Renal Failure in the Elderly

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Theodore H. Yuo and Mark L. Unruh

9.1 Introduction

Among the elderly, defined as those over 65 years of age, kidney disease is common with between 11% and 30% having chronic kidney disease (CKD) [1]. CKD has been associated with increased risk of death and disability as well as increased surgical risk. A proportion of those with CKD progress to end-stage renal disease (ESRD), at which point kidney replacement therapy is required to sustain life. Among elderly patients with CKD, the cause of kidney disease, severity of albuminuria and glomerular filtration rate (GFR) are associated with the likelihood of progression to acute and chronic kidney failure. Dialysis as a form of kidney replacement therapy for treatment of ESRD is a great triumph of modern medicine, saving lives and providing meaningful improvements in quality of life for many patients. When introduced on a wide scale in the 1970s, ESRD patients treated with dialysis through the Medicare entitlement program were typically young, carefully selected, and did not suffer from multiple other medical comorbidities [2]. Over time, though, the population undergoing kidney replacement has changed, and contemporary reports in the United States suggest that patients over 65 years of age are at least half of incident ESRD patients, with the very elderly, those over 80 years of age, representing a significant and growing fraction of the population [3]. Many elderly patients with ESRD have four or more chronic health conditions when they reach ESRD, and many are not considered candidates for kidney transplantation,

M.L. Unruh

T.H. Yuo, MD MSc (⊠)

Chair and Professor of Medicine, Department of Internal Medicine, University of New Mexico School of Medicine, Albuquerque, NM, USA

Assistant Professor of Surgery, Division of Vascular Surgery, Department of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA e-mail: yuoth@upmc.edu

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suggesting that dialysis will be the patient's kidney replacement therapy for the rest of their lives [4]. ESRD patients in general are fragile, with death rates 8–16 times higher than in the general population [5]. The general challenges of caring for elderly patients, compared to younger patients, have been well documented; these include generalized weakness, increased susceptibility to disease, inability to tolerate adverse environments or minor traumas, loss of agility, and age-related physiological changes in addition to attitudes and beliefs of older adults and their caregivers [6]. Further, within the traditional cohort of elderly patients defined as those over 65 years, there are distinctions between the "young elderly" between 65 and 80 years and the "very elderly" older than 80 years, in terms of comorbidities, frailty, dementia, and institutionalization status [7]. Despite these patient characteristics, dialysis access strategies for the elderly share many features with younger patients. This chapter aims to review the indications and potential modalities for renal replacement therapy (RRT) among the elderly with kidney failure. Further, RRT should be planned in a patient-centered fashion, accounting for patient anatomy, surgical history, medical comorbidities, and patient preferences. We will review the outcomes of vascular interventions in elderly ESRD patients and highlight approaches that may be used to attenuate the risk of contrast. Last, we will focus on individualizing decisions for the elderly with advanced CKD receiving either a dialysis access or other vascular procedures.

9.2 Indications for Renal Replacement Therapy

As in the population as a whole, the most common causes of ESRD in the elderly are diabetes and hypertension. Indications for RRT in the elderly are similar to those in younger patients. Historically, fluid overload and signs or symptoms of uremia, despite the poorly understood nature of the uremic syndrome and its somewhat subjective evaluation, were also considered to be indications for dialysis. As such, it is theoretically appealing to postulate that earlier initiation of RRT can remove these toxins and may be associated with decreased morbidity or mortality, as some observational studies suggested [8]. However, after correcting for lead-time bias, this advantage disappears [9]. The question of timing of initiation of hemodialysis (HD) was also explored in the Initiating Dialysis Early and Late (IDEAL) study, which randomized patients to early or late initiation of dialysis, based on estimated GFR (eGFR) [10]. Patients who started HD early at a target eGFR between 10 and 15 mL/min had similar survival and clinical outcomes as patients who started HD late at a target eGFR between 5 and 7 mL/min, or who started HD due to the development of symptoms associated with kidney failure including fluid overload or uremia. While elderly patients per se were not the target population for this study, the average age of participants in the study was 60 years and the overall findings did not differ between patients who were younger than 60 years and those who were older. Of note, there was substantial cross-over among those randomized to the delayed dialysis initiation so that nearly three-quarters of the group started dialysis at eGFR

above 7 mL/min. The degree of cross-over limited the inferences one could draw regarding the impact of delayed start on patient outcomes.

Other authors have noted that assessing kidney function in elderly patients is difficult since the serum creatinine level can be spuriously low due to falling muscle mass, despite steadily declining eGFR as patients age. Further clouding the clinical picture, symptoms associated with uremia are nonspecific, and include anorexia, weight loss, weakness, nausea, and difficulties with sleep and cognition [11].

Given this background, a trial of dialysis in elderly patients may be considered in selected patients who have been well informed of the possible risks and benefits of dialysis, and can cooperate with the treatment and can receive it safely. Recent guidelines published by the Renal Physicians Association (RPA) offer recommendations that incorporate patient preferences and prognostic survival assessments to help guide physicians and patients in the decision-making process [12]. Indications for trials of dialysis include uremia or worsening of congestive heart failure, refractory to maximal medical management. In cases of acute kidney injury, as opposed to chronic kidney disease, when there is a possibility of reversibility of acute kidney failure, dialysis should be offered. Further, patients with atypical presentations of ESRD should be evaluated for treatable causes of kidney failure regardless of patient age. Occasionally, there can be the worry that this attempt at acute treatment may transition inappropriately to a long-term commitment to dialysis. However, while elderly survivors of AKI seem to require more time for total recovery and recover function less completely, they can recover function and generally deserve a trial of dialysis [11]. Ultimately, though, as well described in recent guidelines, "The initiation of dialysis therapy remains a decision informed by clinical art, as well as by science...." [13]

9.2.1 Choice of Dialysis Modality: Hemodialysis (HD) Versus Peritoneal Dialysis (PD)

As in younger patients, the choice of dialysis as kidney replacement therapy in the elderly is influenced by the availability of infrastructure and staff, the burden of comorbidities, specific anatomic contraindications to a particular modality, patient and caregiver ability to adhere to the requirements of the chosen modality, and patient or physician preference. Possible advantages of PD over HD in the elderly include preservation of residual kidney function, avoidance of fluid and electrolyte shifts, more liberal diet, avoidance of vascular access, and decreased transportation time, since this is typically a home modality. On the other hand, HD may be a better choice for patients with hernias, diverticulitis, history of abdominal surgery or other intra-abdominal pathology, morbid obesity, or psychosocial inability to adhere to PD requirements. The requirement for bulky and heavy dialysate consumables is another consideration, which may represent an unanticipated difficulty for elderly patients with limited storage space and physical strength; the employment of home-care assistants may overcome these challenges [14].

Peritoneal dialysis is in general used less frequently than hemodialysis, with approximately 9% of the prevalent US dialysis population using peritoneal dialysis and the balance using hemodialysis. In the elderly, defined as those over 65 years, PD is used even less frequently, with only 7% of the population using PD, though this fraction is growing [15].

There is controversy regarding the possible survival advantage of one modality over the other in elderly patients. In general, there appears to be a benefit to using PD instead of HD initially, but this benefit appears to be lost over time. This has historically been attributed to slower loss of residual kidney function in patients on PD, but more recent analyses have suggested that this effect is overstated and may be due to selection bias [16] or the use of tunneled dialysis catheters (TDCs) in HD patients [17]. In one prospective cohort study of 174 elderly patients older than 70 years in the United Kingdom, the annual mortality and hospitalization rates in PD and HD patients were similar (26.1 vs. 26.4 deaths per 100 person-years and 1.9 vs. 2.0 admissions per person-year, respectively) [18]. Contrary to the reports in younger patients, Windelmayer and colleagues found 16% higher mortality rates for elderly patients that start on PD compared to HD in the first 90 days after dialysis initiation. Mortality rates between 91 and 180 days were equivalent, but were 45% higher after 181 days. This effect was particularly pronounced in those with diabetes [19]. A larger study from Korea with longer follow-up also demonstrated higher mortality in elderly patients started with PD, as compared to patients started with HD, with PD being associated with a 20% higher hazard of mortality. An accompanying meta-analysis again suggested higher mortality with PD, though the magnitude of the increased hazard was only about 10%, but still statistically significant [20]. The possibility of increased mortality rates with PD in elderly patients must be considered and balanced against any possible benefits.

9.3 Selection of Hemodialysis Access: AVF Versus AVG Versus TDC in the Elderly

9.3.1 Kidney Disease Outcome Quality Initiative (KDOQI) Guidelines

The current Kidney Disease Outcome Quality Initiative (KDOQI) guidelines, last updated in 2006, state that patients should have a functional permanent access at the initiation of dialysis therapy. The KDOQI guidelines suggest that a working fistula should have the following characteristics, sometimes called the "Rule of 6s": blood flow adequate to support dialysis (generally greater than 600 mL/min); a diameter greater than 6 mm, with location accessible for cannulation and discernible margins to allow for repetitive cannulation; and a depth of approximately 6 mm [13]. Accordingly, patients should be referred for arteriovenous fistula (AVF) creation at least 6 months before the start of HD. This is in preference to AV grafts (AVG) due to a belief that AVF are superior to AVG due to improved survival, lower costs, better patency, and reduced risk of infection or other complications. This time frame is

suggested to allow for both initial access evaluation as well as additional time for revision to ensure that a working fistula is available at initiation of dialysis therapy [13]. Of note, this recommendation is based on expert opinion; a recent metaanalysis was unable to identify any studies that compared early to late referral for access creation [21].

An additional challenge is accurately predicting when dialysis will need to be initiated [22]. A liberal policy of early surgical referral provides more opportunities for successful access creation and can reduce the likelihood of starting HD with a tunneled dialysis catheter (TDC). This is an important consideration in the elderly, who have a lower rate of maturation compared to younger patients [23]. However, this may also be associated with a higher rate of unused AVF due to unexpectedly slow kidney function decline or competing mortality [24]. One study in the United States Department of Veterans Affairs system focused on patients with GFR less than 25 mL/min. In this group, 25% initiated HD over the ensuing year, while a far lower percentage of elderly patients received permanent access. The majority of elderly CKD patients survived without requiring dialysis, and many died before initiating dialysis [25]. A decision analysis model suggests a GFR threshold of 15-20 mL/min; though due to competing mortality risks, later referral at a lower GFR level would be appropriate for elderly patients [26]. Similarly, another resource suggests using a GFR threshold of 20 mL/min at which point a patient should be referred for AV fistula creation [27]. Ongoing work to establish clinically valid prediction rules for the progression to ESRD may help to individualize the approach to access placement.

Compared to AVF creation, AVG placement is considered to be the second best option in patients that have not yet started hemodialysis, but is better than initiating HD through TDC, according to the KDOQI guidelines. This ranking appears to be valid in the elderly, and is supported by data from analysis of data from administrative databases and the US Renal Data system (USRDS) [28, 29]. There is a concern, though, that successful maturation of an AVF may be a marker of overall improved medical status, and not of an effect of the access type [30, 31]. This selection bias may lead to an overestimate of the benefit of AVF over AVG [32]. More recent analyses that account for the influence of selection suggest that AVF and AVG may be equivalent in certain populations, especially the elderly [33–35].

Finally, dialysis through a TDC is considered inferior to both AVF and AVG due to the tendency for patients receiving HD through TDC to suffer increased rates of mortality, infection, and hospitalization compared to patients receiving AVF or AVG [36]. Further, catheters are associated with less efficient dialysis, the development of central venous stenosis, and an increased number of procedures required to maintain a functioning vascular access, leading to increased expense [37, 38]. This dynamic has also been demonstrated in the elderly [34]. The reasons for this increase in adverse outcomes in TDC patients have been postulated to be related to increased risks for catheter-related septicemia and also sterile inflammation even in the absence of infection [39].

The medical rationale for trying to avoid catheters is clear; however, from the patient's perspective, TDC has the distinct advantage of being in many ways the

least invasive procedure, as it does not require surgery, a maturation period, or being cannulated thrice weekly with large-gauge needles, as AVF and AVG require [40]. This is especially relevant for elderly patients who may be struggling with multiple other medical challenges [41].

9.3.2 Transitioning Patients from TDC to an Internal Access

Despite KDOQI's goal of 50% AVF as a patient's incident vascular access, in 2010 approximately 80% of patients initiated HD through TDC, with approximately 16% started through AVF, and the balance through AVG. This distribution has remained largely unchanged since 2005, and is also seen among elderly patients [42]. Particularly in the elderly, the challenge of facilitating a transition from catheters to an internal access is complicated by the heavier burden of medical comorbidities that this patient population suffers. Extended TDC dependence after HD initiation is more likely to occur in elderly patients and may be related to longer time to maturation, increased need for secondary procedures, and higher primary failure rates [43].

Because of the known disadvantages of prolonged TDC dependence, AVG placement may be more attractive than AVF creation due to higher maturation rates and shorter time to maturation, leading to earlier TDC removal. However, these advantages need to be balanced against more frequent use of secondary procedures to maintain patency, as demonstrated in one study using administrative data from the USRDS [44]. In the elderly, who have short life expectancy, the longer-term risks of AVG use, including infection, limited primary patency, and potentially higher rates of ischemic steal syndrome, may not be as relevant as for younger patients. Recently, analytic tools to predict mortality rates among ESRD patients on HD have been developed, which may assist clinicians with tailoring vascular access options to particular patient needs [45]. As such, further research is necessary in order to better characterize the role of AVF and AVG, and determine the relative trade-offs, and whether different recommendations should exist based on patient age and preference.

9.3.3 Outcomes of Vascular Interventions in Elderly ESRD Patients

9.3.3.1 General Considerations

Both end-stage kidney disease and increasing age are well-known risk factors after many vascular surgical interventions, including repair of infrarenal abdominal aortic aneurysms (AAAs), carotid artery stenting (CAS) and carotid endarterectomy (CEA), and treatments for lower extremity arterial insufficiency [46–48].

Regardless of the presence of ESRD or advanced age, patients with symptomatic or ruptured aortic aneurysms are nearly always managed with either endovascular or open surgical intervention [49]. In these cases, although the perioperative risks are heightened due to the presence of ESRD and elderly status, the alternative of observation and medical management frequently leads to free rupture and death.

Similarly, symptomatic 50–99% stenosis of the extracranial internal carotid artery is usually treated, with some considerations for medical comorbidities and advanced age. Carotid endarterectomy (CEA) is generally the first option, and is preferred in the elderly, with carotid artery stenting (CAS) being reserved for patients with challenging anatomy or with severe cardiac or pulmonary comorbidities [47].

However, the majority of patients undergoing interventions for abdominal aortic aneurysms and extracranial carotid artery occlusive disease are asymptomatic, and in this population, the increased perioperative risk associated with ESRD and elderly status suggests that observation and medical management can sometimes be appropriate.

9.3.3.2 Asymptomatic, Intact Abdominal Aortic Aneurysms

In general, asymptomatic, intact abdominal aortic aneurysms larger than 5.5 cm should be considered for elective repair. At smaller diameters, the long-term benefit of early repair appears to be outweighed by the perioperative risk. At diameters between 4.0 and 5.4 cm, the UK Small Aneurysm Trial showed that compared to observation, early open surgical repair offered no long-term benefit in survival, while also subjecting patients to approximately 6.8% increased risk of mortality in the first 6 months after randomization [50]. Endovascular abdominal aortic aneurysm repair (EVAR) is associated with lower perioperative risks, leading some to suggest that repair at smaller sizes may be appropriate [51]. On the other hand, more recent publications suggest that patients with overall poor life expectancy and those that cannot safely tolerate a minimally invasive procedure should not undergo AAA repair, though the pre-operative identification of these patients can be difficult [52].

Elderly patients with ESRD over age 65 at HD initiation certainly suffer from abbreviated life expectancy, with a median survival of less than 2 years. Among patients who underwent AAA repair, an analysis of the United States Renal Data System (USRDS) found 1557 patients, 261 who had undergone open surgical repair and 1296 who had undergone EVAR between 2005 and 2008. The 30-day mortality after EVAR was lower than after open aortic repair (OAR) (10.3% vs. 16.1%). This perioperative survival advantage associated with EVAR was quickly lost; survival estimates were similar at 66.5% at 1 year (EVAR, 66.2%; OAR, 68%) and 37.4% at 3 years (EVAR, 36.8%; OAR, 40.0%). Median survival was 25.3 months after EVAR and 27.4 months after OAR [53].

Of note, current European Society for Vascular Surgery clinical practice guidelines state that AAA patients who undergo repair should have life expectancy of at least 3 years, which is longer than the median survival of patients who underwent AAA repair in the USRDS [54]. Meanwhile, American College of Cardiology Foundation/American Heart Association guidelines articulate a life expectancy of 2 years [55]. Ideally, criteria can be developed to assist with selecting patients with the necessary life expectancy, but in the absence of extenuating

clinical circumstances, delaying prophylactic repair of asymptomatic AAAs in elderly ESRD patients until the AAAs reach a fairly large size threshold may be an appropriate strategy.

9.3.3.3 Asymptomatic Carotid Artery Occlusive Disease

In asymptomatic patients with 60–99% stenosis of an extracranial carotid artery, the benefit of carotid revascularization in asymptomatic patients can confer durable reduction in the risk of stroke, but this is dependent on excellent surgical technique. Perioperative stroke and death rates need to be less than 3%. However, it is also predicated on the patient's life expectancy, particularly in asymptomatic patients who are only expected to derive the full preventive advantages if they anticipate a life expectancy of at least 3 years [47]. This life expectancy may not be realized in patients with multiple medical comorbidities, particularly elderly patients with ESRD [41]. Although such patients have been shown to have potentially acceptable perioperative outcomes after CEA, long-term survival is poor, leading to calls for a conservative, nonoperative approach to the management of asymptomatic carotid disease for this population [56].

The development of CAS has been presented as an alternative to CEA for certain high-risk patients. Current guidelines define "high risk" as patients with medical risk factors, principally cardiac and pulmonary comorbidities, in addition to challenging anatomy like a high carotid bifurcation, the presence of a tracheal stoma, or extensive scar tissue due to radiation therapy or previous surgery [47]. In the Carotid Revascularization Endarterectomy Versus Stenting Trial, CAS appeared to be associated with lower rates of post-operative cardiac complications, but higher rates of stroke [57]. As such, the use of CAS as opposed to CEA or medical management in asymptomatic patients is still controversial, with specialty guidelines offering varying recommendations [58]. Society for Vascular Surgery guidelines recommend that CAS be reserved for high-risk patients with symptomatic carotid artery stenosis. Asymptomatic patients are best managed with CEA or medical management if they are at high risk for open surgery or if they have limited life expectancy [47].

For a patient with asymptomatic carotid artery stenosis, the relationship between perioperative risk, life expectancy, and the ongoing risk reduction after a successful intervention was recently described mathematically. The investigators of this decision analysis created a generalized model, identifying a critical life expectancy that was a function of perioperative complication rates and the absolute risk reduction that could be expected after successful surgery. As applied to patients with ESRD who have a short life expectancy, in order for either CEA or CAS to be superior to medical management, the intervention would need to be associated with either very low periprocedural complication rates or have very high absolute risk reduction [59].

These challenges were highlighted in a recent analysis of USRDS data, which focused on asymptomatic patients who underwent CEA and CAS. In this study, 2131 asymptomatic patients underwent carotid revascularization (1805 CEA, 326 CAS). Perioperative combined stroke or death rate was similar at 10.1% after CEA and 10.9% after CAS. Median survival after surgery was approximately 2.0 years

for CAS and 2.5 years for CEA. Age over 70 years at the time of surgery was predictive of mortality in multivariate Cox proportional hazards modeling. While the rates of stroke with medical therapy alone could not be ascertained in the study, the remarkably short survival after both CEA and CAS is sobering, and is clearly lower than the 3-year guidance offered in contemporary guidelines [60]. As with intact, asymptomatic aortic aneurysm disease, criteria can be developed to assist with selecting asymptomatic, elderly ESRD patients for carotid revascularization. However, in the absence of extenuating clinical circumstances, medical management may be preferable in this population.

9.3.3.4 Lower Extremity Peripheral Arterial Occlusive Disease

Lower extremity peripheral arterial occlusive disease is more prevalent in patients with ESRD, compared to the general population, with rates of approximately 25% in two large prospective studies, in addition to significantly higher rates of cardio-vascular morbidity and mortality [61]. Patients with ESRD who undergo lower extremity revascularization are more likely to suffer post-operative morbidity and mortality compared to patients with normal kidney function [62]. An analysis of the Dialysis Mortality and Morbidity Study in the USRDS showed post-operative mortality rates of 12.6% and 7.5% for bypass and angioplasty, respectively [63].

Given these challenging results, some authors have questioned whether lower extremity revascularization is worthwhile in patients with ESRD [64]. The countervailing concern, though, is the fate of the patient in whom limb salvage is unsuccessful. In an analysis of Medicare data from the 1990s, the rate of amputation was 6.2 per 100 person-years. Further, two-thirds died two years post-operatively after an amputation [65]. Clearly, while outcomes after lower extremity revascularization are challenging, amputation is associated with adverse health outcomes, as well.

In general, both endovascular techniques and open surgical revascularization can be used for limb salvage. In the Bypass versus Angioplasty In Severe Ischaemia of the Leg (BASIL) trial, which was a randomized controlled trial (RCT) that compared a balloon-angioplasty-first strategy versus bypass-surgery-first strategy, outcomes in terms of amputation-free survival were broadly similar, though balloon angioplasty was associated with lower costs [66]. However, among patients who survived at least 2 years, bypass surgery was associated with improved survival, leading to the suggestion that bypass surgery should be offered to patients who could be expected to survive at least 2 years [67]. In order to assist with patient selection, a survival model based on BASIL data was created. Elderly status and impaired kidney function were among the most important predictors of mortality [68]. Extending these findings to the elderly ESRD population with symptomatic peripheral arterial disease would suggest that an endovascular-first strategy that spares the patient some perioperative morbidity may be preferable due to the relatively short survival we expect in this patient population.

9.4 Strategies to Prevent Contrast Nephropathy

Contrast-induced acute kidney injury (CI-AKI) has been defined as an acute decrease in kidney function after intravascular administration of an iodinated contrast medium. The change in kidney function manifests as an increase in serum creatinine level of 25% or 50% relative to baseline, or an absolute change in serum creatinine level of 0.5 mg/dL within 2–5 days [69]. Pre-existing renal functional impairment is likely the most important risk factor for developing CI-AKI and the elderly, many with multiple medical comorbidities including diabetes, are certainly at high risk of chronic kidney failure [70].

A single-institution patient series reviewed outcomes after percutaneous coronary interventions. In their analysis of 8357 patients, hypotension, intra-aortic balloon pump, congestive heart failure, chronic kidney disease, diabetes, age greater than 75 years, anemia, and volume of contrast used were identified as risk factors for the development of CI-AKI [71]. While clearly an unmodifiable risk factor, advanced age needs to be recognized as a marker for increased risk of CI-AKI, and appropriate precautions taken to prevent AKI [72].

The mechanism for CI-AKI is not well defined, and is thought to be associated with a combination of renal vasoconstriction, acute tubular necrosis, reactive oxygen species production, and possibly direct toxicity on renal tubular cells. Regardless, the osmolality of the contrast agent appears to be a key modifiable risk factor, and there have been multiple efforts to create nonionic contrast agents, in addition to reducing their osmolality [73]. A recent meta-analysis of 25 trials demonstrated that CI-AKI after intra-arterial injection of contrast was less frequent with use of the iso-osmolar agent iodixanol (Visipaque), as compared to nonionic low-osmolar agents [74]. Iso-osmolar nonionic agents like iodixanol typically have osmolality of 290–320 mOsm, while low-osmolar nonionic agents like iohexol (Omnipaque) and iopamidol (Isovue) have osmolality around 600 mOsm. Finally, the osmolality of older, high osmolar ionic agents like iothalamate (Conray) is around 1600 mOsm; these agents are rarely used in contemporary practice.

The use of pre-exposure volume expansion is widely accepted. Guidelines published by the Kidney Diseases Improving Global Outcomes (KDIGO) initiative recognize the danger of volume depletion in patients who are already at elevated risk of AKI, like the elderly. The use of intravenous volume expansion with isotonic sodium chloride solution or sodium bicarbonate solutions is recommended over using hypotonic sodium chloride solutions, no intravenous volume expansion, or oral hydration alone [75].

N-acetylcysteine (NAC) is related to the amino acid cysteine and acts as a freeradical scavenger, producing antioxidant and vasodilatory effects. It has been studied as a prophylactic agent against CI-AKI in multiple observational and randomized studies with conflicting results [75, 76]. The results of ten randomized controlled trials were recently reviewed in a meta-analysis, which demonstrated that the combination of N-acetylcysteine (NAC) and sodium bicarbonate isotonic solutions reduced the occurrence of CI-AKI overall but not dialysis-dependent kidney failure. While the effect of NAC is not seen consistently across available studies, oral NAC is inexpensive and relatively safe. As such, current specialty guidelines offer cautious endorsement of the use of oral NAC in addition to isotonic intravenous volume expansion in order to prevent CI-AKI [69, 75].

Several investigator teams have studied prophylactic intermittent hemodialysis (IHD) for contrast-media removal. One major RCT demonstrated a benefit from prophylactic hemodialysis in patients with pre-existing chronic kidney disease. This study randomized 82 patients to normal saline intravascular fluid expansion either with or without a 4 h session of hemodialysis immediately after coronary angiography. Baseline creatinine was 4.9 mg/dL in both groups. Patients randomized to HD were noted to have lower peak serum creatinine levels (6.7 mg/dL vs. 5.3 mg/dL), less need for temporary kidney replacement therapy (35% vs. 2%), and lower need for long-term dialysis after discharge (13% vs. 0%) [76, 77]. Multiple authors have challenged the study's conclusions due to the small sample size and the fact that the renal outcome of serum creatinine concentration was directly impacted by the study intervention of prophylactic hemodialysis. Furthermore, the majority of the studies that have been published have not found any benefit from prophylactic kidney replacement therapy. A recent meta-analysis demonstrated that prophylactic HD held no advantages over standard medical therapy in terms of need for permanent kidney replacement therapy or progression to ESRD. In fact, HD appeared to actually increase the risk of CI-AKI [78].

There are other ungraded recommendations from KDIGO that are particularly relevant to the elderly population.

- Clinicians should assess kidney function in order to identify patients with preexisting, but perhaps underappreciated, chronic kidney disease.
- Alternative imaging methods in patients at increased risk of CI-AKI should be considered.
- The lowest possible dose of contrast medium should be employed in patients at risk of CI-AKI.

The KDIGO recommendations are summarized in Table 9.1.

9.4.1 Considerations for Individualizing Care of Older Patients with ESRD

Dialysis dependence is associated with marked reduction in health-related quality of life (HRQoL) compared to age-matched controls, a finding seen in both North American and international populations [79]. Cross sectional studies have suggested that peritoneal dialysis is associated with improved HRQoL compared to hemodialysis in the general population [80]. While this finding suggests that peritoneal dialysis may be the preferred modality for many patients, it may be related to selection bias, and in any case is difficult to apply to the elderly population, who frequently have difficulty adhering to the self-care requirements. Further, any initial advantage in HRQoL may not be sustained; an observational study focused on

Recommendation	Strength of recommendation
Assess the risk of CI-AKI and, in particular, screen for pre-existing impairment of kidney function in all patients who are considered for a procedure that requires intravascular (i.v. or i.a.) administration of iodinated contrast medium	Not graded
Consider alternative imaging methods in patients at increased risk of CI-AKI	Not graded
Use the lowest possible dose of contrast medium in patients at risk of CI-AKI	Not graded
We recommend using either iso-osmolar or low-osmolar iodinated contrast media, rather than high-osmolar iodinated contrast media in patients at increased risk of CI-AKI	1B
We recommend i.v. volume expansion with either isotonic sodium chloride or sodium bicarbonate solutions, rather than no i.v. volume expansion, in patients at increased risk of CI-AKI	1A
We recommend not using oral fluids alone in patients at increased risk of CI-AKI	1C
We suggest using oral NAC, together with i.v. isotonic crystalloids, in patients at increased risk of CI-AKI	2D
We suggest not using theophylline to prevent CI-AKI	2C
We recommend not using fenoldopam to prevent CI-AKI	1B
We suggest not using prophylactic intermittent hemodialysis (IHD) or hemofiltration (HF) for contrast-media removal in patients at increased risk of CI-AKI	2C

Table 9.1 KDIGO clinical practice guideline for acute kidney injury management associated with radiocontrast administration

Grading scale:

Level 1: "strong"

Level 2: "weak" or discretionary

Quality of supporting evidence: A (high), B (moderate), C (low), or D (very low)

elderly patients found that while initial HRQoL was higher in the PD population, this advantage was not evident at 6 and 12 months after dialysis initiation [18].

For hemodialysis patients, in particular, the causes for reductions in quality of life are likely multifactorial. Pain and depressive symptoms can drive lower mental health scores, and also lead to shortened hemodialysis treatments, increased utilization of emergency services, and hospitalizations [81]. In the recently published Frequent Hemodialysis Network trial, 245 patients were randomized to standard thrice weekly dialysis or a more frequent schedule of dialysis six times per week, with shorter daily sessions. The more frequent schedule was associated with improved self-reported general mental health, although depression scores were not significantly different. Possible mechanisms for this finding include better small molecule clearance, better volume management, reduced inflammation, and more convenient timing of dialysis [82].

Another issue to consider is the impact on caregivers. This is particularly relevant for peritoneal dialysis patients due to the significant home-care that is required. In one observational study of 201 elderly patients, the caregivers for 84 hemodialysis patients were compared to 40 peritoneal dialysis patients, who were both compared to a control group of caregivers of 77 non-elderly hemodialysis patients. Caregivers of peritoneal dialysis patients scored significantly lower on the mental component of the SF-36 than caregivers of hemodialysis patients. The authors hypothesized that this may be related to the challenges of repetitive dialysis exchanges and other medical responsibilities; these can be onerous and lead to feelings of anxiety, stress, resentment, and guilt [83].

While there have been multiple studies investigating the difference in HRQoL between PD and HD, the HRQoL related to hemodialysis access (i.e., AVF vs. AVG vs. TDC) has not been studied as extensively. The existing measures, including the CHOICE Health Experience Questionnaire (CHEQ) and Kidney Disease Quality of Life (KDQOL), have only a handful of broad questions exploring dialysis access type [84, 85]. More recently, the short-form vascular access questionnaire (SF-VAQ) was developed. This is a validated questionnaire evaluating patient satisfaction in a Canadian setting associated with HD access type. HD through an AVF was associated with the highest overall satisfaction, followed by TDC, with AVG having the lowest scores. Interestingly, the study determined that while AVF scored well in terms of outcomes like concerns around hospitalization and bathing, TDC was preferred when it came to physical complaints like pain, bleeding, swelling, and bruising [86].

Recently, quality of life considerations have been explicitly referenced in contemporary guidelines for the management of patients with ESRD [87]. However, there may still be tension between what might be recommended in guidelines and what an individual patient may find preferable, especially in the elderly [88].

Guidelines for ESRD patients often present a uniform approach to management, prioritizing interventions to reduce mortality and manage disease complications. The overall goal is to provide a simplified pathway to guide management rather than address complex issues that may develop for individual patients. Many ESRD patients have multiple comorbid conditions, which can generate conflicting treatment recommendations [89]. In older patients, an individualized approach that considers competing sources of morbidity and mortality can inform clinical decisions. Clinicians, in conjunction with patients and caregivers, can prioritize patient-centered outcomes, even if these outcomes may not be easily explained by a well-described disease process [90].

Key Points

- With regard to management of vascular surgery issues in the elderly patient with renal failure, most recommendations are similar to those for younger patients. However, current guidelines often present a uniform approach to management, whereas older patients with ESRD may benefit from a more individualized approach due to heavy burden of comorbidities and shortened life expectancy.
- Both hemodialysis (HD) and peritoneal dialysis (PD) are reasonable renal replacement therapies in elderly patients with likely similar long-term outcomes, though PD requires significantly more patient resources and can be difficult for elderly patients and their caregivers to implement.

- In patients receiving HD, both arteriovenous fistulas (AVF) and arteriovenous grafts (AVG) are clearly superior to tunneled dialysis catheters as access modalities. AVF are likely superior to AVG, when they mature, but lengthy AVF maturation time can lead to prolonged TDC dependence. In elderly patients, the long-term benefits of AVF need to be balanced against the effects of prolonged TDC dependence on patients with already shortened life expectancy.
- Repair of asymptomatic, intact abdominal aortic aneurysms in elderly patients with renal failure is associated with poor perioperative and long-term outcomes. Delaying surgical intervention, especially in patients with difficult anatomy requiring open repair, may be reasonable in many cases.
- Medical management is the first choice in asymptomatic elderly patients with carotid artery occlusive disease and dialysis dependence. In well-selected patients with good life expectancy and severe extracranial carotid stenosis, carotid endarterectomy (CEA) is reasonable. The role of carotid artery stenting (CAS) in asymptomatic renal failure patients is unclear, and patients with clinical characteristics that make CEA difficult, and hence favor CAS, are likely best served with medical management alone.

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References

- Wiggins J. Why do we need a geriatric nephrology curriculum? Chapter 2. In: American Society of Nephrology Geriatric Nephrology Curriculum. 2009. https://www.asn-online.org/ education/distancelearning/curricula/geriatrics/. Accessed 10 Aug 2015.
- Stevens LA, Weiner DE, Brown WW. The geriatric dialysis patient, chapter 32. In: Henrich W, editor. Principles and practice of dialysis. 4th ed. Philadelphia: Lippincott, Williams & Wilkins; 2009. p. 536–55.
- O'Hare AM, Bowling CB, Tamura MK. Kidney disease in the elderly. In: Gilbert W, editor. National Kidney Foundation primer on kidney diseases. 6th ed. Philadelphia: Elsevier; 2013. p. 437–45.
- Singh P, Germain MJ, Cohen L, Unruh M. The elderly patient on dialysis: geriatric considerations. Nephrol Dial Transplant. 2014;29(5):990–6.
- de Jager DJ, Grootendorst DC, Jager KJ, van Dijk PC, Tomas LM, Ansell D, Collart F, Finne P, Heaf JG, De Meester J, Wetzels JF, Rosendaal FR, Dekker FW. Cardiovascular and noncardiovascular mortality among patients starting dialysis. JAMA. 2009;302(16):1782–9.
- Kane RL, Ouslander JG, Abrass IB, Resnick B. Chapter 1. Clinical implications of the aging process. In: Kane RL, Ouslander JG, Abrass IB, Resnick B, editors. Essentials of clinical geriatrics. 7th ed. New York: McGraw-Hill; 2013.
- Kurella M, Covinsky KE, Collins AJ, Chertow GM. Octogenarians and nonagenarians starting dialysis in the United States. Ann Intern Med. 2007;146(3):177–83.
- Fink JC, Burdick RA, Kurth SJ, Blahut SA, Armistead NC, Turner MS, Shickle LM, Light PD. Significance of serum creatinine values in new end-stage renal disease patients. Am J Kidney Dis. 1999;34(4):694–701.
- Traynor JP, Simpson K, Geddes CC, Deighan CJ, Fox JG. Early initiation of dialysis fails to prolong survival in patients with end-stage renal failure. J Am Soc Nephrol. 2002;13(8): 2125–32.

- Cooper BA, Branley P, Bulfone L, Collins JF, Craig JC, Fraenkel MB, Harris A, Johnson DW, Kesselhut J, Li JJ, Luxton G, Pilmore A, Tiller DJ, Harris DC, Pollock CA; IDEAL Study. A randomized, controlled trial of early versus late initiation of dialysis. N Engl J Med. 2010;363(7):609–19.
- Stevens LA, Weiner DE, Brown WW. The geriatric dialysis patient. In: Henrich W, editor. Principles and practice of dialysis. 4th ed. Philadelphia: Lippincott, Williams & Wilkins; 2009. p. 536–55.
- 12. Guideline recommendations and their rationales for the treatment of adult patients. In: Renal Physicians Association (RPA). Shared decision-making in the appropriate initiation of withdrawal from dialysis. 2nd ed. Rockville: Renal Physicians Association (RPA); 2010. p. 39–92.
- National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations for 2006 updates: hemodialysis adequacy, peritoneal dialysis adequacy and vascular access. Am J Kidney Dis. 2006;48(suppl 1):S1–S322.
- 14. Ho-dac-Pannekeet MM. PD in the elderly a challenge for the (pre)dialysis team. Nephrol Dial Transplant. 2006;21(Suppl 2):ii60–2.
- 15. United States Renal Data System, 2014 annual data report: epidemiology of kidney disease in the United States. Bethesda: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2014.
- Quinn RR, Hux JE, Oliver MJ, Austin PC, Tonelli M, Laupacis A. Selection bias explains apparent differential mortality between dialysis modalities. J Am Soc Nephrol. 2011;22(8): 1534–42.
- Perl J, Wald R, McFarlane P, Bargman JM, Vonesh E, Na Y, Jassal SV, Moist L. Hemodialysis vascular access modifies the association between dialysis modality and survival. J Am Soc Nephrol. 2011;22(6):1113–21.
- Harris SA, Lamping DL, Brown EA, Constantinovici N; North Thames Dialysis Study (NTDS) Group. Clinical outcomes and quality of life in elderly patients on peritoneal dialysis versus hemodialysis. Perit Dial Int. 2002;22(4):463–70.
- Winkelmayer WC, Glynn RJ, Mittleman MA, Levin R, Pliskin JS, Avorn J. Comparing mortality of elderly patients on hemodialysis versus peritoneal dialysis: a propensity score approach. J Am Soc Nephrol. 2002;13(9):2353–62.
- Han SS, Park JY, Kang S, Kim KH, Ryu DR, Kim H, Joo KW, Lim CS, Kim YS, Kim DK. Dialysis modality and mortality in the elderly: a meta-analysis. Clin J Am Soc Nephrol. 2015;10(6):983–93.
- Murad MH, Sidawy AN, Elamin MB, Rizvi AZ, Flynn DN, McCausland FR, McGrath MM, Vo DH, El-Zoghby Z, Casey ET, Duncan AA, Tracz MJ, Erwin PJ, Montori VM. Timing of referral for vascular access placement: a systematic review. J Vasc Surg. 2008;48(5 Suppl):31S–3S.
- Green D, Ritchie JP, New DI, Kalra PA. How accurately do nephrologists predict the need for dialysis within one year? Nephron Clin Pract. 2012;122(3–4):102–6.
- 23. Lok CE, Oliver MJ, Su J, Bhola C, Hannigan N, Jassal SV. Arteriovenous fistula outcomes in the era of the elderly dialysis population. Kidney Int. 2005;67(6):2462–9.
- 24. Tamura MK, Tan JC, O'Hare AM. Optimizing renal replacement therapy in older adults: a framework for making individualized decisions. Kidney Int. 2012;82(3):261–9.
- 25. O'Hare AM, Bertenthal D, Walter LC, Garg AX, Covinsky K, Kaufman JS, Rodriguez RA, Allon M. When to refer patients with chronic kidney disease for vascular access surgery: should age be a consideration? Kidney Int. 2007;71(6):555–61.
- Shechter SM, Skandari MR, Zalunardo N. Timing of arteriovenous fistula creation in patients with CKD: a decision analysis. Am J Kidney Dis. 2014;63(1):95–103.
- Hakim RM. Hemodialysis. In: Gilbert W, editor. National Kidney Foundation primer on kidney diseases. 6th ed. Philadelphia: Elsevier; 2013. p. 437–45.
- Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF, Port FK. Type of vascular access and mortality in U.S. hemodialysis patients. Kidney Int. 2001;60(4):1443–51.
- Xue JL, Dahl D, Ebben JP, Collins AJ. The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. Am J Kidney Dis. 2003;42(5):1013–9.

- Murad MH, Elamin MB, Sidawy AN, Malaga G, Rizvi AZ, Flynn DN, Casey ET, McCausland FR, McGrath MM, Vo DH, El-Zoghby Z, Duncan AA, Tracz MJ, Erwin PJ, Montori VM. Autogenous versus prosthetic vascular access for hemodialysis: a systematic review and meta-analysis. J Vasc Surg. 2008;48(5 Suppl):34S–47S.
- Quinn RR, Ravani P. Fistula-first and catheter-last: fading certainties and growing doubts. Nephrol Dial Transplant. 2014;29(4):727–30.
- Lee T, Barker J, Allon M. Comparison of survival of upper arm arteriovenous fistulas and grafts after failed forearm fistula. J Am Soc Nephrol. 2007;18(6):1936–41.
- Chan MR, Sanchez RJ, Young HN, Yevzlin AS. Vascular access outcomes in the elderly hemodialysis population: a USRDS study. Semin Dial. 2007;20(6):606–10.
- 34. DeSilva RN, Patibandla BK, Vin Y, Narra A, Chawla V, Brown RS, Goldfarb-Rumyantzev AS. Fistula first is not always the best strategy for the elderly. J Am Soc Nephrol. 2013;24(8): 1297–304.
- 35. Yuo TH, Chaer RA, Dillavou ED, Leers SA, Makaroun MS. Patients started on hemodialysis with tunneled dialysis catheter have similar survival after arteriovenous fistula and arteriovenous graft creation. J Vasc Surg. 2015;62(6):1590–7.e2.
- 36. Rehman R, Schmidt RJ, Moss AH. Ethical and legal obligation to avoid long-term tunneled catheter access. Clin J Am Soc Nephrol. 2009;4(2):456–60.
- 37. Lee H, Manns B, Taub K, Ghali WA, Dean S, Johnson D, Donaldson C. Cost analysis of ongoing care of patients with end-stage renal disease: the impact of dialysis modality and dialysis access. Am J Kidney Dis. 2002;40(3):611–22.
- Eggers P, Milam R. Trends in vascular access procedures and expenditures in Medicare's ESRD program. In: Henry ML, editor. Vascular access for hemodialysis-VII. Chicago: Gore; 2001. p. 133–43.
- Kaysen GA. Biochemistry and biomarkers of inflamed patients: why look, what to assess. Clin J Am Soc Nephrol. 2009;4(Suppl 1):S56–63.
- 40. Dinwiddie LC, Ball L, Brouwer D, Doss-McQuitty S, Holland J. What nephrologists need to know about vascular access cannulation. Semin Dial. 2013;26(3):315–22.
- 41. Wright S, Danziger J. Vascular access for hemodialysis in the elderly. Chapter 21. In: American Society of Nephrology Geriatric Nephrology Curriculum. 2009. https://www.asn-online.org/ education/distancelearning/curricula/geriatrics/. Accessed 10 Aug 2015.
- 42. Lok CE, Foley R. Vascular access morbidity and mortality: trends of the last decade. Clin J Am Soc Nephrol. 2013;8(7):1213–9.
- 43. Wasse H, Speckman RA, Frankenfield DL, Rocco MV, McClellan WM. Predictors of delayed transition from central venous catheter use to permanent vascular access among ESRD patients. Am J Kidney Dis. 2007;49(2):276–83.
- 44. Leake AE, Yuo TH, Wu T, Fish L, Dillavou ED, Chaer RA, Leers SA, Makaroun MS. Arteriovenous grafts are associated with earlier catheter removal and fewer catheter days in the United States renal data system population. J Vasc Surg. 2015;62(1):123–7.
- 45. Floege J, Gillespie IA, Kronenberg F, Anker SD, Gioni I, Richards S, Pisoni RL, Robinson BM, Marcelli D, Froissart M, Eckardt KU. Development and validation of a predictive mortality risk score from a European hemodialysis cohort. Kidney Int. 2015;87(5):996–1008.
- 46. Patterson BO, Holt PJ, Hinchliffe R, Loftus IM, Thompson MM. Predicting risk in elective abdominal aortic aneurysm repair: a systematic review of current evidence. Eur J Vasc Endovasc Surg. 2008;36(6):637–45.
- 47. Ricotta JJ, Aburahma A, Ascher E, Eskandari M, Faries P, Lal BK; Society for Vascular Surgery. Updated society for vascular surgery guidelines for management of extracranial carotid disease. J Vasc Surg. 2011;54(3):e1–31.
- Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG; TASC II Working Group. Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg. 2007;45(Suppl S):S5–67.
- 49. Chaikof EL, Brewster DC, Dalman RL, Makaroun MS, Illig KA, Sicard GA, Timaran CH, Upchurch Jr GR, Veith FJ; Society for Vascular Surgery. The care of patients with an abdomi-

nal aortic aneurysm: the Society for Vascular Surgery practice guidelines. J Vasc Surg. 2009;50(4 Suppl):S2-49.

- The UK Small Aneurysm Trial Participants. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. Lancet. 1998;352(9141):1649–55.
- Finlayson SR, Birkmeyer JD, Fillinger MF, Cronenwett JL. Should endovascular surgery lower the threshold for repair of abdominal aortic aneurysms? J Vasc Surg. 1999;29:973–85.
- Fillinger MF. Chapter 127 Abdominal aortic aneurysms: evaluation and decision making. In: Rutherford's Vascular Surgery. 7th ed. Philadelphia: Elsevier; 2010.
- Yuo TH, Sidaoui J, Marone LK, Avgerinos ED, Makaroun MS, Chaer RA. Limited survival in dialysis patients undergoing intact abdominal aortic aneurysm repair. J Vasc Surg. 2014;60(4):908–13.e1.
- Moll FL, Powell JT, Fraedrich G, Verzini F, Haulon S, Waltham M, et al. European Society for Vascular Surgery. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. Eur J Vasc Endovasc Surg. 2011;41(Suppl 1):S1–58.
- 55. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, et al.; Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society for Vascular Medicine, Society for Vascular Surgery. 2011 ACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2011;58(19):2020–4.
- 56. Ascher E, Marks NA, Schutzer RW, Hingorani AP. Carotid endarterectomy in patients with chronic renal insufficiency: a recent series of 184 cases. J Vasc Surg. 2005;41(1):24–9.
- 57. Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W, Mackey A, Hill MD, Leimgruber PP, Sheffet AJ, Howard VJ, Moore WS, Voeks JH, Hopkins LN, Cutlip DE, Cohen DJ, Popma JJ, Ferguson RD, Cohen SN, Blackshear JL, Silver FL, Mohr JP, Lal BK, Meschia JF; CREST Investigators. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med. 2010;363(1):11–23.
- Brott TG, Halperin JL, Abbara S, et al. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/ CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease. Circulation. 2011;124(4):e54–e130.
- Yuo TH, Roberts MS, Braithwaite RS, Chang CC, Kraemer KL. Applying the payoff time framework to carotid artery disease management. Med Decis Mak. 2013;33(8):1039–50.
- Yuo TH, Sidaoui J, Marone LK, Makaroun MS, Chaer RA. Revascularization of asymptomatic carotid stenosis is not appropriate in patients on dialysis. J Vasc Surg. 2015;61(3):670–4.
- O'Hare A, Johansen K. Lower-extremity peripheral arterial disease among patients with endstage renal disease. J Am Soc Nephrol. 2001;12(12):2838–47.
- 62. O'Hare AM, Feinglass J, Sidawy AN, Bacchetti P, Rodriguez RA, Daley J, Khuri S, Henderson WG, Johansen KL. Impact of renal insufficiency on short-term morbidity and mortality after lower extremity revascularization: data from the Department of Veterans Affairs' National Surgical Quality Improvement Program. J Am Soc Nephrol. 2003;14(5):1287–95.
- Jaar BG, Astor BC, Berns JS, Powe NR. Predictors of amputation and survival following lower extremity revascularization in hemodialysis patients. Kidney Int. 2004;65(2):613–20.
- Korn P, Hoenig SJ, Skillman JJ, Kent KC. Is lower extremity revascularization worthwhile in patients with end-stage renal disease? Surgery. 2000;128(3):472–9.
- Eggers PW, Gohdes D, Pugh J. Nontraumatic lower extremity amputations in the Medicare end-stage renal disease population. Kidney Int. 1999;56(4):1524–33.
- 66. Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, Fowkes FG, Gillepsie I, Ruckley CV, Raab G, Storkey H; BASIL Trial Participants. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366(9501):1925–34.
- 67. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, Ruckley CV, Raab GM; BASIL Trial Participants. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: an intention-to-treat analysis of amputation-free and overall survival in patients random-

ized to a bypass surgery-first or a balloon angioplasty-first revascularization strategy. J Vasc Surg. 2010;51(5 Suppl):5S–17S.

- 68. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, Ruckley CV, Raab GM; BASIL Trial Participants. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: a survival prediction model to facilitate clinical decision making. J Vasc Surg. 2010;51(5 Suppl):52S–68S.
- 69. Palevsky PM, Liu KD, Brophy PD, Chawla LS, Parikh CR, Thakar CV, Tolwani AJ, Waikar SS, Weisbord SD. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. Am J Kidney Dis. 2013;61(5):649–72.
- Mehran R, Nikolsky E. Contrast-induced nephropathy: definition, epidemiology, and patients at risk. Kidney Int Suppl. 2006;69:S11–5.
- Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, Leon MB, Dangas G. A simple risk score for prediction of contrastinduced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol. 2004;44(7):1393–9.
- Detrenis S, Meschi M, Bertolini L, Savazzi G. Contrast medium administration in the elderly patient: is advancing age an independent risk factor for contrast nephropathy after angiographic procedures? J Vasc Interv Radiol. 2007;18(2):177–85.
- Rudnick MR, Goldfarb S, Wexler L, Ludbrook PA, Murphy MJ, Halpern EF, Hill JA, Winniford M, Cohen MB, VanFossen DB. Nephrotoxicity of ionic and nonionic contrast media in 1196 patients: a randomized trial. The iohexol cooperative study. Kidney Int. 1995;47(1):254–61.
- Heinrich MC, H
 H
 iberle L, M
 iller V, Bautz W, Uder M. Nephrotoxicity of iso-osmolar iodixanol compared with nonionic low-osmolar contrast media: meta-analysis of randomized controlled trials. Radiology. 2009;250(1):68–86.
- 75. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SL, Herzog CA, Joannidis M, Kribben A, Levey AS, MacLeod AM, Mehta RL, Murray PT, Naicker S. Opal SM, Schaefer F, Schetz M, Uchino S. Kidney disease: Improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl (2011). 2012;2(1):6.
- Fishbane S, Durham JH, Marzo K, Rudnick M. N-acetylcysteine in the prevention of radiocontrast-induced nephropathy. J Am Soc Nephrol. 2004;15(2):251–60.
- 77. Lee PT, Chou KJ, Liu CP, Mar GY, Chen CL, Hsu CY, Fang HC, Chung HM. Renal protection for coronary angiography in advanced renal failure patients by prophylactic hemodialysis. A randomized controlled trial. J Am Coll Cardiol. 2007;50(11):1015–20.
- Cruz DN, Goh CY, Marenzi G, Corradi V, Ronco C, Perazella MA. Renal replacement therapies for prevention of radiocontrast-induced nephropathy: a systematic review. Am J Med. 2012;125(1):66–78.e3.
- 79. Fukuhara S, Lopes AA, Bragg-Gresham JL, Kurokawa K, Mapes DL, Akizawa T, Bommer J, Canaud BJ, Port FK, Held PJ; Worldwide Dialysis Outcomes and Practice Patterns Study. Health-related quality of life among dialysis patients on three continents: the Dialysis Outcomes and Practice Patterns Study. Kidney Int. 2003;64(5):1903–10.
- Rubin HR, Fink NE, Plantinga LC, Sadler JH, Kliger AS, Powe NR. Patient ratings of dialysis care with peritoneal dialysis vs hemodialysis. JAMA. 2004;291(6):697–703.
- Weisbord SD, Mor MK, Sevick MA, Shields AM, Rollman BL, Palevsky PM, Arnold RM, Green JA, Fine MJ. Associations of depressive symptoms and pain with dialysis adherence, health resource utilization, and mortality in patients receiving chronic hemodialysis. Clin J Am Soc Nephrol. 2014;9(9):1594–602.
- 82. Unruh ML, Larive B, Chertow GM, Eggers PW, Garg AX, Gassman J, Tarallo M, Finkelstein FO, Kimmel PL; FHN Trials Group. Effects of 6-times-weekly versus 3-times-weekly hemodialysis on depressive symptoms and self-reported mental health: Frequent Hemodialysis Network (FHN) trials. Am J Kidney Dis. 2013;61(5):748–58.
- Belasco A, Barbosa D, Bettencourt AR, Diccini S, Sesso R. Quality of life of family caregivers of elderly patients on hemodialysis and peritoneal dialysis. Am J Kidney Dis. 2006;48(6):955–63.

- 84. Wu AW, Fink NE, Cagney KA, Bass EB, Rubin HR, Meyer KB, Sadler JH, Powe NR. Developing a health-related quality-of-life measure for end-stage renal disease: the CHOICE health experience questionnaire. Am J Kidney Dis. 2001;37(1):11–21.
- Hays RD, Kallich JD, Mapes DL, et al. Kidney Disease Quality of Life Short Form (KDQOL-SF), version 1.3: a manual for use and scoring. 1997. http://www.rand.org/content/ dam/rand/pubs/papers/2006/P7994.pdf. Accessed 16 Aug 2015.
- Kosa SD, Bhola C, Lok CE. Measuring patient satisfaction with vascular access: vascular access questionnaire development and reliability testing. J Vasc Access. 2015;16(3):200–5.
- 87. Davison SN, Levin A, Moss AH, Jha V, Brown EA, Brennan F, Murtagh FE, Naicker S, Germain MJ, O'Donoghue DJ, Morton RL, Obrador GT. Executive summary of the KDIGO controversies conference on supportive Care in Chronic Kidney Disease: developing a road-map to improving quality care. Kidney Int. 2015;88:457–9.
- Tamura MK, Tan JC, O'Hare AM. Optimizing renal replacement therapy in older adults: a framework for making individualized decisions. Kidney Int. 2012;82(3):261–9.
- Singh P, Germain MJ, Cohen L, Unruh M. The elderly patient on dialysis: geriatric considerations. Nephrol Dial Transplant. 2014;29(5):990–6.
- O'Hare AM, Bowling CB, Tamura MK. Chapter 51. Kidney disease in the elderly. In: S. Gilbert, D.E. Weiner (Eds.), National Kidney Foundation primer on kidney diseases. 6th ed. Elsevier; 2014. Saunders