PTFE, although the number of studies that made up the review was limited.

The HeRO graft is a nontraditional vascular access that comprises a hybrid PTFE graft–catheter system that represents a variation of the prosthetic graft modifications outlined earlier. A recent RCT comparing the HeRO graft to standard-wall PTFE demonstrated no difference in patency (primary patency, 35% HeRO vs 28% standard AVGs; RR, 1.25; 95% CI, 0.54-2.89 and secondary patency 66% HeRO vs 56% standard AVGs at 1 year; RR, 1.19; 95% CI, 0.75-1.89) mortality (HeRO [2%] vs standard graft [0%]; RR, 1.19; 95% CI, 0.44-3.23; risk difference, 0.02; 95% CI, -0.02 to 0.06), or complications.[122] Notably, this trial was designed to compare the safety and efficacy of the HeRO graft in a cohort of patients without central vein occlusions or stenosis. However, the HeRO graft may have its greatest applicability in this subset of patients.

The role of autogenous and nonautogenous biological AVGs has evolved. Their use was largely abandoned with the introduction of PTFE (described earlier). Two recent trials suggest that biologic AVGs may confer some advantage, although the sample sizes were relatively small (<60 patients). Kennealey et al[123] reported that the bovine carotid artery AVG might be associated with improved outcome. Notably, the primary patency (bovine carotid artery AVG [61%] vs PTFE AVG [10%] at 1 year; RD, 51%; 95% CI, 39-61; $P = 0.006$ by Kaplan-Meier analysis; however, the numbers at risk at each time point was not indicated), thrombosis rates (0.34/patient-year versus PTFE AVG [0.77/patient-year] [RR, 0.44; 95% CI, 0.29-0.67; $P = 0.01$ by Poisson regression analysis]), and re-intervention rates (1.45/patient-year versus PTFE AVG [1.99/patient-year] [RR, 0.73; 95% CI, 0.58-0.91]) were significantly lower when compared with PTFE AVG, although there were no differences in the secondary patency (64% vs a PTFE graft [59%] at 2 years; P = NS) or other complications. Mousavi et al[124] reported that the infectious complication rates with nonautogenous human saphenous vein AVG were lower than for PTFE, although there were no differences in patency.

The saphenous and femoral veins have both been used as autogenous AVG materials.[125,126] The saphenous vein is relatively thick walled and does not usually dilate when used for an AVF, similar to the cephalic or basilic veins traditionally used for upper extremity autogenous access. Furthermore, the saphenous vein diameter is not usually large enough to meet the minimal criteria for effective dialysis (ie, ≥4 mm; flow rate, ≥500 mL/min).[127] The mean diameter of the femoral vein is sufficient for effective cannulation (ie, 7 mm), and the length of the femoralpopliteal segment is adequate for brachial-axillary access, although its use in this configuration is associated with a modest incidence of wound complications and AV access steal.[125,128]

A variety of novel techniques and AVGs are currently under investigation, including a totally percutaneous or endovascular arteriovenous graft, fistula,[129] and a bioengineered graft composed of human tissues.[130] Although RCTs have not yet reported their efficacy, they may play a role in the future.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S18 through S20.

Special Discussions

The Work Group discussed the need for the guidelines to be updated in an iterative fashion to allow for new hemodialysis access options and the ability to properly evaluate them and incorporate worthy options in future guidelines.

Implementation Considerations

See Guideline 1.

Monitoring and Evaluation

See Guidelines 11, 12, and 14-19.

Future Research

- Further define the optimal nonautogenous graft material for an AV access.
- Further validate the benefits identified for the current biologic grafts.
- Further develop novel techniques and graft materials for the creation of autogenous and nonautogenous AV access.

Guideline 5. CVC Configuration and Materials

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: CVC Configuration and Materials

5.1 **KDOQI suggests that the choice of tunneled HD CVC *type and design* be based on the clinician's discretion and best clinical judgment. (*Conditional Recommendation, Low Quality of Evidence*)**

Rationale/Background

Identifying the type of CVC with the lowest complication rate is important for patients who are dependent on CVC for chronic HD—whether for short-term or long-term use.

However, RCTs comparing various CVC types and designs do not consistently demonstrate, with moderate- or high-quality evidence, significant differences in primary-assisted patency, CRBSI, or thrombosis rates. Catheter types evaluated in these clinical trials include the following:

- Tesio-Cath twin catheter system versus LifeCath Twin catheter system (MedComp)[131]
- Palindrome Symmetric Tip versus HemoStar Long-Term CVCs (staggered tips) (Medtronic)[132]
- Palindrome Symmetric Tip versus Medcomp (step-tip) CVCs[133]
- Ash Split (split-tip) (MedComp) versus PermCath (Medtronic) or Optiflow (step-tip) (Bard Access Systems) catheters[134,135]

Detailed Justification

The following summarizes key evidence-based CVC comparisons:

Twin Catheter Systems: Tesio Versus LifeCath Twin Tunneled CVCs

One RCT (n = 80) compared the Tesio-Cath (ovoid cuff) versus the LifeCath Twin (cuboidal cuff); both CVC types have 2 free-floating lumens and were placed in the right internal jugular vein. Study follow-up was 12 months.[131] There was no significant difference in CVC survival (92% for the Tesio-Cath group vs 86% for the LifeCath Twin group) or CRBSI (0.40/1000 CVC days [Tesio group] and 0.51/1000 CVC days [LifeCath Twin group]; P = 0.7). Rates of hospitalization for infection and CVC-related mechanical complications were higher in the LifeCath Twin group compared with the Tesio-Cath group (0.94 vs 0.24 per 1,000 CVC days, respectively; P = 0.02). This was associated with the greater need for urokinase infusions in the LifeCath Twin group (0.51 per 1,000 CVC days) versus none in the Tesio-Cath group.

Palindrome Symmetric Tipped Versus HemoStar Staggered Tipped Tunneled CVC

A number of studies found no significant difference in primary assisted patency, CRBSI, or thrombosis rates when comparing Palindrome symmetric tipped versus HemoStar staggered tipped tunneled CVC as follows: 1 RCT (302 CVCs inserted in 239 participants)[132] reported no statistically significant difference in infection and thrombosis-free CVC survival (after censoring for CVC design–unrelated removal) or CRBSI (0.24 and 0.10 per 1,000 CVC days [HR, 2.26; 95% CI, 0.44-11.96]) in the Palindrome and HemoStar CVC groups, respectively). Although rates of thrombosis or CVC removal due to thrombosis did not differ between groups, the need for a urokinase infusion was lower for the Palindrome group versus the HemoStar group: 17 versus 35 (HR, 0.58; 95% CI, 0.49-0.68).

Urokinase is rarely used in the United States today. It is unknown whether the decreased urokinase use in Palindrome CVCs would also apply with other more commonly used thrombolytic agents, such as recombinant tissue plasminogen activator (TPA).

Palindrome Symmetric Tip Versus Medcomp Step-Tip Catheter

One RCT (n = 97) of 2 months' duration showed that CVC survival at 2 months was significantly higher in the symmetric tip group compared with the step-tip group, 91%

versus 69% (P = 0.02).[133] For the indication of decreased blood flow rate, fewer CVCs were removed in the symmetric tip CVC group compared with the step-tip CVC group (6% vs 22%; P = 0. 04).

Ash Split-Tip Catheter and Permcath or Optiflow Step-Tip Catheters

There were 2 RCTs.[134,135] One study compared the Ash Split with the PermCath catheter (N = 69).[134] CVC survival at 12 months after censoring for recovery of kidney function AVF creation, peritoneal dialysis, and transplantation was higher in the PermCath group compared with the Ash Split group (74% vs 49%) with no difference between groups in CVC removal due to sepsis, rates of infection, or CVC occlusion requiring removal. The other study compared the Ash Split to the Optiflow catheter (n = 132).[135] In this study, overall CVC survival at 180 days was higher in the Ash Split CVC (75%) compared with the Optiflow CVC (55%; P = 0.02).

Study details and evidence quality are provided in Supplement 3, Tables S21-S29.

Special Discussions

- The ERT did not find significant evidence of benefit of coated catheters, and therefore, these were not included in this Guideline. However, the Work Group believed it was a potential area of future research.

Future Research

- More clinical studies are needed to identify the ideal hemodialysis CVC that meets the criteria of long survival times, low CVC complication rates (dysfunction and CRBSI), and potentially lower patient complication rates (vascular stenosis and thrombosis). Scientific advances will need to focus on vascular biology and the design of biocompatible CVC materials to minimize complications of hemodialysis CVC for the select patients who are not candidates for an AVF or AVG.
- Future CVC designs, materials and coatings should also focus on the impact of CVC on the development of central stenosis, infection risk, vessel injury, and/or thrombosis.
- All CVC design studies should report results using consistent definitions and outcomes.

Guideline 6. Timing, Preparation, and Planning for Creation/Insertion of Dialysis Access

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Education on ESKD Modalities and Dialysis Access

6.1 **KDOQI considers it reasonable for adult and pediatric patients with an eGFR <30 mL/min/1.73 m^2 (CKD G4) with *progressive* decline in kidney function, to be *educated* on all *modalities of kidney replacement therapy* (KRT) options, including transplantation, so that timely referral can be made for the appropriate modality and creation of a functional dialysis access, if necessary. (Expert Opinion)**

Note: For pediatric patients, calculate eGFR by Schwartz formula.

6.2 **KDOQI considers it reasonable for adult and pediatric patients with a kidney transplant with an eGFR < 30 mL/min/1.73 m^2 (CKD G4) with *progressive* decline in kidney function, to be *educated* on all *modalities of KRT* options, including potential retransplantation, so that timely referral can be made for the appropriate modality and creation of a functional dialysis access, if necessary. A re-review of the patient's ESKD Life-Plan should occur. (Expert Opinion)**

Note: For pediatric patients, calculate eGFR by Schwartz formula.

6.3 **KDOQI considers it reasonable for PD patients with complications refractory to therapy and/or with circumstances that make PD less conducive than HD to be educated on all kidney transplant and HD options, so that timely referral can be made for the appropriate modality preparation and creation of a functional dialysis access, if necessary. A re-review of the patient's ESKD Life-Plan should occur. (Expert Opinion)**

Note: See Special Discussions.

6.4 **KDOQI considers it reasonable and important to ensure that the predetermined dialysis access is usable to provide the prescribed dialysis when the patient is ready to initiate the planned dialysis (eg, an AV access is mature and ready for cannulation for HD). (Expert Opinion)**

6.5 **KDOQI considers it reasonable that in patients who have unplanned or urgent dialysis starts with a CVC, the ESKD Life-Plan is established with a dialysis access plan within 30 days of dialysis start. (Expert Opinion)**

Statements: Referral for AV Access

In some facilities, referral of the patient for assessment by the vascular access team/surgeon for appropriate dialysis access is a different process than referral for the actual creation/insertion. However, for simplicity, the Guideline recommendations have been combined, keeping in mind variable timeframes between assessment for and creation of vascular access.

Nondialysis CKD Patients

6.6 **KDOQI considers it reasonable that in nondialysis CKD patients with *progressive* decline in kidney function, referral for dialysis access assessment and subsequent creation should occur when eGFR is 15-20 mL/min/1.73 m^2. Earlier referral should occur in patients with unstable and/or rapid rates of eGFR decline (eg, >10 mL/min/year). (Expert Opinion)**

Note: Nondialysis CKD patients include patients who have a failing transplant.

Hemodialysis Patients

6.7 **KDOQI considers it reasonable that in HD patients with recurrent vascular access problems, prompt referral for assessment and creation of a new AV access should be made to allow adequate time for specialist consult and follow-up, as well as possible AV access failure and correction, and should consider individual patient circumstances and competing risk of death. (Expert Opinion)**

Note: Recurrent vascular access problems include recurrent need for CVC use and/or ≥3 corrective interventions/6 months.

When PD Is the Modality of Choice

6.8 **KDOQI considers it reasonable and ideal to place a PD catheter at least 2 weeks before the anticipated need of the PD treatments. (Expert Opinion)**

6.9 **KDOQI considers it reasonable for an urgent PD catheter to be placed for immediate PD as necessary under the direction and care of experienced personnel in conducive environments. (Expert Opinion)**

Rationale/Background

Timely referral for appropriate KRT modality education and choice is necessary to allow adequate time for the preparation, creation, and use of a functional dialysis access when it is needed at dialysis initiation. It is the first of many important steps required to attain "the right access, in the right patient, at the right time, for the right reasons," one of the guiding principles of the Guideline.

These 2019 Guideline statements regarding modality and vascular access education are almost identical to the 2006 KDOQI guideline,[13] although this Guideline emphasizes the Expert Opinion basis due to the paucity of rigorous evidence to support recommendations.

Key differences in the statements for the timing of education and referral for vascular access creation/insertion include using referral criteria that do not depend solely on GFR criteria and recognizing the challenges of creating vascular access based on a predicted time of dialysis start. A range of patient populations that may need vascular access is also recognized.

Detailed Justification

Appropriate and well-balanced education and preparation are required for patients to choose the most suitable KRT modality and corresponding access, suitable for each patient's own circumstances (see Guideline 1 on ESKD Life-Plan).

It has become increasingly evident that despite clinicians' best efforts, predicting when a patient will initiate dialysis is challenging at best—and mostly inaccurate. Several studies have demonstrated that neither GFR alone nor a time duration before dialysis start is reliable, and using such criteria to base vascular access decisions leads to variable results.[136] Patient and process-of-care factors play contributing roles of varying degrees, depending on the different circumstances associated with each combination of interactions.

This Guideline attempted to find a balance between achieving a functional AV access at dialysis initiation with potential unnecessary procedures that may occur if a predialysis patient's kidney function does not decline or due to the competing risk of death. The competing risk of transplant or transfer to PD should be less of an issue if appropriate and timely modality education and preparation occur, corresponding to the patient's ESKD Life-Plan. Given the lack of prospective studies evaluating different GFR thresholds for vascular access creation, a well-conducted simulation study supports an eGFR referral of 15-20 mL/min/1.73m^2.[137] Studies have also demonstrated increasing postcreation procedure rates with longer time away from starting dialysis beyond 6 to 9 months, with no greater proportion of patients initiating dialysis with an AVF.[138] Such a time frame makes intuitive clinical sense given the time now required to ensure AVF maturation and usability, with an average time to cannulation of 132 days in the United States (USRDS 2017, chapter 3)—for AVF that do not fail.[139] The corresponding AVF that failed to mature was 35.9%. A 6- to 9-month time frame from dialysis initiation would allow time to create a new AV access to be used for dialysis start should the first one fail; the challenge, again, is being able to predict the start time. Thus, it is critical to allow time for surgical referral and creation, plan for risk of AV access failure and correction, and consider trajectory of progression (if predialysis) or CVC exposure time (if on dialysis), along with the competing risk of death when referring for AV access creation.

Table 6.1. Suggested Indications for Creation/Insertion of a Vascular Access in Peritoneal Dialysis Patients

- Recurrent peritonitis, especially if due to poor connection technique (Gram-positive) or bowel leak (mixed Gram-negative)
- Ultrafiltration failure, especially in the presence of oliguria or anuria and persistent volume overload
- Decline in physical status considered to be the result of underdialysis (adherence issues or loss of residual kidney function)
  - Note: This is a relative indication and should not be construed as implying that loss of RKF is itself an indication for vascular access creation.
  - Caution: The patient nonadherent to PD may very well be nonadherent to HD and vascular access creation.
- Change in status of the patient, such that self-dialysis is no longer feasible
  - For example, intercurrent event, such as stroke, death, or other loss of a caregiver
- Significant noninfectious complication
  - For example, recurrent hernias, dialysate leaks including hydrothorax

Special Discussions

Patients transferring to HD, after failing PD, frequently start HD with a CVC.[140] Special efforts to examine the reasons for this and reduce CVC use in this population are required.

Suggested indications for the creation/insertion of a vascular access in PD patients (Table 6.1) are provided and based on Expert Opinion.

Future Research

- Validation of suggested criteria using both eGFR criteria and progressive decline in kidney function is required
- Validation of criteria to refer PD patients for HD vascular access
- Use of prediction equations (eg, the Kidney Failure Risk Equation) to assist with timing of access–does this really help?[141]
- Develop and validate approaches to reduce potential damage to central and peripheral vessels by providers throughout the health care system while waiting for AV access creation.
- Investigate in which patients the decline of eGFR appears to slow or halt after AVF creation, and why this may occur

Statement: Vessel Preservation

6.10 **KDOQI considers it reasonable to protect all central and peripheral arteries and veins from damage whenever possible, including the avoidance of peripherally inserted catheters and unnecessary venipunctures, for patients on dialysis or with CKD where dialysis access is expected in the future (CKD G3 -G5). (Expert Opinion)**

Note: Other scenarios where vessel (artery or vein) damage may occur that should be avoided include (1) radial artery access for coronary interventions and 2) venous cardiovascular implantable electronic devices; alternatives such as epicardial/leadless pacing should be considered whenever possible.

Rationale/Background

Central and peripheral vessel damage may contribute to CVC dysfunction and limit future options for AV access creation and usability in CKD and ESKD patients. Due to the growing age and comorbidities of this population, the risk of and exposure to potentially vessel-damaging conditions and interventions are high. For example, venipuncture itself and infusion of sclerosing medications though peripheral intravenous catheters may result in damage and/or thrombosis of peripheral vein segments that may later be used for AV access creation or CVC insertion. In addition, catheterization of central veins for non-HD requirements such as internal jugular and subclavian lines for acute and chronic care, transvenous pacemakers, and defibrillators are associated with stenosis or loss of central vein patency. Central stenosis is a serious complication that may prohibit successful AV access creation, maturation, or use. PICCs are known to damage veins with subsequent thrombosis in many cases. There is also the risk of clot propagation into the central veins. Loss of these veins can have a dramatic impact on patient morbidity and mortality with loss of current and future HD vascular access sites.[142-144] Patients should be educated regarding these risks and encouraged to advocate for their own vessel protection, along with the nephrology community's support. An informative website on saving veins can be found at www.saveyourvein.org, which serves as an example of a public platform educating on the importance of saving veins. It can be used by patients and professionals. Indeed, caregivers involved in the delivery of care to CKD stage 4/5 patients should be educated regarding the implications of venous and arterial access use, and institutional policies directed toward addressing these concerns are strongly suggested.

Detailed Justification

A case-control study (N = 120) demonstrated that the prior placement of a PICC was associated with a subsequent lower frequency of AVF use[144] (odds ratio, 3.2; $P < 0.001$,) even after adjustment for patient sex, artery and vein diameters, and prior CVC insertion. An observational study using USRDS data found that of 6,487 HD patients with PICCs placed within 2 years before and after AV access creation were independently associated with lower likelihoods of transition to any working AV access.[142]

One study examining the presence of central vein stenosis (CVS) in association with PICCs reported a 7% rate of overall CVS.[145] However, this is likely an underestimation of the true incidence of CVS associated with PICCs, because the study was limited to patients undergoing serial extremity venography. In a prospective study examining

thrombosis associated with PICC placement, all patients underwent ultrasound examination of the arm at 28 days after PICC insertion or at time of PICC removal and found an overall thrombosis rate of 71.9% (partial or complete obliteration of vessel lumen).[146] Unfortunately, the national effort to reduce the use of PICCs among CKD and ESKD patients has not achieved its objective. Notably, McGill et al[147] reported from their urban teaching hospital that >30% of patients with CKD have had a PICC and that >50% were placed in their nondominant arm.

Angiographic comparisons of stenosis rates between subclavian and jugular HD CVC insertions found that both were associated with stenosis, with 42% of subclavian veins stenosed after CVC insertion.[148] Finally, the use of a CVC (including PICCs and catheters inserted at the subclavian and jugular veins) was found to be associated with a 14-fold increased risk of an upper extremity DVT.[149] Vein loss may be extrapolated from DVT formation.

In a consensus statement regarding cardiovascular implantable devices in CKD and ESKD patients, it was noted that such patients derive a reduced survival benefit from implantable cardioverter defibrillator treatment compared with patients with normal kidney function, with a 2.7-fold higher risk of mortality.[150] With regard to CVS, 64% of patients developed stenosis.[151] Options to avoid upper body central veins include femoral vein placement (with its own risks of infradiaphragmatic venous damage), epicardial placement, subcutaneous implantable cardioverter defibrillator placement, leadless pacers, and possibly wearable defibrillators.[152,153]

Finally, with regard to radial artery access for cardiac interventions, a meta-analysis of the literature noted a radial artery occlusion rate of <1% to 33%. The conclusion was that radial artery occlusion was common.[154] Given the fact that radial artery patency is integral to future radiocephalic AVF creation, femoral arterial access for coronary interventions should be strongly considered.

Special Discussions

- Alternative options to PICCs are needed—potential options suggested were pediatric internal jugular vein catheters/small bore catheter; however, whether or not their use translates into less vessel damage and CVS is unknown.
- The "Choosing Wisely" campaign should be fully supported in CKD/ESKD patients to "save the vein" and avoid PICCs whenever possible.

Implementation Considerations

- Strategies to avoid PICCs and vessel damage, such as venipuncture in the back of the wrist and use of small-bore internal jugular CVCs should be studied
- Avoid PICCs for <7 days of infusion—use a peripheral intravenous line, preferably on the back of the hand
- Consider femoral venous access for central vein access
- Continuous quality improvement within/across institutions
- PICC placement in CKD patients in hospital requires approval by nephrology department

Monitoring and Evaluation

- Use of PICCs only when there are no other options

Future Research

- Feasibility and use of other options for blood access
- Radial access impact on future VA creation
- Midline catheter insertion effect on future VA creation
- Does use of small-bore internal jugular CVC reduce central venous stenosis?
- Determine if use of small-bore internal jugular CVCs instead of PICCs is practically feasible and effective for patient care
- Rigorously evaluate the impact of radial artery access for cardiovascular and other procedural interventions on the creation and outcomes of AV access for HD

Statements: Multidisciplinary Team Approach

6.11 **KDOQI considers it reasonable to educate on, coordinate, and manage all aspects of dialysis access using a multidisciplinary team within the resource capacities and feasibilities of each facility. (*Expert Opinion*)**

6.12 **There is inadequate evidence for KDOQI to make a recommendation on the use of a multidisciplinary team to reduce the rate of CVC use or increase the use of AVF.**

Rationale/Background

As described previously (Guideline 1), the ESKD Life-Plan is a strategy for living with ESKD, ideally formulated by the patient and a multidisciplinary team (coordinated CKD management team). A patient-centered approach to HD vascular access considers multiple aspects of a patient's needs and dialysis access eligibility, specifically considering the patient's current medical situation, current and future life goals, preferences, social support, functional status, and logistic and other practical feasibilities. For the purposes of dialysis access, this team should include but is not limited to the following professionals and supportive members: nephrologist, access surgeon, radiologist, nurse, social worker, and patient family member or other supporter.

Placement of any dialysis access, but particularly an AV access, requires education of the patient and family, as well as coordination of visits around timely surgical consultation and follow-up visits. Given the limited ability of individual nephrologists to attend to the multiple and complex aspects of vascular access care, most kidney care programs have established multidisciplinary vascular access

teams.[155-157] The multidisciplinary VA team ensures timely referral for vascular access when appropriate, tracking, and monitoring patients' vascular accesses for complications and outcomes. Often central to the team is a vascular access coordinator (VAC) who coordinates and/or schedules the patient for procedures. In addition, the vascular access coordinator is key to educating patients on the risks and benefits of each vascular access choice, addressing any patient concerns, and facilitating appropriate use of the vascular access.[158]

Detailed Justification

Although the multidisciplinary team approach appears ideal, the majority of studies of multidisciplinary team care were at high risk of bias.[159-167] Only 1 study that evaluated a care coordinator,[168] 1 study evaluating multidisciplinary care,[165] and 1 study evaluating patient education[169] were extracted and analyzed (Supplement 3, Table S30).

Multidisciplinary Care

Wilson et al[165] (N = 3,636) analyzed patients starting HD in the DaVita system with follow-up for 360 days. An Incident Management of Patient, Actions Centered on Treatment (IMPACT) program for patients before and early in dialysis was instituted at selected clinics to manage predialysis and early dialysis issues, including initiating HD with an AV access. The multidisciplinary team included a nephrologist, nurses, dietitians, social workers, and clinical care providers and involved structured intake, referral services, patient education, patient management checklists and timelines, and monitoring outcomes. Usual care also included patient education and other interventions, but not in a formalized manner. Patients in the IMPACT program were propensity-matched to patients receiving usual care in a 1:2 ratio, and treatment groups were well balanced for baseline characteristics. Use of an AVF or AVG versus a CVC was not significantly different among IMPACT patients (50%) versus usual-care patients (47%) (RR, 1.06; 95% CI, 0.99-1.14) at 90 days.[165] However, use of an AVF or AVG versus a CVC was significantly higher among IMPACT patients (63%) versus usual-care patients (48%) (RR, 1.31; 95% CI, 1.22-1.41) at 360 days.[165]

The success of the multidisciplinary team has historically been measured by increasing the rate of use of the AVF.[170-173] However, there are a number of other important outcomes, including the rate of VA-related procedures and complications. Recently, Gill et al[174] performed an observational study of vascular access outcomes in the first year of HD treatment before (2004-2005, pre-team period) and after implementation of an access team (2006-2008, early team period; 2009-2011, late team period). Access team implementation did not affect the probability of CVC-free use of the AVF (OR, 0.87; 95% CI, 0.52-1.43, for the early and OR, 0.89; 95% CI, 0.52-1.53 for the late-team period). Patients underwent an average of 4 to 5 total access-related procedures during the first year of HD, with higher rates in women and in people with comorbidities. CVC-related procedure rates were similar before and after team implementation; relative to the pre-team period, AVF-related procedure rates were 40% (20%-60%) and 30% (10%-50%) higher in the early-team and late-team periods, respectively. One difficulty in interpreting the results of this study is that concurrent with the implementation of the access team was the widespread implementation of Fistula First policies in the study centers. The use of AVG was very low (<1%) in the centers involved in the study. Although the CVC rates were similar, the rates of procedures increased in AVFs of women and those with greater comorbidities, factors associated with poor AVF maturation and outcomes. It is unclear if results would have differed if those high-risk patients had received AVG instead. This highlights the need to evaluate the use of multidisciplinary vascular access team to help patients delineate an appropriate ESKD Life-Plan with the corresponding appropriate vascular access, including evaluation of feasibility for AVF.

Vascular Access Coordinator

Data on the true impact of a VAC for improving VA outcomes is lacking. Sixty percent of HD programs reported having at least 1 VAC in a 2013 Dialysis Outcomes and Practice Patterns Study survey of 72 US sites, but they did not report whether an access team was present.[170,174] The percentage of patients using an AVF or a CVC did not differ across facilities with or without at least 1 VAC. The percentage of use of one type of vascular access or another is insufficient for evaluating the usefulness of a VAC. It is not only the percent use that matters but for those using a particular vascular access, it matters whether or not that use is appropriate, safe, and provides patient satisfaction and support for their dialysis to help them achieve their own goals. Having a VAC has been shown to increase the odds of successful unassisted AVF maturation, the ideal form of AVF maturation. Indeed, VACs have the expertise, skills, and capacity to build relationships with patients and multiple team members to educate, coordinate, guide, and manage vascular access for the patient[175,176]—typically much better than solely physicians and surgeons. For example, having a dedicated vascular access nurse or coordinator to assist physicians and staff with management of CVC-related infections has been reported to reduce CVC treatment failure rates and death from sepsis.[177-179] However, further research is required to generate more specific evidence to support vascular outcomes that can be attributable to the work of VACs.

Future Research

Further research is needed to identify new strategies to deliver optimal, personalized, and patient-centered vascular access care. Data on the true benefits of a multidisciplinary vascular access team are limited. The success of a multidisciplinary vascular access team is dependent on

the defined outcome measure. If it is increasing the use of AVFs, there are conflicting data from observational studies using different compositions of teams and roles of the team members. Additionally, these types of studies require accurate information regarding vascular access use across a patient's ESKD lifespan, which is challenging and requires high-quality data assessing time periods of vascular access use with and without a CVC.

Currently, there are no data on the benefit of multidisciplinary teams on patient trust and confidence in making dialysis access–related decisions, in their quality of life or satisfaction with their dialysis access. Futures studies may also determine the impact of a VAC and multidisciplinary teams on health care spending, which may or may not show benefit by shifting care from physicians to lower-cost providers. This may also enhance patient engagement and promote shared decision making. These important outcome measures should be evaluated in future studies.

Guideline 7. Patient and Vessel Examinations: Preparatory Considerations

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Patient Clinical Examination

7.1 **KDOQI recommends that a physical examination focused on vascular anatomy be the basis for the initial assessment and planning of vascular access creation. (*Conditional Recommendation, Very Low Quality of Evidence*)**

7.2 **KDOQI considers it reasonable to have greater emphasis on and more training in preoperative clinical examination to assess patients and their vessels to determine the type and location of their vascular access. (*Expert Opinion*)**

Rationale/Background

The most appropriate AV access creation requires careful preoperative evaluation. Among many factors, the characteristics of the patient's vascular anatomy, cardiovascular system, and life expectancy will influence the ideal type and location of access (Figs 1.1-1.6). The decision to create an AVF after a thorough preoperative evaluation is aimed at reducing the primary failure rate and improving the cumulative patency rates with few or no additional interventions. The common techniques used in clinical practice include clinical examination and duplex ultrasound evaluation, as previously recommended in the 2006 KDOQI guideline (1.4.1, 1.4.2, and 1.4.3).[13] A detailed history and physical examination focused on evaluating the vascular anatomy and cardiovascular system, as outlined in Table 7.1, remains relevant. The belief that vessel mapping with duplex ultrasonography is better than clinical examination remains contentious. Preoperative vessel mapping to evaluate the arteries and veins using duplex ultrasonography has been recommended in the past based solely on Expert Opinion. The potential benefits outlined were selection of vessel based on luminal size and

Table 7.1. Focused Preoperative Physical Examination for Vascular Access Planning and Creation

Consideration	Relevance
Physical examination of arterial system Character of peripheral pulses Allen test Bilateral upper extremity blood pressures	• An adequate arterial system is needed for AV access; the quality of the arterial system will influence the choice of AV access site. • Abnormal arterial flow pattern to the hand may contraindicate the creation of a snuffbox or radiocephalic AVF.
Physical examination of venous system Evaluation for edema Assessment of arm sizes comparability Examination for collateral veins Evaluation of veins: Augmented palpation Examination for evidence of prior central or peripheral venous catheterization Examination for evidence of arm, chest, or neck surgery/trauma	• Equality or discrepancies of blood pressure values inform the suitability of arterial inflow and access in the upper extremities. • Edema indicates venous outflow problems that may limit usefulness of the associated potential vascular access site or extremity for vascular access placement. • Differential arm size may indicate inadequate veins or venous obstruction that may influence success of AV access created and choice of vascular access site. • Collateral veins are indicative of venous obstruction, as discussed. • Palpation augmented by tourniquet ± warm stimulus (eg, water) will inform venous characteristics (eg, distensibility). Selective venous mapping may be helpful (Guideline Statement 7.3 and Table 7.2)
Cardiovascular evaluation Examination for evidence of heart failure	• Use of CVCs is associated with central venous stenosis; previous placement of venous catheters, pacemakers, etc may have damaged target vasculature necessary for vascular access (Guideline Statement 6.10). • Vascular damage associated with previous surgery or trauma may limit access sites (Guideline Statement 6.10). • Poor cardiac output or ejection fraction may affect success of AV access created (eg, low output may increase risk of maturation failure). • AV accesses may alter cardiac output.

Abbreviations: AV, arteriovenous; CVC, central venous catheter.

distensibility with manual occlusion of blood flow, thus ensuring that the most appropriate vessel is used to create a successful AV access. However, duplex ultrasonography has several disadvantages that include measurement errors due to operator skill and circumstances (eg, the skills and interpretation of a lab technician vs the surgeon creating the access may differ, the condition of the patient as cold/dehydrated vs warm/well hydrated may influence results, environment of outpatient clinic vs intraoperative ultrasonography may be important, etc), patient inconvenience, higher costs to health care system, and delays in creating AV access.

Detailed Justification

Two RCTs and 1 observational study compared preoperative vessel mapping by duplex ultrasonography to physical examination for assessment of AVF creation.[180-182] The majority of patients were predialysis, with hypertension and diabetes. The median age was 66 years, more than half were white, and 60% were men. The minimum follow-up was 6 months after AVF creation. There was no statically significant difference in AVF primary failure (21.5% vs 31.1%; RR, 0.69; 95% CI, 0.45-1.08]) or primary patency (62.5% vs 52.5%; RR, 1.19; 95% CI, 0.97-1.45) between the 2 groups. However, secondary patency was greater with preoperative ultrasound compared with physical examination alone (81.6% vs 65.2%; RR, 1.18; 95% CI, 1.01-1.37). There was no difference in those with vessel mapping compared with physical examination for frequency of postoperative interventions (20.1% vs 22.9%; RR, 0.88; 95% CI, 0.36-2.15); unnecessary creation before dialysis start, transplant, or death (12.1% vs 11.9%; RR 1.02; 95% CI, 0.49-2.13); or mortality (7.5% vs 4.7%; RR, 1.58; 95% CI, 0.53-4.70). The studies were not powered to assess the potential harm, especially to detect the number of unnecessary AV access creations (Supplement 3, Table S31).

Statements: Vessel Mapping for Vascular Access

7.3 **KDOQI suggests selective preoperative ultrasound in patients at high risk of AV access failure (Table 7.2) rather than routine vascular mapping in all patients (*Conditional Recommendation, Low Quality of Evidence*).**

7.4 **KDOQI considers it reasonable to use various imaging studies as needed to evaluate the suitability of vessels for AV access creation such as ultrasonography for peripheral vessels (including intraoperative ultrasound) and venography for suspected central vein occlusion, while considering the patient's clinical circumstances and residual kidney function. (*Expert Opinion*)**

Table 7.2. Examples of Risk Factors For Which Vessel Mapping May Be Beneficial

Clinical Problem	Risk Factors
Fistula failure	Elderly age, female, comorbidities (eg, peripheral vascular disease, coronary artery disease), small pediatric patients
Peripheral vessel damage	Ipsilateral: PICC insertion, other iatrogenic (eg, venipuncture), self-inflicted (eg, IVDU), disease states (eg, vasculitis), radial artery harvesting for CABG
Central venous stenosis	Multiple CVCs; prolonged CVC duration; cardiac implantable electronic device; PICC; surgery or trauma to neck, chest, upper extremity
Limitations to physical examination	Morbid obesity, suboptimal conditions (eg, patient dehydrated or vasoconstricted), poor skin integrity, patient refusal

Note: When central venous stenosis is suspected, ultrasound has low sensitivity for detecting central vein stenosis, and venogram should be performed when possible to confirm and locate lesions.
Abbreviations: CABG, coronary artery bypass graft; CVC, central venous catheter; IVDU, intravenous drug use; PICC, peripherally inserted catheter central.

Rationale/Background

Given the lack of high-quality evidence of preoperative mapping on AVF outcomes over thorough clinical evaluation, there may be utility in selective use of preoperative vessel mapping. Such selective use could be applied to patients considered to be at high risk of AVF failure (Table 7.2), those at risk of or with a history of vessel damage or central stenosis, or those for whom a proper physical examination is not possible or feasible (eg, morbidly obese patients).

Justification

One RCT compared selective versus routine preoperative vessel mapping by duplex ultrasonography for AVF creation (n = 77).[183] The majority of patients were predialysis with hypertension and diabetes, and their median age was 65 years old. There was no statistically significant difference in AVF primary failure rate at 90-day follow-up in those who had selective versus routine vessel mapping (36.0% vs 21.1%; RR, 1.71. 95% CI, 0.81-3.59), postoperative interventions (5.3% vs 5.1%; RR, 1.03; 95% CI, 0.15-6.92) or total complications (12.8% vs 2.6%; RR, 4.87; 95% CI, 0.60-39.79). Primary and secondary patency were not evaluated. The study was too small to properly detect harms, and effect modification was not assessed (Supplement 3, Tables S32 and S33).

Given this set of evidence, the Work Group could not endorse vessel mapping in all patients but wanted to ensure that it could be supported in patients deemed at high risk while supporting the need for further study. The impact of preoperative vessel mapping may be very important and may not be apparent from the studies conducted to date; it is unclear whether the impact of preparative mapping conducted by an independent

imaging facility separate from the operator has the same impact as preoperative mapping conducted by the operator who will be creating the AV access. This is an area that needs to be clarified through research.

Statements: Optimal Vessel Size of Artery and Vein for AV Access Creation

7.5 **KDOQI considers it reasonable that while there is no minimum diameter threshold to create an AVF, arteries and veins of <2 mm in diameter should undergo careful evaluation for feasibility and quality to create a functioning AVF. (*Expert Opinion*)**

7.6 **KDOQI considers it reasonable to evaluate multiple characteristics of vessel quality for AVF creation (size, distensibility, flow, etc). (*Expert Opinion*)**

Rationale/Justification

The previously suggested vein diameter of 2.5 mm and arterial diameter of 2.0 mm have not been validated. The threshold was included in the KDOQI Clinical Practice Guideline for Vascular Access as an Expert Opinion based on a single study by Silva et al in 1998.[184] Despite the routine use of duplex ultrasound, the primary failure rate in the multicenter Dialysis Access Consortium Fistula study was reported to be as high as 60%.[31] Our current knowledge is limited to retrospective single-center studies.[185-187] The studies evaluating vessel size are inconsistent in their reporting regarding the timing (immediate before surgery in the operating room vs imaging suite), distensibility with tourniquet, operator skills (technician vs surgeon), and location (radiocephalic vs brachiocephalic).

The limited clinical evidence meeting guideline criteria for ERT review are summarized:

Allon et al,[28] in a single-center study, evaluated over a 17-month period the effect of routine preoperative mapping on the types of vascular access placed and their outcomes. The minimum vein diameter of >2.5 mm and arterial diameter of >2.0 mm for AVF creation and vein diameter of >4.0 mm for AVG creation were implemented. The study did not report their outcomes based on different tertiles of vessel size. Overall, compared with historical controls, the study reported an increment in AVF creation rate from 34% to 64%, with the greatest improvement in women and diabetic patients. The overall increment in the usability of AVF to support dialysis from the historical cohort was statistically insignificant (46% to 54%; P = 0.34). However, there was substantial increase in the usability of forearm AVFs, although it was not statistically significant (34% to 54%; P = 0.06).

Dageforde et al[188] reported on a retrospective study of 158 patients (mean age, 54 years; diabetes, 56%; body mass index, 32 kg/m^2) with brachiocephalic or brachiobasilic AVF. The study cohort was divided into quartiles based on the vein diameter, with a vein diameter in the lowest group of <2.7 mm and in the highest group of >4.1 mm. Patients with minimum vein diameter of >3.4 mm had a higher maturation rate compared with those with vein diameter of <3.2 mm (79% vs 90%) and 6-, 12- and 24- month patency of 77%, 55%, and 49% vs 90%, 67%, and 58%, respectively.

The variability in reported parameters limits the clinical evidence necessary to make any recommendations on minimal lumen size. Furthermore, it may be important to consider variables other than vessel size; for example, distensibility (defined as increase in internal vein diameter with proximal compression), arterial wall thickness, and resistance index to reactive hyperemia were used in a study of 116 patients by Malvorh.[189] Primary patency rate in patients with increment in internal venous diameter (from 0.226 cm ± 0.063 to 0.335 cm ± 0.115) was 80.2% compared with 19.2% among patients with internal venous diameter increment from 0.219 cm ± 0.097 to 0.245 cm ± 0.126). The study also evaluated internal arterial diameter, baseline arterial blood flow, and resistance index with reactive hyperemia with forearm AVFs. The group with higher maturity had an internal arterial diameter of 0.264 cm ± 0.065 vs 0.162 cm ± 0.066, baseline blood flow of 54.5 mL/min ± 2.81 vs 24.11 mL/min ± 16.81 and resistance index at hyperemia of 0.50 ± 0.13 versus 0.70 ± 0.17. However, the usability was not reported.

Future Research and Educational Needs

There is a paucity of training in vascular access physical examination for the preparation or use of vascular access. The Work Group members believed that there should be a much greater emphasis on and more training in preoperative clinical examination to assess patients and their vessels to determine the type and location of their vascular access.

The impact of preoperative vessel mapping may be very important and may not be apparent from the studies conducted to date; it is unclear whether the impact of preparative mapping conducted by an independent imaging facility separate from the operator has the same impact as preoperative mapping conducted by the operator who will be creating the AV access. This is an area that needs to be clarified through research.

Guideline 8. AV Access Creation

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: Pre-Creation Infection Prevention

8.1 **KDOQI considers it reasonable to conduct a careful history and physical exam by the operator and managing team prior to AV access creation to identify infection risks that should first be managed before proceeding with AV access creation (eg, dental infection, osteomyelitis, etc). (Expert Opinion)**

Statement: Use of Anesthesia for AV Access Creation

8.2 **KDOQI suggests that the choice of anesthesia for AVF creation should be based on the operator's discretion and best clinical judgment, as current evidence shows no difference between regional block or local anesthesia in terms of AVF usability, patency, interventions, or patient experience. (Conditional Recommendation, Low-Moderate Level of Evidence)**

Rationale/Background

A majority of AV access creation procedures require subcutaneous dissection and minimal deep dissection in a circumscribed area of the extremity. Conventionally, these procedures have been performed using local anesthesia and intravenous sedation to increase patient ease. More significant procedures that require extensive tissue dissection such as aneurysm repair or superficialization are usually performed under general anesthesia or regional blocks, based on the operator's discretion.[190] Both regional and general anesthetic have the potential for inducing vasodilation by altering the vascular autonomic tone[191]; the resultant larger vessels (up to 25%)[192] may improve operative ease. Such observations have prompted investigators to evaluate whether the method (type and location) of anesthesia helps to increase AV access creation rates, AV access patency, AVF maturation, patient satisfaction, and operator ease. This topic is new to the current NKF-KDOQI VA Guideline.

Detailed Justification

The success of AVF maturation after creation[31,193] may be associated with the vein diameter used for anastomosis.[104] It is hypothesized that dilation of veins with increased caliber and flow might facilitate and increase AVF creation,[194,195] particularly distal AVF creation. However, it is uncertain whether anesthetic-induced vein dilation and AVF creation are associated with improved AVF maturation and use. In particular, regional block anesthesia has a propensity to dilate superficial veins and increase the blood flow to the limb during the intraoperative and immediate postoperative period.[196] It has been suggested that the resultant increased vein dilation and flow might lead to more distal AV access site selection and creation and that the increased flow in the perioperative phase might increase AVF maturation.[194,195]

The greater availability of duplex ultrasonography has increased the ease, safety, and efficacy of administering regional (supraclavicular and infraclavicular) block for surgical procedures performed in the upper limb.[197]

Six RCTs and 3 observational studies compared the effectiveness and harms of different anesthesia techniques on AV access outcomes[192,198-200]; however, 1 RCT and all 3 observational studies were excluded due to high risk of bias. The evaluated studies showed no difference in AV access patency or failure, patient satisfaction, and complications between groups receiving regional anesthetic using different techniques compared with those receiving local anesthetic during radiocephalic or brachiocephalic AVF creation.

Yildirim et al[201] (N = 100) compared a stellate ganglion block versus local anesthesia for patients undergoing radiocephalic AVF creation. Patients were followed up until their AVF was sufficiently mature for cannulation. Successful cannulation was not significantly different with a stellate ganglion block versus local anesthesia (RR, 1.58; 95% CI, 0.996-2.52). However, the mean maturation time was significantly shorter with stellate ganglion block (mean, 41.4 days) versus local anesthesia (mean, 77.1 days) (mean difference, -36 days; 95% CI, -41 to -31).

Three RCTs compared brachial plexus block versus local anesthesia.[192,199,200] In patients receiving radiocephalic AVF, pooled analysis showed no significant difference in AV access patency, failure, or complications (Supplement 3, Table S34). In the study by Aitken et al,[198] the ability to use the AVF was significantly higher with a brachial plexus block versus local anesthesia among patients who had a radiocephalic AVF created (RR: 1.83; 95% CI, 1.07-3.12) (Supplement 3, Table S35). For those receiving brachiocephalic AVF, the type of anesthesia did not differ in AVF patency, need for secondary interventions, ability to cannulate the AVF, or patient satisfaction.

Reasonably good procedural safety for different regional block techniques performed with ultrasound guidance has been shown.[197] However, regional blocks are also associated with small but significant risks of short- and long-term complications.[202] Thus, the choice of anesthesia technique for AVF creation should be based on institutional experience, operative technique, and patient characteristics to optimize successful AVF creation (Supplement 3, Tables S34-S38).

Special Discussions

The Work Group discussed that creating distal AVF, when appropriate, helps preserve more proximal sites. Vasodilation caused by regional anesthesia may provide an opportunity to identify vessels that were missed or deemed not suitable due to small size during initial evaluation. It is worthwhile to investigate if there is a subgroup of patients

who may benefit from the use of regional anesthetic. Central venous stenosis is an important cause for long-term failure of AVF. Any irritation in and around these veins precipitates development of this problem over time. Long-term effects of regional anesthetic that is infiltrated in the neurovascular bundle that contains the ipsilateral central vein are not known.

Future Research

- Identify a patient population who may benefit from the use of regional anesthesia.
- Evaluate the long-term effect of regional anesthesia on central veins.

Statement: AV Access Anastomotic Configuration and Apposition Methods

8.3 KDOQI considers it reasonable that the choice of anastomotic configuration and apposition method (eg, vascular clips, sutures) for AVF creation be based on the operator's discretion and best clinical judgment, as there is insufficient evidence to prefer one configuration or apposition method over another. (Expert Opinion)

Rationale/Background

Anastomotic configuration is one of many factors considered for its potential influence on AV access primary failure and outcomes. An acute increase in blood flow and a configurational change in the outflow vein are 2 permanent changes that follow AVF creation.[203] Studies have demonstrated that wall shear stress, caused by the altered flow pattern after AV access creation, may lead to venous neointimal hyperplasia,[204,205] which is associated with juxta-anastomotic stenosis (JAS). JAS is consistently seen at the AVG-vein anastomosis of an AVG and AV anastomosis in an AVF[206,207] and is associated with AV access thrombosis and AV access maturation failure.[4] An optimal anastomotic configuration or apposition method might mitigate adverse flow patterns and shear stress[204,208] of the created AV access but may also have unintended consequences, such as venous hypertension.

Detailed Justification

Studies have evaluated anastomosis techniques and tools for AVF creation.[209-211] Mozaffar et al[210] compared side-to-side with end-vein–to–side-artery anastomosis. Primary AVF failure at 6 months was not significantly different with side-to-side (20%) versus end-to-side anastomosis (17%) (RR, 1.20; 95% CI, 0.41-3.51) (Supplement 3 Tables S39-S42).

A French observational study by Sadaghianloo et al[211] compared radial artery deviation and reimplantation (RADAR) technique (n = 53) with historical control standard end-vein–to–side-artery anastomosis (n = 73). Primary AVF patency at 6 months was significantly better with the RADAR technique (93%) versus end-vein–to–side-artery anastomosis (52%) (RR, 1.81; 95% CI, 1.29-2.55). Other outcomes, including secondary AVF patency and interventions, also favored the RADAR technique.

In terms of apposition methods, similar outcomes have been found when anastomotic vascular clips have been compared with sutures (see detailed discussion in Guideline Statement 8.4, AV Access Anastomotic Suture Technique).

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S39-S42.

Special Discussions

The Work Group discussed ERT recommendations related to the RADAR technique. The technique necessitates radial artery transection and is an end-artery–to–side-vein anastomosis. Although bidirectional flow in the cephalic vein may be a reason for increased patency similar to side-to-side AVF, it also poses the risk for development of segmental venous hypertension in the long term; thus, the main reason for selective use of end-to-side anastomosis over side-to-side anastomosis. Transection of the radial artery is a future ischemic risk for patients for whom the procedure fails. Although the RADAR study showed benefits in the short term, the long-term outcome remains to be seen.[211,212] Computational fluid dynamics (CFD) modeling with similar arterial configuration in end-to-end anastomosis has suggested the possibility of developing arterial stenosis related to flow stress.[213,214]

Although the ERT found low to moderate quality of evidence for end-artery–to–side-vein anastomosis over end-vein–to–side-artery anastomosis for AVF creation for better primary patency and need for intervention, the Work Group had reservations. The Work Group believed that, in addition to methodologic issues (nongeneralizability [ie, only radiocephalics were evaluated in the study], limited short-term follow-up, etc), clinical concerns such as potential loss of the artery for future vascular access, potential for venous hypertension, and hand ischemia hampered the Work Group's enthusiasm for this technique.

Implementation Considerations

Avoid: Excessive Depth in AV Access Creation

Regardless of anastomotic technique, AV accesses that lie too deep relative to the surface of the skin can lead to problems with cannulation. This scenario typically arises for obese patients with brachiocephalic AVFs but can occur with the other AV access types and configurations depending on the distribution of fat in the forearm for the radiocephalic AVF and the depth at which the various AVGs and brachiobasilic AVFs are tunneled. This concern is more relevant for the nonmaturing AV access, although it can present later in the life cycle of the AV access.

There are a variety of open surgical techniques to elevate, or superficialize, the AVF relative to the surface of the skin.[215-219] An incision can be made over the course of

the AVF, typically the outflow vein for a brachiocephalic AVF, and the vein can be elevated by re-approximating the underlying subcutaneous tissue. Bronder et al[215] reported an extensive 7-year experience with 296 consecutive patients with excellent long-term results. The subcutaneous tissue overlying the AVF can be resected, effectively resulting in elevation of the AVF by decreasing the distance between the skin and the AVF. Alternatively, the vein can be transposed or rerouted rather than simply elevated, thereby reducing the likelihood of the vein being exposed if the wound were to breakdown. Bourquelot et al[216] have described making a series of transverse incisions over the course of the conduit and undermining the skin to facilitate resecting the excess subcutaneous tissue, while others have described using suction lipectomy.[220,221]

Future Research

The preponderance of stenosis in specific anatomic locations suggests that local hemodynamics plays a significant role in its development. The availability of better imaging techniques and CFD provides an opportunity to model hemodynamics and shear stress patterns.[222] Areas of bends and curves tend to have maximum shear stress gradient that predisposes to VNH.[213,222] Hull et al[223] studied side-to-side CFD models and found a configuration, called the *piggyback Straight Line Onlay Technique* (pSLOT), to have more uniform wall shear stress patterns compared with several other angles. Future rigorous study of this and other techniques based on hemodynamic parameters will be insightful to help limit the development of JAS and consequent stenosis, with the hope of improving AV access longevity.

- Study of hemodynamics (flow, shear stress) as a causative factor for AVF dysfunction outcomes (eg, outflow vein stenosis, JAS)
- Develop AV access–specific CFD modeling
- Clinical evaluation of different anastomotic configurations—identify stress zones and mitigate or avoid them (prevention of stenosis)
- A piggyback straight-line onlay technique has been described but was excluded from ERT appraisal due to the high risk of bias[209]; further rigorous study of this technique may be insightful
- Further rigorous research and long-term follow-up of RADAR technique

Statement: AV Access Anastomotic Suture Technique

8.4 KDOQI considers it reasonable that the choice of suture technique for AV access creation should be based on the operator's discretion and best clinical judgment, as there is insufficient evidence that any anastomotic suture technique is advantageous in terms of AV access patency or complications. (Expert Opinion)

Rationale/Background

Creation of vascular access is associated with a significant risk of primary failure.[31] Suture techniques are one of the many factors that have been studied to evaluate their influence on the surgical outcome of AV access creation. Vessel apposition by suturing can be performed in a continuous or an interrupted fashion. Studies have shown hemodynamic advantage for interrupted anastomosis in the presence of pulsatile flow.[224] Due to difficulties in execution and lack of adequate devices available to perform interrupted anastomosis, continuous suturing is the most prevalent anastomotic technique.

Two new devices[225,226] have been evaluated and may help surgeons to use interrupted suturing to perform vascular access anastomosis.

Detailed Justification

Continuous versus interrupted anastomosis have different hemodynamic profile and compliance patterns at the para-anastomotic site of small vessel anastomosis.[224] The current literature does not provide clarity on the effect of this altered hemodynamic and compliance on long-term AV access outcomes. A recent RCT (n = 78) reported improved primary patency for a partially interrupted anastomosis in radiocephalic AVF but no difference in functional patency[227] compared with continuous sutures. Another retrospective study compared the outcomes of continuous versus interrupted anastomosis in 334 procedures performed in a large cohort of veteran patients and observed an equivalent outcome.[228] A larger multicenter (17 centers) retrospective study reported the long-term performance of 398 AVF (199 clips, 199 sutures) and 740 AVG (401 clips, 344 sutures). Improvements in bleeding complications, primary patency, and cumulative patency were associated with clipped anastomosis in AVF that were patent and used, and in an intention-to-treat analysis, improved patency was also associated with clipped anastomosis in AVG.

Two RCTs assessed the comparative effectiveness and harms of using continuous versus interrupted suture techniques in AVF. Zeebregts et al[229] compared the outcome of VCS clips (Tyco Health/Auto Suture Company) versus 6-0 Prolene (Johnson & Johnson) sutures in 98 patients followed up to 2 years. Walker [230] compared the U-clip device (Medtronic) with continuous 6-0 Prolene suture (Johnson & Johnson) for anastomosis in 31 patients. Pooled data from these 2 trials failed to show a statistically significant difference between continuous versus interrupted techniques; the primary AVF patency at 6 months for clips was 71% and for sutures was 72% (RR, 0.98; 95% CI, 0.73-1.32).[229,230] Secondary patency at 6 months was also not statistically different between clips (86%) and sutures (69%) (RR, 1.25; 95% CI, 0.96-1.64).

Special Discussions

Although interrupted anastomoses appear to have a better hemodynamic profile at the anastomotic site, studies have

failed to show a significant impact on AV access outcome. One retrospective study[231] with a large number of AVF anastomosis (n = 1,345) with a long-term follow-up period (2 years) found significant patency advantage for clips (AnastoClips), suggesting that the beneficial effect of a better hemodynamic profile is possibly small.

The theoretical disadvantage of interrupted anastomosis is the potential for the anastomosis to expand with time, possibly leading to mega fistula. Although this was not demonstrated as a major factor in coarctation repair in cardiac surgery,[232] it may be possible in AVF construction on larger vessels that have a higher propensity of developing flow-related problems. Further study of anastomotic techniques is required.

Statements: Use of Operator-Assisted Maneuvers for AV Access Maturation

8.5 **KDOQI does not suggest the use of allogenic endothelial implants to improve AVF maturation, patency, or clinical usability or to improve AVG graft patency or reduce thrombosis. (*Conditional Recommendation, Very Low Quality of Evidence*)**

8.6 **KDOQI does not suggest the use of pancreatic elastase to improve the patency and clinical use of AVF or AVG. (*Conditional Recommendation, Moderate Quality of Evidence*)**

8.7 **KDOQI considers it reasonable to have a careful individualized approach to operator-enhanced (surgical or endovascular) maneuvers during AV access creation to facilitate AV access maturation, based on the operator's best clinical judgment and expertise. (*Expert Opinion*)**

Rationale/Background

AVF maturation failure and AVG thrombosis remain major clinical problems for hemodialysis patients. Unfortunately, 20% to 60% of AVFs created fail to mature successfully for dialysis use.[77,233] Thrombosis accounts for almost 80% of AVG failures[31,234-236] due to an underlying stenosis at the venous anastomosis.[237-239] At present there are few, if any, effective therapies to enhance AVF maturation and reduce AVG stenosis and thrombosis. Pharmacologic therapies to assist AVF maturation were not addressed in the 2006 KDOQI guideline.[13] Since the 2006 KDOQI guideline, there have been several RCTs evaluating novel biological therapies to assist AVF maturation and prevent AVG thrombosis.

Detailed Justification

The role of adjunctive nonpharmaceutical treatment for AVF and AVG creation specifically focuses on allogeneic endothelial cell implants and pancreatic elastase type I (Supplement 3, Tables S43-S46).

Nonpharmaceutical Biologics to Enhance Maturation

Allogenic Endothelial Cell Implants in AVF[240,241]. Data from Conte et al[240] include 65 maintenance HD patients needing AVF (n = 31) or AVG (n = 34) from combined phase 1 (allogeneic endothelial cell implants [AEC] safety trial) and phase 2 (RCT of AEC vs placebo sponges in a 2:1 ratio) studies. Patients treated with AEC received 2 Vascugel sponges containing human endothelial cells suspended in gelatin medium placed adjacent to the venous outflow vein and anastomosis, with some patients receiving a third sponge for placement next to the arterial anastomosis. Primary AVF patency was not statistically different with AEC (60%) compared with placebo (62%) at 24 weeks (RR, 0.97; 95% CI, 0.52-1.83).[240] There were no thrombosis events for either the AEC or placebo groups.[240] Local wound infections and need for intervention to correct a complication were not significantly different with AEC (4%) versus placebo (0%) (RD, -0.04; 95% CI, -0.20 to 0.13)[240] (Supplement 3, Tables S43-S45 and S52).

Allogenic Endothelial Cell Implants in AVG[240]. In the study by Conte et al,[240] all patients with AVG (n = 34) had 2 Vascugel sponges placed adjacent to the venous anastomosis and outflow vein and were followed up for 24 weeks. Phase 2 AVG patients (n = 30) received a third sponge adjacent to the arterial anastomosis, for a total of 3 implanted sponges. There were no differences in thrombosis or patency between those receiving AEC or placebo. Thrombosis at 30 days was 9% in AEC versus 18% in placebo (RR, 0.48; 95% CI, 0.08-2.96), and primary AVG patency at 24 weeks was 38% in the Vascugel group compared with 23% in the placebo group (RR, 1.44; 95% CI, 0.48-4.27). Local wound infection, thrombosis, and need for intervention to correct a complication at 30 days showed ≤2 events for either treatment arm (Supplement 3, Tabled S46-S48 and S53).

Pancreatic Elastase Type 1 in AVF. Hye et al[242] and Peden et al[243] (n = 229) randomized participants with AVF to pancreatic elastase type 1 (PRT-201) or placebo and followed them for 1 year (Supplement 3, Table S49). Data were available in 188 participants for this detailed justification. The drug was administered directly to the inflow artery, anastomosis, and outflow vein during surgery, over the course of 10 minutes immediately after AVF creation. Primary AVF failure at 2 weeks[243] and secondary AVF patency was not significantly different between 2 two groups.[242] Unassisted AVF maturation, defined as maturation with no prior procedure to restore or maintain patency, at 3 months was higher with PRT-201 (68%) versus placebo (46%) (RR, 1.48; 95% CI, 1.02-2.15).[242] However, hemodynamically significant lumen stenosis at 3 months was not statistically different (RR, 0.93; 95% CI, 0.19-3.43).

In a pooled analysis of the 2 trials, primary AVF patency at 1 year was not statistically different with PRT-201 versus placebo (RR, 1.21; 95% CI, 0.87-1.68).[242,243] At 1 year, primary

AVF patency, the ability to use the AVF (59% for PRT-201 vs 53% for placebo; RR, 1.11; 95% CI, 0.82-1.51),[242] and thrombosis of the AVF were not statistically different (RR, 0.86; 95% CI, 0.31-2.38).[242,243] Neither trial showed differences in any reported harm (stenosis, thrombosis, hypoesthesia, steal syndrome, or need for intervention) (Supplement 3, Tables S50 and S51).

Pancreatic Elastase Type 1 in AVG[244]. Dwivedi et al[244] enrolled 89 patients with AVG and followed them for 6 months. There were 9 study groups grouped by dose levels (low, medium, high). Pancreatic elastase type I (PRT-201) was administered as a series of drops directly to the graft-vein anastomosis and adjacent outflow vein over the course of 10 minutes immediately after AVG creation. At 6 months, AVG thrombosis (42% for PRT-201 vs 46% for placebo (RR, 0.90; 95% CI, 0.48-1.67) and venous stenosis (42% for PRT-201 vs 32% for placebo; RR, 1.30; 95% CI, 0.63-2.65) was not different between groups.[244] At 1 year, primary AVG patency was not statistically different between the PRT-201 (range of 17%-21%, depending on dose) and placebo groups (19%) at all dose levels. Secondary AVG patency (range of 59%-71%, depending on dose) was also not significantly different.[244] Rates of thrombosis, stenosis, and need for intervention to correct a complication at 12 months were not significantly different between groups.

To summarize, 2 RCTs evaluated device or topical therapies that were delivered intraoperatively after AV access creation: pancreatic elastase and allogenic endothelial cells. These therapies are currently not commercially available for use because they are in phase 3 studies. Moreover, the current data from these studies do not suggest benefit at this time in AVF or AVG (Supplement 3, Tables S46-S48).

Intraoperative Devices and Operator-Enhanced Intraoperative Maneuvers

The OptiFlow anastomotic connection device implanted at the time of AVF creation has been evaluated in single-arm studies with comparison with historical control groups showing similar unassisted AVF maturation rates.[245,246] The Optiflow device has not been studied in phase 3 studies and is not commercially available.

Other Surgical Maneuvers

There is very little literature in the area of operator-enhanced (surgery) maneuvers for AV access maturation (Guideline Statements 8.5 and 8.6). Whether a 1-stage versus 2-stage basilic vein transposition is "more beneficial" when creating an upper arm AVF is a common clinical question at the time of AVF creation. Only observational studies are available to address this question, and these largely do not show a benefit of one technique versus the other.[247,248] Further studies comparing these 2 techniques will be necessary before recommendations can be made. Until this issue is resolved, an individualized approach is suggested.

Intraoperative Endovascular Maneuvers

There has been 1 observational study evaluating the role of intraoperative primary balloon angioplasty as a technique to upgrade small-diameter veins during AVF creation in combination with sequential BAM.[249] That study reported a >90% use in this center with primary balloon angioplasty.[249] However, it did not have a comparator group and did not report the number of interventions required to maintain patency after AVF use, and it was also nonrandomized. Primary balloon angioplasty with BAM warrants further scrutiny before further adoption as standard practice.

Special Discussions

The Work Group discussed the clinical trials challenges of intraoperative maneuvers to assist AVF maturation (eg, pancreatic elastase and allogenic endothelial implants, among others) but acknowledged the need to develop drugs, devices, and/or strategies to facilitate AVF maturation and use. BAM was discussed, but the literature was not extracted due to the limited evidence in this area of intraoperative maneuvers for AVF maturation.

Implementation Considerations

None of these therapeutics are available for use at present because the phase 3 studies were terminated before completion and/or they are currently being evaluated in ongoing phase 3 studies, and/or the therapy was ultimately found to be ineffective.

Future Research

- The role of the Fistula Assist device in AVF maturation is currently in early-phase studies and may play a role in AVF maturation. No formal data are available regarding this technology.
- The role of BAM needs to be studied further in the setting of RCTs.
- One-stage versus 2-stage basilic vein transpositions need to be studied further in the setting of RCTs.

Guideline 9. CVC Insertion

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Techniques and Other Considerations for Placement

9.1 **KDOQI recommends the use of image-guided CVC insertions to improve success of insertions. (Conditional Recommendation, Moderate Quality of Evidence)**

9.2 KDOQI considers it reasonable that if fluoroscopy is not used to insert a tunnelled CVC, alternative imaging is used to ensure that the CVC tip has been correctly placed. (Expert Opinion)

Rationale/Background

CVCs were traditionally placed by using anatomic landmarks including vessel pulsation and were typically inserted in the internal jugular vein (right side preferred over left side) or the femoral vein (for short term use). More recently, image-guided placement of CVCs by both fluoroscopic and ultrasound imaging have been assessed and used. The advantages to image-guided insertion of CVCs by trained individuals are increased successful insertion and reduced complication rates. The main complications include hematomas and inadvertent arterial puncture.

The current 2019 NKF KDOQI Clinical Practice Guideline concurs with the prior 2006 KDOQI guideline for vascular access that recommended that CVC insertion should be performed in centers where ultrasound guidance and fluoroscopy are available. Ultrasound guidance should be used for all tunneled, cuffed CVC insertions to minimize insertion complications such as inadvertent arterial cannulation. Furthermore, fluoroscopic localization of the catheter tip was also encouraged to allow for ideal CVC tip location for attainment of maximal hemodialysis blood flow.[13]

Detailed Justification

Successful placement of a CVC requires attainment of the proper location within the vascular system and sufficient HD blood flow rates to achieve prescribed adequate dialysis. Imaging allows the trained operator to localize the target vein and its surrounding structures, thereby detecting any variant anatomy and ensuring patency (because intraluminal thrombosis is not uncommon).[250] Because the anatomic relationship of the right internal jugular vein to the common carotid artery can vary, ultrasound guidance for CVC insertion may reduce the likelihood of inadvertent arterial puncture.[251,252]

The 2019 KDOQI recommendations are primarily based on the greater quality of evidence that image-guided placement of CVC results in a higher likelihood of successful insertion, with weaker evidence that it reduces complications (as will be discussed). In this section, *imaging* refers to fluoroscopic and ultrasound guidance.

A single-center RCT (N = 110) compared the success of ultrasound-guided versus traditional insertion (using anatomic landmarks without ultrasonography) of uncuffed femoral vein CVCs and accounted for physician experience, comparing those with <6 years of experience with those with >6 years of experience. The success rate (defined as insertion of the CVC after no more than 3 attempts) was significantly higher with ultrasound (98% vs 80%; P = 0.002), as was success on the first attempt (86% vs 55%; P < 0.001).[253] Significantly fewer attempts were required to achieve catheterization with ultrasound (mean of 1.16 vs 1.51; P = 0.001). Fewer complications (hematoma or arterial puncture) occurred in the ultrasound group compared with the anatomic landmark group (5.5% vs 18.2%; P = 0.04).[253]

One observational study (n = 202) compared fluoroscopy-guided CVC placement (n =136) to CVC placement without imaging (using a slightly modified traditional technique of introducer insertion without the rigid dilator; n = 66).[250] All CVCs were placed in the internal jugular vein, with the majority (83%) placed on the right side. There was a significantly higher success rate (defined as placement and use of the CVC with adequate blood flow) with fluoroscopy (98% vs 92%; P = 0.03). Significantly more CVCs were placed on the right side in the nonimaging group (91% vs 80%; P = 0.02). This study reported bleeding events and showed no significant difference between groups for major, minor, or total bleeding events. Total bleeding rate was 1.5% in the fluoroscopy-guided placement group and 3.0% in the nonimaging placement group

Overall, KDOQI cannot suggest the use of image-guided CVC insertion based solely on reducing complication rates, because the complication rates are not significantly different with ultrasound-guided versus traditional placement techniques. Given the strength of the available evidence, further high-quality studies on image-guided CVC insertions and complication rates are needed.

Postinsertion imaging should be considered to avoid malpositioning of CVCs.[254,255] Proper location of the CVC tip is at the mid right atrium to avoid vessel and right atrial trauma and consequent complications. Malpositioning can lead to vascular perforation, venous thrombosis, catheter malfunction, and cerebral migration. Such complications have been documented to occur in 1% of CVCs placed into the right internal jugular vein via ultrasound guidance in a retrospective single-center study, where 75% of CVCs were placed by trainees (residents/fellows).[254,255] In a prospective study, 1.4% of right internal jugular vein CVCs were malpositioned when placed by an anesthesiologist with the aid of anatomic landmarks without image guidance.[255]

Factors associated with tunneled CVC tip malpositioning include change in position from supine to upright position, which may be accentuated in obese patients and female patients.[256] Consistent with the 2006 KDOQI guideline, it is reasonable to consider imaging for correct CVC location when catheter dysfunction persists that is unresponsive to conservative maneuvers and TPA administration.[13]

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S54-S59.

Special Discussions

The preferential order of CVC insertion (eg, right internal jugular vein, left internal jugular vein, etc) is addressed in a separate section (Guideline 3).

The proper location of the CVC tip is at the mid right atrium (see Detailed Justification above).

Implementation Considerations

To ensure competency for procedural skills to insert nontunneled (uncuffed) CVC, nephrology fellowship programs have incorporated simulation-based learning. The focus has shifted from tallying the number of procedures performed to a more focused measurement of the necessary components of the process for successful performance of this procedure. Procedural training, which includes placement of nontunneled HD CVC, is also a requirement of the American Board of Internal Medicine and the Accreditation Council of Graduate Medical Education.[257]

Such training is highly desirable for all jurisdictions and personnel—at any level of training or practice—who need to insert CVCs for HD. Given the global nature of HD and travel of HD patients, a minimum level of procedural training for CVC insertion would provide standardization of care.

Future Research

Additional clinical studies are needed to identify the ideal means to insert a CVC for HD. Imaging appears to favorably affect successful placement and may reduce complication rates. Both ultrasound and fluoroscopy have been studied thus far, with the former being most used for placement of the CVC and the latter being used primarily to ensure appropriate CVC tip localization.

Newer technologies include vein-localizing tools based on near-infrared spectroscopy; near-infrared radiation is absorbed by hemoglobin and reflected by neighboring tissues, thereby outlining the vascular tree and allowing visualization of the vessels through the overlying skin.[258] This technology has been used to increase successful placement of PICCs in neonates.[259] Whether this technology has application in adults for CVC placement, and whether it warrants comparison to real-time ultrasonography as an imaging technique to enhance CVC placement, would be subjects for future studies.

Guideline 10. Post–AV Access Creation/CVC Insertion Considerations

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: AV Access Early Postoperative Considerations (0-30 days)—Early AV Access Complications

10.1 **KDOQI considers it reasonable for AV access (AVF and AVG) to be evaluated by a surgeon/operator for postoperative complications within 2 weeks and for an appropriate member of the vascular access team to evaluate for AVF maturation by 4-6 weeks after AV access creation and refer for further investigation if not maturing as expected. (Expert Opinion)**

Note: Ideally, the surgeon/operator evaluating for complications would be the same individual who created the AV access.

Rationale/Background

After creation of an AV access, there are 2 issues that need to be addressed: early surgical complications and usability or maturation of the AV access. Early surgical complications need immediate attention and are best addressed by the surgeon or operator who created the vascular access. A knowledgeable member of the vascular access team (eg, nephrologists and/or nurses skilled in AVF examination) can determine usability and maturation. Typically, an AVG can be used almost immediately (early stick AVG) or at 2 weeks (standard AVG) after creation. An AVF should be evaluated for maturity at 4 to 6 weeks after creation; if concerned, arrangements must be made for further investigations, such as an ultrasound examination.

Detailed Justification

Surgeons typically see patients within 2 weeks after construction of the vascular access to assess wound healing and evaluate for potential complications. Early complications of the vascular access are thrombosis, immaturity, infection, pain, numbness, weakness, and edema of the ipsilateral arm/hand.[260,261] Infections are more common after AVG than AVF placement. The majority of AVG infections occur in the first month after placement.[262] Hand or finger tingling and numbness can occur from soft tissue swelling and hematomas compressing nerves but usually resolves within 4 weeks.[261] Pain, numbness, weakness, and paralysis of the hand and fingers with a warm hand, often occurring immediately after surgery, suggests ischemic nerve damage, a condition called *ischemic monomelic neuropathy* that typically requires immediate ligation of the vascular access.[263] Hand and finger pain with a cold and blue hand suggests ischemia that needs surgical measures to reperfuse the hand[264,265] (Guidelines 18 and 19). Limb edema could result from the surgical procedure itself but, if persistent (>2 weeks), suggests central vein stenosis, especially if the patient currently has or had ipsilateral CVC(s) or other central vein damage/manipulation.[266]

AVF examination for maturity is important especially if patients are dialyzing with a CVC. The earlier AVF immaturity is detected and addressed, the shorter the time the patient receives HD with a CVC. An experienced and knowledgeable member of the vascular access team, such as dialysis nurses and nephrologists skilled in AVF examination, can accurately assess maturity in most AVFs at 4 weeks after creation.[4,127] In 1 study, experienced dialysis nurses were able to predict with 80% accuracy the ability to use AVFs for dialysis.[127] The major causes of AVF failure to mature can be detected by physical examination of the AVF.[267-269] The tools provided by the Fistula First Catheter Last initiative have not been validated but can still be helpful, such as the "AVF Quick Reference" guide.[270,271]

The arm-raising test assesses adequacy of venous outflow, and the augmentation test assesses adequacy of arterial inflow. In addition, the examination may reveal a large accessory vein or collateral vein and stenosis contributing to AVF immaturity. If the physical examination is equivocal, an appropriate follow-up investigation, such as ultrasound examination with Doppler, should be performed. This will help evaluate for causative abnormality and assess AVF maturation progress via AVF diameter and blood flow (brachial artery and AVF). Minimum ultrasound criteria have been established for AVF maturity at 4 weeks using vessel diameter and flow parameters (vessel diameter, 4-5 mm and blood flow, 400-500 mL/min).[127,189,268,272,273] Should a correctable cause for AVF immaturity be found (eg, culprit stenosis or collateral vessels), this should be corrected in a timely manner to facilitate AV access maturation.

Special Discussions

Tools provided by Fistula First Catheter Last initiative have not been validated but were created by a group of multidisciplinary experts in HD vascular access that the Work Group believed might be helpful. See esrdncc.org/en/fistula-first-catheter-last/ffcl-resources/ffcl-professionals/tools-and-resources/.

Implementation Considerations

Routine re-training of relevant health team members (eg, annual basis) on postcreation/postinsertion evaluation and monitoring for complications of AV access and CVC, respectively, should occur to maintain and update knowledge for optimal vascular access care.

Monitoring and Evaluation

Evaluate whether the 2 to 4–week timelines suggested need to be altered according to each facility's logistics and practice patterns and what impact it has on a patient's AV access complications and usability.

Future Research

Validate tools provided by Fistula First Catheter Last for AVF maturation and the impact on AVF usability.

Statements: Postoperative AV Access Maturation

Patient Enhanced

10.2 **There is inadequate evidence for KDOQI to make a recommendation on the use of upper extremity exercise to facilitate postoperative AVF maturation.**

10.3 **KDOQI recommends the use of whole arm rather than finger exercise, if exercise is used to facilitate AVF maturation. (*Conditional Recommendation, Moderate-High Quality of Evidence*)**

Pharmacologic Intervention

10.4 **KDOQI does not suggest the use of heparin as an adjuvant therapy in the perioperative period to improve primary patency or initial use of AV access (AVF or AVG). (*Conditional Recommendation, Low Quality of Evidence*)**

10.5 **KDOQI does not suggest the use of adjuvant clopidogrel monotherapy initiation in the perioperative period to improve AVF maturation and reduce the likelihood of primary failure. (*Conditional Recommendation, Low Quality of Evidence*)**

10.6 **KDOQI does not suggest the use of glyceryltrinitrate to enhance AVF maturation. (*Conditional Recommendation, Low Quality of Evidence*)**

10.7 **KDOQI does not suggest the use of cholecalciferol to enhance AVF maturation. (*Conditional Recommendation, Moderate Quality of Evidence*)**

10.8 **There is inadequate evidence for KDOQI to make a recommendation on the use of clopidogrel-prostacyclin (iloprost) for AVF usability or patency.**

Endovascular and Surgical Intervention

10.9 **There is inadequate evidence for KDOQI to make a recommendation on the preferred use of surgical or endovascular techniques for postoperative maturation. It is reasonable to consider a careful individualized approach to using either surgical techniques or endovascular techniques when needing to intervene on an AV access to enhance maturation postoperatively.**

Rationale/Background

AVF maturation failure and AVG thrombosis remain major clinical problems for HD patients. Unfortunately, 20% to 60% of AVFs created fail to mature successfully for dialysis use.[77,233,234] Thrombosis accounts for almost 80% of AVG failures[235,236] due to an underlying stenosis at the venous anastomosis.[237-239] At present there are few, if any, effective therapies to enhance AVF maturation and reduce AVG stenosis and thrombosis. Patient-enhanced and pharmacologic therapies to assist postoperative AV access maturation and stenosis/thrombosis prevention were not addressed in the 2006 KDOQI guideline.[13] Moreover, the type of intervention (eg, surgical or endovascular) was not addressed in the 2006 KDOQI guideline. Since the 2006 KDOQI guideline, there have been several RCTs evaluating therapies to assist AVF maturation and prevent AVG thrombosis in the early postoperative period.

Detailed Justification

Patient-Enhanced Postoperative Maturation

Among the postoperative interventions to promote AVF maturation that were reviewed, 1 patient-enhanced postoperative procedure and 1 pharmacologic therapy demonstrated significant benefit to improve postoperative maturation. Although commonly practiced, there is inadequate evidence demonstrating the benefit of arm exercises for AVF maturation. Arm exercises after AVF creation should be positively considered, despite some literature suggesting no benefit versus control, in part because it is noninvasive, has little to no harm, and requires minimal costs.

Directed Upper Extremity (Elbow/Wrist/Hand) Postoperative Exercise Program Versus Routine Postoperative Care

Fontsere et al[274] (N = 72) compared isometric exercises along the whole arm postoperatively to usual routine postoperative care, allocating 39 patients to the exercise and 33 patients to the control group. The exercise intervention included repetitive exercise of the elbow, wrist, and hand using a flex band, for a duration of 1 month after AVF creation. The control group was not asked to perform specific exercises. Potentially relevant drug use (eg, anticoagulant) was similar among treatment groups. Clinical AVF maturation, defined as an easily palpable vein by physical examination, with a straight-superficial segment, length of more than 10 cm, sufficient diameter, and good palpable thrill, at 1 month was not statistically different between the exercise group (95%) versus the control group (81%) (RR, 1.18; 95% CI, 0.97-1.42).[274] This nonsignificant result was consistent with that found by using ultrasound criteria for AVF maturation, defined as a draining vein diameter of ≥5 mm, skin-vein distance of ≤6 mm, and brachial blood flow rate of ≥500 mL/min of the exercise (82%) and control groups (74%), respectively (RR, 1.10; 95% CI, 0.85-1.42).[7] There was no difference between the exercise and controls groups for (1) change in mean brachial artery flow (+389 mL/min [exercise] vs +431 mL/min [control]; P = 0.99); (2) change in mean venous diameter (+2.1 mm [exercise] vs +2.5 mm [control]; P = 0.30).[7] Harms, including potential repetitive stress injury, were not assessed. AVF location as an effect modifier was analyzed. Proximal AVF (brachial-cephalic, brachial-basilic) was 50% (19/38) in the exercise group and 68% (21/31) in the control group, with no difference in clinical maturation. Clinical maturation of distal AVF was achieved by 95% in the exercise group and 60% in the control group. However, the effect of location (proximal vs distal AVF) on clinical maturation was not significant (odds ratio [OR], 3.78; 95% CI, 0.74-19.16). The effect of location on maturation became statistically significant when ultrasound measures were used (OR, 6.82; 95% CI, 1.76-26.40). AVF maturation defined by ultrasound criteria for proximal AVF was achieved by 95% in the exercise group and 86% in the control group and in distal AVF was achieved by 69% in the exercise group versus 50% in the control group. Clinical usability was not assessed in this study.

Arm Exercise Versus Finger Exercise

In a single-center study, Salimi et al[275] compared isometric exercises of the whole arm (n = 25) to limited finger movements (n = 25). The intervention group performed exercises at home, using a tourniquet placed 15 cm above the AVF incision site. It included a defined number of exercise repetitions over specific time frames: 4 times a day for 2 weeks after AVF creation that involved the hand, lower arm, elbow, and upper arm. Exercise difficulty progressed over the study period by making the exercises more challenging and adding in the use of light dumbbells (0.5 kg) and flex bands. The comparison group did not have a specified routine but were asked to routinely open and close their fingers.[275] Originally, 55 patients (n = 25 in control group and n = 30 in intervention group) were recruited, but 5 participants in the intervention group who did not comply were not analyzed and not reported. Clinical maturation, defined as a palpable, relatively straight with >10 cm length of the superficial vein and a uniform thrill on palpation, at 2 weeks improved with arm exercises (52%) versus finger exercise (20%) (RR, 2.60; 95% CI, 1.09-6.20). Maturation by ultrasound criteria, defined as draining vein diameter of ≥6 mm, skin-vein distance of ≤6 mm, and blood flow rate of ≥600 mL/min, were considered because AVF ultrasonographic maturation criteria at 2 weeks were not statistically different between the whole arm (88%) and finger (68%) exercise groups (RR, 1.29; 95% CI 0.9501.76). The change in flow rate at 2 weeks was

not statistically different with arm exercise (+431 mL/min) versus finger exercise (+316 mL/min) (mean difference, 114 mL/min; 95% CI, -41.0 to 269). There was no difference between groups for (1) mean change in the draining vein diameter: -2.32 mm (whole arm exercise) versus +1.63 mm (finger exercise) (mean difference, +0.72 mL/min; 95% CI, -0.20 to +1.64) or (2) mean change in the skin to vein distance: -1.95 mm (whole arm exercise) versus 1.80 mm (finger exercise) (mean difference, -0.15; 95% CI, -1.01 to 0.71).[275]

Pharmaceutical Treatment Postoperative Maturation

Heparin in AVF and AVG. Four trials with a total of 336 participants[276-279] evaluated heparin for AV access maturation; the statistics provided here are for this combined cohort. D'Ayala et al,[278] Bhomi et al,[276] and Wang et al[279] were eligible to be pooled together and resulted in a study population with mean age of 52, and 54% male. Primary patency was reported in 3 trials[276,278,279]: short-term primary patency (<60 days) was not different with heparin or no adjunctive treatment (RR, 1.01; 95% CI, 0.64-1.60). The ability to use the AVF for dialysis at 3 months did not differ between participants who received heparin versus no adjunctive treatment (RR 1.13; 95% CI, 0.82-1.57). Harms reporting was inconsistent across studies. Two trials reported hematomas.[276,279] Bhomi et al had no hematomas in either group, whereas there was no statistical difference in hematomas with heparin (12%) versus no heparin (5%) in Wang et al (RR, 2.68; 95% CI, 0.30-24.1). AVF thrombosis was reported by Chen et al[277] and occurred in 13% of the heparin-treated group and 17% in the no-heparin group (RR, 0.80; 95% CI, 0.34-1.89). None of the trials assessed the effect modification of patient, vessel, or care delivery characteristics.

Clopidogrel. Two trials with low risk of bias enrolled a total of 970 participants.[280] Dember et al[31] randomized 877 patients to clopidogrel 300 mg the first day after AVF creation, followed by clopidogrel 75 mg daily or placebo treatment for 6 weeks and were followed up until 150 to 180 days after AVF creation or 30 days after initiation of dialysis, whichever occurred later. Ghorbani et al[280] randomized 93 patients in a separate study, 46 to clopidogrel 75 mg daily versus 47 to placebo control daily, 7 to 10 days before AVF creation up to 6 weeks postoperatively. These 2 studies were eligible for pooling, which resulted in a study population with mean age of 51 years and 58% male. (Primary failure, defined as thrombosis 6 weeks after AVF creation, favored the treatment group at 6 weeks in Dember et al: RR, 0.63; 95% CI, 0.46- 0.86.[31]) At 8 weeks, the primary failure outcome in Ghorbani et al showed no statistical difference between treatment arms (RR, 0.26; 95% CI, 0.06-1.14). The pooled failure rate that was not statistically different with clopidogrel (11%) versus placebo (19%) (RR, 0.55; 95% CI, 0.29-1.03). The ability to use the AVF was not different with clopidogrel (38%) versus placebo (41%) at 6 weeks (RR, 0.94; 95% CI, 0.79-1.13) or at 6 months (clopidogrel [52%] vs placebo [51%]; RR, 1.02; 95% CI, 0.69-1.51). Serious harms, bleeding, and thrombosis were reported by 1 or both studies[31,280] and were not statistically different with clopidogrel versus placebo. Dember et al reported no statistical difference in surgical or percutaneous interventions with clopidogrel (1.6%) versus placebo (2.3%) (RR, 0.69; 95% CI, 0.27-1.81). No trial assessed the effect modification of patient, vessel, or care delivery characteristics.

Glyceryl-Trinitrate. Field et al's single-center trial[281] randomized 99 to the glyceryl-trinitrate group and 101 to the placebo group. Of these, 167 patients completed surgery, 86 received glyceryl-trinitrate transdermal patch, and 81 received a placebo patch applied near the anastomosis/incision site and then dressed, immediately after surgery. Patients were told to remove the patch after 24 hours and were followed for 6 weeks. Radiocephalic or brachiocephalic AVF were included. Data from 167 of the 200 randomized patients was used in the analysis. Primary fistula failure at 6 weeks was not significantly different with glyceryl-trinitrate patch (28%) versus placebo (23%) (RR, 1.19; 95% CI, 0.71-2.0). Venous diameter mean change showed no statistical difference between the glyceryl-trinitrate patch (+2.2 mm) versus placebo (+2.3 mm) (mean difference, -0.10; 95% CI, -0.66-0.46).[281]

Cholecalciferol. Wasse et al[282] randomized 52 prevalent HD patients scheduled to have AVF creation within 4 weeks to oral vitamin D3 (cholecalciferol) 200,000 IU weekly (n = 25) or placebo (n = 27) for 3 weeks and followed them for 6 months. Eight participants died, were lost to follow-up, or never received permanent access, leaving 44 participants in the study. Nine (20%) of these 44 participants ended up receiving AVGs instead of AVFs. The ability to use the AVF at 6 months was not statistically different between cholecalciferol (45%) and placebo (54%) (RR, 0.83; 95% CI, 0.45-1.53).

Clopidogrel and Iloprost. Abacilar et al[283] randomized 96 participants to a combination of clopidogrel and iloprost (n = 40) or placebo (n = 46) and followed them for 1 year. Those on treatment were given 75 mg/day of clopidogrel and 200 mg/day iloprost (clopidogrel/iloprost) starting 7 to 10 days before surgery and continuing for 52 weeks. Primary failure was lower with clopidogrel/iloprost (8%) over placebo (30.4%) at 4 weeks (RR, 0.26; 95% CI, 0.09-0.74). Primary patency was higher with clopidogrel/iloprost (85%) versus placebo (68%) at 3 months (RR, 1.28: 95% CI, 1.02-1.61). Maturation was better with clopidogrel/iloprost (87%) versus placebo (67%) at 3 months (RR, 1.28; 95% CI, 1.01-1.61). There was no statistical difference in rates of adverse events with clopidogrel/iloprost (18%) versus placebo (13%) (RR, 1.38 95% CI, 0.52-3.58) or reoperations (0% in clopidogrel/iloprost vs 4% in placebo; RR, 0.20; 95% CI, 0.01-4.06).[283]

Although clopidogrel/iloprost in 1 study showed significant benefit to improve primary patency and maturation,[283] consideration of use should be individualized in the elderly and frail population. Detailed evaluation of the study by Work Group members revealed study inconsistencies that raised caution and led the group to lower its recommendation. Indeed, the KDOQI Work Group discussed the clopidogrel/iloprost study at length and believed that a larger, rigorously designed and conducted RCT to evaluate this drug regimen's effect to improve AV access outcomes would be needed. Furthermore, a much larger RCT with more than 900 patients[31] evaluating clopidogrel only versus placebo did not demonstrate significant benefit to improve clinical AVF use but did demonstrate significant benefit to reduce early thrombosis. Thus, the true benefit of clopidogrel to improve AVF maturation needs further evaluation.

Other Interventions

Data extraction on the type of intervention, endovascular versus surgery, used to intervene on a nonmaturing AV access was not performed. Formal comparative studies directly evaluating these 2 methods in salvaging nonmaturing AVFs are lacking. The studies published to date, primarily regarding AVFs, have shown conflicting results.[284-288] RCTs will be needed to determine the appropriate type of intervention used to intervene for a nonmaturing AVF. Moreover, recently, a more aggressive approach to AVF maturation failure in which repeated long-segment angioplasty procedures (BAM) has been used to sequentially dilate up the peri-anastomotic venous segments. Two single-center studies evaluating BAM techniques to salvage nonmaturing AVFs have been published. These 2 studies demonstrated that a large proportion of immature AVFs could be salvaged for successful use on dialysis, but postintervention primary unassisted patency rates were poor, and the number of postmaturation angioplasties per year to maintain function was high.[289,290] Prospective and randomized studies of BAM compared with standard of care need to be performed in the future.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S60-S89.

Special Discussions

Additional Work Group discussion determined that there is a need to (1) provide a uniform recommendation on when to abandon an AV access; (2) determine the best methods to evaluate for postoperative maturation, including physical examination techniques and imaging; (3) provide uniform definitions of AV access maturation and patency that are relevant for both clinical and study purposes; and (4) create consensus guidelines to determine the best protocols to intervene for nonmaturing AVF (eg, < and >6 weeks) and early AVG problems.

Implementation Considerations

Although some of these studies did not meet the prespecified primary outcome, several important secondary outcomes were achieved; thus, use of these therapies must be considered on an individual basis. Moreover, therapies such as clopidogrel, which is an antiplatelet agent, require special consideration for use in the elderly and/or frail population, who have a high risk of falls or other bleeding events.

Future Research

The Work Group determined several areas for critical future research in this area, which include (1) the role of surgical versus endovascular procedures to enhance AVF maturation; (2) the potential role of protocol-driven AVF maturation (eg, BAM), in particular, the short- and long-term risks and benefits of this procedure; (3) the potential role of external assistance, such as the Fistula Assist device in AVF maturation and others, that may be in development or early-phase clinical studies and may be promising.

Statements: Timing of CVC Removal

Noncuffed, Nontunneled Catheters (NT-CVC)

10.10 **KDOQI considers it reasonable to limit the use of temporary, noncuffed, nontunneled dialysis catheters to a maximum of 2 weeks due to increased risk of infection, and this should be considered only in patients in need of emergent access. (Expert Opinion)**

Cuffed, Tunneled CVC

10.11 **KDOQI considers it reasonable that in HD patients for whom a cuffed, tunneled CVC is the most appropriate permanent dialysis access, there is no maximum time limit to CVC use, but regular evaluation is required to determine if the CVC remains the most appropriate dialysis access. (Expert Opinion)**

Note: Appropriate uses of a cuffed, tunneled CVC for chronic hemodialysis include the following:

1) *All other AV access options have been exhausted (after thorough multidisciplinary evaluation)*
2) *Temporary switch from another modality (eg, PD, due to PD-related complications such as pleural leak, transplant–acute rejection, etc), but the patient is expected to return to that modality after the complication is adequately resolved*
3) *Awaiting live-donor kidney transplant with established surgical date (<90 days)*

4) *Very limited life expectancy (eg, <6-12 months)*
5) *Clinical conditions that would worsen with AV access (eg, HF with EF<15%, nontreatable skin lesions where cannulation/scratching significantly increases infection or rupture risk, etc)*
6) *Patient choice after proper informed consent (eg, competent, >85-year-old elderly woman with high risk of AV access failure, needle phobia, and unknown life expectancy)*

Note: The above points regarding appropriate use of CVC are discussed in Guideline Statement 2.2.

Rationale/Background

In patients for whom an AV access has not been created, is not ready for use, or is not possible, HD can be performed with a HD catheter. In the United States, 80% of patients were using a CVC at HD initiation in 2015, which has changed little since 2005.[139] At 90 days after initiation of dialysis, 68.5% of HD patients were still using a CVC.[139] The type and duration of CVC use during this time must be considered because it may have implications for patient well-being.

Nontunneled, noncuffed catheters (NT-CVCs) serve a temporary role for acute clinical situations where immediate HD is needed and/or there are immediate barriers or contraindications to placement of a cuffed tunneled catheter (CVC). Sepsis, lack of image guidance, and uncorrectable coagulopathy are examples of such barriers. It is known that cuffed, tunneled CVCs have a lower risk of infection than NT-CVC.[291,292] Therefore, NT-CVC use should be limited. A related question of when to switch from a NT-CVC to a tunneled CVC in patients who do not recover from AKI has not been addressed by prospective studies. However, 1 study noted that the need for dialysis in acute kidney injury (AKI) often exceeded 3 weeks.[293]

The prior 2006 KDOQI guideline Statement 2.4 recommended that there should be a plan to (1) discontinue or (2) convert any short-term catheter (NT-CVC) to a long-term catheter (CVC) within 1 week. As for maximum CVC dwell time, there may be concerns about CVC durability and of the CVC becoming incorporated or scarred into the venous wall over a prolonged period of time. Complications related to these concerns have been reported, such as breakage and migration of CVC parts, incorporated and retained CVC sections that have caused fatal sepsis, etc.[294] Although resistant adherent CVCs, also known as *stuck catheters*, can be removed by endovascular techniques, if unsuccessful, it may require open heart surgery to extract scarred in CVCs.[295] Despite these reports, no studies have ascertained an ideal dwell time. Furthermore, other opinion-based guidelines[296,297] now recommend against routine change of CVCs, including the prior 2006 KDOQI guideline. Furthermore, there are newly described techniques that allow minimally invasive removal of stuck catheters[298,299] in situations where the cuffed, tunneled CVC is a valid choice for vascular access but needs removal or exchange.

Detailed Justification

In terms of short-term use, in 1 study, the infection rate increased exponentially after 1 week with actuarial analysis of 272 catheters (37 CVC vs 235 NT-CVC) showing a difference in infection rates by 2 weeks.[291] Also, infection rates per 1,000 days at risk for NT-CVC were more than 5 times greater versus internal jugular CVC and almost 7 times greater with femoral NT-CVC.[291]

In HD catheters for AKI or urgent/emergent HD starts, a prospective multicenter RCT comparing NT-CVC to CVC (internal jugular vein location) in critically ill patients found a significant reduction in CVC-related sepsis with CVC.[300] A single-center retrospective study found that mean CVC dwell time in patients who eventually recovered from AKI was 34 days, with only 15 of 76 (20%) patients recovering kidney function within 1 week.[293]

In terms of long-term use of HD catheters, although there are concerns regarding stuck HD CVC with possible embolization of fragments during removal attempts, there have been recent techniques that now allow for extraction percutaneously. These include laser extraction similar to pacemaker lead extraction and intraluminal CVC dilation that dislodges the CVC from vessel walls.[298,299]

Special Discussion

Although uncommon, complications such as resistant adherent CVCs, also known as a *stuck catheters*, may require management by operators with prior specialized experience.

Monitoring and Evaluation

Regular re-evaluation of the patient's use of CVC required, including whether the patient should receive conservative care.

Future Research

- Testing long-term durability of dialysis catheters
- Materials to prevent resistant adherent CVCs (stuck catheters); do newer removal techniques prevent stuck catheters in the long term?

Guideline 11. Vascular Access Use

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: Vascular Access General Monitoring

11.1 **KDOQI considers it reasonable to assess or check the vascular access and surrounding area by physical exam prior to every cannulation (if AV access) or connection (if CVC) for potential complications. (Expert Opinion)**

Statements: AV Access Cannulation

Please review Guideline Statement 11.1.

11.2 **KDOQI recommends rope ladder cannulation as the preferred cannulation technique for AVFs. (Conditional Recommendation, Moderate Quality of Evidence)**

11.3 **KDOQI considers it reasonable to limit AV access buttonhole cannulation only to special circumstances given the associated increased risks of infection and related adverse consequences. (Expert Opinion)**

11.4 **KDOQI considers it reasonable to avoid buttonhole cannulation in synthetic PTFE grafts due to potential serious consequences. (Expert Opinion)**

11.5 **KDOQI suggests that when select buttonhole cannulation is performed, the use of buttonhole cannulation devices to facilitate cannulation should be at the discretion and expertise of the cannulator. (Conditional Recommendation, Low Quality of Evidence)**

11.6 **KDOQI considers it reasonable to use skilled cannulators with established high rates of cannulation success to perform initial AV access cannulations on patients to help avoid primary infiltration injury of the AV access. (Expert Opinion)**

11.7 **KDOQI considers it reasonable to have structured training and supervision of dialysis technicians and nurses before and during their initial cannulation attempts, and regular training updates to maintain cannulation competency. (Expert Opinion)**

11.8 **KDOQI considers it reasonable to support and educate eligible patients on self-cannulation of their AV access (AVF or AVG). (Expert Opinion)**

Note: To be clear, any consideration of buttonhole cannulation refers only to AVF and certain AVG materials. AVG made of PTFE should not be accessed by buttonhole cannulation, due to risks of "one-siteitis" and its serious consequences.

Note: See Guideline Statement 12.2 for use of ultrasound for AV access cannulation.

Rationale/Background

Once an AV access is created and nurtured to "readiness for cannulation," the next important step is AV access cannulation. The first cannulation is often a source of anxiety for the patient—and often for the cannulator as well. Problems with cannulation can lead to a range of complications, from mild infiltration injury to major hematomas or blood loss requiring blood transfusions, and even loss of the AV access. Mild infiltration injury can occur as frequently as >50% of all AVF and major infiltrations of 5% to 7%.[3] Thus, it is critical to ensure that cannulators have received adequate training and mentoring to facilitate and achieve successful cannulation. A successful cannulation is one where 2 needles of adequate size are inserted into the AV access at the right depth and angle to facilitate prescribed dialysis and in which this is achieved with minimal pain or no complications. Different cannulation techniques can be applied effectively[301] but require skilled cannulators who have received adequate initial and ongoing training[302] and continued close monitoring of the AV access.

Detailed Justification

Technique

There were 5 unique RCTs and 7 observational studies reviewed on cannulation technique. Three trials (total N = 265)[303-305] compared buttonhole cannulation versus rope-ladder (RL) cannulation. Neither AVF survival nor pain with cannulation was statistically different with buttonhole versus RL cannulation. For example, MacRae et al[303,304] showed no difference in AVF survival (RR, 1.04; 95% CI, 0.81-1.34). Although pain was not different between techniques, lower use of lidocaine with buttonhole cannulation was reported.

Patient satisfaction was also not significantly different with buttonhole versus RL.[305] Chow et al[305] reported the Kidney Disease Quality of Life scale, which includes the Short Form (SF) Health Survey. The SF-12 physical and mental composite scales were described as showing no significant difference between groups. (The SF-12 physical composite score had mean of 35.80 [buttonhole] vs 33.88 [RL]; the SF-12 mental composite score had a mean of 42.58 [buttonhole] vs 44.39 [RL].)

The need for surgical or endovascular intervention was also not significantly different between buttonhole and RL.[304] At 1 year, MacRae et al[304] found the rate of surgical intervention with buttonhole (0.09 per patient-year at risk) versus RL (0.11 per patient-year at risk) (RR, 0.79; 95% CI, 0.33-1.89) and the rate of endovascular intervention with buttonhole (0.90 per patient-year at risk) versus RL (0.72 per patient-year at risk) (RR, 1.28; 95% CI, 0.78-2.10). No other intermediate outcomes were reported.

Hematomas were reported with varying results.[303,305] MacRae et al[303] found significantly fewer hematomas per dialysis session with buttonhole (295 per 1,000 dialysis sessions) versus RL (436 per 1,000 dialysis session) at 8 weeks (RR, 0.68; 95% CI, 0.58-0.79). In contrast, Chow et al[305] reported significantly more hematomas with buttonhole (12%) versus RL (0%) at 26 weeks (RD, 0.12; 95% CI, 0.01-0.23). There was no difference with thrombosis or exit site infections. For example, pooled analysis of 3 trials showed that exit site infections with buttonhole cannulation had RR of 4.41 (95% CI, 0.16-123.5)[304-306] (Fig 11.1).

Of importance was the risk of serious AV access–related infections. *Staphylococcus aureus* bacteremia was significantly more frequent with buttonhole (13%) versus RL (0%) at 1 year (RR, 19; 95% CI, 8-46; RD, 0.13; 95% CI, 0.05-0.21).[304] The quality of evidence for this harm was strong compared with the quality of evidence for other findings of the cannulation technique.

Tables of studies, evidence quality, and risks of bias are provided in Supplement, 3 Tables S90-S97.

Aids to the Buttonhole Cannulation Technique

Two trials examined cannulation aids (total n = 226) and assessed outcomes at 1 year. Vascular access failures were significantly lower with buttonhole-peg cannulation (0%) versus usual care (different-site) (13%) in 1 trial (RR, 0.06; 95% CI, 0.03-0.15; RD, -0.13; 95% CI, -0.21 to -0.05).[307] Total interventions (fistuloplasty or thrombectomy) were significantly lower with buttonhole-peg cannulation (19%) versus usual care (39%) in 1 trial (RR, 0.48; 95% CI, 0.26-0.89).[307]

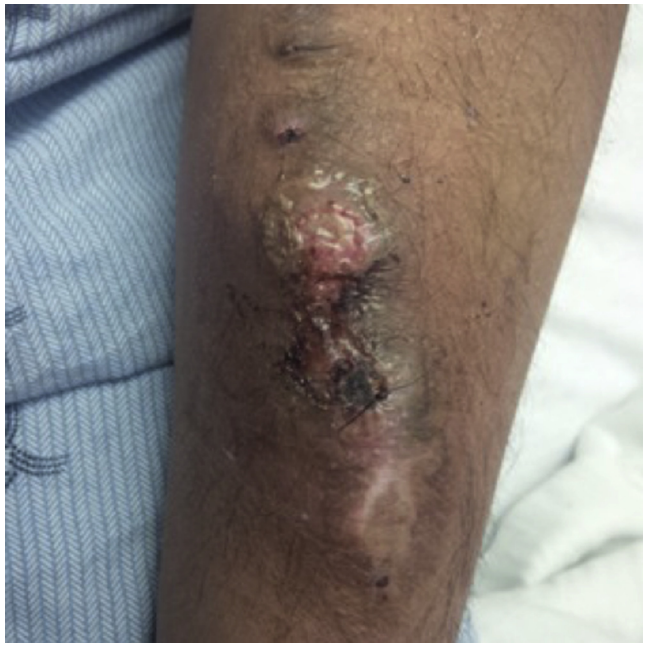


Figure 11.1. Buttonhole infection.

Vaux et al[307] reported that enlargement of existing aneurysm was significantly lower with buttonhole-peg cannulation (23%) versus different-site technique (67%) (RR, 0.34; 95% CI, 0.12-0.99). However, development of a new aneurysm did not differ: buttonhole-peg cannulation was 4% versus different-site technique at 17% (RR, 0.27; 95% CI, 0.06-1.17).[307]

Of note, using a buttonhole cannulation aid was associated with increased risk of cannulation site infection (whereas not using one was not, as discussed). Exit-site infections were significantly higher with buttonhole-peg cannulation (3%) versus different-site technique (0%) in a pooled analysis of data from the 2 trials (RR, 4.60; 95% CI, 2.31-9.18).[307,308] Again, the quality of this evidence was stronger than the other outcomes.

Special Discussions

Given the high risk of infectious harms with buttonhole cannulation (eg, *S aureus* bacteremia) and low evidence of clinical benefit with buttonhole (eg, no difference in AV access survival, surgical, and endovascular interventions or patient comfort), the Work Group agreed on a cautious approach to accessing the patient's lifeline with a decision to prefer the RL cannulation technique. However, they recognized that circumstances do exist where buttonhole cannulation may be necessary (Table 11.1). The Work Group commented that, for in-home HD patients who cannot cannulate using the RL technique, the infection risk associated with buttonhole cannulation is similar to a well–cared-for CVC[309-313]; thus, the decision to continue with an AVF with buttonhole cannulation or insert CVC must be carefully considered, weighing the risks and benefits or both in the context of the patient's ESKD Life-Plan. The potential risks of "one-siteitis" and its consequences in synthetic grafts made of materials such as PTFE can be serious; therefore, the Work Group took a cautious approach to avoid buttonhole cannulation in these circumstances. The use of buttonhole cannulation in other nonautogenous graft materials, such as bovine or other biological material, is limited,[314] so the Work Group cannot comment on this. In the absence of evidence, the Work Group considers it reasonable to use the same precautions as with native AVF cannulation until data are available.

In such situations where buttonhole cannulation is appropriate, careful establishment of the buttonhole with proper training, retraining, and close monitoring is

Table 11.1. Circumstances Where Buttonhole Cannulation May Be Acceptable

AVF has only a short or small segment for cannulation
Enlarging or large aneurysm to prevent its further expansion
Failure of rope-ladder cannulation for cannulators (eg, home hemodialysis) who have established excellent hygiene and cannulation technique

required. Although the buttonhole-peg has potential advantages, it is also associated with increased risks of cannulation site infection, whereas buttonhole without aids does not appear to share that risk (but has a high risk of bacteremia). Thus, the decision to use a buttonhole aid must be carefully considered in an individualized manner, considering the characteristics and skills of both the patient and cannulator, respectively.

The skill and experience of a cannulator is intuitively important for cannulation outcomes, although there are no rigorous studies reporting on this. The use of expert cannulators to perform initial AVF cannulations was discussed; however, there are no widely accepted or standardized definitions of *expert cannulator*. Ideally, all nurses, technicians, patients, and physicians cannulating an AV access should have a level of proficiency such that both new and established AV accesses can be cannulated with the same degree of comfort, reliability, and success.

The specific details on the mechanics of accessing the AV access, for example, clean or aseptic technique, were not discussed but should follow universal infection control guidelines and adhere to specific dialysis unit/institutional policies. The use of graduated needle sizes, advancing blood flow rates, and so on should be individualized to meet the prescribed dialysis needs to achieve patient goals. Here, consideration of the ESKD Life-Plan is very important. For example, a patient on home nocturnal dialysis may be self-cannulating with needles and blood pump speeds that are quite different (eg, Qb of <300 mL/min) than a patient being cannulated by a technician with 14-gauge needles to satisfy a Qb of 450 mL/min in a 3- to 4-hour facility dialysis session (as may be the case in some US facilities).

Furthermore, since the last Guidelines, the prior "Rule of 6s" has been assessed by the National Institutes of Health Hemodialysis Fistula Maturation Study. Although blood flow, vein diameter, and depth were shown to be important, when using criteria of fistula blood flow of 600 mL/min, vein diameter of 6 mm, and depth of 2 mm below the skin, the likelihood of maturation success was approximately 50%, with greater depths having poorer maturation outcomes (in other words, a depth of 6 mm would likely be less successful, if maturation was only 50% with a depth of 2 mm).[315] Thus, the cannulation criteria needs to be revisited and studied further. The principals of having a vein of adequate length and diameter that is easily accessible (ie, not too deep and properly located to allow for comfortable needle cannulation) continue to hold. Cannulation criteria may, in part, be dependent on needle size and blood pump speed needed to achieve adequate dialysis. This is supported by the observed variation in cannulation times and successes around the world in studies comparing cannulation practices patterns.[85,316,317]

Finally, the use of ultrasound-guided cannulation was discussed at length among Work Group members. Due to the reliance on operator expertise, resources required, mixed patient and user feedback, and the paucity of literature to support its widespread use, the Work Group supports its use in select patients until further research is available. Select patients where ultrasound guidance may be useful include first or new AVF cannulation where a cannulator *experienced and competent with ultrasound-guided cannulation* deems that it may aid in cannulation, in an AVF with prior infiltration injury, or to avoid cannulation complications (Guideline Statement 12.2).

Implementation Considerations

Training and retraining of cannulators is critical to ensure maintenance of competency of cannulation skills. The use of cannulation simulation may be beneficial and should be studied.

Monitoring and Evaluation

New or altered cannulation protocols should be monitored in a continuous quality improvement manner to establish that change has made an improvement (eg, a reduction in the rate of infiltration injury).

Future Research

- Study of criteria for AV access readiness to cannulate
- Rigorous study of use of ultrasound-guided cannulation—its safety, efficacy, and impact in busy dialysis units—is needed
- More study of the details of the mechanics of cannulation at a patient level (eg, needle size and type, angle, retrograde/antegrade, graduated flow rates under varying circumstances) for best patient and dialysis outcomes is required
- Evaluating different simulation models and techniques for improving cannulation success—does it improve cannulation competency, reduce cannulation complications, and improve patient satisfaction?
- Define *expert cannulator* and how such expert cannulators can maintain their expertise and be best maximized to improve overall cannulation success within a dialysis unit or for the individual patient
- Rigorous studies to evaluate the use and outcomes associated with alternative cannulation-assistive devices
- The safety, efficacy, and patient satisfaction with using plastic cannulae
- Safety of buttonhole cannulation in nonautogenous, biologic graft materials

Statements: CVC System Connect and Disconnect Procedure Considerations

Please review Guideline Statement 11.1.

11.9 **KDOQI suggests the use of a catheter care protocol for exit site and hub care to reduce catheter-related bloodstream infections and treatment of catheter dysfunction. (*Strong Recommendation, Moderate Quality of Evidence*)**

11.10 **KDOQI considers it reasonable, in addition to correct hand hygiene/washing, to use aseptic**

technique and masks for patients and staff performing catheter connection and disconnection procedures. (Expert Opinion)

11.11 KDOQI considers it reasonable to cleanse the catheter hub when connecting and disconnecting the catheter with a chlorhexidine based solution. If chlorhexidine is contraindicated (eg, sensitivity, allergy), povidone-iodine solution (preferably with alcohol) is a reasonable substitute and should be used. (Expert Opinion)

11.12 KDOQI considers it reasonable at the time of catheter dressing change to cleanse the skin surrounding the catheter exit site with a chlorhexidine based solution. If chlorhexidine is contraindicated (eg, sensitivity, allergy), povidone-iodine solution (preferably with alcohol) is a reasonable substitute and should be used. (Expert Opinion)

11.13 There is inadequate evidence for KDOQI to make a recommendation on the specific chlorhexidine formulation to use for infection prophylaxis, and this should be based on the clinician's best clinical judgment and local practical considerations.

11.14 There is inadequate evidence to demonstrate a difference in catheter-related infections with the use of transparent film dressing compared with nontransparent dressing; thus, the choice of catheter dressing material should be based on the clinician's discretion that considers the patient's circumstances and uses best clinical judgment.

11.15 KDOQI considers it reasonable to use a topical antiseptic or antibiotic barrier at the catheter exit site in addition to cleansing until the exit site is healed to reduce the risk of catheter-related infection. (Expert Opinion)

11.16 There is inadequate evidence to demonstrate a difference in catheter-related infections between the use of various antiseptic or antibiotic topical exit site barriers; thus, the choice of topical exit site barrier should be based on the clinician's discretion and best clinical judgment.

11.17 KDOQI considers it reasonable to follow these catheter care practices (Expert Opinion):

- The frequency of catheter dressing change should be based on the clinician's discretion and best clinical judgment, with a minimum of once weekly
- Catheter dressings should be protected against wet and dirty environments, particularly when the exit site is not yet fully healed (eg, avoid swimming and showering)

Note: See Guideline Statements 21.2 and 21.3 for statements on CVC connectors to prevent CVC dysfunction or bacteremia and Guideline Statements 24.3-24.5 for statements on intraluminal strategies for the prophylaxis of CVC-related infections.

Rationale/Background

Hemodialysis CVCs, when compared with AV access, are associated with a 2- to 3-fold higher risk of infection-related hospitalization and associated costs due to catheter-related blood stream infections (CRBSI).[67,318,319] Contamination of the external and internal CVC surface through both the extraluminal and intraluminal pathways, respectively, involves the transfer of organisms during CVC manipulation, such as during dressing changes or connection and disconnection of the CVC. The transfer of organisms are from either the health providers' or patients' hands (if patient does own CVC care), the patient's skin, or surrounding clothing to the CVC exit site opening and tunnel (extraluminal pathway of organism entry) or to the external or internal surfaces of CVC hubs or caps (extraluminal or intraluminal pathway)[297,320] (Fig 11.2). As such, some guidelines have recommended (1) minimal manipulation of the CVC to reduce the risk of infection, (2) limiting access of HD vascular access to personnel who are adequately trained, and (3) need for regular re-training

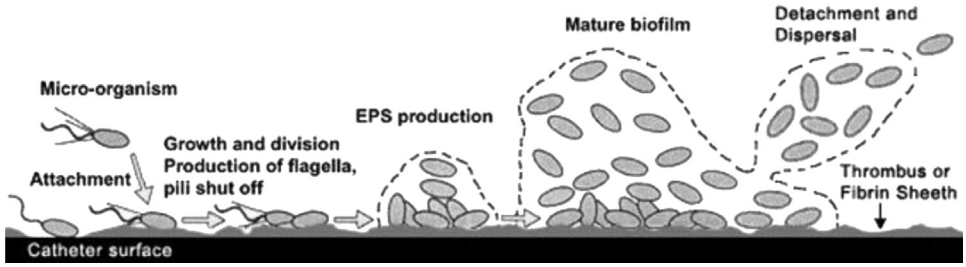


Figure 11.2. The pathogenesis of biofilm formation. Abbreviation: EPS, extracellular polymeric substance. Reproduced from Lok[665] with permission of Elsevier; original image © 2006 by the National Kidney Foundation, Inc.

of individuals handling HD catheters (or any dialysis access).[321] As a result, many dialysis units restrict accessing the CVC to the provision of HD, unless in emergency situations. The prior 2006 KDOQI guideline recommended CVC dressing changes at each dialysis session.[320] The current guideline differs by suggesting only the necessary minimal manipulation of CVC until the exit site and tunnel are healed to reduce the risk of infection. This Guideline suggests the preferred use of chlorhexidine for CVC and exit site cleansing, unless contraindicated, similar to prior recommendations.

Detailed Justification

Vigilant CVC care is required, including regular inspection of the CVC, tunnel, and exit site, and adherence to CVC care protocols. Both the patient and the HD staff should follow universal precautions and hygienic measures. The 2006 KDOQI guideline recommended that staff manipulating CVCs should wear a mask and clean or sterile disposable gloves; however, the data supporting masks are extrapolated from studies of their use during CVC insertion.[322,323] During CVC insertion, the risk of infection is high due to direct exposure of the vessel and bloodstream to the external environment. Whether or not masks are required is unclear in situations where the exit site is healed. However, extra protection is theoretically afforded if the health care provider or patient inadvertently sneezes, coughs, or spits (eg, while talking) during CVC care. The use of sterile gloves (vs new clean gloves) is also controversial, particularly when the use of no-touch techniques is strictly enforced.

Hub Care

Risks of contamination of the hub and infection include (1) contact of the exposed CVC hub with a nonsterile surface (eg, bedside desk) or object (eg, hand) (2) prolonged exposure to the air (3) improper cleansing of the hub, and (4) patient or provider breathing on the exposed hub.[324] Thus, it is important to reduce the hub exposure time, and diligent hub cleansing is required. Doing so can result in a marked (almost 4-fold) decrease in CRBSI rates,[325] approaching a rate of 1 episode/1,000 catheter days.[325] Thus, adopting protocols that incorporate limiting hub exposure time and increasing protection by vigorously "scrubbing the hub" is very important and is supported by these and other guidelines.[296,297]

Catheter and Exit Site Cleansing

One cluster RCT (n = 422 facilities) compared a new CVC care protocol involving exit site disinfection with 2% chlorhexidine and 70% alcohol swab sticks and 70% alcohol pads for hub care to current practice (no specific disinfectant, no scrubbing of CVC hubs[326]). Significantly fewer blood stream infections were reported in the intervention facilities. A patient-level analysis, adjusted for a cluster effect, yielded an RR of 0.79 (95% CI, 0.78-0.81). Adverse events were reported only for the intervention facilities, which included chlorhexidine sensitivity. A total of 184 local, non–life-threatening events were reported in 82 study participants.

In a pilot RCT (n = 105), a 2% chlorhexidine in 70% isopropyl alcohol solution was compared with chlorhexidine solutions (either 0.5% chlorhexidine in alcohol [81% of control group] or 0.05% aqueous chlorhexidine [19% of control group]) for CVC exit site antisepsis.[327] Follow-up was 12 months. Overall, fewer CVC-related infections were noted in the intervention group compared with the control group, but the difference was not significant (RR, 0.49; 95% CI, 0.18-1.34). There were also no significant differences between groups for specific types of infection (ie, CRBSI or exit site). Skin sensitivity reaction was reported in 4 participants in the 2% chlorhexidine in 70% alcohol group (Fisher exact test, $P = 0.12$)

Given this evidence, the Work Group strongly suggests using a CVC care protocol that involves chlorhexidine and, if circumstances permit, using chlorhexidine gluconate 1% or 2% and 70% alcohol solution.[296,297] Additional research by the Work Group found chlorhexidine skin cleansing to be superior to povidone-iodine and alcohol in the prevention of CVC-related infection.[328-330] If chlorhexidine is contraindicated (eg, skin sensitivity or allergy), povidone-iodine 10% in 70% ethanol should be used.[331] The antiseptic solution should be applied using friction, for at least 30 seconds, and allowed to air-dry without wiping or blotting, to promote adherence of the dressing material to the skin and reduce the likelihood of skin breakdown and infection. Multidose cleansing solution bottles are discouraged due to the risk of cross-contamination. All cleansing solutions should be single use, for example, a disposable swab stick or pad.[297]

Exit Site Barriers and Dressings

The routine application of topical antiseptic/antibiotic ointments at the CVC exit site has been shown to be associated with a 75% to 93% reduction in the risk of CRBSI.[332-334] Topical ointments that have been studied include mupirocin, povidone-iodine, and Polysporin triple-antibiotic ointment. A 6-year prospective follow-up study using a Polysporin triple-ointment application at the exit site of HD catheters has not demonstrated microbial resistance or loss of efficacy for infection prophylaxis, with bacteremia rates consistently <1.0/1,000 catheter days.[309] Medical-grade honey has been shown to have equivalent efficacy to mupirocin for CRBSI.[335] Such findings are supported by the ERT. For example, bacteremia occurred in 12% with medical-grade honey and 10% with mupirocin prophylactic application at the CVC exit site ($P = 0.78$).[336] Bacteremia-free survival also did not differ between these groups (HR, 0.94; 95% CI, 0.27-3.24).

Given the reduction in CRBSI using topical antiseptic or antibiotic barriers compared with placebo or no barrier, but no significant differences between types of antiseptic/antibiotic barrier, the Work Group suggests the choice of barrier based on the clinician's best clinical judgment and

local practices. Whether the benefit exists after exit sites are fully healed is unclear. However, it is important to recall that exit sites require re-healing after each CVC exchange. As with the use of any intraluminal solutions, any cleansing solution or antiseptic/antibiotic used topically should be compatible with the CVC material.

All dressing material should be applied using no-touch or aseptic techniques. *No-touch technique* means that all open ports and ends of CVCs are not touched with hands or gloves (see http://antt.org/ANTT_Site/home.html). Recent data indicate that there is no significant difference between transparent, semipermeable dressings, and standard gauze dressings with respect to CVC exit site colonization or CRBSI.[337-339] This is also supported by the ERT. For example, 1 small RCT (n = 66) compared 2 dressings: a sterile transparent film and a traditional sterile gauze and hypoallergenic micropore dressing.[340] No significant difference in CVC-related infection (12% intervention, 9% control; P = 0.69) was found.[340]

Both patient and environmental factors should be considered when selecting dressing type and the frequency of change (discussed earlier). Dressings should not be submerged in water and should be changed when they become damp, loose, soiled, nonocclusive, or nonadherent, and only trained dialysis care providers (including patients) should change CVC dressings. Regular retraining is highly desirable to maintain competency and reduce the risk of infection.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S98-S109.

Assessment of CVC Patency

Routine flushing with 0.9% normal saline is used to maintain CVC patency and has become a standard of practice when accessing and de-accessing CVCs. Flushing of CVC lumens is intended to prevent the mixing of incompatible medications or solutions within the CVC lumen and assists in clearing the CVC of blood) **or** fibrin buildup.[341] Typically, a 5- to 10-mL syringe is used; given the lack of evidence for syringe size, the CVC manufacturer's instructions may be used as a guide. However, the clinician is expected to use his/her best clinical judgment and follow local CVC care protocols.

Table 11.2. Example of CVC Connect and Disconnect Procedures

Suggested Method to Access CVC
Step 1: Explain the procedure to the patient. Ask him/her to minimize talking and turn the head the opposite direction of the CVC.
Step 2: Perform hand hygiene. Remove any gauze or tape securing the CVC or covering CVC limbs.
Step 3: Ensure that both limbs of the CVC are clamped. Place clean or sterile pad/towel under the CVC so that the limbs are on top of the pad/towel.
Step 4: Perform hand hygiene and prepare supplies, maintaining sterility. Put on gloves.
Step 5: Ensure clamp on CVC is closed. Remove the Luer lock cap and clean the hub ("scrub the hub")[297] with chlorhexidine (or povidone if chlorhexidine not tolerated). Ensure that the disinfected hub does not touch nonsterile surfaces. If closed system, high-flow, needleless-style caps are used; follow the manufacturer's recommendations and CVC care for cleaning and changing of caps. Repeat with the second port. *Optional for Step 5:* Before removing the Luer lock cap, disinfect the caps and part of the hub with an antiseptic pad, using a separate antiseptic pad for each hub or catheter limb.
Step 6[a]: Attach syringe, unclamp CVC, and aspirate 2 to 5 mL of blood and CVC locking solution from lumen. Reclamp CVC. Detach syringe and attach to dialysis circuit. Repeat with second port. *Optional for Step 6*: If no resistance is felt with aspiration of blood and CVC locking solution, attach a 5- to 10-mL syringe of 0.9% normal saline and flush lumen using turbulent flushing technique.
Step 7[b]: Initiate dialysis.
Step 8: Discard the syringe and used materials.
Suggested Method to Disconnect CVC
Step 1: Explain the procedure to the patient, retransfuse patient's blood as per unit protocol, perform hand hygiene, and prepare supplies for CVC locking.
Step 2: Close the clamp on the CVC lumens and bloodlines. Disconnect 1 bloodline from 1 CVC lumen and clean the CVC hub.[c]
Step 3: Attach a 5- to 10-mL syringe with 0.9% normal saline to CVC lumen, unclamp CVC, and flush lumen.
Step 4: Remove normal saline syringe from lumen, attach syringe with CVC locking solution to lumen, and instill locking solution volume as per unit CVC care protocols.[d]
Step 5: Close clamp on lumen, remove syringe, clean the hub, and apply sterile Luer lock cap.
Step 6: Repeat steps with second lumen.
Step 7: Discard used supplies.

Abbreviation: ANTT, aseptic no touch technique; CVC, central venous catheter.

[a]If limbs do not aspirate or flush freely, ensure clamps are open and rule out external causes of resistance (kink in CVC limb or patient position).[342] If problems persist, the CVC may indicate fibrin or thrombus formation or CVC tip malposition (Guidelines 22 and 24). A gentle back-and-forth motion (irrigate) may promote CVC patency. After irrigation, flush lumen (eg, with 10 mL of normal saline) using turbulent flushing technique to ensure that blood is cleared from the CVC lumen (optimize line patency). Observe for bleeding if anticoagulant (locking) solution cannot be removed (aspirated).

[b]If line reversal is necessary to initiate dialysis treatment, follow unit protocols and practices for next steps. If patency is established, initiate dialysis.

[c]Follow "scrub-the-hub" protocol.[297]

[d]Locking solutions may include anticoagulants, antiseptic/antibiotic, or thrombolytic locks and their combinations. Caps must be replaced every time the catheter is accessed and de-accessed. If closed-system, high-flow needleless caps are used, follow unit protocols and manufacturer's recommendations.

It is recommended that the aseptic no-touch technique (see http://antt.org/ANTT_Site/home.html) be practiced when accessing and de-accessing the CVC and that 1 lumen be accessed at a time to reduce the time blood remains in the lumen (Table 11.2).

Care of Hemodialysis Central Venous Catheters and Patient Education

To facilitate CVC care, the following actions should be strongly considered[4]:

1) Educate patients (see following), health care personnel, and relevant administrators regarding the acceptable appropriate indications for CVC use (Guideline Statements 1 and 2.2) and proper procedures for safe and optimal CVC care and use, including prophylactic measures for CVC-related infections.
2) Periodically assess knowledge of and adherence to guidelines for all individuals (including patients and relevant family/patient supporters) involved in CVC access, use, and maintenance.
3) Designate only trained individuals who demonstrate competence for the access, use, and maintenance of CVC.Patient teaching and instructions should include, but are not limited to, the importance of the following:
   - Initial CVC care, including when sutures should be removed
   - Frequent hand washing
   - Avoid pulling, tugging, or using sharp objects (eg, scissors) around the catheter
   - What to do if the dressing becomes soiled or wet
   - What to do if bleeding occurs
   - What to do if the CVC falls out
   - What to do if a limb clamp breaks and falls off
   - What to do in the case of pain, fever or chills, or redness or discharge seen at the CVC exit site or tunnel
   - Whom to call with questions or concerns, with the correct contact details

Patients should be provided written instructions on CVC care and up-to-date contact information for reporting any vascular access concerns such as bleeding or signs of infection (fever, chills, and/or purulent discharge).

Implementation Considerations

- The concern of the often rapid turnover of dialysis technicians, leading to inadequate training and/or competency to care of all types of vascular access
- The use of any intraluminal or extraluminal cleansing solutions, antiseptics, antibiotics, medicines, or anticoagulants should be compatible with the CVC material
- Provision of training, auditing, and feedback for frontline staff with respect to CVC care, connection, and disconnection procedures

Monitoring and Evaluation

- Monitor for CVC exit site healing
- The Centers for Disease Control and Prevention (CDC) Audit and Checklist[343] may also be helpful

Future Research

- Study whether sterile gloves are required if strict no-touch technique is used for CVC manipulation and care
- Study whether masks are required for each CVC dressing change and manipulation, if the patient has head turned away and both patient and provider do not talk. Exception is if patient or provider has respiratory signs/symptoms.
- Determine if there is benefit of topical barriers after exit site and tunnel are fully endothelialized and healed.
- Validate tests to determine exit site healing
- Determine if a patient can safely shower when the exit site and tunnel are fully healed
- Determine if a patient can safely eliminate the use of dressings altogether when the exit site and tunnel are fully healed, if the patient properly cleanses

Guideline 12. AV Access Cannulation Complications

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: AV Access Cannulation Complications

12.1 **KDOQI considers the following therapeutic interventions for cannulation injury reasonable to follow:**
- **Any size infiltration: apply ice for a minimum of 10 minutes and refrain from maximizing the blood pump speed. (Expert Opinion)**
- **If the infiltration is moderate, the needle should be withdrawn and manual pressure held over the infiltration site. (Expert Opinion)**
- **If the infiltration is significantly large, in addition to the above, a decision on the necessity for dialysis that day is required—if dialysis is required, a site proximal to the infiltration injury should be cannulated; if this is not possible, reattempt at the area of injury should not proceed until manual pressure and ice is applied for 30 minutes. (Expert Opinion)**

- **If a hematoma develops, close assessment of the site, the AV access, and the adjacent extremity should be made, including measurement of swelling, assessment of the presence of flow in the AV access both proximal and distal to the hematoma, and circulation to the associated extremity. (Expert Opinion)**

12.2 **KDOQI considers it reasonable to use ultrasound to help determine direction of flow and proper needle placement in the AV access of select patients as needed and performed by trained operators, to prevent cannulation complications. (Expert Opinion)**

Rationale/Background

Despite cannulation being an integral component of the HD procedure, there is very limited evidence to support practice. Knowledge, skill, and ability among cannulating nurses/dialysis personnel varies significantly across jurisdictions, with little to no minimum standards or standardization. Basic knowledge of vascular anatomy, patient-centered care, and the importance of provider-patient therapeutic relationships should be components of all cannulation training programs to reduce the frequency of complications. The complications that occur as a result of cannulation not only cause significant discomfort and distress to patients but, in some cases, may negatively affect their ability to have a functioning dialysis access in the future. For example, a single infiltration injury that occurs before successful 2-needle cannulation is associated with 56% lower odds of overall AVF maturation.[158] Infiltration injury is associated with frequent imaging, interventions, and prolonged need for a CVC.[3] Indeed, unsuccessful cannulation attempts are associated with poorer AVF maturation success and outcomes.[158] Currently, complications related to cannulation are not consistently or well documented as part of the dialysis treatment.

Cannulation site bleeding can usually be corrected by direct pressure but occasionally requires the placement of a skin suture. Pressure should be applied directly to the bleeding site, and care should be exercised not to occlude the AV access outflow distal to the bleeding site because of the potential to increase the intraluminal AV access pressure to arterial levels. A "bad stick" that results in a significant hematoma often requires placement of a CVC and deferral of further AV access cannulations until the hematoma is resolved, a period that may last up to 3 months.[3] Bleeding from a vascular access needle site that needs a skin suture or results in a very large hematoma is very suggestive of a venous outflow stenosis and requires a referral for a diagnostic angiogram.

Detailed Justification

Complications and Management

- Infiltration of the vein can occur when a needle is inserted and the tip is inadvertently advanced beyond the vein, perforating the side or back wall and resulting in some degree of swelling, bruising, and/or pain.
- Hematomas can develop as a result of an infiltration of the vein or due to leaking of blood around the puncture site during cannulation, during a dialysis treatment, or after removal of a needle at the end of a dialysis treatment. The size of hematomas can vary significantly, from a small diffuse area to a large, firm mass that can potentially compress the vessel, resulting in thrombosis of the AV access. The development of significant hematomas can also result in the development of stenosis at the site of hematoma. Every effort should be made to avoid these.
- Pain of various degrees is common and can occur in various sites, at various times, and with various intensity. Pain can develop at the time of cannulation, during the dialysis treatment at the site of or surrounding a site of cannulation, or along the arm or hand and continue after dialysis as a result of a hematoma, infiltration of the vein, or irritation of an adjacent nerve.
- Management of cannulation complications such as infiltration and resulting hematoma is dependent on the extent of swelling, pain and patient anxiety. The sharing of knowledge and providing support to the patient and family cannot be minimized. Providing comfort measures and/or analgesic administration must be assessed on an individual basis.

Prevention of Cannulation Complications

- AV access check or assessment before cannulation is required. Ensuring that flow is present in the AV access and determining the direction of flow to ensure optimal dialysis is required before needle placement. Observation of the full AV access and adjacent limb and auscultation and palpation along the AV access can detect many defects and aid in appropriate selection of sites for cannulation. The use of bedside ultrasound by a trained operator to aid in cannulation has been associated with an increase in nurse confidence and patient comfort and can help determine direction of flow within the AV access, but there is limited evidence at this point to recommend use in all patients. Please see Special Discussions under Guideline 11 for discussions about the use of ultrasound to aid cannulation.
- Appropriate selection of cannulation sites based on assessment and input from patients can help avoid associated complications.

- Use of experienced cannulators to cannulate AV accesses at risk of complications should be attempted whenever possible. Cannulators should determine at the time of assessment if they anticipate any challenges with cannulation and seek expert advice and guidance. If a cannulator is unsuccessful cannulating an AV access, a maximum of 2 attempts is recommended before seeking expert advice.
- The use of smaller-gauge and Teflon needles should be considered when cannulating smaller and more fragile vessels. Although these needles may limit blood flow, consideration of longer, more frequent, or individualized prescription based on the patient's dialysis needs and goals may enable noncomplicated use of the AV access and avoid insertion of a CVC.
- When appropriate and possible, self-cannulation in well-trained patients may be beneficial.
- Documentation of complications of cannulation should be reviewed as part of each cannulator's training and evaluation.

Special Discussions

- Centers with limited opportunities for staff to cannulate dialysis accesses face particular challenges. Accessing online resources and expertise should be considered to ensure the provision of adequate care to patients.
- The Work Group acknowledged that there is limited evidence to support the recommendations related to cannulation and management of cannulation-related complications, limiting them to Expert Opinion only. Even when reviewing the literature in areas such as peripheral venipuncture and arterial cannulation, the evidence is opinion based.
- When appropriate and possible, self-cannulation in well-trained patients may be beneficial to improving patient comfort and reducing anxiety in cannulating the AV access.

Future Research

- Rigorous studies examining cannulation practices, challenges to achieving complication-free cannulation, and strategies to mitigate barriers to successful AV access cannulation is needed
- To study the role of cannulation complication documentation and review whether or not it improves quality of cannulation and AV access outcomes

Guideline 13. AV Access Flow Dysfunction—Monitoring/Surveillance

Note: "AV access flow dysfunction" refers to clinically significant abnormalities in AV access (AVF or AVG) flow or patency due to underlying stenosis, thrombosis, or related pathology. This is in distinction to other types of AV access complications.

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Appropriate Use of Monitoring/Surveillance for AV Access Flow Dysfunction

Physical Examination (Monitoring)

13.1 **KDOQI recommends regular physical examination or check of the AVF, by a knowledgeable and experienced health practitioner, to detect clinical indicators of flow dysfunction of the AVF. (Conditional/Strong Recommendation, Moderate Quality of Evidence)**

See Table 13.2 for clinical indicators

13.2 **KDOQI recommends regular physical examination or check of the AVG, by a knowledgeable and experienced health practitioner, to detect clinical indicators of flow dysfunction of the AVG. (Conditional/Strong Recommendation, Moderate Quality of Evidence)**

See Table 13.2 for clinical indicators.

13.3 **KDOQI considers it reasonable for nephrology trainees and health practitioners involved with clinical HD patient care to be properly trained in physical examination of the AV access to monitor for and detect AV access flow dysfunction. (Expert Opinion)**

Surveillance to Facilitate Patency

13.4 **There is inadequate evidence for KDOQI to make a recommendation on routine AVF surveillance by measuring access blood flow, pressure monitoring, or imaging for stenosis, that is additional to routine clinical monitoring, to improve access patency.**

Note: In other words, monitoring of vascular access is primary, while surveillance findings are supplementary, and action should not be based solely on surveillance findings.

13.5 **KDOQI does not suggest routine AVG surveillance by measuring access blood flow, pressure monitoring, or imaging for stenosis, that is additional to regular clinical monitoring, to**

improve AVG patency. (Conditional Recommendation, Low Quality of Evidence)

Note: In other words, monitoring of vascular access is primary, while surveillance findings are supplementary, and action should not be based solely on surveillance findings.

Investigation of Abnormalities Detected by Clinical Monitoring

Please refer to Guideline Statements 15.1-15.3.

Statements: Surveillance and Pre-emptive Intervention for AV Access Stenosis Not Associated With Clinical Indicators

Endovascular Intervention to Improve Patency

13.6 **KDOQI does not recommend pre-emptive angioplasty of AVFs with stenosis, not associated with clinical indicators, to improve access patency. (Conditional Recommendation, Moderate Quality of Evidence)**

13.7 **KDOQI does not recommend pre-emptive angioplasty of AVGs with stenosis, not associated with clinical indicators, to improve access patency. (Conditional Recommendation, Moderate Quality of Evidence)**

Surgical Intervention to Improve Patency

13.8 **There is inadequate evidence for KDOQI to make a recommendation on pre-emptive surgical interventions in AVFs with stenosis, not associated with clinical indicators, to improve access patency.**

Statement: Pre-emptive Intervention for AV Access Stenosis Associated With Clinical Indicators

13.9 **KDOQI considers it reasonable for patients with consistently persistent clinical indicators and underlying AV access stenosis to undergo pre-emptive angioplasty of their AV access to reduce the risk of thrombosis and AV access loss. (Expert Opinion)**

Rationale/Background

In this Guideline, *AV access flow dysfunction* refers to clinically *significant abnormalities* in AV access (AVF or AVG) flow or patency due to underlying stenosis, thrombosis, or related pathology. This was previously referred to as *AV access dysfunction*, which encompassed many forms of dysfunction (or abnormalities of AV access); however, the Work Group wanted to distinguish AV access dysfunction due to stenosis or thrombosis from other causes of dysfunction, such as aneurysms. Thus, the terminology *AV access flow dysfunction* is used in distinction to other types of AV access complications.

AV access flow dysfunction is a common problem, typically associated with underlying stenosis and/or thrombosis. The development of progressive vascular access stenosis with subsequent failure of the vascular access contributes significant morbidity to patients and costs to the health care system.[344] The fundamental principle for performing routine vascular access monitoring and surveillance is to detect and correct the stenosis to minimize or avoid reduced dialysis clearance (dialysis dose protection), reduce the rate of thrombosis, and improve AV access function. Indeed, vascular access function was globally ranked as a top priority for patients and health care providers clinically and as a research target, so much so that it has become the core outcome measure for vascular access clinical trials.[345]

Rationale for Physical Examination/Monitoring

A variety of methods have been proposed for screening the AV access for early detection of stenosis before the AV access becomes dysfunctional.[346-351] Clinical monitoring strategies include physical examination (inspection, palpation, and auscultation) of the vascular access to detect signs that suggest the presence of pathology. This monitoring is ideally conducted when the patient is not on dialysis. Abbreviated forms, such as the "One-Minute Access Check" (esrdncc.org/en/resources/lifeline-for-a-lifetime/step-eight-the-one-minute-access-check/), are rapid and effective and can be conducted by patients and providers before dialysis.[352] Such monitoring can be supplemented by review of routine laboratory studies regularly obtained in the dialysis unit, dialysis adequacy (urea reduction ratio or Kt/V, documented recirculation), difficulties in cannulation or achieving hemostasis after needle withdrawal, and other clinical signs. Although these different techniques and methods are available for identifying vascular access flow dysfunction, the scientific evidence for the optimal methodology is lacking. A small number of RCTs have been performed evaluating different monitoring techniques. Dynamic venous pressure (DVP) can be measured on most dialysis machines; however, the utility of DVP at blood flows (Qb) of 150 to 200 mL/min in detecting stenosis or predicting AV access thrombosis is very limited, because DVP is dependent on a variety of factors, such as the needle gauge and the length of the dialysis needle.[353] AV access recirculation and declines in URR or Kt/V may help indicate AV access stenosis, but by themselves cannot be sole indicators, because many variables affect their measurements, and they have not been rigorously studied. Following the trend of these monitoring measures (URR, Kt/V, recirculation, etc) may be a helpful accompaniment to physical examination and should be properly studied. Physical examination of the

AV access by an experienced individual has high sensitivity and specificity.[267,354,355] The physical examination is easily available, requires minimal training, is cost efficient, and takes minimal equipment and time. Several studies have examined the use of the physical examination to detect AV access flow dysfunction (ie, stenosis within the AVF[267,355] and AVG[351,356]). The value of physical examination (monitoring) is that if AV access flow dysfunction is suspected with appropriate matching clinical indicators, further investigation and preventive intervention, such as with angioplasty, could be performed to improve outcomes (eg, preventing thrombosis).

Rationale for Surveillance

The rationale underlying AV access surveillance is to detect and correct stenosis within the AV access before the development of thrombosis, to improve the patency of the AV access by reducing the risk of thrombosis. Clinical indicators associated with AV access stenosis (Table 13.2) include reduced dialysis clearance without other known cause, excessive bleeding after needle withdrawal, high venous and arterial pressures at the prescribed blood flow,[357] and indicators on physical examination (see earlier discussion on AV access monitoring). Surveillance procedures, requiring specialized equipment and operator skills, have been studied to detect stenosis before the development of a clinical indicator. These include AV access flow (Qa) measurement[348,358,359] by a variety of methods, including ultrasound dilution method (UDM) and duplex ultrasound to measure Qa and visualize anatomic abnormalities.[360,361] The use of dynamic and static venous pressure has also been used as a surveillance tool[362]; dynamic venous pressure measures are now considered as supplementary to clinical monitoring.

Several important questions arise when considering AV access surveillance to reduce thrombosis and improve AV access patency: (1) What is the diagnostic value of surveillance for detection of stenosis? (2) What are the validated diagnostic thresholds by surveillance indicators (eg, Qa, change in Qa/time) that accurately diagnose stenosis that will lead to future thrombosis? (3) What factors, other than stenosis, contribute to abnormal surveillance indicators? (4) What is the appropriate intervention when stenosis is detected by surveillance in the absence of

Table 13.1. Routine AV Access Monitoring by Physical Examination

Exam Steps	Fistula (Normal)	Graft (Normal)	Flow-related Dysfunction or Poor Maturation (Abnormal)	Infection, Steal Syndrome, or Aneurysm/Pseudoaneurysm[a] (Abnormal)
Look	Well-developed main venous outflow, no irregular/dilated areas or aneurysm formations, adequate areas of straight vein that can be used for 2-needle, rope-ladder cannulation Vessel collapses when arm is elevated above head	Uniform-sized graft in a loop or straight configuration No irregular areas or aneurysm or seroma formations with organized site rotation used for cannulation	AVF with poor maturation—multiple venous outflow veins (accessory veins), poorly defined cannulation areas **AVF:** Stenosis can occur in artery or any venous outflow vein Look for a narrowing of the outflow vein, abnormal pulsations, or aneurysm formations **AVF or AVG:** Dilated neck veins or surface collateral veins in the arm or neck above the vascular access	**Infection:** Redness, swelling, induration, drainage, or pus **Steal syndrome:** Extremity/hand discoloration, skin ulceration due to poor arterial blood flow to the hand Check nail beds, fingers and hand for unusual skin changes **Aneurysm** Abnormal areas of dilatation with overlying skin thinning
Listen with a stethoscope	Low-pitch continuous diastolic and systolic	Low-pitch continuous diastolic and systolic	High-pitch discontinuous systolic only	**Steal syndrome** AVF may have a very strong bruit
Feel with your fingers	Thrill at the arterial anastomosis and throughout the entire outflow vein that is easy to compress	Thrill strongest at the arterial anastomosis but should be felt over entire graft and be easy to compress	**AVF:** Pulse at the site of a stenotic lesion—may be water-hammer in quality and feel **AVG:** Thrill and/or pulse strong at the site of stenotic lesion pulse has a water-hammer feel An AVG with a low intra-access blood flow feels mushy Local area of the graft that feels mushy or irregular in shape can be a site of aneurysm formation	**Infection** Warm or painful to touch, swelling **Steal syndrome** Feel bilateral limbs (hands and fingers) and compare for the access limb to be the same as the nonaccess limb Compare temperature, grip strength, and range of motion and any complaints of changes in sensation or pain If the access limb has any major differences than the nonaccess limb, consider steal syndrome

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft.
[a]Also see Guidelines 16 through 19 for specific complications.

Table 13.2. Clinical Indicators (Signs and Symptoms) Suggesting Underlying Clinically Significant Lesions During Access Monitoring

Procedure	Clinical Indicators	
Physical examination or check	• Ipsilateral extremity edema	354,365
	• Alterations in the pulse, with a weak or resistant pulse, difficult to compress, in the area of stenosis	378
	• Abnormal thrill (weak and/or discontinuous) with only a systolic component in the region of stenosis	239
	• Abnormal bruit (high pitched with a systolic component in the area of stenosis)	360
	• Failure of the fistula to collapse when the arm is elevated (outflow stenosis) and lack of pulse augmentation (inflow stenosis)	267
	• Excessive collapse of the venous segment upon arm elevation	
Dialysis	• New difficulty with cannulation when previously not a problem	379
	• Aspiration of clots	239
	• Inability to achieve the target dialysis blood flow	360
	• Prolonged bleeding beyond usual for that patient from the needle puncture sites for 3 consecutive dialysis sessions	
	• Unexplained (>0.2 units) decrease in the delivered dialysis dose (Kt/V) on a constant dialysis prescription without prolongation of dialysis duration	

clinical indicators? and (5) What is the AV access patency outcome after intervention of *stenosis not associated with a clinical indicator,* and does this differ from intervention of stenosis detected by clinical examination?

What Is the Diagnostic Value of Surveillance for Detection of Stenosis?

Surveillance methods can detect stenosis; however, there are valid issues regarding the accuracy and reproducibility of this detection, which may vary based on the method of surveillance and the indicator used. Stenosis within the AV access is thought to be reflected by reductions in AV access flow and alterations in AV access circuit pressures. However, flows and pressures are influenced by factors other than the presence of stenosis, including the location and degree of the stenosis, variations in the hemodynamics over the course of dialysis (eg, timing, blood pressure), and cannulation technique and AV access characteristics.[362-364] Thus, repeat measurements and trending of surveillance results are important to confirm abnormal surveillance results, if surveillance is done. The location of the stenosis can influence the diagnostic characteristics of the surveillance tool, and an AV access can have multiple stenoses, not reliably detected with a single surveillance tool, especially if measured in isolation.[365] Additionally, the AVG and the AVF have different pathophysiology for development of stenosis, occurring at different rates, at different locations, and with different hemodynamic consequences based on their configurations.[366]

What Are the Validated Diagnostic Thresholds by Surveillance Indicators (eg, Access Flow Rate, Change in Access Flow Rate) That Accurately Diagnose Stenosis That Will Lead to Future Thrombosis?

The various surveillance techniques available to detect AV access stenosis differ in their ability to accurately and reliably detect AV access flow dysfunction beyond clinical examination.[13,367] In addition, when using a given surveillance method to detect significant stenosis that would prompt intervention, there is still a need for standardized diagnostic thresholds with sufficient sensitivity to detect clinically significant stenosis but with good specificity to avoid unnecessary interventional procedures. Issues regarding surveillance reliability and reproducibility (see above) add to the challenge of defining and validating diagnostic thresholds. As such, the required validated thresholds for intervention have not been established for all methods of AV access surveillance.

What Factors, Other Than Stenosis, Contribute to Abnormal Surveillance Indicators?

Variables to consider (discussed above) include factors related to the hemodialysis procedure, patients' response to it (eg, hypotension), the AV access, and AV access circuit anatomy and physiology.[362,363] In addition, the expertise and reliability of the operator obtaining the measurement may contribute to abnormal surveillance indicators.

This Guideline focuses on the evidence available, or the lack thereof, for answering the remaining patient-important and clinically relevant questions (4) and (5): What is the appropriate intervention when stenosis is detected by surveillance in the absence of clinical indicators? and What is the AV access patency outcome after intervention of stenosis *not associated with a clinical indicator*, and does this differ from intervention of stenosis detected by clinical examination?

The brief answers are as follows:

What is the appropriate intervention when stenosis is detected by surveillance in the absence of clinical indicators? Do nothing—do not intervene in the absence of clinical indicators.

What is the AV access patency outcome after intervention of stenosis not associated with a clinical indicator, and does this differ from intervention of stenosis detected by clinical examination? (1) For AVF, the data are unclear and more study is required; (2) for AVG, the data do not demonstrate improved patency with surveillance and subsequent pre-emptive intervention on AVG with no clinical indicators, compared with routine clinical examination.

Detailed Justification

The 2006 KDOQI Vascular Access Work Group previously recommended AV access surveillance with preemptive angioplasty of stenosis to improve AV access outcomes.[13] This was based on the best available evidence at that time that supported the premise that use of surveillance for the early detection of AV access stenosis and its preemptive correction compared with deferred correction would improve AV access outcomes. There has been controversy over the interpretation of this recommendation based on previous and more current evidence. Over time, the nephrology community has recognized that *surveillance for stenosis in isolation is not clinically meaningfully without also examining the effect of the subsequent intervention on clinically important outcomes*, which, in this case, would include AV access thrombosis, patency, and intervention rates. Many studies have been underpowered to show either benefit or harm from surveillance strategies. Multiple factors discussed earlier contribute to the heterogeneity of the results and interpretations of the studies in this area and have contributed to the change in the recommendations for AV access surveillance.

Physical Examination

The physical examination is easily available, requires minimal training, is cost efficient, and takes minimal equipment and time. Several studies have examined the use of the physical examination to detect AV access flow dysfunction (eg, stenosis within the AVF[13,364,365] and AVG[361,362]).

Diagnostic Accuracy of the Physical Examination to Detect Stenosis in the AVF. Two observational studies compared physical examination with angiography for monitoring and diagnosing dysfunction with AVF.[267,354] Coentrao et al[354] analyzed data resulting from physical examinations by 11 general nephrologists and 1 nephrology resident who received 6 months of training on conducting physical examinations to identify AV access flow dysfunction. Diagnostic physical examination results were compared with those of angiography for detecting AV access stenosis. Clinical criteria for AV access flow dysfunction prompting angiography were applied according to the prior 2006 KDOQI guideline.[13] Physical examination included inspection of the arm, chest, neck, and face; palpation of the entire AVF tract; arm elevation; pulse and thrill abnormalities; and pulse augmentation tests. AVF dysfunction was classified into 4 major disorders: inflow stenosis, outflow stenosis, coexisting inflow/outflow stenosis and AVF thrombosis. Stenosis by angiography was defined as 50% luminal narrowing compared with the normal vascular segment located adjacent to the stenosis according to 2006 KDOQI guideline.[13] Thrombosis of the AVF was ascertained by the presence of clots in the arterial and/or venous sides of the AVF. The agreement beyond chance between the nephrologists' physical examination and angiography for the assessment of AVF dysfunction was moderate (kappa = 0.49; 95% CI, 0.40-0.57). and near-perfect when the physical examination was done by the trained nephrology resident (kappa = 0.86; 95% CI, 0.77-0.95). The agreement was similar for both forearm and upper arm AVFs.

Asif et al[267] (n = 147) compared results of a complete physical examination of the AV access conducted by an interventional nephrologist to angiography. Similar criteria for AV access flow dysfunction were used as in the Coentrao et al study.[354] The diagnostic accuracy of physical examination was poor for central vein and AVF body stenosis, moderate for inflow and coexisting inflow and outflow stenosis, and good for outflow stenosis.

Diagnostic Accuracy of the Physical Examination to Detect Stenosis in the AVG. Leon et al[356] conducted preprocedure physical examinations on 43 consecutive patients referred for angiography to manage AVG dysfunction. Physical examination findings and diagnosis were each recorded and secured in a sealed envelope. Angiography from the feeding artery to the right atrium was performed. The angiographic images were reviewed by an independent interventionalist with expertise in AV access procedures who was blinded to the physical examination results. The agreement beyond chance between physical examination and angiographic findings was strong for the diagnosis of vein-graft anastomotic stenosis (kappa = 0.52) and moderate for intragraft stenosis (kappa = 0.43) and inflow stenosis (kappa = 0.40). The findings of this study demonstrate that physical examination can assist in the detection and localization of stenoses in AVGs.

Surveillance

Surveillance of the AVF. The use of physical examination is an accepted, standard, evidence-based practice for the assessment and monitoring of the AV access for access flow dysfunction, infection, and vascular integrity. Only 1 study compared the addition of surveillance methods to routine clinical examination for detecting stenosis and reported AVF outcomes, with variable results, depending on the type of surveillance and outcome examined.[368]

The need to address whether or not surveillance methods can detect AVF dysfunction and stenosis and its incremental benefit beyond clinical examination (monitoring) is important to focus efforts for education, training, and the attainment of expertise in the relevant method for detecting AVF flow dysfunction.

Clinical Monitoring Plus Blood Flow (Qa) Surveillance Versus Clinical Monitoring Alone. A single-center RCT (n = 137) of AVF surveillance compared clinical monitoring plus intra-access blood flow (Qa) surveillance using UDM versus clinical monitoring alone.[347] The clinical monitoring group was referred to angiography if stenosis was clinically suspected. Participants in the UDM Qa surveillance group were referred to angiography if stenosis was clinically suspected or Qa was <500 mL/min at baseline or if Qa fell by >20% once Qa was <1,000 mL/min. Patients in the UDM Qa surveillance group were twice as

likely to have stenosis detected compared with those in the clinical monitoring alone group (HR, 2.27; 95% CI, 0.85-5.98; P = 0.09 [NS]), with a trend for the stenosis to be detected earlier in the UDM Qa surveillance group. The area under the curve demonstrated moderate prediction of >50% stenosis (0.78; 95% CI, 0.63-0.94; P = 0.006) in the UDM surveillance group. The study primary outcome was the time to detection of an angiographically significant AVF stenosis (defined as a ≥ 0% reduction of the normal vessel luminal diameter on angiography accompanied by a hemodynamic [in the case of the Qa surveillance group], functional, or clinical abnormality [in the case of the control group]) was not significantly different with clinical monitoring plus UDM Qa surveillance versus clinical monitoring alone (P = 0.20).

In summary, the use of surveillance methods in addition to clinical monitoring in AVF appears to increase the rate of detection of AVF stenosis and the rate of AVF intervention.

Surveillance of the AVG. Several previous studies have examined the effect of surveillance in addition to clinical monitoring in AVG.[351,360,364,369] Most of the studies did not specifically examine the rate of detection of stenosis but, rather, a clinical outcome of thrombosis or patency. The ERT did not include these studies because their publication dates were outside the prespecified window of dates for data extraction. However, the Work Group believed it was important to discuss previous studies that examined clinical monitoring alone and clinical monitoring plus surveillance in AVGs.

One blinded RCT (N = 112) compared clinical monitoring (DVP and physical examination) plus monthly Qa measurement by UDM versus clinical monitoring alone.[351] The Qa surveillance group was referred for angiogram if Qa was <650 mL/min or there was a 20% decrease in Qa from baseline, whereas the clinical monitoring alone group were referred for significant changes in dialysis adequacy or physical examination or for high DVP. Percutaneous angioplasty was performed for stenosis ≥50% compared with the adjacent vessel. The rates of AVG thrombosis per patient-year at risk were 0.51 and 0.41 in the surveillance and clinical monitoring groups, respectively (P = 0.57). Stenosis was detected more frequently in the surveillance group because of the increased use of angiograms and was accompanied by an increase in interventions: 51 interventions (0.93/patient-years at risk) in the Qa surveillance group versus 31 interventions (0.61/patient-years at risk) in the clinical monitoring alone group.

In summary, the use of surveillance methods in addition to clinical monitoring in AVG appears to increase the rate of detection of AVG stenosis and the rate of AVG intervention.

Surveillance and Preemptive Repair

The aim of interventions to prevent AV access flow dysfunction (ie, to improve patency or access function) is to improve patient and vascular access outcomes, with greater net benefit than harm, compared with no interventions (see the Background/Rationale for this section). There is limited evidence to provide guidance on the role of appropriate methods to prevent clinically insignificant stenosis (ie, stenosis that may be associated with abnormal findings on surveillance but without accompanying clinical indicators) in AVFs and AVGs. The available literature for AVF and AVG is provided in subsequent sections.

Surveillance and Preemptive Repair in Asymptomatic AVFs. One observational study using data from the Fresenius Medical Care North America centers (N = 35,716) compared elective percutaneous angioplasty (PTA) with no treatment for the prevention of AVF and AVG (AV access) dysfunction. Patients were referred for PTA based on Qa of <400 mL/min or change >30% for AVF and <600 mL/min for AVG. In the AVF subgroup, patients who received angiography and PTA were matched to control individuals not receiving an intervention (matched on vascular access type, access age, intra-access blood flow rate using the method of ionic online clearance, and single-pool Kt/V). Follow-up was for 1 year after intervention with angiography and PTA. The key findings are[370] (1) secondary patency was not significantly different with elective angiography and PTA versus no treatment and (2) thrombosis was not significantly different with elective PTA versus no treatment. The primary outcome was 1-year AV access survival (cumulative patency) from the date of first intervention, and it was not significantly different with elective PTA versus no treatment (54.8 vs 47.8 per 100 access years; HR, 1.06; 95% CI, 0.98-1.15). Several secondary outcomes were evaluated. Embolism with upper-arm thrombosis was not significantly different with elective PTA versus no treatment for AVF and AVG combined (0.86% vs 0.03% events per procedure; attributable risk increase, 0.83%; 95% CI, 0.56-1.12). This outcome was not reported separately by AV access type. Other harms were not reported for this comparison.

In contrast, a prospective study was conducted in patients who did not meet prior KDOQI Qa criteria for intervention but *had abnormal clinical monitoring* findings, for example, on physical examination. A single open RCT of AVFs (n = 58) assessed AVF with subclinical stenosis and Qa >500 mL/min (but abnormal physical examination result, Qa of <900 mL/min and elevated static venous pressure) who had prophylactic repair (pre-emptive intervention group) versus observation (repair at the time of AVF thrombosis).[349] Subclinical stenosis was angiographically defined as >50% reduction in vessel diameter compared with the adjacent segment. Prophylactic repair in the pre-emptive intervention group was by either PTA or surgery, whereas the observation arm underwent stenosis repair only after the onset of AVF dysfunction (defined as clinical abnormality) or a Qa of <400 mL/min (n = 3). AVF loss was lower in the pre-emptive PTA group than the

observation alone group: 5 (18%) versus 13 (43%), respectively (corresponding AVF loss rates [event/AVF-year] were 0.066 and 0.186; P = 0.041). Thrombosis rates were significantly lower in the pre-emptive PTA group than observation alone group: 21% versus 50%, respectively. The use of temporary CVC and associated CVC infection rates were not significantly different between groups.[349]

In addition to the described studies extracted by the ERT, when finalizing the KDOQI guideline statements, the Work Group considered other RCTs[347,348,371,372] in this area outside the prespecified window of data extraction. The Work Group believed that these previous RCTs help place the reported data in the appropriate context. There is further discussion about these specific studies in the "Special Discussions" section that follows.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S132, S134-S138, S145, and S147-S151.

Surveillance and Preemptive Repair in Asymptomatic AVGs. There was 1 RCT (N = 64) in AVG comparing pre-emptive intervention of asymptomatic stenosis versus observation (repair at the time of thrombosis).[373] AVGs with elevated static venous pressure values underwent diagnostic angiography. If there was a stenosis producing at least a 50% reduction in lumen diameter and the static venous pressure ratio was ≥0.4, patients were then randomized to the pre-emptive intervention arm (prophylactic repair by PTA) or surgery (if PTA was unable to be performed or was unsuccessful). The observation arm had intervention only after an AVG thrombosis event or if there was clinical evidence of AVG dysfunction. Participants were followed for 3.5 years. Mortality (19% in the pre-emptive intervention arm and 13% in observation arm), AVG loss (14 patients [44%] in each arm), and time to AVG abandonment did not differ between groups. The rates of thrombosis were significantly lower with pre-emptive intervention than with observation (44% vs 72%). Dember et al[373] reported no other differences between groups.

In AVGs, 1 observational study by Chan et al[370] (N = 35,716), used data from the Fresenius Medical Care North America centers to compare elective angioplasty versus no treatment for prevention of AVF dysfunction (described earlier) but also included a subset of patients with AVG who had elective angioplasty versus no treatment. Similar to the AVF cohort, in AVGs, follow-up was for 1 year after intervention with angiography and PTA. This study had these main findings: (1) secondary AVG patency was not significantly different with elective angiography and PTA versus no treatment and (2) thrombosis was not significantly different with elective angioplasty versus no treatment. The primary outcome was 1-year access survival (cumulative patency) from date of first intervention and was not significantly different with elective PTA versus no treatment (51.7 vs 52.7 per 100 access years; HR, 0.95; 95% CI, 0.86-1.05).

Similar to our discussion in the earlier AVF section, in addition to the described studies extracted by the ERT, when finalizing the KDOQI guideline statements, the Work Group considered other RCTs[351,360,373-376] in this area outside the prespecified window of data extraction. The Work Group felt that these previous RCTs help place the above data in the appropriate context. There is further discussion about these specific studies in the "Special Discussions" section that follows.

In summary, in clinical practice, many centers use surveillance techniques with the intention to detect early dysfunction in AVF and AVG with the premise that early identification and correction of stenosis may prevent clinically significant dysfunction, such as a thrombotic event. However, in clinical practice, it is difficult to predict which stenosis (anatomic abnormality) will progress into a clinically significant functional abnormality, such as an occlusive thrombosis. Intervening on stenoses that are clinically asymptomatic may lead to unnecessary interventions, and, subsequently, more interventions to maintain patency—which does not appear to be improved with pre-emptive intervention.[373] Thus, given the evidence available from the literature, our recommendations are to intervene only on AVFs and AVGs that have clinically relevant dysfunction when detected on routine clinical monitoring (eg, abnormal physical examination findings, low Kt/V without other cause, persistently inadequate blood flow rates to provide prescribed dialysis without other cause than the AV access, high venous pressure during dialysis, etc) We do not recommend interventions in AVG and AVFs that do not have clinically significant dysfunction (Supplement 3, Tables S133, S139, S140-S144, S146, and S152-S156).

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S110-S156.

Special Discussions

Overall, there were very few studies that evaluated methods to prevent AVF and AVG dysfunction that were of high-quality evidence, per ERT. The Work Group discussed and considered previous RCTs[347,348,351,360,371,373-377] not included in the data extraction (Table 13.3) in developing the guidelines and determined that these previous RCTs were important in the overall context of developing the guideline statement. Only 1 previous study demonstrated improved longevity with surveillance in AVGs,[376] with the remaining studies showing no statistical benefit compared with clinical monitoring in improving thrombosis or cumulative survival. In AVFs, several studies showed benefit of surveillance techniques compared with clinical monitoring; however, they too, had methodologic concerns (eg, group contamination, generalizability).

The Work Group recognizes that duplex ultrasound is valuable and has different characteristics than specific surveillance techniques for intra-access flow; however, the ERT evidence was limited. The Work Group encourages further research in all monitoring and surveillance techniques and strategies (see Future Research in this section).

Table 13.3. Additional Randomized Controlled Trials of AVG Surveillance

Reference	Surveillance Method	Patients, n		PTA/year		Thrombosis/year		Primary Outcome	Result
		Con	Sur	Con	Sur	Con	Sur		
Lumsden et al[374]	Doppler ultrasound	32	32	0	1.5	0.47	0.51	AVG Survival	No difference
Ram et al[375]	1. Ultrasound dilution (monthly) 2. Duplex ultrasound (quarterly)	34	32 35	0.22	0.34 0.65	0.68	0.91	AVG Survival	No difference
Moist et al[351]	Access flow	53	59	0.61	0.93	0.41	0.51	1. Time to AVG Thrombosis 2. AVG survival	No difference No difference
Dember et al[373]	Static DVP	32	32	0.04	2.1	1.03	0.89	AVG survival	No difference
Malik et al[376]	Ultrasound	92	97	NR	NR	NR	NR	AVG survival	Benefit for surveillance
Robbin et al[360]	Ultrasound	61	65	0.64	1.06	0.78	0.67	AVG survival	No difference

Abbreviations: Avg, arteriovenous graft; Con, control; DVP, dynamic venous pressure; NR, not reported; PTA, percutaneous balloon angioplasty; Sur, surveillance.

There was no evidence-grade literature on evaluating multidisciplinary care in the prevention of AV access flow dysfunction (primary and secondary prevention). However, given that a multidisciplinary effort is essential to achieve a successful vascular access, including disciplines such as nephrology, surgery, interventionalist, and dialysis nursing, a multidisciplinary team is also likely crucial to identifying clinically important AV access flow dysfunction, referring for intervention, and proceeding in a timely manner, if necessary.

Implementation Considerations

A multidisciplinary program comprising nephrologists, surgeons, interventionalists, vascular access coordinators, and dialysis nurses to provide coordinated care is likely essential to prevent asymptomatic AV access complications. Development of curriculum is necessary for implementation into training programs for nephrology fellows and health practitioners evaluating and caring for the AV access.

Monitoring and Evaluation

Important considerations when implementing new monitoring and surveillance programs include considering the processes of care and practice patterns at each individual dialysis center, because monitoring and surveillance may be different. Thus, changes in implementation of monitoring or surveillance within a dialysis unit may affect usual established protocols.

Table 13.4. Performance and Agreement Beyond Chance Between Physical Examination and Ultrasonography

	Complete PE	Edema	AVF collapse	Thrill	Pulsatility
True positive, n	47	1	41	19	40
True negative, n	28	42	12	30	28
False positive, n	14	0	30	12	14
False negative, n	10	56	16	38	17
Sensitivity, % (95% CI)	82 (72-93)	2 (0-6)	71 (59-84)	33 (20-47)	70 (57-83)
Specificity, % (95% CI)	67 (51-82)	100 (99-100)	29 (14-43)	71 (57-86)	67 (51-82)
PPV, % (95% CI)	77 (66-88)	100 (50-100)	57 (45-69)	61 (43-80)	74 (61-87)
NPV, % (95% CI)	74 (58-89)	43 (33-53)	43 (23-63)	44 (32-57)	62 (47-78)
LR+, % (95% CI)	2.47 (1.59-3.86)	—	1.00 (0.78-1.29)	1.17 (0.64-2.13)	2.11 (1.33-3.33)
LR-, % (95% CI)	0.26 (0.14-0.48)	0.98 (0.95-1.02)	1.00 (0.53-1.88)	0.93 (0.72-1.22)	0.45 (0.28-0.70)
Overall accuracy, % (95% CI)	76 (67-85)	43 (33-54)	46 (36-57)	51 (40-61)	69 (59-78)
κ (95% CI); *P* value	0.5 (0.32 to 0.67); <0.001	0.02 (-0.02 to 0.04); 0.388	-0.25 (-0.4 to 0.1); 0.956	-0.05 (-0.24 to 0.14); 0.614	0.37 (0.18 to 0.55); <0.001

Note: The physical examination was performed before the HD session by a single nephrologist and was divided into 3 steps. Pulse and thrill were evaluated following the model described by Beathard.[380,381] Physical examination was considered positive for the presence of stenosis if at least 1 of the signs suggestive of stenosis was detected regardless of the step. Stenosis was also identified by the presence of edema and collateral circulation in AVF arm. Stenosis prevalence = 58%.

Abbreviations and definitions: κ, Cohen's kappa coefficient (agreement beyond chance); CI, confidence interval; LR+, positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value;

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Future Research

The Work Group proposed the following topics as important areas for further research: (1) RCTs, with adequate methodology and power to delineate the role, if any, of the current and future surveillance and intervention methods, within a strategy to improve AV access patency; (2) specific studies evaluating the impact of pre-emptive intervention in patients with clinical indicators; (3) more comparative studies of physical examination/clinical monitoring and imaging studies (± surveillance methods) in various clinical scenarios (eg, on/off dialysis) to better define its sensitivity, specificity, predictive values, and accuracy of detecting clinically significant lesions, to expand on data (example of data in Table 13.4); (4) validation of the indicators on clinical monitoring of clinically significant stenosis; (6) consideration and proper study of the use of new technology or methods, including point-of-care ultrasound, to facilitate monitoring or surveillance of vascular access; (5) identification of subgroups of patients who may benefit from earlier angiographic intervention; (6) indications for endovascular versus surgical intervention; and (7) potential impact of multidisciplinary care for improved AV access patency.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S110-S156.

Guideline 14. AV Access Flow Dysfunction—Prevention

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Noninvasive Primary and Secondary Prevention of AV Access Flow Dysfunction

Note: "AV access flow dysfunction" refers to clinically significant abnormalities in AV access (AVF or AVG) flow or patency due to underlying stenosis, thrombosis, or related pathology. This is in distinction to other types of AV access complications.

Fistulas

14.1 **KDOQI suggests that the use of adjuvant far-infrared therapy to improve AVF primary patency be based on individual circumstances, feasibility, and the clinician's best judgment and expertise. (*Conditional Recommendation, Moderate Quality of Evidence*)**

14.2 **KDOQI does not suggest the routine use of fish oil or aspirin to prevent AVF flow dysfunction. (*Conditional Recommendation, Low-Moderate Quality of Evidence*)**

14.3 **There is inadequate evidence for KDOQI to make a recommendation on the use of simvastatin and ezetimibe to reduce AVF interventions or thrombosis.**

14.4 **There is inadequate evidence for KDOQI to make a recommendation on the use of clopidogrel-prostacyclin to improve AVF primary failure.**

Grafts

14.5 **KDOQI suggests careful consideration of potential individual patient benefits, risks, and circumstances prior to the use of combination dipyridamole (200 mg) and aspirin (25 mg) twice daily to improve AVG primary unassisted patency. (*Conditional Recommendation, High Quality of Evidence*)**

14.6 **KDOQI suggests the use of oral fish oil supplementation, in patients with newly created AV grafts, to reduce patient morbidity (ie, reduce frequency of thrombosis and related corrective interventions). (*Conditional Recommendation, Moderate Quality of Evidence*)**

14.7 **There is inadequate evidence for KDOQI to make a recommendation on the use of oral fish oil supplementation to prolong AVG cumulative patency.**

14.8 **There is inadequate evidence for KDOQI to make a recommendation on the use of simvastatin and ezetimibe for reducing AVG interventions and thrombosis.**

Rationale/Background

Arteriovenous Fistula

AVF maturation failure remains an important clinical problem for HD patients and has been reported in observational studies to range from 20% to 60%.[77,233,234] In fact, a multicenter RCT in the United States reported that up to 60% of AVFs created failed to mature successfully for dialysis use.[31] At present, there are very few effective therapies to prevent AVF dysfunction. The 2006 KDOQI guideline recommended interventions in AVF in the presence of inadequate flow to support dialysis, hemodynamically significant venous stenosis, aneurysm formation, and ischemia.[13] These Guidelines recommended a PTA or surgical revision in an AVF with greater than 50% stenosis in either the venous outflow or arterial inflow, in conjunction with clinical or physiologic abnormalities.[13] The previous 2006 KDOQI guideline did not address pharmacologic interventions to prevent AVF dysfunction.[13] Since the 2006 KDOQI guideline, there has been newly published literature evaluating pharmacologic and other therapies to prevent AVF dysfunction.

Far-Infrared Therapy. Four studies (N = 763), all conducted in Taiwan, compared far-infrared radiation with no treatment for prevention of AVF dysfunction.[382-385] One study recruited patients not yet on HD for whom a new AVF was created,[384] 2 studies recruited patients already on HD via AVF for at least 6 months without AVF interventions for at least 3 months,[382,383] and 1 recruited patients on HD via AVF who required 2 or more percutaneous interventions in the past.[385] Participants were followed for 1 year. All 4 and the pooled results reported statistically higher rates of primary patency at 1 year with far-infrared radiation compared with no treatment (RR, 1.24; 95% CI, 1.07-1.45). Lin et al[384] in 2013 reported significantly lower occlusion in the far-infrared radiation group (5%) versus no treatment group (18%) (P = 0.03). Lin et al[382] in 2007 found no difference in thrombosis at 1 year (P = 0.15).

There was no difference in the need for angioplasty between treatment arms; Lin et al[382,383] in 2013 reported angioplasty in 23% versus 25% (P = 0.87). In another study, Lin et al[384] reported 0.11 versus 0.29 angioplasties per day per patient per year (P = 0.10). Lai et al[385] and Lin et al[384] reported no complications or infections in both groups. Lin et al[384] reported shorter hospital stays with the far-infrared radiation versus no treatment (0.40 vs 1.35 days/patient/year; P < 0.01) (Supplement 3, Tables S157 and S158).

Fish Oil. A single RCT by Irish et al[386] (N = 567) compared fish oil versus placebo for prophylaxis of AVF dysfunction. A subset of participants in both groups without indication for aspirin (n = 406) was also randomized to aspirin or placebo. It is unclear how many in each group were concurrently taking aspirin, but analyses controlled for aspirin status. Follow-up was 6 months for adverse events, hospitalizations/emergency department visits, and mortality and 1 year for primary outcomes (primary AVF failure and thrombosis). Study participants were on average 55 years old; 63% were men, 53% were white, and 32% were Asian (Supplement 3, Table S158). There was no significant difference in AVF primary failure, thrombosis, hospitalizations/emergency department visits, or mortality (Table 14.1).

There was no significant difference in adverse events with fish oil versus placebo for bleeding (6% vs 4%) (RR, 1.56; 95% CI, 0.72-3.39) or gastrointestinal events (both 5%) (RR, 1.06; 95% CI, 0.52-2.17).

Primary failure in this study was defined as a composite of thrombosis, AVF abandonment, and cannulation failure.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S158-S160.

Table 14.1. Primary Outcomes for Fish Oil Versus Placebo for AVF

Outcome	Fish Oil, %	Placebo, %	Relative Risk (95% CI)
Primary failure	47	47	1.03 (0.86 to 1.23)
Thrombosis	22	23	0.98 (0.72 to 1.34)
Hospitalizations/ emergency department	38	39	0.99 (0.79 to 1.24)
Mortality	3	3	0.89 (0.35 to 2.27)

Abbreviation: CI, confidence interval.

Simvastatin-Ezetimibe. Herrington et al[387] conducted a secondary analysis of the Study of Heart and Renal Protection (SHARP) trial (N = 2,353) that evaluated the potential impact of simvastatin and ezetimibe on vascular access occlusive events. *Vascular occlusive event* was defined as any vascular access revision procedure (PTA, embolectomy, or surgical repair), any AV access thrombosis event, or the removal of old/placement of new vascular access (AV access or CVC). Analyses were restricted to those participants known to have a pre-existing functioning AVF or AVG at randomization.[387] Participants were on average 59 years old; 65% were male and 94% had an AVF access.[387] There was no significant difference in the need for intervention with simvastatin and ezetimibe versus placebo (19% vs 21%; note that vascular access types were not reported separately; RR, 0.87; 95% CI, 0.74-1.02). Access thrombosis was not significantly different with simvastatin/ezetimibe versus placebo (RR, 0.90; 95% CI, 0.71-1.15), nor was the rate of any vascular occlusive event (27% for simvastatin/ezetimibe vs 32% for placebo) (RR, 0.83; 99% CI, 0.68-1.02).[387] Harms pertaining to vascular access were not reported (Supplement 3, Tables S160-S163).

Clopidogrel and Prostacyclin. There is 1 RCT (N = 96) by Abacilar et al[283] from Turkey comparing clopidogrel in combination with prostacyclin versus placebo to prevent AVF dysfunction. Primary failure at up to 12 months was 8% with clopidogrel-prostacyclin therapy versus 30% with placebo (RR, 0.82; 95% CI, 0.31-0.94). Primary patency was not significantly different with clopidogrel-prostacyclin therapy (60%) versus placebo (39%) (RR, 1.53; 95% CI, 1.00-2.35). There was no significant difference in number of adverse events (tenderness, edema, or hematoma) (18% vs 13%, respectively; RR, 1.38; 95% CI, 0.53-3.58) and bleeding (RR, 0.92; 95% CI, 0.059-14.3) between arms[283] (Supplement 3, Tables S160-S162). This study was discussed at length by the Work Group. There were concerns regarding the methodology and reporting of this study and its potential clinical applications.

Arteriovenous Grafts

Preventing AVG thrombosis and maintaining longevity remains a major clinical problem for HD patients. Thrombosis can account for up to 80% of AVG failures[235,236] due to an underlying stenosis at the venous anastomosis.[237-239] The 2006 KDOQI guideline recommended evaluation and treatment in AVGs of patients with extremity edema persisting for 2 weeks or longer, AVGs at risk for rupture, and stenosis with a >50% decrease in

luminal diameter with clinical and physiologic abnormalities.[13] These Guidelines recommended PTA or surgical revision/repair to prevent AVG dysfunction.[13] Since the 2006 KDOQI guideline, there has been newly published literature evaluating pharmacologic therapies and novel interventions to prevent AVG dysfunction.

Recent studies that assessed pharmacologic therapies to prevent AVG dysfunction include those related to fish oil and dipyridamole.[97,388-390]

Fish Oil. Two North American studies (N = 230) compared fish oil with placebo for patency of AVGs. Lok et al followed participants for 1 year[388] and Bowden et al for 8 months.[389] Primary patency was better at 1 year with fish oil versus placebo in Lok et al (48% vs 32%; HR, 0.68; 95% CI, 0.46-0.99; P = 0.045), but Bowden et al reported no difference at 6 months (mean patency rate, 254.2 days vs 254.1 days). Bowden et al reported the proportion of AVG with thrombosis or required angioplasty, 50% versus 40% (RR, 1.25; 95% CI, 0.56-2.81).[389] Secondary patency was not significantly different with fish oil versus placebo. Lok et al[388] reported that time to intervention was not significantly different with fish oil versus placebo (HR, 0.78; 95% CI, 0.55-1.09). However, fewer interventions per 1,000 access days was reported with fish oil versus placebo (0.39 vs 0.95 interventions per 1,000 access days; 95% CI, 0.20-0.85; P = 0.02).[388] This group also reported a lower rate of thrombosis with fish oil compared with placebo, 1.71 versus 3.41 (RR, 0.50; 95% CI, 0.35-0.72). Bowden et al[389] reported no difference in gastrointestinal distress between patients assigned to fish oil versus placebo, 33% versus 13% (RR, 2.68; 95% CI, 0.62-11.6). The dose and compositions of fish oil used by Bowden and Lok were different.

Tables of study details and evidence quality are provided in Supplement 3, Tables S164 and S166.

Dipyridamole and Aspirin[96,390]. Two publications of 1 North American RCT (N = 649) reported outcomes for the comparison between dipyridamole (200 mg) and aspirin (25 mg) daily versus placebo[96,390] given at the time of AVG creation and followed for 1 year. The participants were on average 59 years old; 39% were male, and 71% were black. Dixon et al[96] showed that AVG unassisted graft patency at 1 year was lower with dipyridamole/aspirin (80%) versus placebo (84%) (HR, 0.82; 95% CI, 0.68-0.98). They reported a median primary patency of 5.8 months with dipyridamole/aspirin versus 4.3 months with placebo (ie, a difference of 6 weeks); however, statistical significance was not reported, and data was otherwise insufficient to calculate significance or assess quality of evidence. There was no difference in hospitalizations between groups (54% vs 52%; HR, 0.93; 95% CI, 0.75-1.15).[96,390] The study did not report further harms of the dipyridamole and aspirin combination.

The study details and evidence quality are provided in Supplement 3, Table S166.

Summary

Arteriovenous Fistula. In AVFs, clopidogrel and prostacyclin has been the only pharmacologic therapy suggested by RCT evidence to be effective to prevent AVF dysfunction.[283] This study reported that clopidogrel and prostacyclin therapy improved primary AVF failure. Although reviewed in a separate section, a multicenter RCT by Dember et al[31] reported that clopidogrel significantly reduced 6-week AVF thrombosis but did not improve AVF suitability for dialysis. A recent RCT evaluating fish oil and aspirin in new AVFs did not show any benefit to improve primary failures, thrombosis, abandonment, or cannulation failure in the fish oil group.[386] A subset of participants without aspirin indication (n = 406) in both groups were also randomized to aspirin or placebo.[386] It is unclear how many in each group were concurrently taking aspirin, but analyses controlled for aspirin status. The results from the aspirin subset were not graded for level of evidence. However, in the aspirin-only analysis, aspirin did not improve primary or secondary outcomes. Also, in a subsequent independent publication, fish oil was found to be associated with reduced rates of AV access interventions.[345] Finally, the far-infrared therapy studies demonstrated significantly improved primary AVF patency rates compared with no treatment. Although several of these pharmacologic and technologic therapies have shown benefit, the Work Group recommends an individualized approach toward implementing these therapies because the sample size was small in several of these studies.

Arteriovenous Grafts. There were 2 major studies evaluating pharmacologic therapies in AVG, fish oil[388] and dipyridamole/aspirin.[96] The fish oil study showed improved primary but not secondary AVG patency. Dipyridamole/aspirin also showed improved primary patency. Clinical practice implementation based on the results of these studies needs to be individualized. Although in combined studies fish oil did not show significant benefit for AVF patency, it was associated with reduced frequency (rate) of thrombosis and interventions, and it prolonged the time to thrombosis. Overall, fish oil has low-risk profile; risks and benefits can be considered within the patient's ESKD Life-Plan.

On the other hand, although dipyridamole/aspirin showed a significant statistical benefit to reduce loss of primary patency, the benefit of the therapy realistically was very modest: primary unassisted patency in the dipyridamole/aspirin group was 28% versus 23% in the placebo group (ie, taking dipyridamole/aspirin delayed loss of primary patency by 6 weeks).[96] However, the risks of potential complications of frailty, falls, and bleeding must be individualized before considering use of this therapy.

Although not reviewed by the ERT for these guidelines, the efficacy of the combination of aspirin and clopidogrel in the prevention of graft thrombosis was evaluated in a Veterans

Affairs Cooperative study.[391] The study was a randomized, double-blind trial conducted at 30 hemodialysis units at Veterans Affairs medical centers. Participants undergoing hemodialysis with an AVG were randomized to receive either double placebos or aspirin (325 mg) and clopidogrel (75 mg) daily. Participants were to be monitored while receiving study medications for a minimum of 2 years. The study was stopped after randomization of 200 participants by the Data Safety and Monitoring Board because of a significantly increased risk of bleeding among the participants receiving aspirin and clopidogrel therapy. The cumulative incidence of bleeding events was significantly greater for those participants compared with participants receiving placebo (HR, 1.98; 95% CI, 1.19-3.28; P = 0.007).[391] Among the vascular access outcomes data reported, there was no significant benefit of active treatment in the prevention of thrombosis (HR, 0.81; 95% CI, 0.47-1.40; P = 0.45).[391] Similar increased major bleeding risks were noted in a well-conducted double-blind RCT of low-dose warfarin (target international normalized ratio [INR], 1.4-1.9) versus placebo to reduce HD graft thrombosis.[392] *Although these studies did now show benefit of an antiplatelet agent or anticoagulant to reduce AVG thrombosis, they more importantly highlight the need for assessing the risks for potential complications of using antiplatelet or anticoagulant agents in an elderly and frail population, where the benefit of the therapy may only be modest or absent.*

Special Discussions

Overall, there were very few studies that evaluated therapies to prevent AVF and AVG dysfunction that were of high-quality evidence. Even in those studies of high quality, careful consideration should be made before using additional therapies based on statistically significant results in the absence of important clinically meaningful differences.

Implementation Considerations

- Some of these therapies, such as far-infrared therapy, may not be widely available outside of Asia.
- Antiplatelet and anticoagulant agents may increase risk of bleeding, and their use needs to be carefully considered in the elderly population and those patients with high bleeding risks.

Monitoring and Evaluation

- Because a number of these therapies have been performed in smaller studies and often nonrandomized studies, adverse events need to be closely monitored and evaluated.
- A number of these agents have adverse events such as bleeding, so these complications must be closely monitored and evaluated.

Future Research

- Far-infrared therapies for AVF and AVG dysfunction in populations outside of Taiwan
- The FISH study did not reach its enrollment target; additional studies of omega-3 fatty acids, including those with different formulations and/or different doses, may provide insight to potential benefits for AV access outcomes.

Guideline 15. AV Access Flow Dysfunction—Confirmation and Treatment

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Radiographic Confirmation of Clinically Significant AV Access Lesion

15.1 **KDOQI considers it reasonable that when clinical monitoring suspects clinically significant AV access lesion (eg, stenosis), further timely and confirmatory evaluation should proceed, including imaging of the dialysis access circuit. (Expert Opinion)**

Notes:

- *A clinically significant lesion is one that contributes to clinical signs and symptoms (see AV Access Monitoring, Table 13.2) without other cause (with or without a change in surveillance measurements, such as change in blood flow [Qa] or venous pressures).*
- *Dialysis access circuit is defined as the continuum from the heart and the arterial inflow through the AV access to the venous outflow back to the heart.*
- *The timeframe, choice, and extent of imaging studies for further evaluation are dependent on local resources and the severity of findings on clinical monitoring; a timeframe of less than 2 weeks was deemed reasonable by the KDOQI Work Group.*

15.2 **KDOQI considers it reasonable to use the smallest volume of iodinated contrast or non-iodinated contrast agents (eg, CO_2 gas) by operators knowledgeable in their uses, contraindications, and risks to obtain the best possible image in all patients with CKD to preserve residual kidney function. (Expert Opinion)**

15.3 **KDOQI considers it reasonable that when further confirmatory imaging studies reveal a culprit lesion responsible for clinical signs and symptoms, the clinically significant lesion is promptly treated. (Expert Opinion)**

Note: A clinically significant lesion is one that contributes to clinical signs and symptoms (see AV access Monitoring, Table 13.2) without other cause (with or without a change in surveillance measurements, such as change in blood flow [Qa] or venous pressures).

Statement: General Treatment of Clinically Significant Stenosis or Thrombosed AV Access

15.4 **KDOQI considers it reasonable to use a careful individualized approach to the treatment of failing or thrombosed AVF and AVG (surgical or endovascular), based on the operators best clinical judgment and expertise considering the patient's ESKD Life-Plan. (Expert Opinion)**

Note: Consider both the patient's individual circumstances and the operator's clinical experience and expertise (ie, reasonable capabilities and limitations); preferably discussed and agreed on by the team managing the patient's vascular access, including but not limited to the patient and one or more of the following: nephrologist, interventionalist, surgeon, vascular access coordinator, cannulators (nurse or technician).

Statements: Treatment of Clinically Significant AV Access Stenosis

Angioplasty

15.5 **KDOQI considers it reasonable to use balloon angioplasty (with high pressure as needed) as primary treatment of AVF and AVG stenotic lesions that are both clinically and angiographically significant. (Expert Opinion)**

Note: Angiographically present stenosis without accompanying clinical signs and symptoms is inadequate to treat/intervene upon.

15.6 **There is inadequate evidence for KDOQI to make a recommendation regarding the use of specialized balloons (drug-coated or cutting) versus standard high-pressure balloons in the primary treatment of AVF and AVG stenosis.**

15.7 **There is inadequate evidence for KDOQI to make a recommendation regarding the optimal duration of balloon inflation time during angioplasty to improve intervention primary patency in the treatment of AVF or AVG stenosis.**

15.8 **KDOQI considers it reasonable that a careful patient-individualized approach to the choice of balloon type for angioplasty of clinically significant AVF and AVG stenosis be based on the operator's best clinical judgment and expertise. (Expert Opinion)**

Stents

15.9 **KDOQI suggests the appropriate use of self-expanding stent-grafts in preference to angioplasty alone to treat clinically significant graft-vein anastomotic stenosis in AVG when the goal is overall better 6-month postintervention outcomes after carefully considering the patient's ESKD Life-Plan. (Conditional Recommendation, Moderate Quality of Evidence)**

Note: Appropriate use avoids cannulation segments.

Note: Overall better 6-month outcomes refer to reduced recurrent AVG restenosis ± improved patency.

15.10 **KDOQI considers it reasonable to first consider the consequences of placement of a stent-graft on future AV access options according to the patient's ESKD Life-Plan, with consultation with the vascular access team if necessary, prior to its placement. (Expert Opinion)**

15.11 **KDOQI suggests that the use of an appropriately placed stent-graft is preferred to angioplasty alone for the treatment of in-stent restenosis in AVG and AVF for overall better 6-month postintervention outcomes. (Conditional Recommendation, Moderate Quality of Evidence)**

Note: Appropriate use avoids cannulation segments.

Note: Overall better 6-month outcomes refer to reduced recurrent AVG and AVF restenosis ± improved patency.

15.12 **KDOQI considers it reasonable to avoid the use of bare metal stents for the treatment of clinically and/or angiographically significant AVG and AVF stenotic lesions. (Expert Opinion)**

Rationale/Background

Maintaining effective functioning AV access (AVF and AVG) is an ongoing challenge that frequently requires remedial treatment for problematic AV accesses (see Table 13.2, Clinical Indicators (Signs and Symptoms) Suggesting Underlying Clinically Significant Lesions During Access Monitoring), especially if AV access thrombosis occurs as a terminal event. Several of these conditions are addressed in separate sections of the Guidelines (Guidelines 16-19). The generic approach to these various failure modes includes appropriate monitoring and imaging to identify the underlying cause and then definitive treatment of the clinically significant culprit lesion. Various endovascular approaches have largely replaced the open, surgical approach and should be used as the first line of treatment, with the surgical approach reserved for endovascular failures, lesions not amenable to endovascular treatment, and those select lesions in which the surgical approach is deemed far more durable.

Stenosis is the most common complication after AV access creation.[393] Venous stenosis is often the result of neointimal hyperplasia[394] and leads to several serious sequelae in both AVF and AVG. Stenosis causes AVF nonmaturation with the attendant reliance on CVCs. AVF maturation failure has been reported in observational studies to range from 20% to 60%.[77,233,234] Furthermore,

a multicenter RCT in the United States reported that up to 60% of AVFs failed to mature successfully for dialysis use.[31] Stenosis also causes dysfunction in mature AVFs resulting in inadequate HD clearance, thrombosis, and eventual abandonment. AVGs are also susceptible to stenosis developing at the graft-vein junction, leading to thrombosis in 80% of AVGs.[235,236,238,239,395] The previous 2006 KDOQI guideline maintained that PTA is the first-line treatment for stenosis in the access circuit.[13] Although this generally remains the case in the modern era of vascular access, several important clinical trials and device innovations are considered that may alter the indications for angioplasty and the types of balloons and stents for treatment of stenosis. The current recommendations update those from the previous Guidelines.

Detailed Justification

Maintaining vascular access function required to provide adequate goal-directed dialysis is an ongoing challenge for all access types and configurations; all have a limited life expectancy. The complication and remediation rates (eg, infection, sepsis, thrombectomy) vary by the dialysis access type (CVC: 0.7 and 2.1 episodes/year; AVF: 0.14 and 0.44 episodes/year; AVG: 0.25 and 0.77, episodes/year, respectively)[396,397] and are detailed in various sections of this Guideline. In addition to the significant morbidity associated with dialysis access complications,[398] procedures to confirm and manage AV access flow–related problems have been deemed the most burdensome to patients, often leading to patient dissatisfaction.[345] It is the responsibility of the treating team to ensure appropriate detection of failing AV access and judicious use of invasive procedures in the diagnosis and treatment of culprit lesions. To provide greater clarity, the Work Group has replaced the term *AV access dysfunction* with 3 more specific terms describing AV access complications: (1) thrombotic-flow related complications or dysfunction; (2) nonthrombotic-flow–related complications or dysfunction, and (3) infection-related complications or dysfunction (see Glossary). It is incumbent on all health care providers who care for HD patients to be familiar with the various vascular access complications and failure modes. It is critical to emphasize that reducing complications and vascular access failure begins before a vascular access is created, with proper patient selection and an appropriate vascular access plan (vascular access creation plan) that considers the entire life cycle of the vascular access (vascular access contingency and succession plans) with the appropriate monitoring and care within the dialysis unit.

Detection and Diagnosis of Clinically Significant Stenosis and Related Complications

A clinically significant stenosis within the HD access circuit is associated with patient signs and symptoms and can lead to abnormal dialysis indicators (Table 13.2). The HD vascular access circuit should be viewed as a continuum from the left side of the heart, through the outflow arterial inflow to the anastomosis and back again, through the peripheral veins (or graft) to the central veins, and ultimately to the right side of the heart. AV accesses can develop lesions, especially stenosis, at any point within this circuit. AVGs typically develop stenoses at the graft-venous anastomoses, whereas AVFs typically develop stenoses in the juxta-anastomotic region and the swing segment for brachial-basilic AVF and the cephalic arch for brachial-cephalic AVF.[399-402] As noted in Guideline 15, the indication for further evaluation and definitive treatment requires the presence of a clinically symptomatic, significant lesion and not simply the presence of a lesion (ie, asymptomatic stenosis).[403,404]

Once routine monitoring reveals a clinically important vascular access problem (Guideline 13), the diagnostic approach is contingent on the clinical suspicion of the underlying lesion (ie, arterial inflow, anastomosis, venous outflow). Duplex ultrasound is effective for examining the AV access from the arterial anastomosis throughout the peripheral venous section (or graft) and may ascertain causes of thrombotic flow–related complications/dysfunction such as neointimal hyperplasia (NH), thickened venous valves, and competing accessory veins. However, it is ineffective for interrogating the central venous outflow, given the limitations of ultrasound and the bony thoracic cavity. Arterial duplex ultrasound can be helpful to image the peripheral arteries but is again limited for assessing the great vessels in the chest. Catheter-based venography and arteriography are invasive procedures but can definitively image the AV access from the anastomosis to the heart (venography) or the whole AV access circuit (arteriography) while serving as a platform for therapeutic interventions. CT arteriography and venography are alternative diagnostic studies for most peripheral vascular interventions but may have practical limitations.[405] These diagnostic procedures may use iodinated contrast that is potentially nephrotoxic and should be used judiciously in patients with CKD/ESKD and residual kidney function—on or off dialysis. Indeed, the choice of contrast needs to be factored into the imaging algorithm. Carbon dioxide can be used as an alternative non-nephrotoxic contrast agent for catheter-based procedures in select cases, although the quality of the imaging may not be sufficient to guide interventions, and caution should be exercised to avoid intra-arterial injection in the upper extremity due to the potential of the gas to pass into the cerebral arterial circulation and cause neurologic events.[406] Intravascular ultrasound can also be helpful in patients with severe contrast allergies.[407] MRI is also an alternative to CT arteriography, although the published experience is limited, and the use of the MRI contrast agent gadolinium is relatively contraindicated due to the risk of nephrogenic fibrosis.[405,408]

Appropriate imaging of the dialysis circuit should identify the culprit lesion and suggest definitive treatment strategies. Venous stenoses throughout the peripheral vein for AVFs and at the venous anastomoses for AVGs are

typically treated with endovascular therapies given their less invasive nature. Notably, these stenoses are typically dense, fibrous lesions from intimal hyperplasia and are distinctly different from arterial atherosclerotic lesions. Anastomotic lesions can likewise be treated with an endovascular-first approach, although they may not be as amenable to angioplasty, and, thus, more suited for open repair. The choice of treatment for atherosclerotic arterial inflow lesions should be based on their natural history, independent of the fact that they involved vessels providing inflow to the AV access. Accordingly, subclavian orifical lesions are typically treated with a combination of balloon angioplasty and intraluminal stenting with the more peripheral lesions (ie, axillary, brachial, radial, ulnar) treated by endovascular methods or open surgical repair using bypass or patch angioplasty.

Angioplasty for Treatment of Clinically Significant Stenoses

High-Pressure Balloon Angioplasty. Venous stenosis from NH is characterized by a concentric thickening and a lumen diameter reduction caused by myointimal cell proliferation.[409] Although there are several putative mechanisms that may promote NH, including an inflammatory reaction secondary to the AVF creation surgery, hemodynamic shear stress, trauma related to needle punctures, and possibly as a direct result of uremia,[410] a durable solution to NH-induced stenosis remains elusive. Re-stenosis at the initial lesion or elsewhere in the previously treated dialysis circuit occurs up to 60% of the time at 6 months.[411] In addition, the usual percutaneous angioplasty (PTA) solution to AV access stenosis is the very mechanism by which NH is induced in the porcine model and vessels progressively injured in HD patients.[412] Due to these fundamental limitations in the efficacy of standard PTA, several innovations were evaluated in this Guidelines. Aside from the special circumstances described herein, standard high-pressure balloon angioplasty remains the treatment of choice for the majority of anatomic and clinically significant AV access stenotic lesions. A clinically significant AV access stenotic lesion is one that is accompanied by clinical signs and symptoms (refer to section Guideline 13 and Tables 13.1 and 13.2) and shows >50% narrowing relative to adjacent normal vein diameter by angiography or ultrasound.

Paclitaxel-Coated Balloon Angioplasty in AVF. An RCT (N = 40) evaluated treatment with paclitaxel drug-coated balloons (PCBs) (Supplement 3, Table S178) compared with high-pressure balloons for treatment of single stenotic lesions in AVFs.[413,414] Patients were followed to 1 year with clinical assessments every 2 months. Both groups received oral aspirin 100 mg daily after angioplasty. Primary patency at 200 days was not significantly different with PCB versus high-pressure balloons (RR, 2.25; 95% CI, 0.83-6.13). However, treatment lesion re-stenosis-free survival was significantly superior in the PCB group compared with the high-pressure balloon group (PCB, 308 days vs balloon, 161 days; HR, 0.47; 95% CI, 0.23-0.96; P = 0.03), as was access circuit primary patency (ACPP) (median days): 270 versus 161 days (HR, 0.48; 95% CI, 0.23-0.97). Thrombosis at 1 year did not differ (RR, 2.0; 95% CI, 0.2-20.3).[414] Another small RCT (N = 10) compared PCB with plain balloon versus plain balloon alone for treatment of stenotic AVF where each access circuit had 2 lesions, 1 treated with PCB and the other without. Each patient acted as his/her own control and was followed for 1 year.[415] A high-pressure balloon was used if a plain balloon did not adequately treat the target lesion. Primary patency at 1 year was not significantly different with PCB and plain balloons versus plain balloon alone (20% vs 0%; P = 0.47). Angioplasty-

Table 15.1. Outcomes of Paclitaxel-Coated Balloon Angioplasty in AVGs and AVFs

Outcome	Paclitaxel-coated PTA	Plain balloon PTA	RR, HR, or P value
Primary patency at 1 year (all AV accesses)	No difference	No difference	RR, 7.0 95% CI, 0.95-51.8
Median primary patency (all AV accesses), years	0.64	0.36	*P* = 0.0007 adjusted HR, 0.23 95% CI, 0.10-0.50
Primary patency at 1 year (AVG), %	38	0	*P* = 0.003
Median primary patency (AVG), years	0.62	0.21	*P* = 0.002 unadjusted HR, 0.22 95% CI, 0.08-0.57
Primary patency at 1 year (AVF), %	29	14	*P* = 0.26
Median primary patency (AVF), years	0.78	0.43	*P* = 0.15 unadjusted HR, 0.42 95% CI, 0.13-1.44

Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; AVG, arteriovenous graft; CI, confidence interval; HR, hazard ratio; PTA, primary balloon angioplasty; RR, relative risk.

free days were significantly greater with PCB and plain balloons versus plain balloon alone (251 vs 103 days; P < 0.01).

Paclitaxel-Coated Balloon Angioplasty in AVG. One RCT (N = 40) compared paclitaxel-coated balloon versus plain balloon for PTA in stenotic AV access (14 AVF [n = 14] and 26 AVG) at 1 year[413] (Table 15.1).

Thrombosis was not significantly different with PCB versus plain balloon (RR, 1.0; 95% CI, 0.16-6.42). Angiographic restenosis was significantly lower with PCB versus plain balloon (RR, 0.68; 95% CI, 0.49-0.96), as was the need for repeat angioplasty procedures (RR, 0.63; 95% CI, 0.44-0.92).

A recent meta-analysis found that paclitaxel-coated stents and balloons used in patients with peripheral arterial disease for claudication was associated with an increased 5-year mortality. A causative factor, if any, has not been ascertained—it is unclear if this finding is relevant to the HD patient population and vascular access.[416]

Cutting Balloon Angioplasty. Two RCTs compared cutting balloon angioplasty with high-pressure balloon angioplasty for the treatment of stenosis in AVF.[417,418] One Canadian trial (N = 48; 39 analyzed), included participants with de novo stenoses. Another Singapore-based study (N = 77; 71 analyzed) included participants with stenoses for whom conventional pressure balloon angioplasty had failed who were randomized to cutting balloon PTA versus high-pressure balloon PTA. Average age of the AVF was approximately 15 months in the Canadian trial and 22 months in the Singapore trial.[418] Clinical treatment success, defined as the ability to perform at least 1 successful dialysis procedure using the AVF after angioplasty, was 96% and did not differ between groups (RR, 1.00; 95% CI, 0.95-1.05). Technical treatment success, defined as <30% residual stenosis, did not differ at 95% and 98% in the cutting and high-pressure arms, respectively (RR, 0.98; 95% CI, 0.91-1.05]. Overall, 6-month primary patency did not differ between groups.

Study details and evidence quality are provided in Supplement 3, Table S167.

Angioplasty Balloon Inflation Time. One RCT (N = 48) compared a 1-minute inflation time with a 3-minute inflation time during PTA of AV access stenosis.[419] Most were AVF (88%), with an average age of 692 days. There were 40 stenoses in the 27 participants allocated to the 1-minute group and 36 stenoses in the 21 participants allocated to the 3-minute group. Results were reported up to 6 months. Treatment success, defined as a reduction of stenosis to less than 30% of the luminal diameter or a reduction of the mean gradient to less than 10 mm Hg in peripheral or to less than 5 mm Hg in central lesions, did not differ statistically between groups (75% in the 1-minute group vs 89% in the 3-minute group ; P = 0.12). Primary patency did not differ between groups at any of the postintervention intervals of 1, 3, or 6 months. Kaplan-Meier estimates of 6-month patency were 63% and 47% for the 1- and 3-minute duration groups, respectively. An observational trial (N = 75) analyzed prospectively collected data from a vascular access database of stenotic AVGs and AVFs with 223 interventions (178 with 30-second inflations and 45 with 1-minute inflations).[420] Demographics and baseline characteristics were similar across groups. Immediate technical success and patency in the first 3 months did not differ (HR, 0.86; 95% CI, 0.34-2.20). After 3 months, however, a 1-minute inflation time was associated with greater incidence of AV access failure (adjusted HR, 1.74; 95% CI, 1.09-2.79).

Stents for Treatment of Clinically Significant Stenoses

See Table 15.2 for indications for stent use in AV access.

Stents-grafts in AVG. Two RCTs evaluated stent grafts for treating AVG stenosis: Haskal et al[421] and Vesely et al[422] compared treatments for AVG venous anastomotic stenosis using angioplasty with placement of stent-grafts versus angioplasty alone. Haskal et al conducted a

Table 15.2. Indications for Stent-Graft Use in AV Access

Please note that the indications for stent graft use is for 6 month outcomes only.

The numbers of patients at risk in the individual studies were too small for the ERT to determine impact on 12- and 24-month outcomes.

Studies have not sufficiently or consistently shown stent graft use to improve AV access thrombosis rates or cumulative AV access survival beyond 6 months.

The indications below are relevant to AV accesses in the absence of central vein occlusion. Before the use of a stent-graft, clinicians should first consider the impact of its placement on (1) the current access's ability to be cannulated without harm and (2) the patient's ESKD Life-Plan and subsequent vascular access creation and use.

- Recurrent clinically significant graft-vein anastomotic stenosis in AVG
- Recurrent graft-vein anastomotic thrombosis in AVG
- In-stent re-stenosis in AVF and AVG
- Treatment of ruptured venous stenotic segment of AVF and AVG
- Treatment of highly select AV access aneurysm/pseudoaneurysm (see AV access aneurysms section)

Note: Overall better 6-month outcomes refer to reduced recurrent AVG restenosis ± patency (target lesion and AV access circuit). To achieve consensus in the Guidelines, Table 15.2 reflects the Work Group's very considered decision to incorporate and balance the available evidence with expert opinion (eg, Guideline Statements 15.9-15.11), considering clinical practice and the long-term needs of patients, with the limited follow-up time and numbers from the available evidence. This highlights the need for further rigorous study of stent-graft use in AV accesses, which considers the findings on clinical monitoring and surveillance that lead to the indications for investigation and treatment, and the need for longer follow-up, including the impact of treatments on future AV access creation and use.

multicenter RCT (N = 190) that compared angioplasty with placement of a stent-graft (self-expanding nitinol polytetrafluoroethylene stent [Flair Endovascular Stent Graft, Bard Peripheral Vascular]) to high-pressure angioplasty alone to treat AVG venous anastomotic stenosis. Participants were followed for 6 months. Treatment groups were similar at baseline, except for more anastomoses at the axillary vein among the angioplasty-alone group. Thrombosed accesses were excluded, and a mandatory 6-month angiogram was performed. Vesely et al conducted a multicenter RCT (N = 293) that compared angioplasty with placement of a stent-graft (self-expanding polytetrafluoroethylene stent with a heparin bioactive surface and an external nitinol structure (Viabahn Endoprosthesis With Heparin Bioactive Surface, WL Gore) to angioplasty alone to treat AVG venous anastomotic stenosis.[422] Participants were followed for 24 months. Treatment groups were similar at baseline, except for more Hispanic/Latino participants among the angioplasty-alone group. Thrombosed AVGs were included, and follow-up was conducted per individual site standard of practice with no mandatory angiogram. Outcomes were reported for both intent-to-treat and per-protocol populations; only the intent-to-treat outcomes were extracted and analyzed by the ERT. Because Vesely et al also reported primary patency for patients with stenosis versus thrombosis separately, the outcomes for patients with stenosis were pooled with outcomes from Haskal et al and analyzed.

In a pooled analysis, treatment area primary patency (TAPP) by angioplasty with stent graft versus angioplasty alone at 6 months was significantly higher among stenotic lesions (RR, 1.71; 95% CI, 1.11-2.64) and among all lesions (stenotic and thrombotic) (RR, 1.50; 95% CI, 1.14-1.97) in Vesely et al.[422] However, in the shorter term, TAPP was not significantly different for angioplasty with stent graft versus angioplasty alone among stenotic lesions at 2 months (RR, 1.04; 95% CI, 0.90-1.21). ACPP by angioplasty with stent graft versus angioplasty alone at 6 months was significantly higher in a pooled analysis among stenotic lesions (RR, 1.58; 95% CI, 1.30-2.20) and in the study by Vesely et al, among all lesions (stenotic and thrombotic) (RR, 1.46; 95% CI, 1.06-2.01). However, in the Haskal et al study, ACPP was not significantly different for angioplasty with stent graft versus angioplasty alone among stenotic lesions at 2 months (RR, 1.03; 95% CI, 0.88-1.19).

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S168-S177.

Several intermediate outcomes evaluated showed that angioplasty with stent graft, compared with angioplasty alone, had (1) higher freedom from subsequent intervention (32% angioplasty with stent graft vs 16% angioplasty alone; P = 0.03),[421] (2) lower risk of restenosis (RR, 0.52; 95% CI, 0.40-0.68), (3) longer median time to loss of TAPP among all lesions (2,013 days for angioplasty with stent vs 108 days for angioplasty alone),[423] and 4) longer median time to loss of ACPP among all lesions (126 days for angioplasty with stent s 91 days for angioplasty alone). Tests for significance were not reported and were not calculable in time-to-event analyses.

Haskal et al[421] and Vesely et al [422] did not report other intermediate health outcomes. Harms associated with treatment, including infection (RR, 2.84; 95% CI, 0.59-13.72), pseudoaneurysm (RR, 2.37; 95% CI, 0.47-11.90), and vessel rupture (RR, 2.84; 95% CI, 0.30-26.82), were not significantly different for angioplasty with stent graft versus angioplasty alone in Haskal et al. Adverse events within 30 days, whether major (risk difference, -0.01; 95% CI, -0.03 to 0.005; RR, undefined) or minor (RR, 2.04; 95% CI, 0.38-10.97) were not significantly different for angioplasty with stent grafts versus angioplasty alone in Vesely et al.

The Work Group discussed these studies and their implications at great length. Concerns raised included the fact that the Haskal et al study[421] used protocol angiograms to detect lesions, which may not have been clinically significant; thus, the generalizability and relevance to clinical practice was questioned. There was also no difference in clinically important thrombosis. After the literature review and data extraction by the ERT, another study was published (RENOVA, by Haskal et al), which was similar in design as the prior Haskal study but with longer follow-up.[424] The Work Group reviewed and considered this study as well. All studies that reported 12- and 24-month outcomes had low numbers of remaining patients at risk, leaving uncertainty in interpretation (for example, in Haskal et al, at 12 months, the total number of evaluable patients at risk was 9, and at 24 months it was 0, for ACPP).

The Work Group statements reflect the consideration of the outcomes of all 4 published studies and their clinical interpretation, application, and relevance in light of the Work Group concerns.

Stent-grafts in AVF. Two RCTs evaluated stent grafts for treating AVF stenosis.[425,426] Shemesh et al[425] and Rajan et al[426] compared treatments for cephalic arch stenosis; Shemesh et al compared angioplasty with a stent graft versus angioplasty with a bare-metal stent, whereas Rajan et al compared angioplasty with a stent graft versus angioplasty alone. The ERT did not extract data for analysis from the Rajan et al study, due to the study's high risk of bias.

Shemesh et al (N = 25) compared the 2 groups for treating recurrent cephalic arch stenosis within 3 months of a previous successful PTA of a brachiocephalic AVF, with up to 15 months follow-up (mean, 13.7 months).[425] The stent graft was a self-expanding nitinol stent covered by expanded polytetrafluoroethylene (Fluency Plus, Bard

Peripheral Vascular, Angiomed GmbH & Co Medizintechnik KG). The bare-metal stent was a self-expanding nitinol stent (Luminex, Bard Peripheral Vascular, Angiomed GmbH & Co Medizintechnik KG). Stent grafts, compared with bare-metal stents showed (1) higher primary patency (HR, 4.09; 95% CI, 1.9-20.3; P = 0.002) and (2) no difference in secondary patency (P = 0.29 by log-rank test) at 1 year.

Interventions for re-stenosis were significantly fewer with a stent-graft versus a bare-metal stent during total follow-up (RR, 0.46; 95% CI, 0.22-0.96), as were overall interventions per patient-year (RR, 0.47; 95% CI, 0.36-0.61). Re-stenosis was defined as >50% stenosis at 3 months as determined by angiography. Re-stenosis at 3 months was significantly lower with a stent-graft (RR, 0.26; 95% CI, 0.07-0.97). Of note, no sample size determination was made, and methodology for randomization was not provided. The Work Group had discussions about these studies and shared concerns about making statements based on the small numbers in these studies and, therefore, refrained from doing so.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S168-S177.

Stent-Graft for In-Stent Restenosis. The next study was discussed by the Work Group, but it did not meet entry criteria for retrieval and review by ERT due to its publication date. A multicenter RCT (N = 275) by Falk et al[427] evaluated the efficacy of stent-graft versus angioplasty alone for the treatment of in-stent re-stenotic lesions in the venous outflow of the AV access circuit of AVGs and AVFs.[427] Primary endpoints were ACPP at 6 months and safety through 30 days; secondary endpoints were evaluated through 24 months. ACPP at 6 months was significantly higher in the stent-graft group (18.6%) versus the angioplasty group (4.5%; P < 0.001), and freedom from safety events (30 days) was comparable (stent graft, 96.9%; angioplasty, 96.4%; P = 0.003 for noninferiority). TAPP was superior for the stent-graft group (66.4%) versus the angioplasty group (12.3%) at 6 months (P < 0.001). ACPP and TAPP for the stent-graft group demonstrated similar outcomes in central and peripheral vein subgroups (P < 0.001). Of note, overall or secondary access patency was not assessed.

Thrombolysis—Endovascular and Surgical

Despite efforts at prevention of thrombosis, either via pharmacologic prophylaxis or angioplasty of stenosis, access thrombosis frequently occurs. Percutaneous thrombectomy remains an essential endovascular procedure, with a variety of approaches to this procedure. The method chosen depends on operator experience, available resources, and patient factors. Although immediate success to provide at least 1 effective dialysis session after the procedure can be achieved in 80% to 95% of thrombosed AVGs and AVFs,[428] long-term patency after thrombectomy remains elusive, with reported rates of 25% to 50% at 6 months and 10% to 20% at 1 year.[429] For AVGs, a meta-analysis of 8 RCTs compared surgical thrombectomy to endovascular therapy for thrombosed AVGs and found outcomes to be comparable.[430] With regard to AVFs, only observational studies on the treatment of thrombosed AVFs were identified that also showed similar primary outcomes of surgical and endovascular interventions.[431]

Surgery

Open surgical repair is generally reserved for recurrent lesions, those not amenable to endovascular treatment, and those for which the outcomes associated with the endovascular approach are poor.[432,433] There are a variety of open surgical techniques for these peripheral venous lesions, including interposition grafting and patch angioplasty, with the choice typically dictated by the extent of the lesion. Notably, Romann et al[434] reported that failure of balloon angioplasty for AVF stenoses was correlated with the length of the lesion, with those >2 cm having a higher failure rate, suggesting that these may be better treated with an open approach. Brachiocephalic AVFs and brachiobasilic AVFs frequently fail due to development of stenoses at the cephalic arch and "swing segment" (proximal hinge for the mobilized basilic vein). Both of these lesions are amenable to endovascular treatment, but the surgical alternative may be more durable and remains an option for recurrent lesions after failed endovascular treatments. Two series have reported favorable surgical results for the cephalic arch stenoses,[435,436] although a systematic review failed to identify a superior approach among the open and endovascular options.[437]

Special Discussions

- Should stents and their variations be used, it is important to avoid placing them at AV access cannulation segments to preserve AV access functionality and use.
- Overall, there were very few studies that evaluated therapies to prevent AVF and AVG dysfunction that were of high-quality evidence.
- See commentary in Detailed Justification section for Work Group discussion of stent-graft use.

Implementation Considerations

- Close follow-up and documentation of the effects of stent-graft use on short- and long-term outcomes for the currently affected and future AV accesses

Monitoring and Evaluation

- Because a number of these therapies have been performed in smaller and often nonrandomized studies, adverse events need to be closely monitored and evaluated.

Future Research

- Study the patient and AV access outcomes and impact of (1) ultrasound-guided angioplasty and (2) intravascular ultrasound-guided angioplasty, to limit contrast exposure in CKD/ESKD patients with residual kidney function and urine output
- Stent-grafts versus bare-metal stents for treatment of central vein stenosis requires more RCT evaluation, with larger numbers, rigorous conduct, and analysis.
- More RCT evaluation of stent-grafts for vascular access management (primary or secondary) with clinical-based (rather than angiogram) outcomes are urgently required.
- Study is needed in AVFs for multiple modalities of treatment (eg, stent-grafts, drug-eluting balloons, etc).
- Comparative methods of AV access thrombolysis (eg, surgical vs endovascular) with a variety of short- and longer-term AVF and AVG outcomes
- Increasing evidence in the following areas:
  - The use of specialized balloons (drug-coated or cutting) versus standard high-pressure balloons in the primary treatment of AVF and AVG stenosis
  - The optimal duration of balloon inflation time during angioplasty to improve intervention primary patency in the treatment of AVF or AVG stenosis
  - The secondary use of drug-coated balloons after successful angioplasty with high-pressure balloons for treatment of stenosis in AVF and AVG
- Impact of timing of recurrence of stenosis on choice of treatment modality
- Use of stent grafts in locations other than graft-vein anastomosis or cephalic arch in brachiocephalic AVFs
- Optimal treatment of in-stent stenosis that occurs in stent-grafts
- Study outcomes with surgically corrected occluded AV accesses that are followed by a completion angiogram/imaging ± further corrective procedure. How does this strategy compare with historical surgical correction without completion imaging or with endovascular management?
- The optimal timing of angioplasty/thrombolysis or thrombectomy in thrombosed AVF and AVG
- Studies to determine the best measurement that defines a successful procedure outcome: for example, should it be a percent relative improvement in lumen size or an absolute lumen diameter or other measurement? When should it be measured after the treatment (eg, PTA) (during the procedure or after?)

Statements: Treatment of Thrombosed AV Access

15.13 KDOQI considers it reasonable that management of each episode of AV access thrombosis is at the operator's/clinician's best judgement and discretion, and involves the consideration of the patient's dialysis access Succession Plan that is consistent with the ESKD Life-Plan, given the compromised AV access patency after either endovascular or surgical treatment. (Expert Opinion)

Note: Operators/clinician's discretion carefully considers both the patient's individual circumstances and the operator's/clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations). The Succession Plan is a critical component of the P-L-A-N (see Monitoring and Evaluation discussion in Guideline 1).

15.14 KDOQI considers it reasonable to surgically treat a failing AV access in the following circumstances: (1) endovascular treatment failures, (2) clinically significant lesions not amenable to endovascular treatment, and (3) situations in which the surgical outcomes are deemed markedly better. (Expert Opinion)

Note: Situations when surgical outcomes are anticipated to be better than alternative options should be first discussed and agreed upon by the team managing the patient's vascular access, including but not limited to the patient and one or more of the following: nephrologist, interventionalist, surgeon, vascular access coordinator, and cannulation expert, if possible.

Rationale/Background

Fully occlusive thrombosis represents the terminal event for the failing AV access and accounts for 65% to 85% of all AV access abandonments.[438] Although the contributory cause of the terminal thrombotic event is usually obvious (eg, low flow related to venous outflow stenosis in AVG), patients can present with de novo thrombosis without any clear failure mechanism.[439] The clinical priorities include providing necessary effective dialysis, clearing the intraluminal thrombus, and definitively treating the underlying cause of the failure.

The diagnosis of a thrombosed AV access is often obvious on physical examination but can be confirmed with duplex ultrasound. Patients with an emergent need for dialysis (eg, volume overload, hyperkalemia) should be dialyzed through a temporary nontunneled CVC prior to definitive treatment of their AV access thrombosis.

Detailed Justification

Both endovascular and open surgical approaches for treating thrombosed AVGs are acceptable, with the choice determined by the local practice and expertise, underlying condition, and patient preference. Although earlier reports suggested superior outcomes with the surgical approach, more recent reports have suggested that both approaches for AVGs are comparable, likely reflecting the overall evolution in the endovascular therapies.[431,440,441] Furthermore, there are a number of different endovascular approaches, although none has proven superior.[438] Importantly, open surgical and endovascular approaches should not be viewed as competing but rather complementary, because there are a variety of hybrid approaches

that involve both (eg, open surgical thrombectomy with combined balloon angioplasty of central vein stenosis).[442,443] There has been a gradual evolution in the approach to thrombosed AVFs with the earlier version of the 2006 KDOQI guideline recommending abandoning the AVF to more recent attempts at AVF thrombectomy and AV access salvage.[395,444] A meta-analysis by Kuhan et al[441] emphasized the lack of long-term data with little quality evidence to guide the management of thrombosed AVFs. The contraindications to AV access thrombectomy include pulmonary hypertension and right-left intracardiac shunts due to the potential risk of embolization and AV access infection.

Regardless of the approach, thrombectomy should be performed in a timely fashion relative to the event, particularly for AVFs, given the pathophysiology of the thrombotic process and the underlying inflammatory response. Although it is possible to remove AVG thrombus up to 30 days, early thrombectomy has been associated with better long-term results.[445] Sadaghianloo et al[446] reported that thrombectomy within <6 hours was associated with a better technical outcome and improved midterm results. Practically, early thrombectomy helps minimize and/or eliminate the need for dialysis with a CVC. However, patients may still require a CVC for dialysis to manage volume overload or electrolyte abnormalities prior to AV access thrombectomy.

Although the reported technical success rates for AV access thrombectomy, both endovascular and surgical, have been good, the longer-term patency rates have been poor, underscoring the critical importance of considering the next AV access option (ie, AV access succession plan) even before each thrombotic event.[438,447,448] Simoni et al[449] reported from a large device registry that the technical success rate of the AngioJet (Boston Scientific, Marlborough, MA) percutaneous thrombectomy device was 92%, although the patency rate for AVGs and AVFs was 53% and 86%, respectively, at 3 months. Similarly, Quencer and Friedman[438] reviewed that the patency rates after thrombectomy ranged from 25% to 50% at 6 months and 10% to 20% at 12 months for both AVGs and AVFs. Accordingly, repeated thrombectomy of the same AV access is likely not justified.

Definitive treatment requires identifying and correcting the underlying cause of the AV access thrombosis. Completion imaging should be done after either endovascular or surgical thrombectomy to confirm that the culprit lesion is corrected.

AV accesses thrombosis within the early postoperative period (<30 days) is often due to technical issues (eg, anastomotic stenosis) or the choice of an inadequate artery/vein combination (eg, diminutive vein) for an AVF. AV access thrombectomy and/or revision is/are possible if there is an identified technical defect, although definitive treatment usually requires constructing a new AV access. Chemical thrombolysis is a relative contraindication in the early postoperative period due to the associated bleeding risk.

Implementation Considerations

All of the HD vascular access types and configurations have a limited life expectancy and, accordingly, will ultimately fail or start to fail (ie, failing access). It is incumbent on the various health care providers who care for dialysis patients to recognize these dysfunctional accesses and be familiar with the various failure modes (AV access complications). Rosenberg et al[450] reported that it is possible to teach nonmedical professionals the requisite physical examination skills to recognize failing AV access in a short duration of time. Furthermore, it is important to engage the patients themselves and challenge them to assume responsibility for the care and maintenance of their vascular access. The ultimate goal is to maintain safe, effective dialysis with the fewest number of interventions in a patient-centric, cost-effective manner. Any intervention should consider the impact on current and future accesses; for example, viable/useful cannulation segments should be avoided when using stent grafts. It is the hope that early recognition and definitive treatment of the failing and thrombosed vascular access will result in improved vascular access functional survival.

Monitoring and Evaluation

The identification of failing and thrombosed AV access should be part of the routine monitoring protocols (Guideline Statement 11.1 and Guideline 13). It is important for the various health care providers to be cognizant of the various failure modes such that they can initiate the appropriate referral and/or remedial treatment, as part of the vascular access contingency plan. At that time, consideration and planning for the next dialysis access or kidney replacement modality (as appropriate) should begin in accordance with the individual patient's ESKD Life-Plan strategy.

Future Research

- Define and validate the optimal monitoring strategies for the dysfunctional AV access
- Define and validate the thresholds for intervention for the dysfunctional AV access
- Define the optimal open and endovascular treatment(s) for the dysfunctional and thrombosed AV access
- Define outcome metrics for the dysfunctional and thrombosed AV access
- Determine outcomes with surgically corrected occluded AV accesses that are followed by a completion angiogram/imaging ± further corrective procedure(s). How does this strategy compare with historical surgical correction without completion imaging or with endovascular management?

Guideline 16. AV Access Infection

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: AV Access Infections

Monitoring and Prevention

16.1 **KDOQI considers it reasonable to educate the patient on washing the access arm using antiseptic to clean the skin prior to every cannulation. (Expert Opinion)**

16.2 **KDOQI considers it reasonable to check the vascular access and surrounding area prior to every cannulation for signs and symptoms of infection. (Expert Opinion)**

Note: This check should be done by patient and cannulator (if patient does not self-cannulate).

See special considerations from Guideline Statements 11.2, 11.3, and 11.7 that are relevant to this section.

Diagnosis

16.3 **KDOQI considers it reasonable to use radiologic imaging to help confirm the diagnosis of AV access infection; however, physical examination remains the hallmark for assessing for infection. (Expert Opinion)**

Note: Radiologic imaging includes duplex ultrasound, ± CT scan, PET, and nuclear medicine scans (eg, indium scan).

Note: Signs of infection include erythema, skin breakdown, purulent discharge, and presence of exposed graft.

16.4 **KDOQI considers it reasonable to investigate and closely monitor for metastatic complications (eg, endocarditis, spinal abscesses, septic arthritis) in patients with buttonhole infection from particularly dangerous organisms such as *S aureus*, Gram-negative bacteria, and fungal organisms. (Expert Opinion)**

Note: Investigations include 2D echocardiography, MRI, joint aspirate, and other, as appropriate.

Treatment

16.5 **KDOQI considers it reasonable to obtain cultures and sensitivities of the blood and any available infected AV access vessel/material, surrounding tissue, or drainage prior to initiating antibiotic therapy. (Expert Opinion)**

16.6 **KDOQI considers it reasonable for infected AV access the rapid initiation of empiric broad-spectrum antibiotics and timely referral to a surgeon knowledgeable in the management of vascular access complications. (Expert Opinion)**

16.7 **KDOQI considers it reasonable to have strict follow-up of culture results with the appropriate change in antibiotics based on organism sensitivities, with antibiotic duration according to extent of vascular access infection and surgical intervention. (Expert Opinion)**

16.8 **KDOQI considers it reasonable that the specific surgical treatment for AV access infections (with concurrent antibiotics) should be based on the patient's individual circumstances considering the extent of infection, offending organism, and future vascular access options. (Expert Opinion)**

Rationale/Background

Both AVFs and AVGs (collectively referred to as *AV access*) can become infected. The underlying mechanisms are somewhat different, but the management principles including systemic antibiotics and source control are similar and grounded on standard principles of managing infected vascular prostheses. The incidence of AV access infections is relatively low, particularly for AVFs. However, the spectrum of potential sequelae of AV access infections are broad and range from mild limited cellulitis to extensive graft involvement mandating total explant; the systemic consequences can range from localized pain and fever to overwhelming sepsis and death. Treatment requires early recognition and management to prevent sequelae. The definitive treatment of AV access infections should be chosen within the context of the patient's ESKD Life-Plan dialysis access needs, with consideration for preserving/maintaining future vascular access options. Prevention and monitoring for ongoing or recurrent infection are critical. The current recommendations are consistent with the recommendations from the previous KDOQI Guidelines.

Detailed Justification

AVF and AVG infections are a major clinical problem, often leading to hospitalization and increased mortality.[396,451,452] AVG infections have been reported to occur in up to 1.6% to 35% of patients, with an overall incidence of positive blood cultures of 0.31/1,000 days.[453,454] The incidence of AVF infections is typically, but not always, lower,[455] and this may be modified by different cannulation techniques, with buttonhole cannulation putting AVF at greater risk of infection.[303,312,456] AVGs that have been

abandoned in the past are also sources for infection. AVFs have a median infectious complication rate of 0.11/1,000 days[457] and positive blood culture rate of 0.08/1,000 days.[458]

The underlying mechanisms responsible for the development of AV access infections are likely multifactorial and include both patient and system-related issues (Supplement 4). Skin organisms *S aureus* and *Staphylococcus epidermidis* account for 70% to 90% of AV access infections[459-461] in the upper extremity, with a higher incidence of Gram-negative organisms in lower-extremity AV accesses.[462] AV access infection may be polymicrobial, with a variety of causative organisms, including fungi.[264,460,463-466] Attaining blood and relevant AV access cultures (wound, soft tissue, tunnel, or drainage) *before* initiating antibiotics is critical.

Patients with AV access infections require timely detection, diagnosis, and treatment to prevent poor outcomes. Presenting signs and symptoms range from mild cellulitis around the cannulation site to bacteremia and overwhelming sepsis.

The physical examination and routine laboratory studies are usually sufficient to establish the diagnosis. However, additional imaging can help corroborate the diagnosis and define the extent of AV access involvement. In particular, Duplex ultrasound can be used to confirm patency, interrogate the integrity of the AV access wall, confirm the presence of any aneurysms/pseudoaneurysms, document the presence of fluid around the vein/nonautogenous access, and help determine the extent of the infection[264,467] Ultrasound cannot differentiate the type of fluid around the AV access (ie, hematoma vs seroma vs abscess), which requires clinical corroboration. Other imaging studies can be used, including CT, PET, indium scans, and technetium scans, although they are rarely necessary and not as universally available.[264,454,467,468] PET and nuclear medicine scans may help exclude an occult infection in a thrombosed, nonfunctional AVG.

General Treatment

Blood cultures should always be obtained when an AV access infection is suspected. Cultures of the infected skin, soft tissue, AV access site, or tunnel (eg, obvious abscess or purulent drainage) may help confirm causative organism and infection source. Cultures should also be obtained at the time of any surgical intervention or AV access excision. Antibiotic therapy should be altered accordingly to culture sensitivity results. Most antibiotic regimens can be administered with dialysis, avoiding longer-term intravenous AV access. Consultation with infectious diseases experts to find the most convenient and appropriate antibiotic regimen per culture results may be helpful. PICCs should be avoided in CKD and ESKD patients as highlighted throughout the guidelines (Guideline 6).

Treatment of AV access infections includes immediate initiation of broad-spectrum antibiotics (after attaining relevant cultures) for both Gram-positive and Gram-negative organism coverage (eg, vancomycin, piperacillin/tazobactam) and control of the infectious nidus (ie, source control). Ideally, the infected AV access should be avoided for dialysis, although it is possible if the infection is minimal. Otherwise, a CVC should be inserted and used until the AV access infection is resolved or if, not salvageable, until a new AV access can be established.

Specific Medical Management

Antibiotics alone may be adequate treatment for limited localized AV access infections (eg, buttonhole track infection in AVF). However, the optimal treatment should be patient individualized, and requires a multidisciplinary team approach with early involvement of an experienced AV access surgeon (Supplement 4 AV Access Infections). Notably, AVG infections can rarely be treated with antibiotics alone because once the prosthetic material becomes infected, it is almost impossible to clear the infection.

The optimal duration of antibiotic therapy depends on the patient's circumstances and extent of infection. For example, extensive AV access infections involving the artery and vein should likely undergo an extended course of parenteral antibiotics similar to the treatment of patients with endocarditis (eg, ≥6 weeks); input from infectious diseases experts is suggested for guidance in complex cases.

Specific Surgical Management

Definitive surgical treatment of AV access infection requires careful individualized consideration of the extent of the infection, the offending organism, the type of AV access (ie, AVF vs AVG), the location of the infection (ie, anastomotic vs nonanastomotic), the extent of the infection (ie, localized vs diffuse), the presence of systemic signs, the presence of bleeding, and, importantly, future dialysis access options. Both AVF and AVG infections can lead to erosion of the skin and life-threatening hemorrhage, underscoring the importance of a timely, definitive surgical treatment as needed. Surgical treatment options can be broadly categorized as strategies designed to salvage the AV access and those designed to excise the AV access (Supplement 4). AV access salvage options include those for in situ and extra-anatomic reconstruction (with the reference being the anatomic course of the infected AV access) for localized infections, where close follow-up and surveillance are mandatory, given the risk of recurrent infection and the potential for anastomotic disruption and significant bleeding. AV access excision options include strategies for both complete and subtotal AV access excision and are considered for infections involving the full length of the AVG (see Supplement 4 for surgical details).

Key Surgical Management Points to Remember

- Salvage of the AV access may be possible if the infection is localized; in an AVG infection, this may be possible

only if the adjacent segments are uninvolved and well incorporated.
- If the infected segment is limited, graft replacement through an uninfected field with excision of the involved segment, may be possible.
- Extensive AV access infections, especially AVG, require total graft excision with definitive treatment of the arterial and venous anastomosis.

Note: Potential options include vein patch angioplasty, vein bypass, and ligation, depending on extent of infection and circumstances.

Preventative strategies should always be used and include avoiding or limiting CVCs, optimizing the use of AVFs where appropriate, avoiding the creation of lower-extremity AV accesses whenever possible, use of autogenous or nonautogenous biologic grafts in patients at high risk for infection, use of the appropriate prophylactic perioperative antibiotics, strict sterile technique at the time of AV access creation, appropriate cannulation techniques (Guideline 11), and mandatory routine AV access monitoring with a low threshold for intervention with any evidence of infection.

Buttonhole cannulation has been associated with significantly higher risks of infection compared with rope-ladder cannulation technique and should be avoided whenever possible. Buttonhole infections are more likely to be Gram-positive and more virulent (eg, *S aureus*), often with serious metastatic consequences such as endocarditis, septic arthritis, or spinal abscesses. Should metastatic complications be detected, rapid treatment with consultation from infectious diseases experts is necessary to prevent serious or catastrophic outcomes.

Special Discussions

Although this information refers to all AV accesses, great attention must be paid to lower-extremity AV accesses due their higher complication rate, including infectious complications (more likely to involve Gram-negative organisms).[58,462,469,470]

Early post-AV access creation (<1 month) soft-tissue infections are commonly associated with the inherent surgical trauma from creation and/or any break in sterile technique. They can typically be treated with a course of systemic antibiotics but require long-term monitoring.

Although the current recommendations build on those from the previous KDOQI Guidelines, the ERT did not identify relevant publications for the treatment of AV access infections using their search criteria. The previous Guidelines defined outcome measures for lifetime use of AVF (<1%) and AVG (<10%); however, the current Guideline has not defined similar measures due to the lack of appropriate evidence, especially those using current measures (eg, rates/1,000 access days vs percent use).

Guideline 17. AV Access Aneurysms

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: AV Access Aneurysms

Recognition and Diagnosis

17.1 **KDOQI considers it reasonable to check AV access for aneurysms/pseudoaneurysms at each dialysis session by knowledgeable care providers, including but not limited to dialysis technicians, nurses, nephrologists, and vascular access coordinator. (Expert Opinion)**

17.2 **KDOQI considers it is reasonable to proactively educate patients on emergency procedures for aneurysm rupture and to obtain proactive surgical assessment when clinical findings suggest an AV access aneurysm/pseudoaneurysm to be at risk of complications. (Expert Opinion)**

Note: An aneurysm/pseudoaneurysm that is considered at risk of complications is one with evidence of associated symptoms or skin breakdown.

17.3 **KDOQI considers it is reasonable to obtain emergent surgical assessment and treatment for AV access aneurysm/pseudoaneurysm complications such as erosion or hemorrhage. (Expert Opinion)**

17.4 **KDOQI considers it reasonable to use duplex ultrasound to corroborate the physical examination suggesting an AV access aneurysm/pseudoaneurysm and to obtain information on the size, presence of stenosis/thrombus, and impact on the AV access (including flow rate [Qa] and status of the arterial inflow and the venous outflow). (Expert Opinion)**

Management

17.5 **KDOQI considers it reasonable that the presence of an aneurysm/pseudoaneurysm alone in the absence of symptoms (ie, asymptomatic) is not an indication for definitive treatment. (Expert Opinion)**

17.6 **KDOQI considers it reasonable to avoid cannulating the access segment(s) that involve the aneurysm/pseudoaneurysm if there are**

alternative sites. In the rare scenario where there are absolutely no suitable alternative cannulation sites, the sides (base) of the aneurysm/pseudoaneurysm should be cannulated (ie, avoid the top). (Expert Opinion)

17.7 **KDOQI considers it reasonable to obtain appropriate imaging of the arterial inflow and venous outflow to assess volume flow or stenotic problems that may need correction prior to or during definitive treatment of symptomatic aneurysm/pseudoaneurysm. (Expert Opinion)**

17.8 **KDOQI considers it reasonable that surgical management is the preferred treatment for patients with symptomatic, large, or rapidly expanding AV access aneurysm/pseudoaneurysm (see "Treatment–Definitive" below). (Expert Opinion)**

17.9 **KDOQI considers it reasonable that a definitive surgical treatment is usually required for anastomotic aneurysms/pseudoaneurysms. (Expert Opinion)**

Treatment–Definitive

17.10 **KDOQI considers it reasonable that open surgical treatment should be deemed the definitive treatment for AV access aneurysms/pseudoaneurysms with the specific approach determined based on local expertise. (Expert Opinion)**

Note: The approach may include a plan for staged repair of multiple aneurysms to avoid bridging CVCs in the perioperative period.

17.11 **KDOQI considers it reasonable to use covered intraluminal stents (stent-grafts) as an alternative to open surgical repair of AV access aneurysms/pseudoaneurysms only in the special circumstances such as patient contraindication to surgery or lack of surgical option, due to the associated risk of infection in this scenario. (Expert Opinion)**

17.12 **KDOQI considers it reasonable that, should a stent graft be used to treat AV access aneurysms/pseudoaneurysm, cannulation over the stent-graft segment be avoided when possible. (Expert Opinion)**

Note: The use of stent grafts to manage aneurysms/pseudoaneurysms is not an FDA-approved indication.

Prevention

17.13 **KDOQI considers it reasonable that appropriate cannulation techniques should be implemented to reduce the occurrence of AV access aneurysms/pseudoaneurysms (Guideline 11). (Expert Opinion)**

Rationale/Background

The hemodynamic changes resulting from AV access creation lead to vessel dilatation and AV access enlargement. These hemodynamic changes are likely exacerbated by the repeated cannulations and injury to the vein or graft material and, along with increased intraluminal pressures from any outflow stenosis, can cause pseudoaneurysms or aneurysms. The reported incidence has ranged from 5% to 60% in clinical series.[471,472] Al-Jaishi et al[457] reported an incidence of 0.04 per 1,000 patient days. The incidence and natural history of AV access aneurysms/pseudoaneurysms are somewhat undefined, partly because of their imprecise definitions. Aneurysms/pseudoaneurysms can lead to skin erosion with hemorrhage, AV access dysfunction, pain, and cannulation difficulties. All symptomatic AV access aneurysms/pseudoaneurysms with skin erosion/ulceration and hemorrhage that represent a risk for a true life-threatening surgical emergency merit immediate assessment and appropriate treatment. The size of an AVF aneurysm alone is not an indication for surgical treatment, although cannulation through the aneurysmal segment should be avoided. The optimal treatment approach is individualized to the patient's AV access and ESKD Life-Plan, within the constraints of local expertise. An endovascular approach using a covered intraluminal stent may be a helpful temporizing measure in urgent or emergent settings, although it is not recommended for more routine indications. The current recommendations are consistent with the previous KDOQI Guidelines.

Detailed Justification

After creation of an AVF, hemodynamic forces in both the artery and the vein are altered, leading to an increase in vessel diameter, blood flow, and blood volume throughout the circuit. These physiologic changes are integral to the maturation process of AVFs, although they can become problematic or pathologic if the outflow vein continues to dilate and becomes aneurysmal. The presence of an outflow stenosis leading to increased intraluminal pressure,[473] repeated cannulations, and genetic predisposition contributes to aneurysm formation. A true aneurysm is defined as a circumscribed dilation of all 3 layers of the vessel wall, whereas a pseudoaneurysm is essentially an extraluminal "blood flow through" defect (ie, hole) in the vessel or prosthetic AV access that is walled off or contained by the surrounding soft tissue (Fig 17.1). An aneurysm in the *arterial* circulation is defined as a vessel that is 1.5 times greater than the normal, expected blood vessel diameter (eg, normal

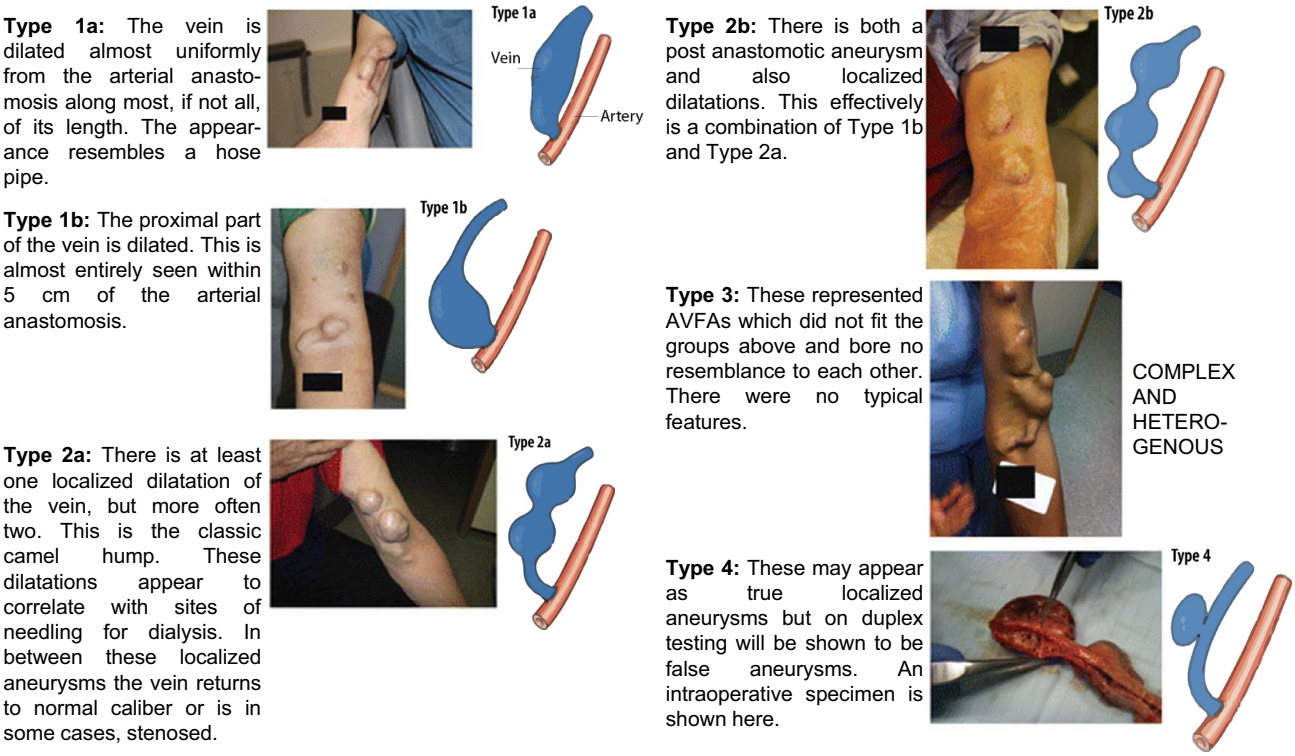

Figure 17.1. Valentini Classification according to shape of the AV aneurysm. Adapted from Valenti et al[666] with permission of SAGE Publications, Inc; original image © 2014 Valenti et al.

infrarenal aorta, 2 cm; aneurysmal aorta, 3 cm). The definition of an aneurysmal AVF is somewhat confusing because a mature AVF is essentially an "aneurysm" given the strict definitions for arterial aneurysms. Balaz and Bjorck[471] have attempted to clarify this issue and have defined an AVF aneurysm as an enlargement of all 3 vessel layers with a diameter of >18 mm or roughly 3 times the diameter of the outflow vein of a mature AVF. However, other classification systems exist.[474] Aneurysms can develop anywhere along the course of the AV access circuit, including the inflow artery,[475] but they typically occur in the outflow vein. Indeed, the distribution of the aneurysmal segments in the outflow vein has been used as part of a classification scheme.[474]

Pseudoaneurysms usually occur due to vessel wall defects from repeated cannulations in the same location and are noted intraoperatively as having Swiss cheese appearance. Although they develop in AVFs, they are more common in AVGs. Given the strict definition given, true aneurysms are unlikely to occur in the prosthetic segment of an AVG because it requires a dilation of all 3 vessel walls. Pseudoaneurysms can also develop at the site of anastomosis in the AVF or AVG, although the responsible mechanisms are somewhat different and include technical defects related to the procedure and infection.

The majority of AV access aneurysms/pseudoaneurysms are typically asymptomatic, but they can be associated with multiple complications and/or lead to AV access dysfunction. Most worrisome, the aneurysms/pseudoaneurysms can lead to thinning and subsequent erosion of the overlying skin and life-threatening hemorrhage. Jose et al[476] reported that the incidence of AV access–related fatal hemorrhage (all etiologies, not just related to aneurysm/pseudoaneurysm) was 1 for every 1,000 patient years and likely occurs every decade in a dialysis unit. Aneurysms/pseudoaneurysms often contain laminated thrombus that compromise AV access function, thereby limiting available cannulation sites.[471] Aneurysms/pseudoaneurysms can be associated with high-output congestive heart failure and pain, and they become cosmetically unacceptable to patients.

The diagnosis of an AV access aneurysm/pseudoaneurysm is made by physical examination and can be corroborated with Duplex ultrasound. Ultrasound can also detect peri-access fluid, intraluminal thrombus, and inflow/outflow stenoses and quantitate aneurysm/pseudoaneurysm diameter and intra-access flow rates. It is critical to determine if the aneurysm/pseudoaneurysm is symptomatic and/or at risk for ulceration and rupture. Therefore, it is important to have routine, objective measures of aneurysm/pseudoaneurysm growth and development, and with greater frequency if worrisome signs or symptoms develop (Table 17.1). Some signs and symptoms, such as AV access flow dysfunction, thrombosis, unacceptable cosmetic appearance, pain, and

Table 17.1. Physical Examination Findings That Are Clinically Relevant to Differentiate Between Aneurysm/Pseudoaneurysm That Do Not Require Urgent Intervention and Those of Urgent Concern

Physical Examination Findings	Nonurgent: Monitor Closely Aneurysm/Pseudoaneurysm	Urgent: Rapid Attention Aneurysm/ Pseudoaneurysm
Size	Not enlarging	Enlarging
Overlying skin	Can be pinched easily (supple, mobile skin)	Thin, shiny, depigmented
Skin erosion	None	Ulcers, scabs
Arm elevation sign	Collapses	May not collapse
Bleeding from puncture sites	Uncommon	Often prolonged

difficult cannulation, are either obvious or are addressed elsewhere in the Guidelines.

All symptomatic AV access aneurysms/pseudoaneurysms should be evaluated and managed. Patients with threatened skin or ulceration overlying their aneurysms/pseudoaneurysms should be treated urgently or emergently to prevent significant hemorrhage. Patients with aneurysm/pseudoaneurysm-related AV access flow dysfunction, thrombus, or limited cannulation sites require treatment to maintain AV access to provide effective dialysis. Patients with high-output congestive heart failure merit treatment to potentially reverse any contribution from the AV access. Patients with pain and/or unacceptable cosmetic disfigurement due to their aneurysm/pseudoaneurysm need an individualized treatment plan that considers the risks associated with potential loss of their AV access. However, aneurysm/pseudoaneurysm *size alone is likely not an indication* for treatment in the absence of symptoms or threatened skin.[471,472] AV access aneurysms/pseudoaneurysms do not usually spontaneously rupture like aneurysms in the arterial circulation. However, rapidly enlarging AV access aneurysms/pseudoaneurysms merit closer follow-up and a lower threshold for intervention. Large, asymptomatic AVG pseudoaneurysms may require careful monitoring and active treatment because they are essentially fed by a large opening in the prosthetic material that is walled off or contained by the surrounding tissue. Lazarides et al[477] have suggested that 12-mm AVG pseudoaneurysms be repaired because they exceed the typical 6-mm graft diameter 2-fold. All anastomotic aneurysms/pseudoaneurysms require evaluation and active consideration for repair because their etiology and natural history are likely different than those involving the outflow vein or length of the graft. Finally, all infected AV access aneurysms/pseudoaneurysms merit treatment (Guideline 16).

The treatment goals for patients with symptomatic access aneurysms/pseudoaneurysms should be to prevent acute complications by managing the precipitating cause (eg, high inflow or a venous outflow stenosis) and modifying the involved AV access segment(s), maintain AV access function, prevent further complications, and avoid CVC use. Unfortunately, the quality of the available evidence to guide treatment is limited, and there are no RCTs. Open, surgical repair remains the standard of care, and it is feasible to salvage the AV access in the majority of cases; patency rates after revision range from 52% to 100% at 1 year.[471,472,477-479]

The optimal approach and timing are dictated by the extent of the aneurysm/pseudoaneurysm (ie, focal versus diffuse), the quality of the involved tissue, and the presence of any infection. Alternative treatments include aneurysmorrhaphy and interposition grafting with the choices among the latter including both autogenous and prosthetic conduits tunneled in situ or extra-anatomically (ie, Wang and Wang[479]). In certain instances (eg, 2 involved segments), a staged approach may be used to allow continued access use and avoid a CVC. A variety of creative aneurysmorrhaphy techniques have been described involving diameter reduction over a catheter mandril,[480] endo staples,[481] and reinforcement with an external mesh wrap.[482] Aneurysmorhaphy may not be feasible if the vein wall comprising the involved segment is severely degenerated or calcified, and in situ interposition grafting with prosthetic material is contraindicated in an infected field. AV access ligation is an appropriate alternative to AV access salvage in certain situations but usually requires excision of the aneurysm/pseudoaneurysm due to the potential to develop thrombophlebitis and the cosmetic appearance of the thrombosed segment.[472] A full assessment of the arterial inflow and venous outflow of the AV access and correction of any contributory lesions is integral to the treatment algorithm given the high prevalence of associated lesions.[452,471] Any concurrent AV access dysfunction may be related to culprit high inflow or outflow stenosis rather than the associated aneurysm/pseudoaneurysm.

Intraluminal covered stents have been used to treat AV access aneurysms/pseudoaneurysms.[478,483,484] This endovascular approach is minimally invasive and may play a significant role as a *temporizing measure* for patients with active bleeding or ulceration without compromising future definitive treatment. The potential downsides to the use of an intraluminal stent include the potential size mismatch between the inflow/outflow sections, potential insertion in an infected field (eg, acute placement for ulceration/bleeding), potential loss of cannulation zone (secondary to stent as well as surrounding nonresorbable chronic thrombus with propensity for infection), and lack of incorporation within the aneurysm/pseudoaneurysm. Additionally, covered stents were not designed for

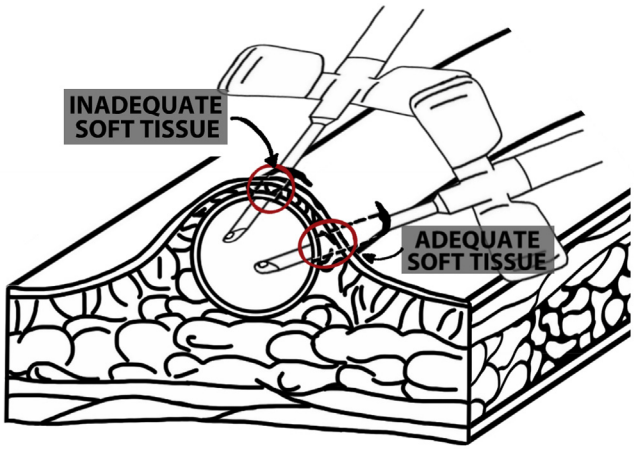

Figure 17.2. Creating a longer tract using the lateral approach. Reproduced from Wilson & Shenoy[667] with permission of SAGE Publications, Ltd; image © 2014 Wichtig Publishing.

repeated cannulation, and they are not approved by the US Food and Drug Administration for AV access salvage. Zink et al[484] reported a complication rate of 29% with the use of covered stents for salvaging AV access, including aneurysms/pseudoaneurysms, with the specific complications including migration, fracture, erosion, and rupture.

The optimal treatment for the majority of asymptomatic aneurysms/pseudoaneurysms is expectant management or no intervention. The involved segment of the AV access should not be used for cannulation, and the cannulation technique should be optimized, as outlined elsewhere in the Guidelines (Guideline 11). Indeed, optimal cannulation techniques are critical through the life cycle of the AV access to help prevent aneurysm/pseudoaneurysm formation. In the rare scenario that no alternative cannulation sites are available, the side of the aneurysms/pseudoaneurysm (base) that has adequate healthy skin and subcutaneous tissue should be used (Fig 17.2).[485] It is important to educate patients with aneurysms that are at risk of bleeding regarding specific emergency measures such as occluding the inflow of the access and elevation of the limb above the level of the heart to control bleeding and calling for help (911), should an aneurysm rupture.[486] There are no published recommendations for surveillance or serial imaging, although the AV access should be monitored by physical examination at each dialysis session per routine as detailed in the following sections.

The *definitive* treatment for anastomotic aneurysms/pseudoaneurysms is dictated by their etiology. Anastomotic disruption in the early postoperative period due to a technical reason (eg, suture fracture, inadequate suture bite) should be treated by revision of the anastomosis.

Those related to infection, typically AVGs, require removal of all infected material and then arterial repair or revascularization as outlined elsewhere in the Guidelines (Guideline 16).

Special Discussions

Skin erosion or active hemorrhage from an AV access aneurysm/pseudoaneurysm is a surgical emergency that requires early recognition and definitive treatment. The bleeding can usually be controlled by direct pressure on the site or often by occluding the AV access inflow at the anastomosis and temporized by a suture incorporating the surrounding soft tissue. Compression of the AV access outflow (ie, distal to the bleeding site) should be avoided because it increases the intraluminal access pressure and potentially increases the bleeding. Patients should be taken directly to the operating room for definitive repair without delay, even if the temporary measures are successful in controlling the hemorrhage.

AV access aneurysms/pseudoaneurysms can contribute to AV access thrombosis and their presence can complicate AV access thrombectomy. The treatment strategies for thrombosed AV accesses with aneurysms/pseudoaneurysm should consider the management of chronic intraluminal thrombus and management of the precipitating cause. The outcomes, particularly for thrombosed AVFs, are likely inferior to those that do not involve aneurysms/pseudoaneurysms. Cull et al[444] have described a useful technique that includes an incision over the arterial anastomosis to remove the arterial plug and then complete thrombus removal by manually "milking" the thrombus out of the lumen.

The preceding discussion is relevant for aneurysms/pseudoaneurysms that involve both AVFs and AVGs. However, it is worth re-emphasizing that aneurysms occur only in AVFs and that pseudoaneurysms are primarily a problem of AVGs that results from degeneration of the graft due to repeated cannulation in the same location. Accordingly, the treatment decisions need to factor in the natural history of the AV access type (ie, AVF vs AVG), the etiology of the underlying problem, and the overall ESKD Life-Plan. The treatment of AVG pseudoaneurysms typically requires an interposition prosthetic graft tunneled in situ or extra-anatomically with the choice partially dictated by the presence of any infection; aneurysmorrhaphy is not an appropriate treatment option.[477]

Implementation Considerations

The optimal treatment for patients with AV access aneurysms/pseudoaneurysms, particularly for patients with skin ulceration or bleeding, requires early recognition and definitive treatment. It is incumbent on all personnel who care for HD patients to recognize the ominous symptoms associated with AV access aneurysms/pseudoaneurysms and initiate the appropriate treatment algorithm. Indeed, AV access ulceration and hemorrhage should be viewed as a failure of care given the typical thrice-weekly dialysis sessions. Care should be provided within the context of a multidisciplinary team involving dialysis technicians, dialysis nurses, nephrologists, interventionalists, and

surgeons involved with vascular access, given the complexity of the treatment algorithm.

Monitoring and Evaluation

Assessment, Identification, and Documentation

All dialysis providers should be able to assess, recognize, and diagnose aneurysm/pseudoaneurysm formation in an AV access. The size of the aneurysm/pseudoaneurysm should be measured at minimum in 2 dimensions, preferably with ultrasound imaging (as described) and documented in the medical records at least every quarter along with the overlying skin changes. This frequency was established by consensus of the Work Group given that there are no published recommendations for surveillance or serial imaging, although the AV access should be examined at each dialysis session per routine (as described). Close monitoring of an enlarging aneurysm/pseudoaneurysm or those that show signs or symptoms of concern (Table 17.1) with low threshold for surgical intervention (as described) should be the guiding principle.

Patients should also be instructed on the appropriate assessment and monitoring of their AV access and provided instructions for emergency care and appropriate contacts for definitive treatment.

Future Research

- Validate the definition and classification schemes for access aneurysms/pseudoaneurysms.
- Define natural history of AV ccess aneurysms/pseudoaneurysms.
- Define the optimal treatment strategy for access aneurysms/pseudoaneurysms.

Guideline 18. AV Access Steal

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: AV Access Steal

18.1 **KDOQI considers it reasonable that strategies to both prevent and treat AV access steal should be developed and implemented before AV access creation, to reduce the risk of AV access steal and related morbidity, respectively. (Expert Opinion)**

18.2 **KDOQI considers it reasonable that post AV access creation, patients should be monitored closely for signs and symptoms associated with AV access steal and managed appropriately with consideration of individual circumstances as follows: (Expert Opinion)**

- **Mild to moderate signs and symptoms require close monitoring for progression of ischemia and worsening of signs and symptoms.**
- **Moderate to severe signs and symptoms often require urgent treatment to correct the hemodynamic changes and prevent any longer-term disability.**

18.3 **KDOQI considers it reasonable that patients with signs and symptoms consistent with AV access steal should be referred urgently to a surgeon/interventionist familiar with the diagnosis and options for the definitive treatment of AV access complications, particularly AV access steal. (Expert Opinion)**

18.4 **KDOQI considers it reasonable that the optimal treatment of AV access steal should be determined based on the patient's clinical presentation, local expertise, and resources. (Expert Opinion)**

Rationale/Background

The construction of an AV access can compromise the perfusion of the extremity distal to the anastomosis, resulting in symptoms consistent with acute or chronic ischemia, commonly referred to as *steal syndrome*. This occurs most commonly after brachial artery–based AV accesses, although it can occur after radial artery–based or lower-extremity accesses. It may occur shortly after AV access creation or several years later, with an increase in intra-access flow or with development of arterial disease of the inflow and outflow vessels. It is important to consider strategies to reduce the incidence of steal syndrome (Table 18.1).

The clinical symptoms of steal syndrome can range from mild numbness to severe motor compromise, and from skin ulceration to gangrene that necessitates major amputation. Several preoperative clinical predictors can identify patients at high risk of steal syndrome (Table 18.2) who may benefit from mitigation strategies. It is important to be familiar with clinical signs and symptoms (Table 18.3) because the diagnosis is largely a clinical one, although findings can be corroborated with noninvasive testing to confirm the hemodynamic changes. The natural history of steal syndrome is poorly defined, but moderate to severe symptoms rarely resolve without definitive treatment. Treatment options (Table 18.4),

Table 18.1. Strategies to Reduce the Incidence of AV Access Steal

Assessment of arterial inflow imaging with correction of inflow stenoses
Correct inflow stenosis or use contralateral extremity
Avoid distal brachial artery–based procedures
Avoid large conduits

Abbreviation: AV, arteriovenous.

Table 18.2. Clinical Predictors of AV Access Steal

Advanced age
Female sex
Diabetes mellitus
Peripheral vascular disease
Large outflow conduits
Multiple prior permanent access procedures
Distal brachial artery–based procedures (ie, near antecubital fossa)
Prior episode of AV access steal

Abbreviation: AV, arteriovenous.

aimed to correct the hemodynamic changes and potentially reverse the symptoms, should be viewed as complementary with the optimal choice based on the clinical scenario. Timely recognition and remediation are crucial to avoid long-term complications with the ideal goal being to reverse symptoms and salvage the AV access. The importance of early recognition of AV access steal and early referral to an appropriate surgeon (ie, knowledgeable in the management of AV access steal) were part of the previous KDOQI Guidelines.[13]

Special Discussions

As mentioned above, AV access steal occurs less frequently after radial artery–based AV accesses than after brachial-based procedures.[488,489] Given the dual blood supply to the hand through the radial and ulnar arteries, the resultant hemodynamic changes may differ. Notably, the AVF can serve as a pressure sink that can "steal" blood from the hand or, more specifically, retrograde flow through the AVF from ulnar artery and palmar arch can compromise digital perfusion. The available treatment options are dictated by the underlying causes of the hemodynamic changes but include correction of any inflow lesions, flow reduction, ligation (or embolization) of the distal radial artery to prevent retrograde perfusion, and AV access ligation.[488-491]

The creation of an AV access can result in severe sensorimotor dysfunction distal to the AV access in the setting of only mild to moderate ischemia, termed *ischemic monomelic neuropathy*.[492-494] Although this is likely within the spectrum of AV access steal, it is a distinct entity that has been attributed to the development of severe ischemic neuropathy despite adequate skin and muscle perfusion.

Table 18.3. Signs and Symptoms of Steal

Grade	Severity	Clinical Presentation	Treatment
0	None	None	None
1	Mild	Cool extremity with few symptoms	None
2	Moderate	Intermittent symptoms during dialysis, claudication	Intervention sometimes
3	Severe	Ischemic rest pain, tissue loss	Intervention mandatory

Note: Based on the Society for Vascular Surgery Reporting Standards for AV access steal.[487]

Table 18.4. Treatment Options for AV Access Steal

Ligation (if symptoms are severe, limb loss at risk, or no other option available)
Correction of arterial inflow stenosis
Flow limiting or banding
Proximalization of the arterial inflow
Revision using distal inflow
Distal revascularization and interval ligation

Abbreviation: AV, arteriovenous.

The published experience is somewhat limited, although the condition appears to be increased among patients with diabetes, peripheral vascular disease, and preexisting peripheral neuropathy. Optimal management includes immediate recognition and treatment, typically with AV access ligation and observation, although the sensorimotor symptoms may not be reversible in any approach.[495]

Implementation Considerations

The development of AV access steal symptoms is one of the most worrisome complications associated with AV access creation, given its potential to compromise hand function and potential for digital ischemia. Accordingly, providers constructing AV access should be familiar with and assume complete responsibility of every phase of its management, including preoperative predictors, diagnosis, strategies to reduce its incidence, and definitive treatment.

Monitoring and Evaluation

Given the potential for AV access steal to compromise hand function, all health care providers managing AV access should be familiar with its clinical presentation and appropriate initial management, including timely referral to a surgeon familiar with the various remedial treatments. Patients should be assessed for the signs and symptoms of AV access steal as part of routine AV access monitoring and counseled about the symptoms of steal and the need to share them with their health care providers.

Future Research

- Further define the pathophysiologic changes that lead to the development of steal.
- Further define and establish the predictors for AV access steal.
- Further define and establish strategies to reduce the incidence of AV access steal.
- Further define the natural history of mild to moderate symptoms related to AV access steal.
- Further define and validate the diagnostic criteria for AV access steal.
- Further define the optimal remedial treatments for AV access steal.
- Further define ischemic monomelic neuropathy as a distinct entity from AV access steal.

Guideline 19. Other AV Access Complications

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: Management of AVG Seroma

19.1 **KDOQI considers it reasonable to carefully monitor for complications of AVG seroma and manage based on the patient's individual circumstances and the clinician's best judgment and discretion. (Expert Opinion)**

Note: Operator's/clinician's discretion carefully considers both the patient's individual circumstances and the operator's/clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations).

Detailed Justification

Fluid collections or seromas can develop around prosthetic AVGs in the early postoperative period, frequently near the anastomoses.[496] They may resemble an aneurysms/pseudoaneurysms (Fig 19.1). The seromas are likely due to the transudation of fluid through the graft material itself or disruption of the surrounding lymphatic channels. Daria et al[497] reported the incidence to be 1.7% among 535 AVGs, with higher incidence among those with upper arm (vs forearm) AVGs. The presence of seroma/fluid around the AVG can be confirmed with an ultrasound. The majority of these early seromas are self-limited and tend to resolve without any consequence; however, they can serve as a nidus for infection given the protein-rich nature of the fluid. Seromas that persist or develop after the early postoperative period may necessitate AVG removal and replacement, preferably with a different material tunneled through a different anatomic course. Fortunately, the majority of the AVGs can be salvaged, and the longer-term results are reasonable.[497]

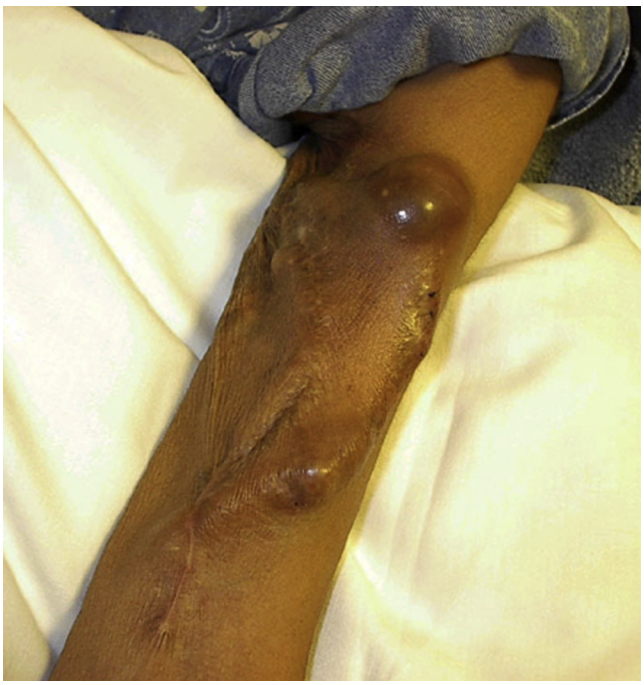

Figure 19.1. Seroma.

Statement: Management of High-Flow AV Access

19.2 **KDOQI considers it reasonable to closely monitor and prophylactically manage AV access with high flows to avoid serious or irreversible complications (eg, high output cardiac failure), based on the patient's individual circumstances and the clinician's best judgment and discretion. (Expert Opinion)**

Note: Operator's/clinician's discretion carefully considers both the patient's individual circumstances and the operatot's/clinician's own clinical experience and expertise (ie, reasonable capabilities and limitations).

Note: Close monitoring refers to physical exam and history on routine dialysis rounds and determination of Qa/CO every 6-12 months, or more frequently as needed.

Detailed Justification

High-Flow AV Access

Increased flow rates through an AV access can lead to a host of problems, including high-output congestive heart failure, pulmonary hypertension, central venous stenosis, venous hypertension, aneurysmal degeneration of the AVF, and AV access-related hand ischemia. The exact threshold to define high-flow access has not been rigorously validated or universally accepted, although an AV access flow rate (Qa) of 1 to 1.5 L/min or Qa of >20% of the cardiac output (Qa/CO) has been suggested.[498] AV access can exacerbate underlying symptoms of congestive heart failure (eg, shortness of breath and fatigue) and even lead to high-output failure, similar to traumatic AVF.[499] Basile et al[500] reported that Qa values of >2.0 L/min were associated with the occurrence of high-output cardiac failure, with a sensitivity of 89% and specificity of 100%, whereas a Qa/CO of ≥20% had a sensitivity of 100% and a specificity of 75%. Not surprisingly, symptoms of congestive heart failure may develop at lower thresholds in patients with underlying heart disease. The frequency of determination of Qa/CO is not established; the Work Group believed a 2-dimensional echocardiogram every 6 to 12 months to help evaluate for cardiac

decompensation and changes in Qa/CO, depending on the patient's circumstances and local resources, was reasonable. AV access flow rates can be reduced by using a variety of flow-reducing therapies or banding (Guideline 18).[501-504] Predictably, occlusion of the high-flow AV access results in a decrease in the cardiac output and improved oxygen delivery.[505]

Guideline 20. Treatment and Prevention of CVC Complications

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: Monitoring/Surveillance of CVC Complications

20.1 **KDOQI considers it reasonable to perform a basic medical history focused on signs and symptoms of CVC-related complications (eg, dysfunction, infection) and physical examination or check of the dialysis catheter, exit site, tunnel, and surrounding area at each catheter dressing change or dialysis session. (*Expert Opinion*)**

Rationale/Background

Although no studies have explicitly studied the value of history, physical examination, check, or inspection for CVC dysfunction, infection, and migration, they are fundamental tools for assessing the HD patient. For example, a history of signs or symptoms of bacteremia/septicemia in a patient with a CVC, should alert the clinician to further assess for the possibility of CVC-related infection. It is common for a patient to appear relatively well but then complain of symptoms of headache, nausea, dizziness, and chills and exhibit signs of vomiting, rigors, and fever 15 to 30 minutes after HD initiation when a CVC-related infection is present. These signs and symptoms may be related to endotoxin release from a CVC containing an infected biofilm, perturbed by the flow incurred by the initiation of dialysis.

Inspection of the CVC exit site may reveal cuff migration that places the CVC at risk of infection and also physical loss of the CVC. Exit-site infection is indicated by the presence of erythema, swelling, tenderness and purulent drainage around the CVC exit and the part of the tunnel external to the cuff. Signs of tunnel infection are swelling, erythema, fluctuance, and tenderness over the CVC tunnel central or proximal to the cuff.

Inspection of the patient on the side of the CVC may also indicate central venous stenosis/occlusion. Common findings are not limited to but include dilated subcutaneous veins and limb swelling.

Special Discussions

Special discussions from the Work Group included (1) the frequency required to evaluate the CVC for adequate prevention of CVC infection and dysfunction and (2) that prior 2006 KDOQI guideline recommend against exchange of CVC.

Implementation Considerations

The Work Group discussed implementation considerations, which included (1) standardizing the use of clinical questions to ask patients pertaining to CVC complications; (2) training and update of dialysis nurses/technicians to identify physical signs of infection, occlusion, stenosis; and (3) identifying key medical personnel to convey information and facilitate a subsequent action plan if an abnormality was identified.

Monitoring and Evaluation

More frequent monitoring and follow-up are required if an abnormality is suspected or found.

Future Research

- Cost benefit of prophylactic vascular access related history/physical examination or check
- Testing long-term durability of dialysis catheters

Guideline 21. Catheter Dysfunction

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Statement: Definition of CVC Dysfunction

21.1 **KDOQI considers it reasonable to assess for CVC dysfunction during each HD session using the following updated definition of CVC dysfunction: failure to maintain the prescribed extracorporeal blood flow required for adequate hemodialysis without lengthening the prescribed HD treatment. (*Expert Opinion*)**

Background/Rationale

Cuffed, tunneled, dual-lumen CVCs have become an acceptable form of HD vascular access when an AV access is not suitable or available, despite the associated high complication rates and mortality risk.[67,455] Maintenance of CVC patency is paramount to providing adequate HD in patients requiring CVCs on either a temporary or long-term basis. A common complication of the CVC is CVC dysfunction, which is associated with reduced dialysis adequacy, increased risk of CRBSI,[506] and mortality.

Although several studies have reported on CVC dysfunction, the rate of occurrence, the time from CVC insertion to dysfunction, and its effect on patients' quality of life, there is no consistency in the definitions used for CVC dysfunction.[506-508]

Detailed Justification

The new Guidelines definition of CVC dysfunction differs from the prior guidelines, which was most suitable for a conventional dialysis prescription of three times a week dialysis, for 3-4 hours per treatment. The updated definition can be applied to a range of dialysis prescriptions (eg conventional HD, incremental HD, short daily HD, nocturnal HD, etc). There are several factors that contribute to the delivery of adequate HD beyond blood flow, including but not limited to the duration, frequency and/or type of dialysis, type of CVC, ultrafiltration variables, degree of recirculation, and weight of the patient. In fact, blood flow may be misleading as an indicator of clearance if there is a significant presence of recirculation, particularly if the lines are reversed.[509] Past definitions of CVC dysfunction have included specific criteria pertaining to blood flow rates, venous and arterial pressure limits, dialysis adequacy based on urea kinetics, and other parameters. The 2006 KDOQI guideline defined CVC dysfunction as failure to maintain extracorporeal blood flow of >300 mL/min at a prepump arterial pressure more negative than -250 mm Hg or failure to attain and maintain an extracorporeal blood flow sufficient to perform HD without significantly lengthening the treatment time.[13] Although it is important to standardize outcomes within a guideline, this recommendation was opinion based and has been interpreted as the need to maintain blood flows >300 mL/min to ensure adequate HD. As a result of these blood flow recommendations, CVCs are often run in the reverse configuration, thrombolytic agents such as recombinant TPA are administered, or CVCs are exchanged when blood flow is consistently ≤300 mL/min. Previous comparisons of CVC mean blood flows of 250, 275, and 300 mL/min did not reliably predict inadequate HD. This was particularly relevant in patients with weights below 70 kg.[510] Furthermore, blood flows of <300 mL/min are often standard in patients receiving long-duration HD, such as nocturnal HD or frequent HD where HD adequacy is excellent.

Additionally, there is uncertainty around the frequency of abnormality, that is, the number of HD sessions to include before defining CVC dysfunction. Patients often experience a single poor HD run with inadequate clearance and then spontaneously resume good runs, providing adequate clearance, without an intervention. These intermittent decreases in clearance can be related to the position of the patient, transient blood pressure drop, interdialytic weight gain, higher levels of hemoglobin, transient partial thrombosis of the CVC that autolyze, and factors not fully understood. The consequences of such intermittent episodes of reduced clearance are unclear, likely due to its variations in frequency and etiologies.[511,512] However, the Dialysis Outcomes and Practice Patterns Study does report an association between number of inadequate HD sessions and increased risk of hospitalizations and mortality, but these data are confounded by HD inadequacy being attributed to shortened HD sessions.[513] It is unknown if a single session of HD with reduced adequacy, as measured by urea clearance but with maintained duration of HD, is associated with the same risk.

The rate of HD CVC dysfunction is variable depending on the specifics of the definitions. Using a combined set of 3,364 patients and 268,363 CVC-dependent HD sessions from Da Vita and the USRDS, CVC dysfunction, defined as a blood flow (Qb) <300 mL/min occurred in 7.1% of HD sessions, and almost two thirds of patients had ≥1 CVC dysfunction session; 30% had ≥1 CVC dysfunction session per month.[514] In an RCT of heparin versus t-PA, CVC dysfunction, defined as peak Qb of ≤200 mL/min for 30 minutes during a HD treatment, mean Qb of ≤250 mL/min during 2 consecutive HD treatments, or inability to initiate HD owing to inadequate Qb, occurred in 20.0% of patients in the TPA group and 34.8% in the heparin group. Others have reported rates varying between 0.5 to 3.0 events per 1,000 catheter-days.[515]

Implementation Considerations

The KDOQI Work Group offers this definition because it allows for intrapatient comparisons and respects differences in definitions of dialysis adequacy used by various studies, institutions, and jurisdictions. It allows for the flexibility required when considering various HD prescriptions according to type, duration, and frequencies of the dialysis regimen.

HD units may want to consider establishing local definitions of CVC dysfunction that incorporate their prescription goals to meet adequacy targets (thereby being consistent with KDOQI definitions) and documenting episode(s) of CVC dysfunction at a predetermined frequency or interval to allow for trending and appropriate intervention

Future Research

To accurately document the rate of CVC dysfunction for comparisons within institutions, across jurisdictions and treatment regimens, it is necessary to standardize the definition of CVC dysfunction. There is an urgent need for the nephrology community to re-evaluate the definition of CVC dysfunction with supporting validation studies, eg, what are the sensitivity, specificity, predictive value of various markers, and timing of intervention for CVC dysfunction? Is earlier intervention better?

Statements: Pharmacologic Prevention of CVC Dysfunction

CVC Connectors to Prevent CVC Dysfunction or Bacteremia

21.2 **KDOQI considers it reasonable to have an individualized approach to use special CVC connectors based on the clinician's discretion and best clinical judgment. (Expert Opinion)**

21.3 **KDOQI considers it reasonable to use an antimicrobial barrier cap to help reduce CRBSI in high-risk patients or facilities; the choice of connector should be based on clinician's discretion and best clinical judgment. (Expert Opinion)**

Intraluminal Agents to Prevent CVC Dysfunction

21.4 **KDOQI considers it reasonable that the choice to use citrate or heparin as a CVC locking solution be based on the clinician's discretion and best clinical judgment, as there is inadequate evidence to demonstrate a difference in CVC survival or complications between these locking solutions. (Expert Opinion)**

21.5 **KDOQI suggests the use of low-concentration citrate (<5%) CVC locking solution, if feasible, to help prevent CRBSI and CVC dysfunction. (Conditional Recommendation, Low Quality of Evidence)**

21.6 **KDOQI suggests that TPA may be prophylactically used as a CVC locking solution once per week to help reduce CVC dysfunction. (Conditional Recommendation, Low Quality of Evidence)**

21.7 **There is inadequate evidence for KDOQI to make a recommendation on the comparative use of the following CVC locking agents for CVC dysfunction or infection prophylaxis: tinzaparin versus unfractionated heparin, taurolidine/citrate versus heparin with or without gentamicin, neutral valve connector (Tego [ICU Medical]) versus citrate (46.7%) locking solution.**

Systemic Agents to Prevent CVC Dysfunction

21.8 **KDOQI recommends against the routine use of prophylactic systemic anticoagulants (eg, warfarin) for the sole purpose of maintaining or improving CVC patency, as there is inadequate evidence of benefit for CVC patency but suggestion of increased risk of harm (Conditional/Strong Recommendation, Low Quality of Evidence).**

21.9 **KDOQI suggests that low-dose aspirin may be used to maintain tunneled CVC patency in patients with low bleeding risk (Conditional Recommendation, Low Quality of Evidence).**

Note: CVC refers to tunnelled hemodialysis CVCs unless otherwise specified.

Rationale/Background

Among incident HD patients in North America, 80% continue to start with a CVC,[516] despite the well-known complications of central vein stenosis,[517] increased risk of subsequent AVF failure,[94,515] and associated likelihood of persistent use of the CVC beyond 90 days.[516,518,519] CVC dysfunction is a common problem and often requires medical or surgical intervention.[520] Use of thrombolytic agents and/or CVC exchange occurs in 20% to 40% of patients dialyzing with CVCs.[506] Both of the latter interventions are associated with high costs.[521] In many cases, CVC dysfunction (previously defined by 2006 KDOQI guideline[13] as "failure to attain and maintain an extracorporeal blood flow of 300 mL/min or greater at a prepump arterial pressure more negative than -250 mm Hg") persists. Besides increases in arterial and venous pressures registered by the dialyzer that necessitate a decrease in blood flow, CVC dysfunction can result in significant recirculation, leading to poor clearance and lower Kt/V. Left untreated, such CVCs require premature removal when they become nonfunctional[522] (ie, with 1 or both lumens that cannot be aspirated).

The onset of CVC dysfunction can occur early or late after insertion, which may help in determining the etiology of the problem and guide subsequent management. Dysfunction noted immediately after the CVC placement is likely due to the positioning of the CVC, preexisting vascular abnormalities (eg, central venous stenosis) or mechanical damage to the CVC (eg, tight suture or perforation). Dysfunction developing after successful initial use is usually due to intraluminal or pericatheter thrombosis, fibrin sheath formation around the CVC, mural thrombus adhering to the CVC tip, or new central venous stenosis.

The following section discusses studies evaluating prophylactic strategies for CVC dysfunction.

Detailed Justification

Connector Maneuvers to Prevent CVC Dysfunction

A closed-system connector has theoretical benefits of limiting environmental contact with microorganisms, reducing biofilm formation and consequent CVC dysfunction and infection. It is left in place during HD sessions and changed every week. An RCT (n = 66) compared a closed-system connector, flushed with saline and attached to the CVC hubs, to 46.7% trisodium citrate lock to evaluate a

composite study endpoint of CVC dysfunction (requiring fibrinolytic therapy or mean Qb ≤250 mL/min during 2 consecutive dialysis sessions) and CVC-related bacteremia.[523] There was no difference in the composite outcome (48% [connector] vs 55% [trisodium citrate]; RR, 0.72; 95% CI, 0.37-1.42]). The 2 groups also did not differ on the individual components of the composite outcome—dysfunction or bacteremia. The need for urokinase to treat thrombotic dysfunction did not differ (14 participants from the connector group and 9 from the trisodium citrate group; P = 0.20). CVC survival rates (free of dysfunction or bacteremia) at 1 year were 0.43 in the connector group and 0.37 in the trisodium citrate group. The study did not report harms. Therefore, given these neutral results, KDOQI suggests that the use of the neutral valve connector be at the discretion of the clinician.

Due to literature search timeline criterion, the ClearGuard studies and data were not retrieved or reviewed by the ERT[524,525]; however, the KDOQI Work Group believed it was important to include in this document. The most recent study by Brunelli et al was a large, 13-month, cluster-randomized, comparative-effective study that evaluated ClearGuard HD barrier cap (single-piece device that applies antimicrobial inside and outside the hub) versus Tego plus Curos (2-piece device that applies antimicrobial to the outside of the Tego cap only). The study outcome was positive blood culture rate as an indicator of bloodstream infection rate. A total of 40 dialysis facilities were enrolled (20 facilities in each group). After a 3-month run-in phase, 1,671 patients (826 control group, 845 Tego plus Curos) qualified for the 13-month intervention phase. The ClearGuard group had 23 positive blood cultures compared with 75 in the Tego plus Curos group (83,064 vs 100,042 CVC days, 0.28 vs 0.75 per 1,000 CVC days, respectively). The incidence rate ratio for CRBSI analysis and access-related blood stream analysis favored the ClearGuard group (0.37; P = 0.003 and 0.32; P < 0.001, respectively).[525] Guideline Statements 21.2 and 21.3 may be relevant to consider in the context of this study until a formal ERT review and analysis for the next Guideline update.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S179-S182.

Intraluminal Agents to Prevent CVC Dysfunction

Anticoagulant Lock to Prevent CVC Dysfunction.

Citrate Versus Heparin. Three European RCTs compared citrate to heparin CVC lock (total N = 542).[526-528] Follow-up was 6 months in 2 studies; 1 study reported results in CVC days.[528] Interventions varied across the studies. One compared a 5% citrate lock to a 5,000 U/mL heparin lock[527] (standard concentrations). Two trials evaluated higher concentrations of citrate: 1 compared 30% citrate lock to a 5,000-U/mL heparin lock,[528] and 1 compared 46.7% citrate lock to a 5% heparin lock.[526] There were more episodes of nonocclusive clot per session in the 5% citrate group compared to the 5,000 U/mL heparin group (14% vs 7%, P < 0.0001).[527] All studies reported on the treatment required for CVC dysfunction. Overall, there was no statistically significant difference between groups (RR, 1.25; 95% CI, 0.53-1.96]). One high-concentration lock study and 1 standard-concentration lock study reported no significant difference between groups for needing treatment with urokinase.[527,528] One study reported no bleeding complications,[526] and 1 study reported significantly lower incidences of major bleeding episodes (3% vs 11%, P = 0.01) and lower persistent bleeding after insertion (4% vs 13%, P = 0.005) in the 30% citrate group compared with the heparin group.[526-528]

Doses of Citrate. There is inadequate evidence for KDOQI to make a recommendation on the use of high- versus low-concentration citrate as a locking solution for HD CVCs. This was not included in the summary of statements to avoid confusion.

One European crossover RCT compared 10% citrate to 5% citrate (n = 28)[556] in tunneled, single-lumen CVCs. Each treatment arm was followed for 3 months. Nonocclusive clot formation was noted in 9.5% of HD sessions with 10% citrate lock and 12.5% of HD sessions with 5% citrate lock (P = 0.04). Urokinase for CVC dysfunction was required in 16 episodes during 10% citrate use and 14 episodes during 5% citrate use. The difference was not significant. There were no episodes requiring a urokinase infusion to restore catheter patency. There were no harms reported.

Doses of Heparin. One RCT[529] (n = 75) and 1 observational study[530] (retrospective review of prospectively collected data; n = 223) compared different heparin concentrations. The RCT compared 5,000 U/mL to 2,500 U/mL and reported outcomes to 24 hours.[529] The observational study compared 3 different heparin locks (5,000, 1,000, and 500 U/mL) after CVC insertion with follow-up to 30 days.[530] In the RCT, there were no episodes of thrombosis within 24 hours in either group.[529] The observational study found no significant differences between heparin concentrations in 2- or 30-day CVC-related infection-free survival, CVC related bleeding[530] or incidence of blood flow less than 250 mL/min.[530]

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S183-S193.

Thrombolytic Lock to Prevent CVC Dysfunction. Recombinant TPA has primarily been used in the treatment of CVC thrombosis. An RCT comparing TPA once per week (with 5,000 U/mL heparin lock after the other 2 HD sessions) to heparin lock 3 times per week, enrolled 225 participants with both incident (first ever) and prevalent CVCs.[531] For 61% of the participants, the CVC was their first dialysis CVC. Follow-up was 6 months, with extended follow-up for those who experienced the primary outcome of CVC dysfunction. The primary study outcome of CVC dysfunction was defined as the first occurrence of decreased blood flow (eg, peak Qb of ≤200 mL/min for 30 minutes during HD, mean Qb of ≤250

mL/min during 2 consecutive HD treatments, or inability to initiate HD due to inadequate blood flow) after protocolized attempts to re-establish patency. There was a significantly higher occurrence of CVC dysfunction in the heparin-only group (40/115; 35%) compared with the TPA group (22/110; 20%) (HR, 1.91; 95% CI, 1.13–3.22) Among CVCs that experienced dysfunction, the need for TPA for immediate management was significantly higher in the heparin group (50% vs 18%, P = 0.01). No significant differences were observed between the TPA and heparin-only groups for reversal of CVC lines for immediate management of CVC dysfunction (TPA, 3/22 [59%], heparin 14/40 [35%], P = 0.07) (or for any serious adverse event (21% [TPA], 30% [heparin]; P = 0.14) or any bleeding (P = 0.93). There is a paucity of rigorous studies comparing various methods of installation of thrombolytic agents (eg, dwell, infusion, push techniques) and their impact on CVC patency outcomes and complications.

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S179, S181, S194 through S207, and S237-S239.

Other Intraluminal Agents to Prevent CVC Dysfunction.

Taurolidine and Citrate Versus Heparin. RCTs (total N = 168) that compared a combined taurolidine and citrate lock (taurolidine/citrate) to heparin lock[532,533] and 1 RCT that compared taurolidine/citrate to a combined gentamicin and heparin lock (gentamicin/heparin) for prevention of CVC complications were identified.[534]

Of the 2 RCTs of taurolidine/citrate versus heparin lock, 1 trial was conducted in the United Kingdom (N = 110),[533] the other in the Netherlands (N = 58).[532] The UK study was of tunneled, cuffed CVC with follow-up of 8,129 and 9,642 CVC days in the taurolidine/citrate and heparin groups, respectively.[533] In the Dutch trial, the majority (76%) of the catheters were for temporary use and nontunneled CVC (NT-CVC)[532]; the median CVC use was 158 days for tunneled CVCs and 28 days for NT-CVCs in the jugular or subclavian vein and 7 days for NT-CVC inserted in the femoral vein.[532] In both trials, the intervention locks contained taurolidine 1.35% and citrate 4%, and the heparin lock control contained 5,000 U/mL.

In both trials, removal of CVC due to thrombosis/occlusion did not differ between treatment groups. In the study of all tunneled CVCs, the need for thrombolytic therapy at least once was twice as great in the taurolidine/citrate group compared with the heparin group: 53% versus 26% (HR, 2.5; 95% CI, 1.3-5.2).[533]

Solomon et al[533] conducted a nonrandomized, 3-arm study (N = 174) as an extension of the RCT conducted in the United Kingdom and compared taurolidine (1.35%), citrate (4%), and heparin (500 U/mL) (ie, TCH) locks versus taurolidine/citrate versus heparin (5,000 U/mL) locks. There was no significant difference for CVC survival between groups.[533] Need for thrombolysis was reduced with the TCH lock (n = 106) compared with the taurolidine/citrate lock (n = 34) (HR, 0.2; 95% CI, 0.06-0.5) but not the heparin 5,000 U/mL lock (n = 34) (HR, 1.4; 95% CI, 0.5-3.9).[535]

The UK trial involving tunneled CVCs reported that heparin-induced thrombocytopenia led to CVC removal in 1 participant in the taurolidine/citrate group and none in the heparin group.[533] The other study reported no adverse events associated with the use of taurolidine and citrate lock solution.[532]

Taurolidine and Citrate Versus Gentamicin and Heparin. There was one RCT (N = 119) evaluating combined taurolidine 1.35% and citrate 4% lock (taurolidine/citrate) versus combined gentamicin 40 mg/mL and heparin 5,000 U/mL lock (gentamicin/heparin).[534] Follow-up was 90 days.

There was no significant difference in the development of CVC thromboses: 9 (12%) in the citrate/taurolidine group versus 11 (15%) in the gentamicin/heparin group (P = 0.63).

Tinzaparin Versus Heparin. One crossover RCT from Canada (N = 42) compared tinzaparin lock to heparin lock.[536] Participants received each of the locks for 7 weeks. All had been using CVCs for more than 3 weeks at the time of enrollment. No significant differences between treatment arms were observed for CVC removal due to failure. Use of alteplase for CVC dysfunction was significantly lower in the tinzaparin group (3.2% vs 6.0% of HD sessions; P = 0.008).

Tables of studies, evidence quality, and risks of bias are provided in Supplement 3, Tables S185, S190, S193, and S208-S217.

Systemic Agents to Prevent CVC Dysfunction

Five studies of systemic anticoagulants for prevention of CVC complications were identified. Three RCTs and 1 observational study compared a systemic antiplatelet or anticoagulant agent to placebo or no intervention.[537-540] One of the RCTs evaluated an antiplatelet drug (aspirin),[539] and 1 RCT and the observational study evaluated an anticoagulant (warfarin).[538,540] One of the RCTs compared an antiplatelet (aspirin) and an anticoagulant (warfarin) to no intervention and to each other.[537] One additional RCT compared systemic anticoagulation after CVC placement to anticoagulant delayed until the first CVC thrombosis or dysfunction event.[541]

Aspirin. There are 2 RCTs (total N = 223) evaluating aspirin compared with either a placebo or no intervention (control group) in participants with CVC.[537,539] One trial was conducted in Iran (N = 185; follow-up 12 months),[539] the other in Saudi Arabia (N = 38; follow-up not indicated).[537] The Iranian trial

compared low-dose aspirin (80 mg/day) to placebo,[539] whereas the Saudi study compared low-dose aspirin (81 mg/day) to no intervention.[537]

Results were mixed for CVC survival outcomes after systemic antiplatelet therapy versus control. The Iranian study reported overall mean CVC survival time to be longer in the aspirin group compared with the placebo group, 5.3 versus 3.9 months (mean difference, 1.40; 95% CI, 0.28-2.52]).[539] The Saudi study reported 68% of the 19 CVC in the aspirin group to be dysfunction-free at 12 months compared with 37% of the 19 CVC in the no intervention group. The authors reported that the difference between groups was significant, but the ERT reanalyzed the results using a Fisher exact test and found no statistically significant difference.[537]

In the Saudi trial, there were fewer participants with at least 1 CVC dysfunction due to CVC thrombosis in the aspirin group than in the no intervention group (21% vs 47%), but when results were reanalyzed by the ERT using a Fisher exact test, the difference was not statistically significant.[537]

Adverse events did not differ between the aspirin and placebo groups in the Iranian trial.[539] The Saudi study reported that no participant in either group experienced a major bleeding event.[537]

Warfarin. Two RCTs (total N = 213) compared warfarin to placebo or no intervention.[537,540] One trial was conducted in Canada (N = 174).[540] The second trial represents the other intervention arm of the study from Saudi Arabia (n = 39) described in the preceding section.[537] The follow-up periods were 709 to 722 participant-months in the Canadian study and 12 months in the Saudi study.[537] Most of the participants received tunneled cuffed CVCs (24% received NT-CVC in the Canadian trial). A low dose of warfarin, adjusted to an INR of 1.4 to 1.9, was compared with placebo in the Canadian study.[540] The Saudi study compared a warfarin dose of 2 to 5 mg/day, targeting an INR of 1.5 to 2.0, to no intervention.[537]

Both studies reported CVC survival outcomes. The Canadian study reported that CVC removal for any reason did not differ between the warfarin and placebo groups (HR, 0.87; 95% CI, 0.42-1.81]).[540] The Saudi study reported that dysfunction-free CVC survival at 12 months was higher in the warfarin group (75%) compared with no intervention (37%) (reported as $P < 0.01$ in the publication and $P = 0.02$ using a Fisher exact test analyzed by ERT).[537] The Saudi trial also reported that 4 (20%) had at least 1 CVC dysfunction due to CVC thrombosis in the warfarin group versus 9 (47%) with no intervention, but the difference was not statistically significant based on the ERT's reanalysis with a Fisher exact test.[537] In the Canadian study, need for an intervention for CVC dysfunction did not differ between the warfarin and placebo groups, at 46% versus 47%, respectively (HR, 0.90; 95% CI, 0.57-1.38).[540]

The Canadian trial reported no difference in major bleeds between treatment groups[540]: 10 (12%) in the warfarin group and 7 (8%) in the heparin group (RR, 1.43; 95% CI, 0.57-3.58]). The Saudi study reported that no participant in either group experienced a major bleeding event.[537]

One observational study from 2 units in the United Kingdom (n = 112 participants with 194 femoral CVCs)[538] observed a total of 20,021 CVC days of use. Prophylactic systemic anticoagulation, typically warfarin with a target INR of 1.5 to 2.5, was compared with a no anticoagulation control group. The control group restricted anticoagulation to patients with CVC dysfunction requiring repeated treatment with urokinase locks.

CVC survival, assessed as CVC removal due to occlusion, did not differ, at 33% in the anticoagulation group and 27% in the control ($P = 0.49$).

There was no difference in the number of CVC-related thromboses between groups, 9% in the prophylactic group compared with 11% (adjusted HR, 0.66; 95% CI, 0.25-1.72). Major bleeding occurred in 5 (6%) of 80 CVCs in the prophylactic group and in 4 (4%) of 108 CVCs in the no anticoagulation group, with an adjusted HR of 1.65 (95% CI, 0.44-6.22). Corresponding rates were 0.7 and 0.4 per 1,000 CVC days.

Warfarin Versus Aspirin. There is inadequate evidence for KDOQI to make a recommendation or suggestion on the use of systemic warfarin versus aspirin for the prevention or treatment of CVC dysfunction. This was not included in the summary of statements to avoid confusion. The detailed justification is as follows.

The RCT from Saudi Arabia by Abdul-Rahman et al,[537] with warfarin and aspirin arms compared to no intervention (described in the preceding section), also provided data comparing warfarin to aspirin. The comparative effectiveness study compared a warfarin group (n = 20) that received a dose of 2 to 5 mg/day, targeting an INR of 1.5 to 2.0, with an aspirin group (n = 19) that received 81 mg/day. Patients were followed for 12 months.

There was no difference between groups for dysfunction-free CVC survival at 12 months: 75% (warfarin) versus 68% (aspirin) ($P = 0.65$) or for at least 1 CVC dysfunction due to CVC thrombosis: 20% (warfarin) versus 21% (aspirin). No participant in either group experienced a major bleeding event.

Warfarin Initiated After CVC Placement Versus Warfarin Initiated After First Thrombosis or CVC Dysfunction Event. One Italian RCT (total N = 144) evaluated warfarin initiated 12 hours after CVC placement (postplacement warfarin group) versus warfarin initiated

after the first thrombosis or dysfunction (postevent warfarin group).[541] In both groups, warfarin was adjusted to an INR of 1.8 to 2.5; follow-up was 12 months for these CVCs.

Fewer participants in the postplacement warfarin group experienced a thrombosis/dysfunction event, 10 (12%; 0.16 events per patient-year) versus 33 (52%; 1.65 events per patient-year) in the postevent warfarin group. Also, fewer participants in the postplacement warfarin group required a CVC replacement due to thrombosis compared with the postevent warfarin group (2% versus 17%, respectively; RR, 0.14; 95% CI 0.03-0.62). No participant in either group experienced a major bleeding event.

Tables of studies, evidence quality, and risks of bias for this section are provided in Supplement 3, Tables S218-S232.

Special Discussions

- Several of these solutions, such as citrate and taurolidine, are not widely available for use in the outpatient setting in the United States.
- The cost effectiveness of using prophylactic thrombolytic locking solutions has not been extensively evaluated.
- Regarding the uses of systemic anticoagulants, the lack of benefit and the potential risks of harm were deemed by the Work Group to be concerns, regardless of whether an INR is targeted (eg, in cases where warfarin is used; the benefits, risks and harms data for warfarin prophylaxis used in other vascular access types and other indications in HD patients were reviewed by the Work Group), especially given the known challenges of consistently achieving a target INR and remaining within the therapeutic range in HD patients.

Implementation Considerations

- Must consider whether each individual dialysis unit has the resources to implement changes in preventive locking solutions.
- The use of any intraluminal or extraluminal cleansing solutions, antiseptics, antibiotics, medicines, or anticoagulants should be compatible with the CVC material
- When the evidence extracted and analyzed by the ERT was inadequate to make a recommendation and there were no associated harms, the Work Group believed it important to support use based on the clinician's discretion and best clinical judgment. The Work Group did not want to place restrictions but instead want to encourage future research to provide the necessary evidence to assist with future clinical practice guidelines development on these topics.

Monitoring and Evaluation

Close monitoring of adverse events related to locking solutions such as citrate.

Future Research

- To prevent CVC dysfunction, better diagnostic tools are required to detect etiology of dysfunction. For example, further research can evaluate the role of 2-dimensional echocardiography to diagnose a catheter-related atrial thrombus.
- The relationship between size of the intraluminal or mural thrombus and symptoms
- Larger multicenter RCTs evaluating citrate and taurolidine
- The role of ethanol as a CVC-locking solution
- The role of nitroglycerin-based CVC lock solution
- The benefit of anticoagulant lock over normal saline for CVC patency has been raised and could be further researched, given the potential for increased risk of adverse events with anticoagulant locks[542-545]
- The cost effectiveness of various doses of prophylactic TPA in high-risk patients eg, 2 mg vs 1 mg installation)
- Rigorous studies comparing various methods of installation of thrombolytic agents (eg, dwell, infusion, push techniques) and their impact on CVC patency outcomes and complications

Guideline 22: Treatment and Management of CVC Dysfunction

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Medical Management of CVC Dysfunction

Conservative Maneuvers

22.1 **KDOQI considers it reasonable for a conservative bedside approach to managing CVC dysfunction prior to other medical or mechanical interventions. (Expert Opinion)**

Pharmacologic Maneuvers

22.2 **KDOQI recommends intraluminal administration of a thrombolytic agent in each CVC port to restore function of dysfunctional CVCs due to**

thrombosis. (*Conditional Recommendation, Moderate Quality of Evidence*)

22.3 **KDOQI recommends the use of alteplase or urokinase plus citrate 4% per limb for restoring intraluminal CVC blood flow in an occluded CVC. (*Conditional Recommendation, Moderate Quality of Evidence*)**

22.4 **KDOQI suggests intraluminal administration of alteplase 2 mg in preference to alteplase 1 mg in each CVC port to restore function of dysfunctional CVCs due to thrombosis. (*Conditional Recommendation, Moderate Quality of Evidence*)**

22.5 **KDOQI suggests administering alteplase by the dwell or push method to treat CVC dysfunction. (*Conditional Recommendation, Low Quality of Evidence*)**

Rationale/Background

Despite the well-known complications of CVC use,[94,515,517-519] CVCs are used in 80% of all incident HD patients.[516] CVC dysfunction is a common problem and often requires medical, endovascular, or surgical intervention[520] in 20% to 40% of patients dialyzing with a CVC.[506] This is inconvenient for patients and costly to the health care system.[521] In the 2006 KDOQI guideline,[13] CVC dysfunction was defined as "failure to attain and maintain an extracorporeal blood flow of 300 mL/min or greater at a prepump arterial pressure more negative than -250 mm Hg." Besides increases in arterial and venous pressures registered by the dialyzer that necessitate a decrease in blood flow, CVC dysfunction can result in significant recirculation, leading to poor clearance and lower Kt/V. Left untreated, such CVCs require premature removal when they become nonfunctional[522] (ie, with one or both lumens that cannot be aspirated, and dialysis cannot be delivered).

Interventions to prevent and treat CVC dysfunction can be categorized by the type of intervention as medical and mechanical interventions. Medical interventions are further subdivided into conservative maneuvers and pharmacologic interventions per se (eg, TPA use). Mechanical interventions are similarly subdivided into fibrin sheath disruption, catheter exchange, and CVC removal with replacement.

Conservative Maneuvers

Due to complex anatomy of the thoracic veins, CVC malposition is common[546] (Guideline 9). In the settings of superior vena cava (SVC) stenosis (itself common in HD patients) and venous aberrations that follow, such as dilatation of the azygous vein, the likelihood of incorrect CVC positioning is even higher.[547] Even if initially appropriately positioned, CVCs can migrate spontaneously, most commonly in the contralateral innominate vein generating an array of complications.[548,549]

CVC dysfunction in these cases is due to direct contact of the CVC tip or its side holes with the vessel wall, causing obstruction of blood flow. A CVC placed through the left internal jugular vein may induce thrombus formation even if its tip moves up into only the upper portion of the SVC[548,549] because of the 90° turn the CVC has to take from the left brachiocephalic vein into the SVC. If the CVC length is too short, its tip will be abutted against the right lateral wall of the SVC, irritating endothelium. If the CVC is found to be malpositioned within the first week of placement, it should be exchanged for one of proper size/length and properly situated. Older CVCs will likely have fibrous tissue formed around the cuff, necessitating subcutaneous dissection and subsequent exchange for a new CVC.

CVC occlusion, a common cause of poor blood flow, may also be caused by kinking or malpositioning. In these cases, CVC dysfunction generally emerges during the first HD session and can be resolved by repositioning if poor position is the culprit.

Use of Intraluminal Thrombolytic

The initial management of CVC dysfunction involves bedside maneuvers. Bedside management includes repositioning the patients (Trendelenburg position) or the use of rapid saline flushes to dislodge a possible thrombus.[550] Reversal of lumens may provide temporary respite and allow for completion of the HD treatment. If these initial bedside maneuvers are unsuccessful, and the CVC remains dysfunctional (ie, cannot be used to provide prescribed HD), consideration should be made for subsequent medical or mechanical intervention.

Persistent CVC dysfunction may be due to intraluminal or pericatheter thrombus or development of a fibrin sheath. Fibrin sheaths may start to develop at the time of CVC insertion, recruiting platelets and other coagulation factors and promoting leukocyte adherence.[551] Over a period of days to months, collagen is deposited near the tip from the venous vessel wall where the CVC is located. If clotting exceeds the endogenous fibrinolytic system's capacity, subsequent CVC thrombosis will ensue.[551] The 3 main types of CVC-related thrombi include intraluminal thrombus, CVC-tip thrombus, and fibrin sheath-thrombus, the most common type of thrombus. Management is directed at these types of thrombi.

The evidence supporting the use of thrombolytic agents for the medical management of CVC dysfunction follows.

One RCT (N = 106) compared intraluminal administration of the recombinant TPA alteplase (1 mg/mL) to urokinase (5,000 IU/mL) in completely occluded CVC[552]; both thrombolytics were allowed to dwell over

40 minutes. The mean duration since CVC insertion was 246 days, and 31% were femoral CVCs. Outcomes were assessed after 1 and 10 HD sessions after the initial alteplase and urokinase administrations. Treatment success, defined as Qb >200 mL/min after dwell, was not significantly different between the thrombolytic groups. Treatment success after 1 dose of alteplase was 95% versus 82% in the urokinase group (P = 0.06). After 10 HD sessions, CVC function was maintained in 93% of alteplase recipients and 86% of urokinase recipients (P = 0.23). CVC removal due to treatment failure occurred in 1 (3%) from the alteplase group compared with 7 (13%) in the urokinase group. No serious harms occurred.

A second RCT (n = 151) compared tenecteplase 2 mg with placebo (administered over a dwell time of 1 hour) in dysfunctional CVC, defined as a blood flow rate <300 mL/min.[553] Outcomes were assessed after 1 treatment session. Treatment success was defined as blood flow rate (Qb) ≥300 mL/min and an increase of 25 mL/min from baseline. Success was greater in the tenecteplase group compared with the placebo group (22% vs 5%). The absolute mean difference was 17% (95% CI, 6-27; P = 0.004). Rates of CRBSI were low and did not significantly differ between groups, at 1% and 4% in the tenecteplase and placebo groups, respectively. There were no significant harms in either group.

Dose of Intraluminal Thrombolytic

One observational study (N = 237) compared high-dose alteplase (2 mg) to low-dose alteplase (1 mg) for the treatment of CVC dysfunction.[554] The treatments were administered over a dwell time of 30 minutes. The time-to-event outcome was defined as the time interval between the first alteplase session until CVC removal due to occlusive thrombus. More CVCs were removed due to unresolved thrombus-related dysfunction in the low-dose group compared to the high-dose group: 19% versus 10%, respectively. After adjustment for potential confounding variables, the risk for CVC removal was much greater in the low-dose group compared with the high-dose group, with an adjusted HR of 2.75 (95% CI, 1.25,-6.04). Mean survival times were 955 days for the high-dose group and 782 days for the low-dose group (P = 0.019).

One RCT (n = 81) compared higher-dose urokinase (100,000 IU lock) with lower-dose urokinase (25,000 IU lock) in participants who experienced CVC thrombosis/dysfunction during a 3-year study period.[555] The treatments were administered over a dwell time of 1 hour. All participants received warfarin therapy to prevent CVC-related thrombosis. Nine study participants with functioning CVC died and were excluded from analysis. Higher-dose urokinase was more effective than lower-dose urokinase in restoring adequate blood flow. Over the 3-year period, 36 and 29 thrombotic events were reported for the higher and lower-dose urokinase groups, respectively. In the higher-dose group, adequate blood flow was returned in all 36 cases after initial treatment 14% (4/29) compared to the cases in the lower-dose group (P = 0.01). Adequate blood flow rate was restored in the remaining 25 cases in the lower-dose group with an additional administration of urokinase 75,000 IU. In the lower-dose group, 14 of the 29 patients (48%) required additional urokinase treatments for more than 2 HD sessions after initial urokinase administration, compared with 3 of 36 patients (8%) in the higher-dose group (P = 0.01). Two in the higher-dose group (5%) and 12 in the lower-dose group (38%) (P < 0.05) had CVC changed due to CVC dysfunction after repeated thrombolytic therapy failed.

Method of Thrombolytic Administration

There was 1 RCT (N = 83) that compared push and dwell protocols for alteplase (2 mg/mL) administration for occluded CVC (Qb, <200 mL/min).[558] The push protocol was completed in approximately 30 minutes. In the dwell protocol, the initial dwell time was 30 minutes. If the CVC was not functional after 30 minutes, alteplase was allowed to dwell for an additional 90 minutes. The majority of participants (71%) had a previous CVC. Nearly 70% of the study CVC had been previously treated with alteplase. Treatment success, defined as Qb ≥300 mL/min for a minimum of 30 minutes and a minimum of 100 mL/min increase in Qb as a result of treatment was not significantly different between the push and dwell groups. Treatment success was 82% (push) versus 65% (dwell) (P = 0.08). CVC survival, defined as time from thrombolytic administration to the next required CVC intervention, did not differ between the push and dwell groups. After censoring for reasons other than CVC interventions for dysfunction and infection, the mean duration before the next required intervention in the push group was 65.5 days versus 59.3 days in the dwell group (P = 0.77). No serious harms were reported

Tables of studies, evidence quality, and risks of bias for this section are provided in Supplement 3, Tables S194-S207.

Monitoring and Evaluation

Tracking frequency of dysfunctional and embedded CVCs.

Tracking frequency of use of thrombolytic agents to treat dysfunctional CVCs.

Future Research

The various methods of managing a CVC that is dysfunctional but also embedded.

Investigate alternate agents, doses, and methods to treat dysfunctional CVC.

Statements: Mechanical Management of CVC Dysfunction

22.6 **KDOQI considers it reasonable that the decision to perform fibrin sheath disruption during CVC exchange for CVC dysfunction be based on the operator's discretion and best clinical judgment. (Expert Opinion)**

22.7 **There is inadequate evidence for KDOQI to make a recommendation on the efficacy of or method of fibrin sheath disruption based on CVC patency outcomes.**

22.8 **KDOQI considers it reasonable that CVC removal followed by replacement at a different site should be the last resort after conservative, medical, and other mechanical (eg, angioplasty, CVC exchange) strategies have all failed to treat CVC dysfunction. (Expert Opinion)**

Detailed Justification

Mechanical Endovascular Fibrin Sheath Disruption

Fibrin sheath formation is a frequent cause of CVC dysfunction, particularly late CVC dysfunction. Recurring use of thrombolytics should in itself raise suspicion of the presence of fibrin sheath around the CVC[559]—a problem affecting 40% to 100% of CVCs.[560-562] Although thrombolytic therapy has been demonstrated to have a high immediate success rate of >80% (as discussed), 2-month patency can be quite low, at approximately 36%.[563] Subsequently, 4 other strategies for restoration of CVC patency have been evaluated. Those included CVC exchange, percutaneous fibrin sheath stripping, angioplasty disruption, and internal snare maneuver.

One RCT[560] (pilot study) and 1 observational study[564] address fibrin sheath disruption. In the RCT, patients with internal jugular CVCs with fibrin sheaths were randomized to CVC exchange over a guidewire (n = 12) or exchange over a guidewire with angioplasty sheath disruption (n = 18). A group of participants with no sheath was also studied (n = 14). There were 2 measures of patency: median time to repeat CVC dysfunction and median time to repeat CVC exchange.[560] The median times to repeat dysfunction were 373 days and 98 days in the sheath disruption and sheath/no disruption groups, respectively (P = 0.22), and 849 days in the no sheath group. The median times to repeat CVC exchange were 411 days and 198 days in the sheath disruption and sheath/no disruption groups, respectively (P = 0.17), and 879 days in the no sheath group. Blood flow and use of thrombolytic dwells were also reported.[560] Mean Qb < 300 mL/min was observed in 15% of those with sheath disruption compared with 22% without disruption and 7% with no fibrin sheath (no significant differences). There was greater use of thrombolytic dwells in the sheath/no disruption group (5.0%) than the sheath/disruption group (2.1%), but the difference was significant only compared with the no sheath group (1.8%).

An observational study, using a local institution procedural database, reviewed all tunneled dialysis CVC exchanged between January 2008 and December 2011 (n = 163).[564] On angiogram, if a fibrin sheath was present, it was disrupted by angioplasty; if no sheath was present, the CVC was exchanged over a guidewire. Patency was determined at 3-month intervals (to 12 months after replacement).[564] The 12-month patencies were 43% in the fibrin sheath disruption group and 52% in the no sheath group. There was no significant association between fibrin sheath disruption and CVC failure (adjusted HR, 1.34; 95% CI, 0.87-2.10]). Neither study reported harm outcomes, and there was no difference in bacteremia rates between groups.

Study details and evidence quality are provided in Supplement 3, Tables S233-S238.

CVC Salvage, Exchange, and Other CVC Strategies

CVC exchange over a guidewire can be performed safely and effectively to treat intrinsic CVC-related thrombosis.[565] However, there are sound reasons (non-RCT evidence) to obliterate the fibrin sheath, if detected, before performing the CVC exchange to prevent early CVC failure after exchange.[560,566] CVC patency is greater in the absence of fibrin sheaths than when CVCs are encased by fibrin sheath (as discussed). Furthermore, Valliant et al,[564] reported that CVC exchange with fibrin sheath disruption did not increase the risk of bacteremia and subsequent CVC dysfunction rates compared with simple over-the-wire exchange. Another retrospective observational study evaluated CVC exchange procedures comparing CVC exchange after creation of a new tunnel and exit site (using the original venotomy site for exchange) (revision group) versus exchange over a wire using the same exit and venotomy site (exchange only group).[567] In the revision group, fibrin sheath disruption was also part of the procedure. Patients with CVC exchange in the revision group had significantly fewer infections (likely due to nondisruption of the exit site and fibrin sheath disruption); repeat procedures were not evaluated.[567]

CVC exchange via a guidewire is also an effective method to treat and prolong CVC patency and preserve and save the exit site, particularly in patients with limited central venous access sites.[568] Guidewire exchange of CVCs has shown to be safe and easily performed with no increase in infectious complications, but at the same time providing similar CVC longevity to de novo CVC insertion.[568]

CVC Replacement

Central vein stenosis (CVS) remains one of the most common vascular access–related complications, with an occurrence rate of up to 40% in prevalent HD patients[517] (Guideline 26). CVC removal, therefore, without

protection of the stenotic vessel by placement of a wire across the stenosis, can lead to thrombosis of the central vessel in which the CVC was placed. In many patients with a long history of ESKD and vascular access problems, the internal jugular and femoral veins may become inaccessible, either due to stenosis or chronic total occlusion. These patients can exhaust all of their vascular access options if the clinician leaves stenotic vessels unprotected.

Guideline 23. Catheter-Related Infection

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statements: Definitions of Catheter-Related Infections

23.1 **KDOQI considers it reasonable to consistently use standardized definitions for CVC-related infections to allow for comparisons across programs/jurisdictions. (Expert Opinion)**

23.2 **KDOQI considers it reasonable to use the KDOQI VA-2019 definitions of CVC-related infections (Tables 23.1 and 23.2), which consider the unique circumstances of a hemodialysis patient. (Expert Opinion)**

Note: In order to harmonize definitions, the KDOQI VA-2019 definitions encompass those of other organizations.

Rationale/Background

Patients dialyzing with a CVC are at increased risks of catheter-related infection (CRI) and have increased morbidity, mortality, and health care costs.[34,67,179,569] Catheter-related infections alone have a reported incidence of 1.1 to 5.5 episodes per 1,000 CVC days.[171,570,571] The hospitalization and mortality rates for patients commencing HD with a CVC is high and has been attributed to the increase in bacteremia/sepsis observed in concert with an increased use of CVCs.[171,569] The financial and patient costs of hospital admissions, antibiotic use, and CVC changes associated with CRI have significant implications.

It is essential that accurate, consistent definitions of CRI be used to accurately report their occurrences to permit comparisons of rates of CRI that may influence practices across jurisdictions in HD patients using CVCs.

Detailed Justification

Several definitions for CRI are cited in the literature, but without consensus among the various associations.[13,297,319] Table 23.1 lists the definitions from the

Table 23.1. Definitions of CVC-Related Blood Stream Infections

KDOQI-2019	KDOQI-2006[13]	CDC[297]	IDSA[319]
Clinical manifestations and at least **1 positive BC** from a peripheral source (**dialysis circuit** or vein) **and** no other apparent source, **with** either positive semiquantitative (>15 CFU/catheter segment, hub or tip) or quantitative (>10^2 CFU/catheter segment, eg, hub or tip) culture, whereby the same organism (species and antibiogram) is isolated from the catheter segment (eg, hub or tip) and a peripheral source (dialysis circuit or vein) blood sample. If available, the following would be supportive: Simultaneous quantitative cultures of blood samples with a ratio of ≥3:1 (catheter hub/tip vs peripheral [dialysis circuit/vein]); differential period of catheter culture versus peripheral BC positivity of 2 hours.	**Definite:** Same organism from a semiquantitative culture of the catheter tip (>15 CFU/catheter segment) *and* from a BC in a symptomatic patient with no other apparent source of infection. **Probable:** Defervescence of symptoms after antibiotic therapy with or without removal of the catheter, in the setting in which BC confirms infection, but catheter tip does not (or catheter tip does, but blood does not) in a symptomatic patient with no other apparent source of infection. **Possible:** Defervescence of symptoms after antibiotic treatment or after removal of catheter in the absence of laboratory confirmation of BSI in a symptomatic patient with no other apparent source of infection.	Clinical manifestations and at least 1 positive BC from a peripheral vein and no other apparent source, with either positive semiquantitative (>15 CFU/catheter segment) or quantitative (>10^2 CFU/catheter segment) culture, whereby the same organism (species and antibiogram) is isolated from the catheter segment and a peripheral blood sample. Simultaneous quantitative cultures of blood samples with a ratio of ≥3:1 (catheter vs peripheral) Differential period of catheter culture versus peripheral BC positivity of 2 hours **OR** Isolation of the same organism from semiquantitative or quantitative culture segment and from blood (preferably from a peripheral vein) of a patient with accompanying symptoms of BSI and no other apparent source of infection.	Bacteremia/fungemia in a patient with an intravascular catheter with at least 1 positive BC and with clinical manifestations of infections (ie, fever, chills, and/or hypotension) and no apparent source for the BSI except the catheter **AND** One of the following should be present: A positive semiquantitative (>15 CFU/catheter segment) or quantitative (>10^2 CFU/catheter segment) culture whereby the same organism (species and antibiogram) is isolated from the catheter segment and peripheral blood. Simultaneous quantitative BC with a >5:1 ratio catheter versus peripheral. Differential time period of catheter culture versus peripheral BC positivity of >2 hours.

Abbreviations: BC, blood culture; BSI, bloodstream infection; CDC, Centers for Disease Control and Prevention; CFU, colony-forming unit; KDOQI, Kidney Disease Outcomes Quality Initiative; IDSA, Infectious Diseases Society of America.

2006 KDOQI guideline, the CDC, and the Infectious Diseases Society of America (IDSA). Of note, the 2009 IDSA guidelines acknowledged the hemodialysis CVC as a separate entity, as did the updated CDC guidelines.[297] In these aforementioned guidelines, the diagnosis of catheter-related bloodstream infections (CRBSI) is obtained through a set of peripheral blood cultures compared with blood cultures obtained from (1) the arterial or venous CVC hub meeting quantitative criteria (3-fold higher count of colony-forming units [CFUs]/mm in the CVC hub culture compared with the peripheral venous blood culture); (2) an arterial or venous CVC hub meeting criteria of differential time to positivity (DTTP), that is, the blood culture from the CVC hub turning positive at least 2 hours before the peripheral blood culture; or (3) the hemodialysis CVC tip growing the same microorganism as the peripheral venous culture. These mentioned guidelines define the peripheral venous culture as one taken from a peripheral vein.

However, the need for a peripheral culture from the peripheral vein was recently challenged in a study that determined the applicability of IDSA criteria for the diagnosis of CRBSI in patients on HD. It determined the diagnostic characteristics of an alternate "real world" approach to diagnosing CRBSI with blood cultures obtained from the dialysis circuit (another peripheral source) rather than the peripheral vein.[12] This study determined that blood culture results were most sensitive, specific, and accurate for the diagnosis of CRBSI, when taken from the HD circuit (the peripheral source) and the venous CVC hub and least sensitive, specific, and accurate when taken from any combination with peripheral vein blood cultures, making venipuncture unnecessary. This study does have some limitations, including a low CRBSI rate and the fact that it was conducted at a single center.

In the present era of accountability for CRBSIs, it is important to note that the current CDC or IDSA diagnostic criteria have not been validated in the unique circumstances of patients with a CVC undergoing HD. This issue is timely because there are several challenges that can influence the rate and accuracy of CRBSI reporting. These include peripheral vein blood cultures not obtained, either because patient veins cannot be accessed or an existing vein needs to be preserved for AV access; suboptimal handling of blood cultures in the outpatient dialysis unit (eg, variable time period before culture bottles are placed in an incubator, differences in temperature during transport to a microbiology laboratory), and use of antibiotic locks for CRBSI prevention, which may interfere with diagnosis. Furthermore, quantitative blood cultures are not routinely available in clinical practice (ie, limited to research settings), and the differential time to positivity criteria has been found to be met in less than one third of cases.

The 2019 NKF-KDOQI CRBSI definition (Table 23.1) is as follows: Clinical manifestations and at least 1 positive blood culture result from a peripheral source (dialysis circuit or vein) *and* no other apparent source, *with* either positive semiquantitative (>15 CFU/catheter segment, hub or tip) or quantitative ($>10^2$ CFU/catheter segment, eg, hub or tip) culture, whereby the same organism (species and antibiogram) is isolated from the catheter segment (eg, hub or tip) and a peripheral source (dialysis circuit or vein) blood sample.

If available, the following would be supportive: simultaneous quantitative cultures of blood samples with a ratio of ≥3:1 (catheter hub/tip vs peripheral [dialysis

Table 23.2. Definitions of CVC Exit Sites and Tunnel Infections

KDOQI 2019	KDOQI 2006[13]	CDC[297]	IDSA[319]
Exit Site Infection			
Hyperemia, induration, and/or tenderness ≤2 cm from catheter exit site. May be associated with drainage from the exit site. It may or may not be associated with bacteremia. If there is exit site drainage, it should be collected and sent for Gram staining, culture, and sensitivities.	Inflammation confined to the area surrounding the catheter exit site, not extending superiorly beyond the cuff if the catheter is tunneled, with exudate culture result confirmed to be positive.	Erythema or induration within 2 cm of the catheter exit site, in the absence of concomitant BSI and without concomitant purulence.	Hyperemia, induration, and/or tenderness ≤2 cm from catheter exit site. May be associated with fever and purulent drainage from the exit site. It may or may not be associated with bacteremia. If there is purulent drainage, it should be collected and sent for Gram staining and culture.
Tunnel Infection			
Tenderness, hyperemia, and/or induration that extends along the subcutaneous tunnel. It may or may not be associated with bacteremia. If there is drainage, it should be collected and sent for Gram staining, culture, and sensitivities.	The catheter tunnel superior to the cuff is inflamed, painful, and may have drainage through the exit site that is culture positive.	Tenderness, erythema, or site induration >2 cm from the catheter site along the subcutaneous tract of a tunneled catheter, in the absence of concomitant BSI.	Tenderness, hyperemia, and/or induration that extends >2 cm from the exit site and along the subcutaneous tunnel. It may or may not be associated with bacteremia. If there is purulent drainage, it should be collected and sent for Gram staining and culture.

Abbreviations: BSI, bloodstream infection; CDC, Centers for Disease Control and Prevention; KDOQI, Kidney Disease Outcomes Quality Initiative; IDSA, Infectious Diseases Society of America.

circuit/vein]) and differential period of catheter culture versus peripheral blood culture positivity of 2 hours.

The 2019 NKF-KDOQI CRBSI definition presented earlier represents a modification of the previous KDOQI and other societal guidelines based on the current evidence.

Table 23.2 provides the minimally revised 2019 NKF-KDOQI definitions for exit-site infection and tunnel infections in addition to the previous 2006 KDOQI guideline,[9] IDSA,[11] and CDC[10] definitions.

Special Discussions

The KDOQI Work Group discussed the importance of good CVC connections and its contributory role in CRBSI when not done properly. CVCs should be accessed and manipulated only by personnel trained and experienced in hemodialysis CVC care (Guideline 11).

Implementation Considerations

Standardized use of CRBSI definitions among dialysis providers to ensure consistent reporting and to allow comparisons between populations/units.

Future Research

- Validate criteria for diagnosis of CRBSI in HD patients
- Further validation studies of diagnostic criteria for exit site and tunnel infections in HD patients

Guideline 24: Prevention of CVC-Related Infection

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: General Prevention of CVC Infection and Use of Infection Surveillance Programs and Infection Control Teams

24.1 **KDOQI considers it reasonable for an infection control program to include an infection surveillance team to monitor, track (in an electronic database), help prevent, and evaluate outcomes of vascular access infections and, in particular, CVC-related infections. (Expert Opinion)**

Rationale/Background

The key to reducing infections in HD patients is incorporating an infection surveillance program. There are several studies documenting that an infection surveillance program can assist in identifying CVC-related infections and result in timely interventions to monitor and treat CVC-related infections and maintenance strategies to prevent CVC-related infections.[572-574] Successful surveillance programs require dedicated teams and resources (including use of an electronic infection tracking system) to monitor clinical outcome measures such as CVC-related infection rates, hospitalizations, and death.[572] Participation in the CDC's National Healthcare Safety Network for bloodstream infection surveillance is encouraged. Multidisciplinary teams have been shown to play an important role in implementing effective surveillance programs.[575] Having a dedicated vascular access nurse or coordinator to assist physicians and staff with management of CVC-related infections has been reported to reduce CVC treatment failure rates and death from sepsis.[177-179] However, probably the most effective strategy to reduce CVC-related infections is avoiding the use of CVCs. Previous studies have also reported that programs that have implemented a vascular access coordinator and vascular access protocols increase use of AVF as the initial vascular access at HD initiation and reduce total number of CVC days.[168]

Specific Prevention of CVC-Related Infection

Routine Monitoring per Guideline 20 is required for the prevention of CVC complications, including CVC-related infections.

Statement: Surveillance of CVC Colonization and Preemptive CRBSI Management

24.2 **There is inadequate evidence for KDOQI to support routine CVC surveillance cultures for colonization and subsequent pre-emptive antibiotic lock installation if culture is positive.**

Rationale/Background

Surveillance of CVC Colonization

CVCs routinely develop a biofilm on their inner surface, often within 24 hours of their insertion. Bacteria in biofilm are a primary source of CRBSI in HD patients with CVCs. It is likely that if the bacterial burden in the biofilm is high, this will result in positive surveillance cultures of the CVC lumen. One potential approach to preventing CRBSI in patients with CVCs is to perform periodic cultures of the CVC lumen immediately before a HD session. Hypothetically, if the culture results are positive, the patient could receive a course of intraluminal antimicrobial lock therapy to eradicate the bacteria in the biofilm.

Detailed Justification

This approach was evaluated in a single-center observational study of 104 patients with tunneled CVC at a hospital in Spain.[576] During a 1-year intervention period, patients underwent surveillance blood cultures from the

CVC lumen every 15 days. If the cultures grew coagulase-negative *Staphylococcus* species within 14 hours or if they grew another pathogen (*S aureus*, *Enterococcus* species, or Gram-negative bacteria) at any time, the patient received a 2-week course of an antibiotic lock at the end of each HD session. The primary outcome, CRBSI, occurred at a frequency of 0.27 episodes/1,000 CVC days during the intervention period versus 1.65 episodes/100 CVC days during the historical control period (no surveillance blood cultures). The authors concluded that this approach could triage patients at high risk of CRBSI, who might benefit from prophylactic antibiotic locks. The ERT graded the quality of this study as very low, with moderate risk of bias.

Special Discussions and Implementation Considerations

The KDOQI Work Group committee had several concerns about this approach, as follows:

- The quality of evidence was graded as "very low" by the ERT.
- This was not an RCT, and moderate bias was evident. The intervention group was compared to a historical control group rather than to a concurrent control group, raising the possibility that the reduction in CRBSI was due to more meticulous aseptic technique, rather than the surveillance and preemptive antibiotic lock.
- This is an extremely labor-intensive and expensive approach. Specifically, in the course of the study, 1,734 surveillance blood cultures were obtained, of which 94.2% had negative results, and 4.6% grew coagulase-negative *Staphylococcus* species in >14 hours. In other words, only 1.2% of cultures resulted in treatment with an antibiotic lock. It is unlikely that such an approach would be feasible in usual clinical practice. Clearly, an indiscriminate approach to CVC surveillance cultures for catheter-related infection is not feasible in normal practice. However, additional studies would be helpful to identify subgroups of patients who may benefit from frequent CVC surveillance cultures and preemptive management of CRBSI.
- It is important to highlight that CVC surveillance cultures are very different from surveillance for catheter-related infections (which the KDOQI Work Group refers to as *monitoring*, and strongly supports).

Future Research

- In addition to determining subgroups of patients who may benefit from CVC surveillance cultures and preemptive management of CRBSI (as described), rigorously designed and implemented studies are required to determine an effective CVC surveillance culture and preemptive management strategy for CRBSI in subgroups of patients at high risk.

Statements: Methods to Prevent CRBSI

Extraluminal Strategies

See Guidelines 11, 21, and 24 on "CVC System Connect and Disconnect Procedure Considerations" and section on "Prevention of CVC Dysfunction."

Intraluminal Strategies

24.3 **KDOQI suggests that the selective use of specific prophylactic antibiotic locks can be considered in patients in need of long-term CVC who are at high risk of CRSBI (eg, multiple prior CRSBI), especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). (*Conditional Recommendation, Low-Moderate Level of Evidence*).**

Note: Under these circumstances and given the current data, KDOQI considers it reasonable for prophylactic use of specific antibiotics: cefotaxime, gentamicin or cotrimoxazole (TMP-SMX). KDOQI cannot support the routine prophylactic use of antibiotic locks with very low supporting evidence (Table 24.1).

24.4 **KDOQI suggests that the selective use of specific prophylactic antimicrobial locks can be considered in patients in need of long-term CVC who are at high risk of CRSBI, especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). (*Conditional Recommendation, Low-Moderate Quality of Evidence*)**

Note: Under these circumstances and given the current data, KDOQI can support the prophylactic use of methylene blue. KDOQI cannot support the routine prophylactic use of antimicrobial locks with very low supporting evidence (Table 24.1).

24.5 **KDOQI suggests that the selective use of once weekly prophylactic CVC locking with thrombolytic agent (recombinant TPA) can be considered in patients in need of long-term CVC who are at high risk of CRSBI, especially in facilities with high rate of CRBSI (eg, >3.5/1,000 days). (*Conditional Recommendation, Moderate Quality of Evidence*)**

Note: Under these circumstances and given the current data, KDOQI can support the prophylactic use of recombinant TPA.

Note: High-risk patients refers to those with prior multiple CRSBI, S aureus nasal carriers.

Rationale/Background

In patients with CVCs, the bacterial biofilm coating the inner surface of the CVC is the major source of CRBSI.[577] Instillation of an antibiotic or antimicrobial lock (in conjunction with an anticoagulant) into the CVC lumen at the end of each HD session may reduce CRBSI by sterilizing the biofilm.

Detailed Justification

CVC Antimicrobial Caps

Please see the discussion on the ClearGuard cap in Guideline 21, under Detailed Justification (connector maneuvers to prevent CVC dysfunction).

Intraluminal Lock Solutions

Please also see the discussion in Guideline 21, under Detailed Justification (other intraluminal agents to prevent CVC dysfunction).

Published RCTs have evaluated a large number of antibiotic CVC lock solutions (gentamicin, cefazolin, cefotaxime, vancomycin, linezolid, vancomycin plus gentamicin, cefazolin plus gentamicin, cotrimoxazole (TMP-SMX), minocycline, or antimicrobial CVC lock solutions (taurolidine, 30% citrate, ethanol, EDTA, methylene blue). Most of these (fairly short-term) studies have demonstrated a substantially lower frequency of CRBSI with an antibiotic or antimicrobial lock solution, compared with an anticoagulant lock solution (such as heparin) (Table 24.1). It is also evident that, in general, the reduction of CRBSI with an antibiotic or antimicrobial lock solution was greatest in studies that observed a relatively high CRBSI rate in the control (anticoagulant-only lock) group.

Table 24.1. Intraluminal Strategies: Effect of Antibiotic and Antimicrobial Catheter Lock Solutions on CRBSI: Summary of Randomized Clinical Trials

Agents Studied	Patients, n	Relative Risk (95% CI)	Anticipated Incidence of CRBSI (95% CI)		Quality of Evidence
Locking Solutions That Can Be Used Selectively for CRBSI Prophylaxis					
Cefotaxime[593-595] (3 RCTs)	227	0.42 (0.25-0.72)	Without antibiotic: 67.5%	With cefotaxime: 23.6%	Moderate
Gentamicin[583-585,596] (4 RCTs)	555	0.18 (0.07-0.46)	Without antibiotic: 22.1%	With gentamicin: 4.0% (1.5-10.2)	Moderate
Weekly TPA[506] (1 RCT)	225	0.30 0.11-0.85)	Heparin: 13%	Weekly TPA: 5%	Moderate
Cotrimoxazole[597] (1 RCT)	87	0.16 (0.04-0.69	Without antibiotic: 4.4 per 1,000 days	With antibiotic: 0.58 per 1,000 days	Low
Methylene blue[598] (1 RCT)	407	0.29 (0.12-0.70)	Heparin: 0.82 per 1,000 days	Methylene blue% 0.24 per 1,000 days	Low
No Significant Effect or Very Low Evidence, Cannot Be Recommended (below)					
Taurolidine/citrate[533,599]	183	0.49 (0.20-1.24)	Heparin: 21.5%	Taurolidine/citrate: 10.5% (4.3%-26.7%)	Low
Vancomycin or linezolid[600] (1 RCT)	152		Without antibiotic: 6.7 per 1,000 days	With vancomycin: 1.2 per 1,000 days With linezolid: 0 per 1,000 days	Very low
Vancomycin + gentamicin[601] (1 RCT)	86	0.18	Without antibiotic: 4.0 per 1,000 days	With antibiotic: 0.7 per 1,000 days	Very low
Cefazolin[602,603] (2 RCTs)	159	0.58 (0.32-1.04)	Without antibiotic: 29.3%	With cefazolin: 17.0% (9.4%-30.5%)	Very low
Cefazolin + gentamicin[604] (1 RCT)	120	0.14	Without antibiotic: 3.12 per 1,000 days	With antibiotic: 0.44 per 1,000 days	Very low
Minocycline[605] (1 RCT)	204	0.32 (0.14-0.71)	Without antibiotic: 4.3 per 1,000 days	With antibiotic: 1.1 per 1,000 days	Not reviewed by ERT
Antimicrobial solutions					
EDTA[606] (1 RCT)	117	0.34 (0.04-3.24)	Heparin: 1.08 per 1,000 days	EDTA: 0.14 per 1,000 days	Very low
Ethanol/heparin[607] (1 RCT)	49	0.17 (0.02-0.63)	Heparin: 13%	Ethanol/heparin: 4%	Very low
Ethanol/citrate[608] (1 RCT)	40		Heparin: 5%	Ethanol/citrate: 0%	Very low
Hypertonic saline[544] (1 RCT)	59	—	Heparin: 10%	Hypertonic saline: 15%	Very low
30% citrate[528] (1 RCT)	291	(0.13-0.36)	Heparin: 4.1 per 1,000 days	30% citrate: 1.1 per 1,000 days	Not reviewed by ERT
46.7% citrate[526] (1 RCT)	232	—	46.7% citrate: 0.7 per 1,000 days	Heparin: 0.7 per 1,000 days	Not reviewed by ERT

Abbreviations: CRBSI, catheter-related bloodstream infection; EDTA, ethylenediaminetetraacetic acid; ERT, evidence review team; RCT, randomized controlled trial; TPA, tissue plasminogen activator.

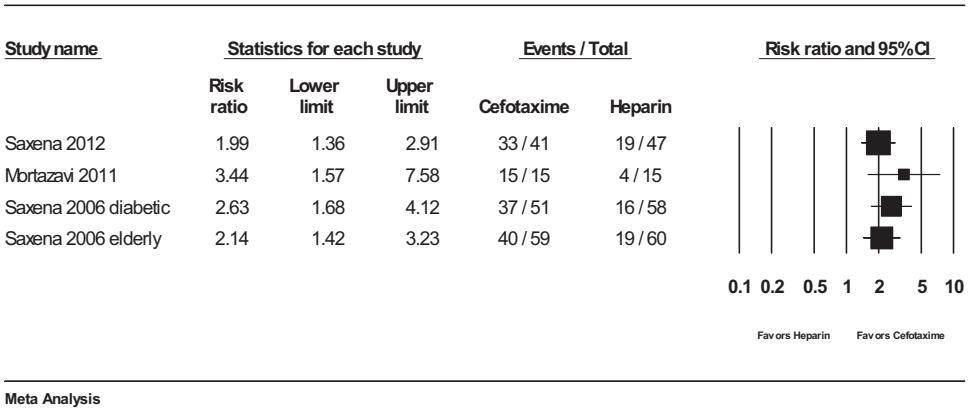

Figure 24.1. Catheter infection-free survival. Abbreviation: CI, confidence interval.

Antibiotic locking agents that had at least moderate evidence for prophylaxis against CRI are discussed in the following sections.

Cefotaxime. Overall CVC-related infections (including CRBSI) based on survival time were significantly lower with cefotaxime locks compared with heparin locks in tunneled CVCs.[578] Four RCTs compared cefotaxime (10 mg/mL) and heparin (5,000 U/mL) locks to heparin (5,000 U/mL) alone[578-582]; of these, 3 specifically indicated use of tunneled, cuffed CVC (N = 30[579] to more than 100,[581,582] with follow-up of 2-12 months). Total sample size could not be determined because of uncertainty about overlap in the separate reporting of the elderly and diabetic populations. The fourth study (n = 208) enrolled those with nontunneled temporary catheters (NT-CVC).[580]

Two studies reported that CRBSI related mortality was lower in the cefotaxime lock groups compared with the heparin lock groups. The difference was not statistically significant in 1 study (10% vs 21%; OR, 0.43; 95% CI, 0.18-1.03).[578] In the other study, it was statistically significant for the elderly group (12% vs 31%; OR, 0.31; 95% CI 0.12-0.81)[582] but not the diabetic group (10% vs 23%; OR, 0.37; 95% CI, 0.12-1.17).[581]

The range of CRBSI rates in both the control and cefotaxime groups were relatively wide,[578] although similarly observed in the studies of elderly (1.7 per 1,000 CVC days [cefotaxime] vs 3.6 per 1,000 CVC days [heparin]) and diabetic (1.6/1,000 CVC days [cefotaxime] vs 3.7/1,000 CVC days [heparin])[581,582] participants. Infection-free survival was found to be significantly higher in the cefotaxime lock groups compared with the heparin lock groups (Fig 24.1).

In the study of temporary NT-CVC, the CRBSI rate was also significantly lower in the cefotaxime lock group (1.7/1,000 CVC days [cefotaxime] vs 3.1/1,000 CVC days [heparin]).[580] This study also reported CRBSI rates by CVC location[580] and found CRBSI rates for femoral vein CVCs (2.16 vs 5.78/1,000 CVC days; P = 0.0001), subclavian vein CVCs (1.16 vs 2.43/1,000 CVC days; P = 0.046), and internal jugular vein CVCs (1.62 vs 3.25/1,000 CVC days; P = 0.036) to be lower in those receiving cefotaxime.

See the tables in this section for study quality of evidence and bias.[578-582]

Gentamicin. The incidence of CRI was lower in the gentamicin/anticoagulant locks compared with heparin locks.

4 RCTs[583-586] and 3 observational studies[587-589] evaluated gentamicin combined with an anticoagulant lock to anticoagulant locks alone for prevention of CRI.[583,585,586,590] One of the studies also compared gentamicin to minocycline/EDTA[585] and the other to taurolidine[534] (Table 24.1)

The 4 RCTs enrolled a total of 555 (range, 41-303) participants, and follow-up periods in total CVC days ranged from less than 3,300 in 2 trials,[583,585] approximately 18,000 in 1 trial,[586] and nearly 40,000 in 1 trial.[590] Two trials were conducted in the United Kingdom,[583,590] 1 in the United States,[585] and 1 in China.[586] Three trials compared gentamicin 4 or 5 mg/mL in either 3% citrate[585] or heparin only (5,000-5,500 U/mL) locks to heparin (5,000-5,500 U/mL) locks.[583,585,586] One trial (n = 303) compared lower-concentration gentamicin 320 μg/mL in 4% citrate lock to lower concentration heparin 1,000 U/mL lock.[590]

Overall, the 4 RCTS showed a significant reduction in the incidence of CRBSI in the gentamicin/anticoagulant group versus the heparin group (RR, 0.18; 95% CI, 0.07-0.46]).[583,585,586,590] There were no significant differences between treatment groups in the incidence of exit site infections.[585,586,590]

Harms associated with preventive procedures were sporadically reported, and events were few (Supplement 3, Table S244).

Cotrimoxazole (TMP-SMX). A single RCT enrolled patients with prevalent subclavian (tunneled) CVC and compared cotrimoxazole (trimethoprim-sulfamethoxazole [TMP-SMX]) (10 mg/mL) and heparin (2,500 U/mL) lock to heparin (2,500 U/mL) lock alone.[591] Median

duration of dialysis was 45 days in the intervention group and 31 days in the control group, with a follow-up of 6 to 12 months.

CRBSI occurred in 4% of the cotrimoxazole group (0.58/1,000 CVC days) and 27% of the heparin group (4.4/1,000 CVC days) (P = 0.002). Cumulative CRBSI-free survival by 365 days was significantly higher in the cotrimoxazole group (77%) compared with the heparin group (47%) (P = 0.02). There were no CRBSI-related deaths. Two of 41 participants (5%) in the heparin-only group were hospitalized after detection of *S aureus* resistant to cotrimoxazole. There were no adverse reactions due to the cotrimoxazole lock solution.

Weekly TPA Locks. A Canadian, multisite, double-blind RCT (N = 225 patients) of incident CVC compared TPA lock once weekly (1 mg per CVC lumen) and heparin lock (5,000 units/mL) twice weekly versus heparin lock thrice weekly. During a 6-month follow-up, definite or probable CRBSI occurred at approximately one third of the rate in the patients receiving weekly TPA locks as compared to standard heparin locks (4.5% vs 13%). The frequency of CRBSI was 0.40 and 1.37 per 1,000 CVC-days, respectively.

Methylene Blue Locks. A multicenter US open-label RCT (N = 407) compared a lock solution containing 0.15% methylene blue, 0.15% methylparaben, and 7% sodium citrate to standard heparin locks (5,000 units/mL).[592] Patients were followed for 6 months for a total of 49,565 CVC-days. The occurrence of CRBSI was significantly lower in the methylene blue group than in the heparin group (0.24 vs 0.82/1,000 CVC-days; P = 0.005). There was no difference in interventions to restore CVC patency between groups (16.4 vs 14.8%, P = 0.38). Of note, after review and retraining of best practices in establishing a baseline practice for the conduct of this study, the control group achieved a low rate of CRBSI of 0.8 episodes/1,000 CVC days.

Tables of studies, evidence quality, and risks of bias for this section are provided in Supplement 3, Tables S179, S181, S237-S239, and S240-S251.

Special Discussions

Several RCTs have found that the use of prophylactic antibiotic or antimicrobial locks reduces the frequency of CRBSI, as compared to conventional anticoagulant locks alone. From that perspective, this approach seems attractive. However, there are several concerns. First, an aliquot of the intraluminal CVC lock solution invariably leaks into the systemic circulation and may cause toxicity. For example, concentrated gentamicin locks resulted in ototoxicity in a subset of patients in 1 study.[609] Similarly, 30% citrate may cause symptomatic hypocalcemia, as manifested by paresthesia in 15% of patients in 1 study.[526] More importantly, the Work Group committee members were concerned about the potential of long-term prophylactic antibiotic locks leading to antibiotic-resistant infections. There are conflicting reports about the potential of prophylactic gentamicin locks to select for infection with resistant bacteria during prolonged use. Landry et al[610] documented this possibility, but 2 other large studies did not observe such a complication.[584,589]

The considered use of antibiotic locks is limited to high-risk patients as defined by the high-risk groups studied in the trials reviewed by the ERT; that is, patients with prior multiple CRBSI and *S aureus* nasal carriage; other potential high-risk patients have not been defined. The facility threshold for use of an intraluminal prophylactic strategy has not been validated and was discussed at length by the Work Group. The Work Group came to a consensus of a baseline CRBSI rate of ≥3.5/1,000 CVC days based on prior literature, potential resource implications, and the finding that high rates of CRBSI can and should be reduced first with retraining and use of best CVC care practices and infection control.[579,592,611]

Implementation Considerations

The potential concern about selection for antibiotic-resistant infections makes the Work Group committee reluctant to recommend antibiotic lock solutions across the board. Thus, our recommendation is to use prophylactic antibiotic locks in those scenarios where the benefit outweighs the potential risk, namely, patients at high risk for CRBSI or units with high rates of CRBSI. These would include patients at high risk of CRSBI (eg, multiple prior CRSBI and persistent, *S aureus* nasal carriers) or facilities with high rates of CRBSI (eg, >3.5/1,000 days). Use of nonantibiotic antimicrobial CVC solutions may be a superior option, due to the low likelihood of selecting for antibiotic-resistant infections.

The RCT using methylene blue highlighted that review, retraining, and implementation of best CVC care practices can achieve a low baseline CRBSI (0.8 episodes/1,000 CVC days),[612] *emphasizing that use of antibiotic lock prophylaxis should be used only in facilities with very high baseline risk of CRBSI even after the implementation of best CVC care and infection control practices.*

Future Research

- Determine and validate patients at high risk of CRBSI, despite confirmed excellent CVC care and infection control practices.
- Effect of risk stratification of patients at high risk of CRBSI and their prophylactic management of CRBSI, including strategies that involve extraluminal (eg, exit site) and intraluminal antimicrobial prophylactic care.
- It is unclear whether prophylactic strategies should be targeted to patients, facilities, or both at high risk of CRBSI; considerations of the effect of widespread prophylactic use of antibiotics and the potential emergence of antibiotic-resistant organisms affecting not only the

patient level but also the facility level must be considered and rigorously studied.

Guideline 25. Treatment of CVC-Related Infection

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation", the Work Group cannot make any recommendation, suggestion or other evidence based guidance (in either direction) based on the very low, low or inadequate quality of evidence amassed by the ERT.

Statement: Management of the Patient With a CVC-Related Infection

25.1 **KDOQI considers it reasonable and necessary to obtain appropriate cultures prior to initiating empiric antibiotics for the treatment of suspected CVC-related infection, with a change in antibiotics according to culture sensitivities. (Expert Opinion)**

Note: See Rationale and Detailed Justification sections for further detailed guidance.

Statement: Management of the CVC in a Patient With a CVC-Related Infection

25.2 **KDOQI considers it reasonable to have an individualized approach to the management of an infected catheter based on the patient's health, dialysis, and vascular access circumstances and should follow the detailed guidance. Options include CVC exchange via guidewire, CVC removal and reinsertion, CVC salvage, and concurrent antibiotic lock (particularly if the CVC is deemed to be the patient's final access). (Expert Opinion)**

Note: See Rationale and Detailed Justification section for detailed guidance.

Rationale and Detailed Justification

CVC-related infections and bacteremia are a significant cause of morbidity and mortality for HD patients. CVC-related infections include exit site infections, infections of the tunnel track, and bacteremia. Bacteremia is the most significant complication because it has the potential to lead to life-threatening sepsis and serious complications, such as endocarditis. The common clinical features of CVC infection include fever or chills, hemodynamic instability, CVC dysfunction, hypothermia, nausea and vomiting, and generalized malaise.[572,613,614] Treatment of the 3 main types of CVC-related infection—exit site infection, tunnel infections, and CVC-related bacteremia—requires careful consideration on how to (1) treat the patient and (2) manage the CVC.

Please see Guideline 23 for definitions of CVC-related infections. Treatment of each type of CVC-related infection must consider local infection control practices and its influence on organism patterns, cultures, and sensitivities. Properly collected cultures must be obtained before initiating empiric antibiotic treatment for all types of CVC-related infections to properly treat the infection and avoid antibiotic resistance.

Exit Site Infections

If drainage is present from the exit site, cultures should be obtained before initiation of antibiotics.[572] If there are signs or symptoms or other concern of systemic infection, blood cultures should also be obtained. Empiric antibiotic treatment should cover Gram-positive organisms and be further modified once culture and sensitivity results are finalized.[572] Duration of treatment for exit site infections typically range between 7 and 14 days.[572]

CVC management of exit site infections: This typically does not require removal; however, this depends on the infecting organism and the response to antibiotic therapy.

Tunnel Infections

When CVC tunnel infections are present, cultures from drainage from the tunnel or exit site and blood cultures from the CVC need to be obtained.[572] After attainment of the appropriate cultures, empiric antibiotics should be initiated to target both Gram-positive and Gram-negative organisms.[572] Antibiotics should be modified once culture and sensitivity results are available. The typical treatment duration for CVC tunnel infections is 10 to 14 days in the absence of concurrent bacteremia.[572] If CVC-related bacteremia is also present, the duration of treatment should be dictated by the management strategy for the CVC-related bacteremia.[572]

CVC management of tunnel infections: If the tunnel infection is not effectively treated with antibiotics, consider CVC exchange with a new subcutaneous tunnel to preserve the venous access site.[615] If not possible, the CVC should be removed and a new CVC placed at a new entry site.[572]

CRSBI or Bacteremia

Patients with suspected CRBSI should have blood cultures obtained from the CVC and peripheral source (dialysis circuit ± peripheral veins; Guideline 23). Broad-spectrum antibiotics that treat both Gram-positive and Gram-negative organisms should be initiated immediately.[572] Due to the high prevalence of methicillin-resistant *S aureus*, empiric therapy should include coverage for methicillin-resistant *S aureus*[318] but should also be guided by the local infection rates, antibiotic sensitivities, and dialysis center policies. Once the final organism and sensitivities are identified, patients should receive long-term antibiotic treatment, according to the CDC or IDSA guidelines, for 4 to 6 weeks for uncomplicated *S aureus*, 7 to

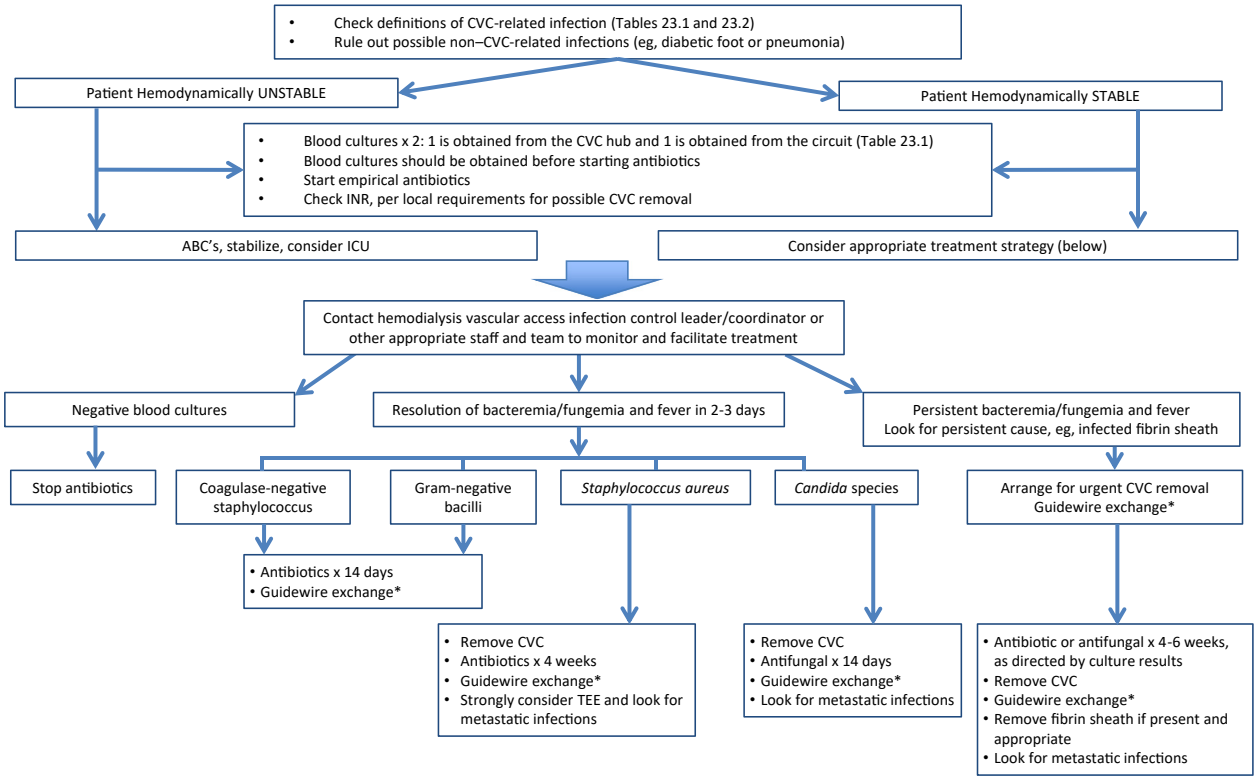

Figure 25.1. Algorithm for CVC-related infection. Special consideration: if the CVC must be salvaged (eg, no other option, embedded, etc), antibiotic lock with concurrent systemic antibiotic may be considered.*If appropriate—that is, no purulence or other signs of infection at exit site or tunnel if exchanging over same site. For tunnel infections, if there is purulence or other signs of infection at exit site or tunnel, exchange may be possible over new noninvolved insertion site using the same side to preserve access. Abbreviation: CVC, central venous catheter.

14 days for Gram-negative bacilli or enterococcus, and a minimum of 14 days with *Candida* species[319] (Fig 25.1).

CVC management of CRBSI: There are 4 main options that involve removing the CVC or retaining the CVC, as follows:

Removing the CVC:

1. CVC removal with CVC exchange over a guidewire at the same site
2. CVC removal with new CVC replaced at a new site (± "CVC free" duration [whereby the patient has a period when there is no CVC in-situ] with insertion of a temporary CVC as needed for dialysis).

   Several situations necessitate the latter option of immediate CVC removal with delayed CVC placement[318,572]:

   a. Clinically and hemodynamically unstable patients
   b. Persistent fever 48 to 72 after initiation of systemic antibiotics
   c. Persistent bacteremia 48 to 72 hours after initiating antibiotics
   d. Metastatic complications, including suppurative thrombophlebitis, endocarditis
   e. Infections due to *S aureus*, *Pseudomonas aeruginosa*, fungi, or mycobacteria
   f. Presence of a tunnel-site infection[616]

Note: In uncuffed, temporary CVC, CRBSI due to Gram-negative bacilli, S aureus, enterococci, fungi, and mycobacteria warrant CVC removal.

At the time of CVC removal, evaluation for the presence of fibrin sheath (presumably with infected biofilm) and fibrin sheath disruption can be performed (Guideline Statement 26.3).

Retaining the CVC:

1. Retain CVC and use antibiotic CVC lock
2. Retain CVC without use of antibiotic CVC lock

Antibiotic locks with concurrent systemic antibiotics may be an alternative treatment strategy to preserve the CVC. Although there are no RCTs evaluating the role of antibiotic CVC locks in the treatment of CRBSI, there have been several observational studies demonstrating eradication of bacteremia with antibiotic locks in conjunction with systemic antibiotics compared to CVC exchange or removal in conjunction with systemic antibiotics.[572,617,618]

Although the best management of CVC-related infections is to avoid them altogether, it is very unlikely that CVC can be completely eliminated, because 80% of patients initiate HD with a CVC.[516] Thus, there are several core interventions recommended by the CDC that KDOQI

endorses that can be useful to decrease infection rates and complications in patients requiring dialysis with a CVC, and these are covered in Guidelines 24 and 25. These core interventions include[572] (1) infection surveillance and feedback, (2) strictly following proper hand hygiene practices, (3) strictly following proper CVC/vascular access care protocols, (4) staff education and competency, (5) patient education and engagement, (6) CVC reduction efforts, (7) chlorohexidine for skin antisepsis, (8) CVC hub disinfection, and (9) antimicrobial ointment.

Multidisciplinary team surveillance and management of CVC-related infections has been demonstrated to reduce infections and improve outcomes in hemodialysis patients who require a CVC for dialysis access.[309,324]

Future Research

- Clinical sequelae of disrupting a fibrin sheath in patients with CRBSI requires further study.
- Prospective studies comparing treatment of CRBSI using antibiotic locks in conjunction with systemic antibiotics versus CVC exchange or removal in conjunction with systemic antibiotics is needed.

Guideline 26. Other Vascular Access-Related Complications

Please refer to Box 1 to understand the evidence basis for the Guideline Statements.

Note: When a statement indicates that "There is inadequate evidence for KDOQI to make a recommendation," the Work Group cannot make any recommendation, suggestion, or other evidence-based guidance (in either direction) based on the very low, low, or inadequate quality of evidence amassed by the ERT.

Statement: Treatment and Intervention of Asymptomatic Central Venous Stenosis Without Clinical Indicators

26.1 **KDOQI considers it reasonable that if *asymptomatic* central venous stenosis (without clinical indicators) is identified and/or associated with the prior or current presence of a CVC, it should not be treated. (Expert Opinion)**

See Table 26.1 for clinical indicators of central venous stenosis.

Rationale/Background

Stenoses or occlusions in the major intrathoracic veins (ie, central veins—internal jugular, subclavian, brachiocephalic, superior vena cava) can compromise AV access function and lead to ineffective dialysis. These lesions can also lead to marked venous hypertension due to the increased flow associated with the AVF with sequelae ranging from mild to severe symptoms (ie, positive clinical indicators) as characterized by varicosities, arm edema, dermatosclerosis, ulceration, and superior vena cava syndrome (Table 26.1 and Fig 26.1). Female patients can occasionally present with ipsilateral breast edema despite a normal or only moderately swollen extremity. These stenotic lesions can lead to clinical signs and symptoms such as prolonged bleeding after removal of the dialysis cannulas and/or elevated venous pressures during routine monitoring with high AV access recirculation. Central vein stenoses (CVS) or occlusions have been reported to occur in up to 5% to 50% of cases[237,619-622] and represent the Achilles heel of maintaining or creating a functional AV access. They can preclude the placement of an ipsilateral AV access and likely account for the leading etiology of complex or tertiary AV access problems.

The central vein lesions are likely caused by an initial injury to the vascular endothelium that precipitates a local

Table 26.1. Signs and Symptoms (Clinical Indicators) of Central Venous Stenosis

Timing of Occurrence	Sign or Symptom	Comments
Early signs and symptoms	Swelling	Typically asymmetric, affecting the hands and arms
	Pain	Pain that can be attributed to central venous stenosis/occlusion, such as aching and heaviness of an extremity, when other causes have been excluded
	Cutaneous findings	Venous collaterals Skin discoloration (red, purple, or blue discoloration)
Late signs and symptoms	Swelling	More widespread, affecting the arms, head, neck, or trunk (including breasts) Swelling may be unilateral, bilateral, or involve only the head, face, and neck.
	Pain	Persistent pain attributed to central venous stenosis/occlusion (eg, persistent aching, chest or extremity heaviness)
	Cutaneous findings	Venous collaterals Skin discoloration (red, purple, or blue discoloration; chronic pigmentation changes) Lymphatic blistering or weeping Stasis ulcers Phlebitis Infection (cellulitis, cannulation site abscess) Nonhealing wounds or incisions
	Respiratory compromise	Hoarse voice and/or respiratory distress from laryngeal edema, pleural effusion, or chest (or breast) swelling that can cause restrictive pulmonary compromise
	Neurologic symptoms	Visual or auditory disturbances, exophthalmos, cognitive disabilities, headaches, or seizures when other causes have been excluded

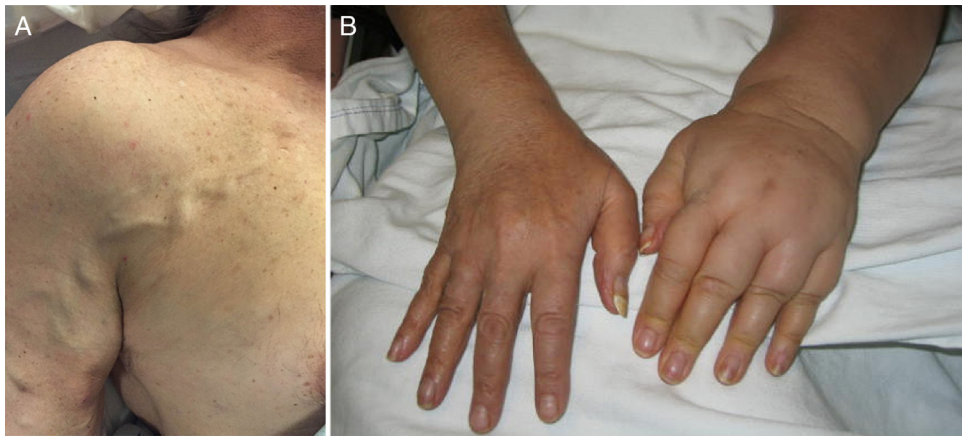

Figure 26.1. Physical findings of central venous stenosis. (A) Venous collaterals evident on the chest and neck. (B) Asymmetric extremities due to venous congestion and arm swelling from central venous stenosis.

inflammatory response that leads to fibrosis. A variety of factors have been shown to compound or exacerbate the various steps of this process, including deep venous thromboses, intravascular CVC, cardiac rhythm devices (eg, pacemakers), and HD AV accesses themselves. Peripherally inserted central catheters (ie, PICCs) have been reported to cause a CVS or occlusion in up to 7% of cases, whereas subclavian catheters have been reported to cause these lesions in up to 50% of cases.[266] Even appropriately positioned (ie, internal jugular inserted) CVCs can lead to CVS and/or occlusions within a relatively brief period of time. The true incidence of CVC-induced CVS/occlusion is unknown. If CVS is incidentally identified on angiographic assessment without clinical symptoms, it is unknown what the natural history of the stenosis is over time. However, overall, CVS/occlusions may represent the worst of the CVC-related complications, underscoring the importance of limiting their use.

Indeed, angioplasty for asymptomatic stenosis is associated with a more rapid progression to symptomatic stenosis[623,624] and should therefore be avoided unless there is a clinical indication to perform an angioplasty. In patients with symptomatic CVS/occlusion, primary patency with angioplasty or angioplasty with stenting is very poor.[2] Although stent grafts have demonstrated improved patency in peripheral stenosis, outcomes for central lesions are uncertain based on small retrospective studies.

The current Guidelines differ from prior KDOQI guidelines as they recommended treatment of CVS with PTA but without clarity regarding whether clinical symptoms were also present as an indication for intervention. Stent placement was recommended for (1) acute elastic recoil of >50% or (2) stenosis recurrence within 3 months. Elastic recoil itself has been poorly defined.

Detailed Justification

In 2 retrospective studies that assessed central vein patency in patients with asymptomatic versus symptomatic CVS, both studies recommended against intervention for asymptomatic stenosis. The first study excluded patients with CVCs but found that treatment of asymptomatic CVS greater than 50% in the setting of HD access maintenance procedures was associated with more rapid stenosis progression and escalation of lesions, compared with a nontreatment approach.[623] In the second study, primary central vein patency at 12, 24, and 36 months in asymptomatic/pauci-symptomatic patients and symptomatic patients with CVS were 77% ± 6% versus 55% ± 9%, 71% ± 7% versus 35% ± 9%, and 67% ± 7% versus 18% ± 9%, respectively ($P = 0.002$).[624]

Angioplasty and/or angioplasty and stenting for CVS are associated with relatively poor patency. In 1 retrospective study, primary patency of 76% was equivalent for angioplasty or angioplasty with stenting at 30 days, with 12-month rates of 29% for angioplasty and 21% for stenting.[2] However, in another retrospective study in HD patients without CVCs, primary patency (time from intervention to next intervention) was 24.5 months in the angioplasty group and 13.4 months in the stent group.[625]

Special Discussions

The Work Group discussed the signs and symptoms that may require confirmatory diagnosis and intervention, including

- Ipsilateral facial, neck, breast or extremity swelling (without other cause)
- Repeated thrombosis of an upper arm access in the absence of other causes within 6 months
- Pain in the extremity related to venous obstruction
- Neurologic symptoms in the absence of other etiologies
- Venous pressure is highly variable and dependent on many patient and HD factors and their interactions. Therefore, intervention should not be based solely on venous pressure, but other signs and symptoms should be present as well.

Future Research

- Understanding the natural history of CVS
- Prospective studies on intervention of symptomatic CVS

Statement: Investigation and Treatment of Symptomatic Central Venous Stenosis With Clinical Indicators

26.2 **Same as guidelines for "AV Access Flow Dysfunction–Confirmation And Treatment"**

See Guideline 15. See Table 26.1 for clinical indicators of central venous stenosis.

Rationale/Background

As discussed for asymptomatic central venous stenosis.

Detailed Justification

Close routine clinical monitoring will detect signs and symptoms suggestive of clinically significant CVS and venous hypertension (Guidelines 11 and 13). The culprit lesion can usually be confirmed with catheter-based and CT venography, given the limitations of ultrasound in the thoracic cavity. CT venography offers the advantage of being noninvasive and the potential to image all 4 extremities at the same time, although the timing of the contrast injection and image acquisition can be challenging.

Patients with mild symptoms can improve over time with the development of collaterals, and it is not uncommon to see patients with a functional AV access and no arm edema despite a CVS/occlusion.[626] Intervention is not indicated for asymptomatic lesions or those associated with minimal symptoms[624] (Guideline 13).

The treatment indications for CVS/occlusions include persistent moderate/severe clinical signs and symptoms (Guideline 13) and/or related ineffective dialysis. It is relatively common for patients to develop some arm edema after AV access construction, likely related to the operative trauma and mild venous hypertension. This usually resolves in the first 2 to 6 weeks postoperatively with the resolution of the inflammation from the surgical trauma and the development of venous collaterals.

The endovascular approach with balloon angioplasty is the first line of treatment for these symptomatic CVS/occlusions. Intraluminal stenting is reserved for angioplasty failures. Although the early technical success rates for the endovascular treatment are excellent and can exceed 90%,[266] the longer-term 6- and 12-month primary patency is poor, at 50% and 25%, respectively.[627-629] Notably, Yan et al[630] reported that balloon angioplasty of the central vein lesions had little impact on the AV access flow, although it was effective in relieving the symptoms. Intraluminal stenting should be reserved for recurrent stenosis, given the uncertainty of outcomes.[266,629] Indeed, stents should be used with caution (or avoided altogether) in the region of the thoracic outlet due to the potential for extrinsic compression and stent fracture from the overlying structures. Placing stents over pacer wires can complicate their removal. Thus, pacer wires can be removed (and the pacer re-sited) *prior to* the placement of an intraluminal stent; however, it may be simpler to create another AV access on the contralateral extremity (if possible), particularly given that the sclerotic lesions associated with the pacer wires tend to be refractory to balloon angioplasty.

Covered stents afford some theoretical appeal because the intimal hyperplasia does not develop within the covered segment, although it can develop at the proximal and distal ends of the stent. Furthermore, the covered component of the stent can inadvertently cover or "jail" important collaterals or the major central veins (eg, internal jugular). Caution must be exercised when using intraluminal stents. A careful tiered approach for de novo and recurrent lesions progressing from balloon angioplasty to bare metal stents followed by covered stents should be considered in the context of the patient's Life-Plan and the vascular access contingency and successions plans.[629]

There are a variety of open surgical options for patients with CVS/occlusions associated with their vascular access. However, these are considered secondary or tertiary options and are largely dictated by the anatomy in terms of available patent inflow and outflow veins. Potential options including axillary-jugular bypass, axillary-axillary bypass, axillary-femoral bypass, axillary-atrial bypass, or the jugular vein turndown procedure.[631,632] Alternatively, associated venous hypertension may be reduced by limiting the flow through the AV access by using some variant of a banding or flow-limiting procedure (Guideline 18).

The Hemoaccess Reliable Outflow (HeRO) Vascular Access Device (Hemosphere, Inc) can be used as a hybrid alternative (ie, combination endovascular/open surgical approach) access once the occlusion is bypassed.[633] The HeRO graft is a 6 mm (inner diameter) PTFE graft that is coupled to a 19 Fr (outer diameter) CVC. Although typically used as a new AV access configuration, the HeRO graft can be used in combination with an existing AVF or AVG to provide the "central vein runoff," provided that the delivery sheath for the CVC can be passed through the lesion.[633,634]

Statement: Management of CVC Fibrin Sheath Associated With Clinical Problems

26.3 **KDOQI considers it reasonable that when a CVC fibrin sheath is associated with adverse clinical manifestations (CVC dysfunction and/or infection), a CVC exchange with or without balloon disruption of the fibrin sheath should be performed. (Expert Opinion)**

Rationale/Background

Fibrin sheaths are a known cause of CVC dysfunction and infection that cannot be treated with thrombolytic therapy alone. CVC exchange alone or exchange with balloon disruption likely results in disruption of the fibrin sheath.[635,636] The fibrin sheath is composed of smooth muscle cells and vascularized connective tissue that originates at the venotomy site and grows along the CVC.[561,637] Once growth extends to the tip of the CVC, the sheath acts as a valve, interrupting aspiration of blood from the CVC but not return of blood through the CVC. Because thrombolytics dissolve acute clot (<14 days) and not tissue, they are ineffective against fibrin sheaths. Also, fibrin sheaths can harbor bacteria. A prior typical management strategy for suspected CRBSI is to remove the CVC, wait 48 to 72 hours, and reinsert a new CVC. The presence of an infected fibrin sheath and its consequences was often not considered in the setting of CRBSI. Disrupting the fibrin sheath may eliminate CRBSI and has been shown not to increase bacteremia rates[564]; thus, its disruption may assist in eliminating a source of recurrent infection.

The prior 2006 KDOQI guideline stated that a fibrin sheath causing CVC malfunction can be treated with CVC exchange with or without balloon disruption. No statement was made in the prior guidelines regarding disrupting fibrin sheaths to prevent or treat bacteremia.

Detailed Justification

In a randomized prospective pilot study, 47 long-term HD patients with secondary, refractory CVC dysfunction underwent guidewire exchange to replace their CVCs. Fibrin sheaths were present in 33 (70%) of the 47 patients. In 18 patients who were randomly assigned to disruption, the median time to repeat dysfunction was 373 days compared with 97.5 days in patients who did not undergo disruption ($P = 0.22$), and the median time to repeat CVC exchange was 411 and 198 days, respectively ($P = 0.17$). Although significance was not obtained due to the small sample size, the study highlighted a high incidence of fibrin sheaths and a trend toward improved function with balloon disruption.[560] Another study found the incidence of fibrin sheath formation for dysfunctional CVCs to be 76%.[638]

In an animal study assessing whether fibrin sheath presence results in increased CVC-related infection and persistent bacteremia, the fibrin sheath group exhibited a 50% infection rate versus 0% in the no fibrin group ($P < 0.01$).[639] There is no comparable published study in humans.

Special Discussions

There is very limited literature on fibrin sheaths and their impact in HD patients. The current data are comprised of small series, mostly retrospective in nature. Thoughts regarding bacteremia are anecdotal. The Work Group acknowledges that our suggestion of considering balloon disruption is based on limited data.

Implementation Considerations

Clinicians should carefully consider and balance an increase in intervention rate and potential complications with balloon angioplasty compared with simple CVC exchange.

Future Research

- RCTs comparing thrombolytics versus catheter exchange versus catheter exchange with fibrin sheath disruption would be highly beneficial and needed
- The associations of fibrin sheath incidence with CRBSI and impact of disruption and antibiotics versus antibiotics alone on CVC malfunction and infection are important to investigate and define

KDOQI VASCULAR ACCESS GUIDELINES GOALS AND TARGETS

Targets are clinical metrics or thresholds that can be used in tracking provider performance measurement.

Overarching Goal: to achieve reliable, functioning, complication-free dialysis access to provide prescribed dialysis while preserving future dialysis access site options as required by the individual patient's ESKD Life-Plan.

Rationale for Targets

1. Establish and Document the Patient's P-L-A-N

The concept and rationale for the ESKD Life-Plan is detailed in Guideline 1. A template example is given in Supplement 2. The ESKD Life-Plan should be determined with the patient and interdisciplinary team and reviewed on an annual basis. Such an approach is consistent with Centers for Medicare & Medicaid Services conditions of coverage Patient Assessment ruling 494.80 and Patient Plan of Care 494.90. Section 494.80 states that a facility's interdisciplinary team is responsible for providing each patient with an individualized and comprehensive patient assessment of his or her needs. Section 494.90(a) states that a facility's interdisciplinary *team must develop and implement a written, individualized comprehensive plan of care* that meets all of the requirements of §494.90. The comprehensive plan must be documented and maintained in the patient's record.

In particular, subsections 8 and 9 of condition 494.80 indicate that the following should be specifically done, consistent with the philosophy of these guidelines of obtaining "the right access, in the right patient, at the right time, for the right reasons" by using an individualized P-L-A-N, as follows:

(9) Evaluation of the patient's abilities, interests, preferences, and goals, including the desired level of participation in the dialysis care process; the preferred modality (hemodialysis or peritoneal dialysis), and setting, (for example, home dialysis), and the patient's expectations for care outcomes.

(8) Evaluation of dialysis access type and maintenance (for example, arteriovenous fistulas, arteriovenous grafts, and peritoneal catheters).

Furthermore, subsection 5 of condition 494.80 indicates the following:

(5) *Vascular access.* The interdisciplinary team must provide vascular access monitoring and appropriate, timely referrals to achieve and sustain vascular access.

GOALS AND TARGETS	
ESKD Patient on HD Life Plan Target	
1	All ESKD patients on HD Life-Plan goal: Establish and Document the Patient's P-L-A-N, to be reviewed and updated annually*: Components: a) Patient Life-Plan: 1-2 year (short term) and 5 year plan (long term) b) Access Needs: i) Creation Plan, ii) Contingency Plan, iii) Succession Plan ** consistent with CMS condition of coverage (494.90)*
AV Access (Fistula or Graft) Target	
2	All AV access (Fistula or Graft) Intervention goal = "1-2-3" interventions as follows: 1. For each 1 AV access creation 2. There should be ≤2 interventions to facilitate AV access use 3. There should be ≤3 interventions to maintain AV access use per year *Access use refers to successful use of AV access with 2-needle cannulation to achieve prescribed dialysis.*
Central Venous Catheter Target	
3	All CVC, regardless if the CVC is cuffed or not, tunneled or not, "final CVC" or not: Infection goal = Catheter-related bloodstream infection rate of <1.5/1000 catheter days

The hemodialysis patient must be evaluated for the appropriate vascular access type, taking into consideration co-morbid conditions, other risk factors, and whether the patient is a *potential candidate* for AVF placement. The patient's vascular access must be monitored to prevent access failure, including monitoring of AVG and AVF for symptoms of stenosis.

In terms of implementing the ESKD Life-Plan, the conditions of coverage stipulate the following:

Standard: Implementation of the patient plan of care.

(1) The patient's plan of care must—
(i) Be completed by the interdisciplinary team, including the patient if the patient desires; and
(ii) Be signed by team members, including the patient or the patient's designee; or, if the patient chooses not to sign the plan of care, this choice must be documented on the plan of care, along with the reason the signature was not provided.

These specifications in the Centers for Medicare & Medicaid Services conditions of coverage are in alignment with the current 2019 KDOQI guideline.

2. Intervention Goal for AV Access

AV access interventions are often necessary to facilitate an AV access for it to be usable for dialysis and/or to maintain its patency and use. However, unnecessary interventions can lead to reductions in patient quality (eg, discomfort/pain, inconvenience) and increased costs to the health care system. Currently, there is no guidance regarding intervention thresholds over which a patient and care team should consider alternate vascular access options, but this should be included as part of the vascular access contingency plan (ie, how many interventions should a patient tolerate before abandoning the current AV access). The only exception to limiting repeated interventions beyond the suggested thresholds is if the AV access is the patient's "destination" vascular access (ie, no other AV access options are feasible), and heroic attempts may be required to continue its prolonged use.

The thresholds for interventions to facilitate and maintain AV access use are based on available data from the current literature (Box 3). Furthermore, greater interventions to either facilitate or maintain an AVF have not demonstrated superior survival compared with AV accesses with fewer interventions.[640,641]

3. CRBSI Goal for Central Venous Catheters

The 2 most significant complications of CVC use are CVC dysfunction (Guidelines 21 and 22) and CVC-related infection, especially CRBSI (Guidelines 23-25). Although CVC dysfunction may be frequently inconveniencing to the patient due to necessary medical or interventional treatment, it is infrequently life threatening. On the other hand, CRBSI pose significant risks to patient morbidity and mortality. Although the 2019 KDOQI guideline's P-L-A-N permits an individualized approach to vascular access choice and use of CVC under specific circumstances, it is critical that, should a CVC be the appropriate vascular access for a patient, processes are followed to limit the risk of CVC related infections, particularly CRBSI (Guidelines 11, 21, 24, and 25). Evidence clearly demonstrates that prophylactic measures can significantly reduce CVC infection rates, and national data demonstrates that a target CRBSI rate of 1.5 or fewer infections/1,000 CVC days is possible.

Such data are derived from a national database, CROWNWEB, which is reported to the National Healthcare Safety Network. Each dialysis facility tracks HD-related bloodstream infections that are submitted on a monthly basis, reviewed by the National Healthcare Safety Network and CDC (CDC is the measure steward), and reported via the National Quality Forum. The most updated report (National Quality Forum #1460) on bloodstream infections (BSI) in HD units reported "in facilities all using a uniform method of measuring and reporting BSI has facility-specific rates that ranges 0-30.8 BSI per 100-patient years," which is equivalent to 0.84/1,000 CVC days. The pooled mean BSI for CVC among facilities reporting was 4.2 per 100 patient months, equivalent to 1.38/1,000 CVC days. Thus, a targeted rate of <1.5/1,000 CVC days is reasonable. Prophylactic measures have been demonstrated to have risk reductions for CRBSI of 22% to 60% (Guideline 24),[524,642,643] and should be used to achieve this target.

Comparison to 2006 KDOQI Guideline Targets

Due to changes in patient demographics and practice patterns, many of the prior 2006 KDOQI guideline targets are no longer clinically relevant and require re-evaluation, or the targets have been achieved or have become standard of care (eg, establishing a continuous quality improvement process). Over the past decade, we have gained great insight due to clinical experiences and research. For example, we now know that targeting thrombosis for AVFs does not result in improvement in AV access survival/longevity and that intervention may be counterproductive. Understanding the role of patient, vessel, and surgical factors for superior AV access survival and assessing the patient for eligibility for different AV access types and what is "right" for that individual patient is a priority in these guidelines.

The Overarching Goal is to provide functional, complication-free dialysis access while preserving future dialysis access site options as required by the individual patient's ESKD Life-Plan. Hence, the current targets differ from the prior guidelines in focusing on the major components that might interfere with achieving this overarching goal, and by doing so, also encompass many of the prior guideline targets.

Box 3. Interventions

First Author	Type of Study, Number of Patients, and Type of AV Access	Duration of Follow-Up	Number of Interventions	Rate	Comments
AV Fistulas: Interventions to Facilitate Maturation or Use (BEFORE First Cannulation)					
Yang, 2017[644]	Retrospective, observational, case-controlled SAVF: n = 60 EAVF: n = 60	SAVF: 183 d (6 mo) EAVF: 319 d (11 mo) SAVF: 6 mo EAVF: 6 mo	Unknown	SAVF: 3.43/patient-year EAVF: 0.59/patient-year SAVF: 3.43/patient-year EAVF: 0.78/patient-year	CMS Data 2011-2013 (SAVF cohort) NEAT Study (EAVF cohort) Facilitative and maintenance procedure, so cohorts include CKD non-HD and prevalent HD patients
Kimball, 2011[645]	Retrospective chart review AVF: n = 150 Upper arm: 54% Lower arm: 46%	12 mo Median: 10 mo	Unknown	Mean number: 2 interventions/AVF (range, 1-10)	On HD using AVF (n = 48) Not on HD patent AVF (n = 34) On HD failed AVF (n = 26) Not on HD failed AVF (n = 42) Interventions are facilitative and maintenance
Falk, 2006[646]	Retrospective AVF: n = 154 IAVF: n = 65	Unknown	113 in 65 immature AVFs	1.7 interventions/IAVF	
Shenoy, 2005[647]	Retrospective AVF: n = 398 cAVF: n = 199 sAVF: n = 199	Unknown	53	cAVF: 0.22 interventions/AVF-year sAVF: 0.37 interventions/AVF-year	Accesses placed between 1996 and 1999 Does not specify facilitative or maintenance procedures
Perera, 2004[648]	Retrospective AVF: n = 100	3 y	51	0.53 interventions/patient/y	Facilitative and maintenance procedures included
AV Fistulas: Interventions to Maintain Function/Patency (AFTER Successful Cannulation and Established Use)					
Harms, 2016[73]	Retrospective Prospective data base AVF: n = 289 NIAVF: n = 143 IAVF: n = 146	AVF: 6.5 y Mean follow-up: 2.3 y	Unknown	All AVF: 0.63 interventions/y NIAVF: 0.46 interventions/y IAVF: 0.84 interventions/y	50.5% of AVFs needed intervention before HD
Lee, 2011[287]	Retrospective Prospective data bases AVF: n = 173	Median: 672 d	Unknown	0IAVF(96): 0.76 interventions/y 1IAVF(54): 1.37 interventions/y 2IAVF(23): 3.51 interventions/y	Database UC and UAB 2005-2007 Follow-up from time of cannulation, so only maintenance procedures Of 173 patients, 77 needed facilitative interventions
Falk, 2006[646]	Retrospective AVF: n = 154 MAVF: n = 63	Mean: 317 d	209	3.3 interventions/AVF 1.75 interventions/AVF-year	—
Manns, 2005[344]	Prospective AVF: n = 157	12 mo	Unknown	AVF surgery: 1.39/PY AVF angiogram: 0.81/PY AVF angioplasty" 0.43/PY	Data from Southern Alberta Transplant Program Database (ALTRAbase)
AV Grafts: Interventions to Facilitate Maturation or Use (BEFORE First Cannulation)					
Shenoy, 2005[647]	Retrospective AVG: n = 745 cAVG: n = 401 sAVG: n = 344	—	635	cAVG: 0.86/AVG-year sAVG: 1.73/AVG-year	Accesses placed between 1998 and 1999 Does not specify facilitative or maintenance
AV Grafts: Interventions to Maintain Function/Patency (AFTER Successful Cannulation and Established Use)					
Harms, 2016[73]	Retrospective Prospective data base AVG: n = 310	AVG: 6.5 y Mean follow-up: 2.01 y	Unknown	All AVG: 1.58 interventions/y No intervention AVG: 1.48 interventions/y Intervention AVG: 2.2 interventions/y	17.7% AVGs needed intervention before HD

(Continued)

Box 3 (Cont'd). Interventions

AV Grafts: Interventions to Maintain Function/Patency (AFTER Successful Cannulation and Established Use)					
Manns, 2005[344]	Prospective AVG: n = 33	12 mo	Unknown	AVG surgery: 1.70/PY AVG angiogram: 1.33/PY AVG angioplasty: 0.94/PY	Data from Southern Alberta Transplant Program Database (ALTRAbase)
Perera, 2004[648]	Retrospective AVG: n = 131	3 y	170	0.92 interventions/patient/y	Facilitative and maintenance procedures included

Abbreviations: AV, arteriovenous; AVF, arteriovenous fistula; AVG, arteriovenous graft; cAVF, clip arteriovenous fistula; EAVF, endovascular arteriovenous fistula; IAVF, arteriovenous fistula with intervention for maturation; MAVF, mature arteriovenous fistula; NIAVF, no-intervention arteriovenous fistula; PY, patient-year; sAVF, suture arteriovenous fistula; SAVF, surgical arteriovenous fistula.

RESEARCH RECOMMENDATIONS

Future Research for Hemodialysis Vascular Access and Related Topics

Effective and appropriate application of the individualized ESKD Life-Plan strategy described in this Guideline requires a broader perspective than focusing solely on the creation of a specific vascular access or the monitoring and management of an existing vascular access. The Life-Plan approach requires consideration of the patient's current and future goals and preferences, as well as his/her current and future medical condition(s). To appropriately consider all of these aspects will require additional knowledge on patient preferences, more accurate tools to predict the timing of the need for dialysis, and better data on the expected outcomes associated with various approaches to dialysis access creation and preservation. To truly individualize the choices, each of these research areas will need to address potential differences across patient subgroups to allow evidence-based decision making for specific patients.

Timing of the Need for Dialysis

Planning for initial dialysis access in CKD requires some knowledge of the urgency of the need for dialysis. The Work Group agrees that assessment for vascular access should occur if the patient has a ≥50% risk of needing KRT within 2 years and/or has an eGFR of ≤15 mL/min/1.73m^2; however, this is based on Expert Opinion only. Tools to predict risk of ESKD, using eGFR and/or other commonly obtained variables, have been developed recently,[649-652] including the 4-variable Kidney Failure Risk Index.[653] The current limited evidence supporting the validity of these prediction tools is based on a single evaluation of each participant's status, which may change quickly. Future studies will require repeated assessments to determine whether a patient has crossed a threshold where dialysis access evaluation or creation is deemed appropriate. Only recently has a dynamic prediction tool been published.[652] Although this tool uses updated information, it does not take full advantage of the patient's history and previous experiences.

Numerous prediction tools have been developed, but few have been validated in other populations, and even fewer have been subjected to an evaluation of their impact.[654] The impact of utilizing a risk prediction tool and associated practices on vascular access specifically has, to our knowledge, not been evaluated for any specific tool. Much work remains in how best to implement vascular access–related clinical decisions based on the projected probability of kidney failure for a specified time horizon or the estimated time to kidney failure. Again, the best approach may differ based on a specific patient's characteristics and preferences, which must be addressed in these evaluation studies.

The other piece of the puzzle for optimizing the timing of vascular access creation, of course, is the time required from creation to use. Additional research is needed on appropriate time for cannulation and how to objectively and reliably determine readiness for cannulation in traditional and newer vascular access types, and methods to aid in AV access maturation.

Expected Outcomes Associated With Various Approaches to Vascular Access Creation and Preservation

National programs, including the Centers for Medicare and Medicaid Services's breakthrough initiative, Fistula First, have aggressively campaigned for greater use of AVFs and set goals of at least 66% AVF use and less than 10% CVC use among prevalent HD patients.[655] Despite these efforts, more than 80% of ESKD patients initiate HD with a NT-CVC or CVC, and CVC use remains common among prevalent HD patients.[44,139] Numerous studies have raised serious questions about this one-size-fits-all approach to vascular access, finding substantial heterogeneity across patients in the benefit derived from immediate AVF creation.[656-658] The Work Group hypothesizes that a more patient-specific approach will result in more appropriate vascular access choices.[20,659]

Multiple factors must be considered to apply the ESKD Life-Plan strategy to vascular access creation decision making, including the urgency of the need for a functioning AV access versus the expected time required for maturation; the infection risk associated with CVC use during maturation versus the expected long-term benefit of an AV access; the probability of maturation failure of an AVF versus the potential long-term benefit over an AVG; the patient burden associated with the planning, creation, and complications associated with each vascular access; and the potential need for future vascular accesses. Although data exist to provide useful estimates based on patient characteristics for some of these, such as predicting the probability of maturation,[660] there remain significant gaps in our knowledge. Additional research is needed to provide estimates for each of these variables across various patient and vessel characteristics to inform patient-centered, evidence-based decision making algorithms.

In the meantime, KDOQI has provided an app (www.myvascularaccess.com) that can be used to facilitate dialysis access decision making, based on evidence gained through the UCLA RAND Appropriateness Method. This tool requires further validation and research into the impact on its implementation. It is important to emphasize that it is only one tool, amongst others to assist with getting "the right access in the right patient, at the right time, for the right reasons". A multidisciplinary approach that involves the patient and family members/supporters to fully understand and evaluate the patient for the ESKD Life-Plan and dialysis access is central to achieving the overarching goal.

Patient Preferences

In addition to the clinical outcomes associated with choosing any specific vascular access, numerous studies have found that vascular access is a major concern of patients faced with ESKD.[661-663] Issues such as physical disfigurement from an AVF and the pain and fear of needle cannulation are of great concern to patients, but these have been overlooked by initiatives such as Fistula First.[664] Research has uncovered substantial heterogeneity in utilities assigned to various factors across patients by age, sex, and country.[661] Additional research is recommended to identify characteristics about processes and health outcomes associated with vascular access that are most relevant to patients' decisions.

Specific Research Recommendations Pertaining to Individual Guidelines

Please also see the accompanying list of topics of Potential Future Research for Hemodialysis Vascular Access and Related Topics under each Guideline topic.

ESKD Life-Plan Strategy

The overall impact of the ESKD Life-Plan Strategy must be critically evaluated. This evaluation should include measures of patient satisfaction, using a validated instrument, associated with each type of vascular access, the incidence of unnecessary dialysis access creations/placements, and the impact of potential outcomes (eg, complications, procedures, hospitalizations) on patient satisfaction and overall patient burden.

The ESKD Life-Plan may consider alternate environments for dialysis that may be more suitable for some patients; as such, further research may help determine and validate strategies for the ideal vascular access for these environments, such as home HD.

Timing, Preparation, and Planning for Creation/ Insertion of Vascular Access/ Vessel Preservation

- Validate ESKD prediction equations in large CKD populations for their use to facilitate vascular access creation and use (eg, kidney failure risk equation). Test whether use of prediction equations to assist with timing of vascular access creation results in improved readiness and/or additional unnecessary vascular access creation/ insertions.
- Develop and validate strategy/criteria for timing of referral of PD patients for HD vascular access creation.
- Develop and validate strategy/criteria for referral of transplant patients for HD vascular access creation.
- Develop algorithms for individualized vascular access site selection based on available locations, urgency of need, and feasibility to provide lifelong access.
- Develop and validate accurate patient-specific estimates of the predicted duration of HD and predicted probability of AVF maturation.
- Assess feasibility of alternative options for blood access.
- Assess the impact of a transradial approach for endovascular interventions (eg, cardiovascular or other) on future vascular access creation and outcomes.
- Determine whether small-bore internal jugular vein catheters result in a lower incidence of central venous stenosis than larger internal jugular vein catheters.
- Determine whether the use of small-bore internal jugular catheters instead of PICCs may reduce central venous stenosis.
- Determine and validate the criteria and timing of creating an AV access in a "failing" PD patient.
- Determine and validate the criteria and timing of creating an AV access in a "failing" kidney transplant patient.
- Investigate in which patients the decline of eGFR appears to slow or halt after AVF creation, and why this may occur.

Patient and Vessel Examinations Preoperative Considerations

- Determine the optimal training methods for preoperative clinical examination to assess patients and their vessels to determine the most suitable type and location of their vascular access.
- Studies are needed to examine the influence of radial-approach angiograms on future vascular access outcomes.
- Develop and validate approaches to reduce potential damage to central and peripheral vessels by providers throughout the health care system.
- Research and develop tools for patient education and vessel preservation to optimize vascular access choice, creation, and use.

Vascular Access Types: Incident and Prevalent Patients

- Develop and test risk prediction models to assist patient-specific decision making regarding choice of vascular access. Because it is unlikely that randomized trials will be performed to compare different initial or subsequent vascular access types, we must rely on high-quality observational data to inform these algorithms. Specifically, data on expected probability of maturation, likely length of time until cannulation, incidence of various complications, and likely length of AV access survival will be needed, ideally for numerous strata of patient characteristics (eg, age, sex, race, life expectancy, number and severity of comorbid conditions). For specific areas where existing data are lacking, provide conflicting results, or are susceptible to substantial bias, new analyses and studies will be required.

- Develop, validate, and implement the standardized definitions for maturation, patency, and specific complications to provide consistency across studies and allow development of decision-making tools.

Vascular Access Locations

- Determine whether large arteries (>2 mm) with higher baseline flows are associated with greater risk of flow-associated problems.
- Identify criteria for upper arm as first AV access choice.
- Evaluate the impact of real time ultrasound evaluation of vessels by the operating surgeon on identifying the optimal type and location for AV access creation and its impact on maturation and use.

AV Access Creation

- The preponderance of stenosis in specific anatomic locations suggests that local hemodynamics play a significant role in its development. The availability of better imaging techniques and CFD models provide an opportunity to model hemodynamics and shear stress patterns. New CFD models, specific for AV access, should be developed and validated for assisting AV access decision making.
- Studies of hemodynamics (eg, flow, shear stress) as a causative or predictive factor of AV access outcomes, including outflow vein and juxta-anastomotic stenosis, are needed.
- Evaluate a variety of anastomotic configurations and techniques, including the end-to-side and side-to-side configurations, the piggyback straight-line onlay technique (pSLOT), and the radial artery deviation and reimplantation (RADAR) technique.
- Investigate technologies to assist with AVF maturation, including The Fistula Assist Device in AVF Maturation, and the role of BAM in the setting of RCTs.
- Evaluate ultrasound-based objective criteria to assess suitability for AV access.
- One-stage versus 2-stage basilic vein transpositions need to be studied further in the setting of RCTs.
- Evaluate novel techniques for surgical and percutaneous creation of autogenous AV access.
- Determine whether endoAVF creation can result in a clinically durable and cost-effective AV access compared with traditional surgical AV access creation and maintenance.

Novel Materials and AV Access

- Validate the potential benefits of current biologic grafts.
- Develop and test novel nonautogenous graft materials and creation techniques.
- Develop and test novel techniques for surgical and percutaneous creation of autogenous AV access.
- Clinical trials are needed to identify the optimal CVC with the best long-term durability and survival and lowest incidence of complications, including central venous stenosis, vessel injury or thrombosis, CRBSI, and CVC dysfunction.
- Develop and test novel CVC materials to minimize complications.
- Catheter insertion: Additional clinical studies are needed to identify the ideal means to insert a NT-CVC or tunneled CVC for HD. Imaging appears to favorably affect successful placement and may reduce complication rates.
- Newer technologies include vein-localizing tools based on near-infrared spectroscopy. Studies are needed to determine whether this technology has application in adults for CVC placement and whether it warrants comparison to real-time ultrasound as an imaging technique to enhance CVC placement.
- Post–AV access creation/CVC insertion considerations: Test the impact of resources provided by the Fistula First Catheter Last Work Group Coalition on AVF maturation and usability.
- Study the indications for secondary interventions (surgical and endovascular) to help AV access maturation.

Vascular Access Use

- Test the safety, efficacy, and impact on health care resources and patient outcomes of ultrasound-guided cannulation in busy, operating dialysis units.
- Identify best practices for mechanics of cannulation, including needle type and size, angle of insertion, and graduated flow rates.
- Test effectiveness of simulation models and other techniques for improving cannulation success, reducing complications and improving patient satisfaction.
- Define *expert cannulator* and determine how such expert cannulators can maintain their expertise and be best used to improve overall cannulation success within a unit and for individual patients.
- Identify obstacles to achieving complication-free cannulation and strategies to mitigate such obstacles.
- RCTs to assess standard needles versus plastic cannulas in preserving AV access patency and reducing complications.
- RCTs to assess impact of needle size and pump speed on long-term AV access patency.
- Assess impact of manual compression versus mechanical clamp use after needle withdrawal on access patency/stenosis (AV access flow dysfunction).
- Evaluate outcomes associated with alternative cannulation devices.
- Evaluate the safety, efficacy, and patient satisfaction with using plastic cannulae.

AV Access Flow Dysfunction

AV access flow dysfunction refers to clinically significant abnormalities in AV access (AVF or AVG) flow or patency due to underlying stenosis or thrombosis-related pathology.

- Determine which indicators from a clinical monitoring examination are most strongly predictive of clinically significant stenosis.
- Assess the impact of annual mandatory physical examination skill assessment for all stakeholders on recognizing early AV access flow dysfunction (similar to BLS for cardiac arrest).
- Adequately powered RCTs are needed to determine which surveillance protocols and thresholds for intervention improve overall AV access patency. Studies should identify indications and relative benefits/harms of earlier (pre-emptive) interventions.
- Clinical studies are needed to determine the most appropriate indications for endovascular versus surgical intervention.
- Define and validate specific outcome metrics for interventions for dysfunctional and thrombosed AV access.
- Determine outcomes with surgically corrected occluded accesses that are followed by a completion angiogram/imaging ± further corrective procedure. How does this strategy compare with historical surgical correction without completion imaging or with endovascular management?
- Clinical studies are needed to test the potential impact of multidisciplinary care on AV access patency.
- The effect of far-infrared therapy on AVF and AVG dysfunction needs to be tested in RCTs in a variety of dialysis populations.
- RCTs of omega-3 fatty acids are needed to test their impact on AV access outcomes and define the optimal formulation and dose.
- Study the patient and AV access outcomes and impact of (1) ultrasound-guided angioplasty and (2) intravascular ultrasound guided angioplasty, to limit contrast exposure in CKD/ESKD patients with residual kidney function and urine output.
- Stent-grafts versus bare-metal stents for treatment of central vein stenosis requires more RCT evaluation, with larger numbers and rigorous conduct and analysis.
- More RCT evaluation of stent-grafts for vascular access management (primary or secondary) with clinically (rather than angiogram) based outcomes are urgently required.
- Study is needed in AVFs for multiple modalities of treatment (eg, stent grafts, drug-eluting balloons, etc).
- Comparative methods of AV access thrombolysis (eg, surgical versus endovascular) with a variety of short- and longer-term AVF and AVG outcomes.
- Increasing evidence in the following areas:
  - The use of specialized balloons (drug-coated or cutting) versus standard high-pressure balloons in the primary treatment of AVF and AVG stenosis.
  - The optimal duration of balloon inflation time during angioplasty to improve intervention primary patency in the treatment of AVF or AVG stenosis.
  - The secondary use of drug-coated balloons after successful angioplasty with high-pressure balloons for treatment of stenosis in AVF and AVG.
- Impact of timing of recurrence of stenosis on choice of treatment modality
- Use of stent grafts in locations other than graft-vein anastomosis or cephalic arch in brachiocephalic fistulas.
- Optimal treatment of in-stent stenosis that occurs in stent-grafts.
- The optimal timing of angioplasty/thrombolysis or thrombectomy in thrombosed AVF and AVG.
- Studies to determine the best measurement that defines a successful procedure outcome. For example, should it be a percent relative improvement in lumen size or an absolute lumen diameter or other measurement? When should it be measured after the treatment (eg, PTA) (during the procedure or after?)

AV Access Infection

- Study the impact of aseptic versus sterile cannulation in AVG infection.
- Evaluate the role of intra-access pressure and cannulation infiltration in development of AVF cannulation site infections.

AV Access Aneurysms

- Assess AV access flow rates on incidence and prevalence of aneurysms.
- Evaluate the role of intra-access pressure in causation of AVF outflow vein aneurysms.
- Assess the impact of size documentation in medical record on overall awareness and active intervention by stakeholders.
- Study the natural history to better determine, manage and prevent incidence of AV aneurysm rupture, and fatal hemorrhage.
- Evaluate techniques for AVF salvage and CVC avoidance while managing aneurysms and bleeding complications.

AV Access Steal

- Further define and establish the predictors for AV access steal.
- Further define and establish strategies to reduce the incidence of AV access steal.
- Further define the natural history of mild to moderate symptoms related to AV access steal.
- Further define and validate the diagnostic criteria for AV access steal.
- Further define the optimal remedial treatment for AV access steal.

- Further define ischemic monomelic neuropathy as a distinct entity from AV access steal.
- Develop and research the utility and validity of definitions for steal based on AVF function (high-flow steal vs low-flow steal).

Treatment of Other AV Access Complications

- Evaluate and develop CVC avoidance techniques to manage AV access complications

Treatment and Prevention of CVC Complications

- Evaluate the cost/benefit of routine physical examination and history on CVC use and/or complications.
- RCT comparing normal saline, 1:1,000 heparin, and 4% citrate as routine CVC lock solution.
- Study the incidence of both central vessel and right atrial thrombus with noninfected dysfunctional CVC and develop management guidelines, potentially based on the size and location of the thrombus.

Catheter Dysfunction

- Develop and validate a standard definition of CVC dysfunction applicable to unique patient circumstances to allow comparisons across institutions, studies, and treatment regimens. Estimate the sensitivity, specificity, and predictive value of specific markers of dysfunction.
- Assess the impact of earlier intervention—and types of interventions—for CVC dysfunction.
- Tracking the frequency of dysfunctional and embedded CVC and the various methods of managing a CVC that is dysfunctional but embedded.

Prevention of CVC Dysfunction

- Confirm benefit of 1 mg versus 2 mg TPA in maintenance of CVC patency, both short and long term.

Catheter-Related Infection

- Further develop and validate criteria for CRBSI in hemodialysis patients.
- Validate diagnostic criteria for exit site and tunnel infections.

Prevention of CVC Infection

- Rigorously designed and implemented studies are required to determine an effective surveillance and preemptive management strategy for CRBSI in subgroups of patients at high risk.
- Determine predictors of CRBSI in patients receiving standard infection control practices.
- Evaluate the impact on incidence of CRBSI of strategies that involve extraluminal exit site and intraluminal antimicrobial prophylactic care. Studies should be performed at both the patient and facility level and evaluate the potential emergence of antibiotic resistant organisms.
- RCT to assess impact of taking a shower on CRBSI with healed CVC exit site.

Other Vascular Access-Related Complications

- The natural history and predictors of CVS need to be understood in greater detail.
- Effective interventions for symptomatic CVS need to be developed and validated.
- Randomized controlled trials for treatment of catheters with a fibrin sheath are needed to compare effectiveness of thrombolytics, catheter exchange, and catheter exchange with fibrin sheath disruption on outcomes of patency and infection.
- The association of fibrin sheath incidence with CBRSI needs to be evaluated.
- The effectiveness of fibrin sheath disruption plus antibiotics compared with antibiotics alone needs to be evaluated in terms of CVC dysfunction and incidence of infection.
- Characterizing catheter-related central vein thrombosis versus atrial thrombosis and its management principles.

Multidisciplinary Approaches to Vascular Access

- Role of associate degree–level training for dialysis technician rather than hands-on training only. Standardizing training curriculum.
- Impact on development and implementation of a standardized dialysis access training curriculum for all stakeholders (nephrologist, nurses, surgeons, radiologist) involved in AV access care.

Endovascular Procedures

- Cost comparison between interventions, PTA, and use of stent-grafts and/or drug-eluting balloons for maintaining overall access patency.
- Comparison between drug-eluting balloons and stent-grafts for overall access patency.
- Comparison between different drug-eluting balloons and different stent-grafts.
- Drug dose comparison study on impact of drug coated balloons on venous stenosis in dialysis accesses.
- Determine if and what the role of angioscopy is for guided interventions.

Surgical Procedures

- Skills and training needs for CVC placement and AV access creation.
- Defining high-flow AV access, its hemodynamic impact and treatment options. Should there be an RCT for treatment options, and if so, what interventions should be evaluated?

BIOGRAPHICAL AND DISCLOSURE INFORMATION

Guideline Development Work Group

Kenneth Abreo, MD

Dr Abreo is Professor of Medicine, Chief of the Division of Nephrology, and Vice Chairman of the Department of Medicine at Louisiana State University Health Shreveport School of Medicine. After completing his Nephrology Fellowship training at the University of California–Davis in Sacramento and the University of Wisconsin in Madison, he joined the Medicine faculty at the University of Kentucky in Lexington from 1982 to 1985 and Louisiana State University Health Sciences Center in Shreveport in 1985. His early research interests were focused on clinical and bench research on aluminum toxicity causing bone disease and anemia in renal failure patients. In the past decade, he has focused on training Nephrology Fellows in interventional nephrology. His current research interests are centered on improving vascular and peritoneal access in dialysis patients. He has played an active role in the American Society of Diagnostic and Interventional Nephrology, most recently as President. He serves on the Editorial Board of the *Journal of Vascular Access*. He has been involved in national and international scientific and educational programs with American Society of Diagnostic and Interventional Nephrology, ASN, NKF, ISN, ANZIN, ERA-EDTA, AVATAR, and VAS. Dr Abreo declares that he has no relevant financial relationships.

Michael Allon, MD

Dr. Allon is Professor of Medicine at University of Alabama at Birmingham, where he serves as the Associate Director for Clinical Affairs and the Medical Director of Dialysis Operations in the Division of Nephrology. He has a longstanding clinical research interest in dialysis and, in particular, in vascular access for hemodialysis. He was the principal investigator for several clinical dialysis trials sponsored by the National Institutes of Health, including HEMO, DAC, and HFM. He has published more than 100 peer-reviewed articles on various aspects of vascular access. Finally, he has been an invited speaker at numerous nephrology meetings on various topics related to vascular access. Dr Allon declares that he has no relevant financial relationships.

Arif Asif, MD, MHCM

Dr Asif is the Chairman of the Department of Medicine at Jersey Shore Medical Center and Professor of Medicine at Seton Hall-Hackensack Meridian School of Health, Neptune, New Jersey. He completed his residency in Internal Medicine at Mercy Hospital and Medical Center, University of Illinois at Chicago, and Fellowship in Nephrology and Hypertension at the University of Miami, Miami, Florida. He also received a Master of Health Care Management and Business Administration degree from Harvard University, Boston, Massachusetts. He is a nationally and internationally recognized expert in hemodialysis vascular access and has organized and chaired multiple scientific meetings on hemodialysis access. Dr Asif has been involved in vascular access research since 2000. He has had numerous funded research projects, received many teaching awards, and developed multiple training programs in the area of dialysis vascular access. He has edited 4 books and authored more than 200 articles and book chapters. Among his many professional editorial responsibilities, he is the Section Editor of the *Journal of Vascular Access* and the Associate Editor of the *American Journal of Kidney Diseases*. He is the Past President of the American Society of Diagnostic and Interventional Nephrology Society and currently serves as the Chair of its Clinical Practice Committee. Dr Asif has consulted for, and received honoraria from, Alexion Pharmaceuticals, Inc, in 2016; consulted for Phraxis, Inc, from 2016 through 2018, and received honoraria from Fresenius USA Marketing, Inc, in 2016.

Brad C. Astor, PhD, MPH

Dr Astor is Associate Professor in the Departments of Medicine and Population Health Sciences at the University of Wisconsin School of Medicine and Public Health. He serves as the Director of Research for the Division of Nephrology. He was a medical device reviewer at the US Food and Drug Administration prior to training as an epidemiologist at The Johns Hopkins Bloomberg School of Public Health. He was a faculty member in the Departments of Epidemiology and Medicine at Johns Hopkins until 2011, when he joined the University of Wisconsin. His research covers several different aspects of kidney disease and its interaction with cardiovascular disease. Other specific areas of interest include predictors of outcomes in kidney transplant recipients and hemodialysis vascular access complications. This research has been pursued in the general population (Atherosclerosis Risk in Communities [ARIC] Study, Multi-Ethnic Study of Atherosclerosis [MESA]) as well as in clinical trials (African American Study of Kidney Disease and Hypertension [AASK]) and observational studies of dialysis patients (Choices for Healthy Outcomes in Caring for ESKD [CHOICE]) and kidney transplant recipients (Wisconsin Allograft Recipient Database [WisARD]). Dr Astor consulted for VascAlert in 2018 and 2019.

Marc Glickman, MD

Dr Glickman is a retired vascular surgeon who has written more than 100 articles on vascular access surgery. He has written several chapters in books on vascular access surgery as well. He was previous President of the Vascular Access Society of the Americas, part of the clinical faculty of the Eastern Virginia Medical School. He has been principal investigator for many vascular access graft studies that are

currently in use today. He has lectured extensively nationally and internationally on vascular access surgery. Dr Glickman received honoraria from Bard Peripheral Vascular from 2016 through 2018 and consulted for WL Gore & Associates, Inc (2016); Merit Medical Systems Inc (2016-2018); LeMaitre Vascular Inc (2016, 2018); Zimmer Biomet Holdings, Inc (2017); and Bard Peripheral Vascular (2018). Dr Glickman has also been employed by Hancock Jaffe (2016 to the present).

Janet Graham, MHScN, CNeph(C)

Ms Graham's career has focused on the care of patients with chronic kidney disease over almost 3 decades. Currently, she is the Clinical Director of Nephrology at The Ottawa Hospital (TOH) and Regional Director of Nephrology Champlain LHIN Ontario Renal Network (ORN), and she recently completed a secondment as Clinical Education and Quality Improvement at the ORN, leading the development and implementation of both clinical education and quality improvement initiatives at the provincial level. Ms Graham's career has spanned the entire care continuum in renal care, and she has held a number of leadership positions at TOH. She holds a Masters of Health Science degree in Nursing and has conducted clinical research in the area of dialysis access, with several publications in this area. Ms Graham declares that she has no relevant financial interests.

Thomas S. Huber, MD, PhD

Dr Huber is Professor and Chief of the Division of Vascular Surgery at the University of Florida College of Medicine. He has a longstanding interest in hemodialysis access and was one of the Principal Investigators for the National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases Hemodialysis Fistula Maturation Study. He has served on the editorial boards of the *Journal of Vascular Surgery* and the *Yearbook of Surgery* while co-editing *Mastery of Vascular and Endovascular Surgery*. He currently serves on the Vascular Surgery Board of the American Board of Surgery. Dr Huber declares that he has no relevant financial relationships.

Timmy Lee, MD

Dr Lee is Professor of Medicine in the Department of Medicine and Division of Nephrology, with a secondary appointment in the Department of Biomedical Engineering at the University of Alabama at Birmingham. He received his medical degree from the Louisiana State University Health Sciences Center in Shreveport and completed his Internal Medicine residency and Nephrology fellowship at the University of Alabama at Birmingham, Nephrology research fellowship at the University of Alabama at Birmingham, and Masters of Science in Public Health degree at the University of Alabama at Birmingham. Dr Lee currently serves as the Associate Director of Interventional Nephrology, Associate Nephrology Fellowship Director, Associate Director of the Nephrology Research Training Center, Associate Section Chief, and Director of the Hemodialysis Program at the Birmingham Veterans Affairs Medical Center. He has been involved in hemodialysis vascular access research since 2002 and has more than 50 publications in vascular access research. He has active research programs in clinical trials and large epidemiologic studies in dialysis vascular access and a laboratory-based translational research program in dialysis vascular access studying human vascular access blood vessel tissue biorepositories and mechanisms of arteriovenous fistula dysfunction using animal models (mouse, rat, and pig). The goal of his research program is to develop novel therapeutics to prevent and treat complications of hemodialysis vascular access dysfunction and improve the delivery and processes of care for patients requiring a hemodialysis vascular access. Dr Lee's research program is currently funded by the National Institutes of Health and Veterans Affairs Medical Center. He serves a counselor in the American Society of Diagnostic and Interventional Nephrology. Dr. Lee served as a consultant for Merck Sharp & Dohme Corporation (2017, 2019) and Boston Scientific (2019).

Charmaine E. Lok, MD, MSc, FRCP(C) (Chair)

Dr Lok is a Professor of Medicine, Faculty of Medicine, at the University of Toronto and Senior Scientist at the Toronto General Hospital Research Institute. She is also associated with the Department of Health Research Methods, Evidence, and Impact, Faculty of Health Sciences, McMaster University. Dr Lok is the Medical Director of both the chronic kidney diseases and hemodialysis programs at the University Health Network–Toronto General Hospital, Toronto, Ontario, Canada. Her research focus is on chronic kidney disease (CKD) and end-stage kidney disease (ESKD) outcomes. She has a special interest in improving dialysis access outcomes and reducing adverse cardiovascular events in CKD/ESKD. She is active in raising awareness of CKD and ESKD and its importance in population health. Dr Lok is involved in a variety of local and international scientific and educational programs including, Canadian Institutes of Health Research (CIHR), Kidney Foundation of Canada (KFOC), Dialysis Outcomes and Practice Patterns Study, National Kidney Foundation (NKF), American Society of Nephrology (ASN), Vascular Access Society of the Americas (VASA), American Society of Diagnostic and Interventional Nephrology, and Kidney CARE Network International. Dr Lok declares that she has no relevant financial interests.

Louise M. Moist, MD, MSc

Dr Moist is a nephrologist at Victoria Hospital, Ontario, Canada and Professor of Medicine, Epidemiology and Biostatistics; Associate Chair of the Division of

Nephrology; and Scientist in the Program of Experimental Medicine at Western University. Her clinical and research interests are focused on chronic kidney disease, with a specific expertise in vascular access for hemodialysis patient. Dr Moist has a number of leadership roles, including The Ontario Renal Network Physician Lead for Dialysis Access, integrating change to improve vascular access practice and reduce catheter use. She has chaired and been involved in several guideline groups, including CSN anemia guidelines, timing of dialysis start, and vascular access. Dr Moist is active in education, clinical care, and research, with more than 150 peer-reviewed academic papers and numerous research grants. She has received the University of Western Ontario award for Excellence for Teaching and for Excellence in Research. Dr. Moist has served on a speaker's bureau and as a consultant for Otsuka America Pharmaceutical (2018) and Janssen Pharmaceuticals (2018). She has also served as a consultant for Boehringer Ingelheim in 2018 and on an advisory board for Novartis (2019), AstraZeneca (2019), and Novo Nordisk (2019).

Dheeraj K. Rajan, MD, FRCP(C)

Dr Rajan completed his Diagnostic Radiology residency at Wayne State University in 1999 and Fellowship in Vascular and Interventional Radiology at the University of Pennsylvania in 2000. Over his career, he has published 100 articles, primarily focused on arterial and dialysis interventions, multiple book chapters, and a textbook titled *Essentials of Percutaneous Dialysis Interventions*. He is a Professor of Medicine and the Division Chief of VIR at the University of Toronto. Dr Rajan also sits on various committees for the Society of Interventional Radiology, Cardiac Care Network of Ontario, and the Ontario Renal Network. He formerly was an Associate Editor for the *Journal of Vascular and Interventional Radiology* and reviews for multiple medical journals. Dr Rajan's current focus is on the percutaneous creation of dialysis fistulas, and he was one of the pioneers for the procedure itself. He also serves as an advisor to multiple start-up and established companies with devices focused on hemodialysis interventions. Dr. Rajan served as a consultant for Becton Dickinson (2018), TVA Medical (2016), and Bard Medical (2016). He also served on a speaker's bureau for Gore Medical (2018) and had stocks/bonds with TVA Medical (2016).

Cynthia Roberts, RN, CNN

Ms Roberts is a Nephrology and Vascular Access Nurse and has for patients with chronic kidney and end-stage renal disease for 28 years. She works with Renal Research Institute, partnering with the University of North Carolina (UNC) at Chapel Hill Nephrology and Hypertension division and UNC Kidney Center. She specializes in developing patient care models that emphasize collaboration of care with dedicated vascular access surgery and interventional clinic systems and nephrology integrated care management. She has multiple publications in ANNA *Nursing Journal and Nephrology News and Issues*, where she served as editor of the vascular access quarterly column. Ms Roberts declares that she has no relevant financial interests.

Surendra Shenoy, MD, PhD

Dr Shenoy is a Professor of Surgery and the Director of the Living Donor Transplantation Program at the Washington University School of Medicine in Saint Louis, Missouri. His clinical and research interests include liver, kidney, and living donor transplantation; liver; and dialysis access surgery. He serves on the Board of Directors and is the immediate past president of the Vascular Access Society of Americas (VASA). He is on the Editorial Board of the *Journal of Vascular Access* and serves as the VASA Editor for the Americas. Dr Shenoy was the Cochair for the working group that was tasked with describing appropriate endpoints for dialysis vascular access trials established by the Kidney Health Initiative of the American Society of Nephrology. He has been actively involved in several clinical research projects related to abdominal organ transplantation and vascular access for hemodialysis. He has published several innovative surgical techniques in the field of transplantation and vascular access. Dr Shenoy consulted for CR Bard, Inc, in 2016 and Bard Peripheral Vascular, Inc, in 2018 and received an honorarium from Getinge USA in 2019.

Tushar Vachharajani, MD

Dr Vachharajani is an Adjunct Professor in the Department of Medicine at the University of North Carolina, Chapel Hill and Chief of Nephrology and Medical Director of the Hemodialysis Program at the Salisbury Veterans Affairs Health Care System, North Carolina. Dr Vachharajani is an interventional nephrologist with international eminence who holds several leadership positions with International Society of Nephrology. He has published more than 70 peer-reviewed scientific papers and several book chapters, and he is an Associate Editor for the *Journal of Vascular Access* (American Society of Diagnostic and Interventional Nephrology [ASDIN]). He served as a Co-Lead on the Access Monitoring Work Group of Fistula First Breakthrough Initiative and as a Chair for the Medical Review Board of ESKD Network 6. He is passionate about training and improving global awareness of dialysis access care through various national and international professional organizations, including ISN, ASN, NKF, ASDIN, AVATAR, ISHD, and Kidney Education Foundation. Besides serving as a Cochair for the Interventional Nephrology Workshop at the World Congress of Nephrology in 2017 and 2019, he has helped organize vascular access symposiums, given scientific presentations, and conducted hands-on workshop in 15 different countries. Dr Vachharajani received the Gerald Beathard Award for Excellence in Teaching and Scholarly Activity from ASDIN. Dr Vachharajani served as a consultant for F. Hoffmann-La Roche AG in 2016.

Rudolph P. Valentini, MD

Dr Valentini is a Clinical Professor of Pediatrics at Wayne State University School of Medicine and the Chief Medical Officer for the Children's Hospital of Michigan (CHM). He served as the Director of Dialysis Services at CHM for 10 years before taking on his role as Chief Medical Officer. He has authored or coauthored a number of articles and book chapters on vascular access in the pediatric hemodialysis patient. This clinical passion has led to a near elimination of central venous catheters for delivery of chronic hemodialysis at his center. He has been an invited speaker at regional and national meetings to speak on the topic of the ideal vascular access choice for the pediatric hemodialysis patient. He was the American Society of Pediatric Nephrology representative and participant on the Center for Medicaid and Medicare Services Technical Expert Panel on Dialysis Vascular Access in 2015. He has also served as the pediatric representative on the Medical Review Committee for the Midwest Kidney Network (formerly Network 11) and was a longstanding member for the Midwest Pediatric Nephrology Consortium review committee. Dr Valentini has received royalties from *UpToDate* (2016 to the present) and World Scientific (2018).

Alexander S. Yevzlin, MD

Dr Yevzlin graduated magna cum laude from Dartmouth College. He did his residency in Internal Medicine at the University of Michigan and fellowship in Nephrology at Northwestern. Dr Yevzlin is currently Professor of Medicine and Director of Interventional Nephrology at the University of Michigan. He has presented and published more than 150 abstracts, invited lectures, and articles. He is an internationally recognized leader in the field of Interventional Nephrology, having edited the first 3 textbooks on the subject, and is a past President of the American Society of Diagnostic and Interventional Nephrology. In addition to his academic contributions, Dr Yevzlin has been involved the invention, design, and reduction to practice of multiple medical devices in his role as Chief Medical Officer, Chief Science Officer, and founder of multiple start-up biotech companies. Dr Yevzlin served as a consultant for AV Medical Technologies (2018), Covidien LP (2016-2018), Lutonix, Inc (2018), and Phraxis, Inc (2016-2018). He also receives interest from stocks in Phraxis, Inc (2016 to the present).

Evidence Review Team

Michelle Brasure, PhD, MSPH, MLIS, is Program Manager and Medical Librarian for the Minnesota Evidence-Based Practice Center. She has extensive experience leading multidisciplinary systematic review teams on a variety of topics. Dr. Brasure reported no relevant financial relationships.

Nancy Greer, PhD, is a senior research associate in the Minneapolis Center for Chronic Disease Outcomes Research and Program Manager for the Minneapolis VA Evidence-Synthesis Program. She has extensive experience in leading multidisciplinary teams in conducting evidence synthesis reports across a wide range of topics. Dr. Greer reported no relevant financial relationships.

Areef Ishani, MD, MS, is the Chief of the Primary Care Service Line at the Minneapolis VA Health Care System and a Professor of Medicine at the University of Minnesota. His primary research interests are in chronic kidney disease, acute kidney injury, and end-stage kidney disease. Dr Ishani reported no relevant financial relationships.

Roderick MacDonald, MS, is a senior research assistant in the Minneapolis VA Center for Chronic Disease Outcomes Research. He has nearly 20 years of experience in conducting systematic reviews across a wide range of topics. Mr MacDonald reported no relevant financial relationships.

Victoria Nelson, MSc, is a research fellow in the Minnesota Evidence-Based Practice Center. Her primary research interests are research methodology, evidence synthesis, health psychology, and behavior change. Ms Nelson reported no relevant financial relationships.

Carin Olson, MD, MS, is a systematic reviewer, medical editor and writer, and physician, working with the Minnesota Evidence-Based Practice Center at the University of Minnesota. Her interests include research methodology (especially relating to meta-analysis and publication bias), research ethics, injury prevention, and cardiopulmonary resuscitation. Dr Olson reported no relevant financial relationships.

Yelena Slinin, MD, MS, is a nephrologist at Kaiser Permanente in California. Her primary research interests are optimal medical care delivery and outcomes of patients with kidney disease, evidence-based medicine, and critical literature appraisal. Dr Slinin reported no relevant financial relationships.

Timothy J. Wilt, MD, MPH, is a Professor of Medicine at the University of Minnesota and Core Investigator in the Center for Chronic Disease Outcomes Research at the Veterans Affairs Medical Center in Minneapolis, Minnesota. He has a research agenda that involves conducting clinical trials, systematic reviews, and meta-analysis to evaluate the effects of health care interventions on outcomes in adults with chronic diseases. Dr Wilt reported no relevant financial relationships.

SUPPLEMENTARY MATERIAL

Supplement 1: Literature Search Strategy (PDF)
Supplement 2: ESKD Life-Plan: Patient-Physician Shared Documentation (PDF)
Supplement 3: Evidence Review Team Tables (PDF)
Supplement 4: Supplement to AV Access Infections (PDF)

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