Considerations in the optimal preparation of patients for dialysis

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Abstract | Every year, more than 110,000 Americans are newly diagnosed with end-stage renal disease and in the overwhelming majority, maintenance dialysis therapy is initiated. However, most patients, having received no predialysis nephrology care or dietary counseling, are inadequately prepared for starting treatment; furthermore, the majority of patients do not have a functioning permanent dialysis access. Annualized mortality in the USA in the first 3 months after starting dialysis treatment is approximately 45%; this high rate is possibly in part due to inadequate preparation for renal replacement therapy. Data from the Dialysis Outcomes and Practice Patterns study suggest that similar challenges exist in many parts of the world. Implementation of strategies that mitigate the risk of adverse consequences when starting dialysis are urgently needed. In this Review we present a step-by-step approach to tackling inadequate patient preparation, which includes identifying individuals with chronic kidney disease (CKD) who are most likely to need dialysis in the future, referring patients for education, timely placement of dialysis access and timely initiation of dialysis therapy. Treatment with dialysis might not be appropriate for some patients with progressive CKD; these individuals can be optimally managed with nondialytic, maximum conservative management.

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Introduction

In 2008, more than 110,000 Americans were started on maintenance dialysis, a life-saving therapy for patients with end-stage renal disease (ESRD).[1] Ideally, when patients begin renal replacement therapy (RRT), they should meet the following conditions: firstly, they should not require hospitalization for the management of untreated acute or chronic complications of uremia; secondly, they should have a thorough understanding of the different treatment options; and thirdly, they should have a functioning, permanent access for the dialysis therapy of their choice.[2]

There is concern that a sizable proportion of patients in the USA are not adequately prepared for initiating dialysis therapy. In 2008, 44% of patients received no predialysis nephrology care and only 25% had received ongoing care by a nephrologist for more than 12 months prior to initiating dialysis.[1] Despite the critical importance of lifestyle management (and the fact that reimbursement is available for such counseling in the USA), fewer than 10% of patients receive dietary counseling prior to starting dialysis.[1] Furthermore, substantial numbers of patients newly diagnosed with ESRD are not offered alternatives to in-center hemodialysis (such as home dialysis or pre-emptive transplantation), even in the absence of medical contraindications.[3,4] More than 80% of patients in the USA initiate hemodialysis therapy with a central venous catheter (CVC); this type of access is associated with significantly higher rates of infectious complications, as well as more long-term non-infectious complications compared with a permanent vascular access.[1,5–7] Inadequate preparation for dialysis in the USA can only partially be accounted for by delayed referral to nephrology specialists; however, as a considerable number of patients who have received more than 1 year of specialist care prior to initiating dialysis are also inadequately prepared for this treatment.[1] In 2006, the annualized mortality in the first 3 months of starting dialysis for patients in the USA was approximately 45%, which was in part due to inadequate preparation of the patient for RRT.[8]

The available data on dialysis preparation practices outside the USA are limited. Findings from studies performed in the 1980s and 1990s indicate a high rate of delayed referrals to a nephrologist in Europe, and contemporary data from Canada also demonstrate a high incidence of suboptimal dialysis initiation.[9–12] Analyses from the Dialysis Outcomes and Practice Patterns Study (DOPPS) further highlight the international scope of this challenge.[13] One in five patients starting hemodialysis

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Key points

- A large gap exists in care in transitioning patients with chronic kidney disease (CKD) to renal replacement therapy; a step-by-step approach is proposed to bridge this gap in care
- Demographic and clinical criteria can help identify those individuals with CKD who would benefit from early preparation for renal replacement therapy
- Iterative multidisciplinary patient education is the first step in preparing patients for dialysis and should offer decision support for selection of dialysis modality or maximum conservative care
- Dialysis access should be placed sufficiently early to preclude the need for central venous catheters
- The decision of when to start dialysis should be individualized based on uremic symptoms and/or the appearance of complications but should not be delayed until patient becomes too sick

in DOPPS-participating countries (USA, Canada, UK, Belgium, Sweden, Germany, France, Spain, Italy, Japan, Australia and New Zealand) first see a nephrologist within 1 month of requiring dialysis.[13] Additionally, over one-half of patients in the UK, Sweden, Belgium and Canada start hemodialysis treatment with a CVC.[5] As such, a high prevalence of suboptimal initiation of dialysis treatment is not unique to the USA.

In this Review we discuss the challenges associated with preparing patients for dialysis therapy and present a practical step-by-step approach to help bridge the gap in care and reduce the high mortality seen in the first few months of starting dialysis (Figure 1). In concert with continued efforts to slow disease progression and delay dialysis, the measures discussed in this Review should be implemented at appropriate times during the course of chronic kidney disease (CKD). The outlined approach is targeted primarily at practicing nephrologists although individual components might be relevant to other specialists providing care to patients with CKD (such as internists, family practitioners, endocrinologists and geriatricians). Discussion of other areas of care in patients with CKD and ESRD (such as the management of high-risk pathology including diabetes mellitus and hypertension, treatment of anemia and provision of vaccinations, and social support), although of importance, are beyond the scope of the Review.

Step one: identify patients for RRT

Renal replacement therapy

An estimated 13% of adults in the USA have CKD, and approximately 700,000 have stage 4 CKD (glomerular filtration rate [GFR] 15–29 ml/min/1.73 m^2).[14] Long-term follow-up of population-based cohorts suggests that many individuals with CKD are unlikely to exhibit sufficient progressive decline in renal function to require dialysis. Over a 5-year follow-up of members of the Kaiser Permanente Northwest Division (a large, non-profit, group-model health maintenance organization, which provided comprehensive, prepaid medical coverage to approximately one-fifth of the population of a US city), only 17% of patients with stage 4 CKD required dialysis but, notably, 45% of patients had died before requiring dialysis.[15] In contrast to the findings from this unselected cohort, in a study involving 4,231 Canadian

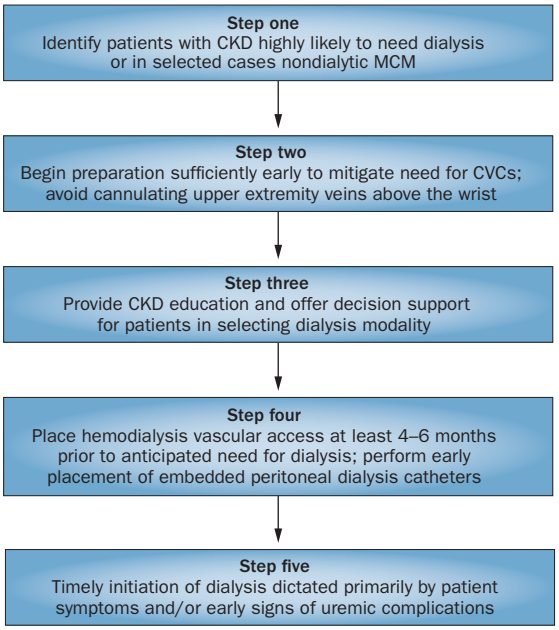

Figure 1 | A proposed step-by-step approach to help prepare patients for dialysis. Abbreviations: CKD, chronic kidney disease; CVCs, central venous catheters; MCM, maximum conservative management.

patients with stage 4 CKD who had been selected because they had been referred to nephrologists, only 7% of study participants died before needing dialysis, but 24% of patients were found to require dialysis support.[16] These data suggest that targeting all patients who have CKD with an estimated GFR (eGFR) below a certain threshold (<30 ml/min/1.73 m^2) for RRT preparation might be inappropriate. Instead, focusing on individuals who have at least one additional characteristic associated with a high probability of reaching ESRD, in addition to a low eGFR, would better identify those who would benefit from preparation for future dialysis (Box 1).

With advancing age, the likelihood of dying prior to initiating dialysis far exceeds the likelihood of starting dialysis therapy. In a US population of veterans with CKD and a mean eGFR of 18 ml/min/1.73 m^2 at cohort entry, 67% of those aged 18–44 years initiated dialysis within 2 years and 22% died during this time. By contrast, in the group of patients who were 85 years of age or older only 17% had initiated dialysis within 2 years, but 41% of this age group died during this time.[17] If all study participants had begun preparation for dialysis at cohort entry, the ratio of unnecessary to necessary dialysis access surgery would have been 0.5:1 for the group of patients aged 18–44 years, but 5:1 for those aged 85 years and older. Similar results have been demonstrated in several other cohort studies.[18–20] Patient age should, therefore, be an important consideration when deciding whether to begin preparation for RRT. Indeed, many elderly patients have stable reductions in eGFR and, in our opinion, only those individuals with progressive loss of renal function should be referred for planning RRT.

Increasing albuminuria within each eGFR strata for CKD stages 1–5 is associated with a substantial increase

in the risk of requirement for future dialysis.[21,22] Routine measurement of the albumin–creatinine ratio on spot urine samples could help physicians identify individuals with reduced eGFR who are more likely to have progressive CKD and, therefore, require referral to prepare for future RRT. Analyses of large patient cohorts also consistently identify high blood pressure, high levels of serum phosphorus, and/or low hemoglobin levels, as additional predictors of future dialysis requirement.[16,19]

No single characteristic can reliably identify which individuals with advanced CKD are likely to progress to ESRD. It is important, therefore, that at every clinical encounter physicians consider each patient with advanced CKD with respect to the discussed characteristics using demographic, clinical and laboratory information (Box 1), and ensure that preparation for RRT begins sufficiently early for individuals likely to reach ESRD. Moreover, all patients with advanced CKD could benefit from patient education tailored to each individual's probability of dialysis need in the future.

Box 1 | Characteristics associated with progression to ESRD

- Young age
- Decline in renal function over time
- Presence of albuminuria
- Presence of underlying primary renal disease (such as diabetic nephropathy, renovascular disease, or primary glomerular diseases)
- High blood pressure
- Development of CKD complications (such as increased serum phosphorus and/or decline in hemoglobin levels)

Abbreviations: CKD, chronic kidney disease; ESRD, end-stage renal disease.

Box 2 | Key elements of nondialytic maximum conservative management

- Interventions to slow rate of decline of native renal function
- Dietary counseling to prevent hyperkalemia
- Diuretics for management of hypervolemia
- Correct anemia to manage symptomatic fatigue and prevent blood transfusions
- Phosphate binders to relieve symptoms associated with hyperphosphatemia
- Referral for hospice care, if appropriate

Nondialytic maximum conservative management

Although dialysis prolongs the lives of many individuals with ESRD, the burden of RRT might not justify the potential benefits of treatment in certain patients, such as the elderly.[23] However, as illustrated by the North Thames Dialysis Study, judgment on the appropriateness for RRT should not depend solely upon chronological age but should instead be based on a composite assessment of the health and functional status of the individual.[24] Results from studies suggest that there are subgroups of patients who have a low likelihood of benefiting from dialysis therapies.[25–27] For example, initiating dialysis does not reverse the progressive decline in functional status of nursing home residents; rather, the decline in functional status seemingly accelerates after dialysis initation.[25] For certain individuals with advanced CKD, nondialytic, maximum conservative management (MCM) might, therefore, be superior to initiating dialysis;[26] this suggestion highlights the importance of considering the appropriateness of dialysis for individuals with CKD early in the disease course. Assessment of disease management requires shared decision-making between patients, their family members, and the treating physicians.[27]

Most of the data on the principles of management and outcomes of patients with advanced CKD who elect to have MCM are derived from the UK.[26,28,29] In most of the published studies to date, the life expectancy of patients with advanced CKD who choose MCM is shorter than that of patients with matching characteristics who choose RRT; the median life expectancy of patients with stage 5 CKD who forgo RRT has been reported to range from 14 months to 23 months.[20,26,28,29] However, the primary goal of care in patients who opt for MCM should be focused on symptom management to enhance quality of life and ensure patient comfort (Box 2).[26,30]

In selected individuals, maximizing renoprotective therapies can be an important component of MCM. Traditionally, renin–angiotensin–aldosterone system (RAAS) blockade has been used to slow CKD progression; however this intervention might be limited by hyperkalemia in individuals with advanced CKD. Furthermore, findings from a UK study demonstrated that discontinuing angiotensin-converting-enzyme (ACE) inhibitors and/or angiotensin-receptor blockers (ARBs) in patients with advanced CKD was associated with a significant increase in eGFR.[31] For these reasons, continued use of ACE inhibitors or ARBs should be periodically re-evaluated in individuals who choose MCM and, in fact, discontinuing drugs from these classes might facilitate patient management.

Additional dietary interventions can be considered in certain patients who elect MCM. These interventions include: low-protein diets (0.6–0.8 g/kg daily); ketoanalog-supplemented very-low-protein diets; or nutritional supplements with low amounts of protein, phosphorus, and potassium.[32–34] A vegetarian diet might serve as another adjunct as it provides reduced amounts of protein and less digestible phosphorus, for example phytate-based phosphorus.[35] However, dietary restrictions can be onerous and should be considered on an individual case-by-case basis. Correction of metabolic acidosis can also slow the decline in renal function.[36] Other therapies are in development that may slow the decline of renal function, for example drugs that adsorb uremic toxins (such as indoxyl sulfate and oral antioxidants) and anti-inflammatory modulators (such as bardoxolone methyl).[37–39] Some patients who choose MCM might benefit from referral for hospice care, which can be provided either in the patient's home or at a hospice facility.

Step two: begin preparation for RRT

Preparation for RRT should begin early enough in the course of CKD to allow time for patients to consider different treatment options and to establish a permanent functioning access for the dialysis modality of choice. If pre-emptive living donor kidney transplantation is appropriate, the patient should undergo the procedure before they need temporary dialysis to minimize

morbidity resulting from dialysis access. In addition, allowing adequate time for patients to consider their options enables individuals who would be appropriate for MCM to consider this option as well. However, preemptive transplantation is uncommon, and limited evidence suggests that when given a choice most patients choose to have dialysis rather than MCM.[1,26] As such, the overwhelming majority of individuals who reach ESRD are likely to require maintenance dialysis and appropriate preparation should be incorporated early in their management plan.

In determining how early to begin preparation of patients for dialysis, it is useful to consider that in our experience it can take 1–3 months of iterative CKD education for patients to accept potential need for RRT, and also to decide which therapy best meets their expectations and fits their lifestyle. Sufficient time should also be allocated for placement and maturation of dialysis access. The mean time for arteriovenous fistula maturation for patients in the USA is approximately 3 months, although shorter times (of approximately 1 month) have been reported in Europe and Japan.[40] Moreover, a substantial proportion of new fistulae fail to achieve suitability for dialysis treatment; therefore, the first vascular access should be placed sufficiently early to allow enough time to either revise the initial access, or for a second access to be placed and mature prior to initiation of dialysis.[31,32] In our opinion, therefore, preparation for RRT should begin about 9–12 months prior to the anticipated dialysis need. Of note, CKD progression rates can change over time making it challenging to precisely anticipate the need for dialysis.[41] In our opinion, it follows that education about CKD, dialysis therapies, dialysis access, and MCM should be initiated in individuals with an eGFR 20–30 ml/min/1.73 m^2. Furthermore, in our opinion a vascular access should be placed in patients with an eGFR 15–20 ml/min/1.73 m^2, in whom progression to ESRD seems likely.

As most patients are likely to require hemodialysis at some stage of their disease, preservation of veins is a critical aspect of advanced planning. Most patients undergoing hemodialysis will require several arteriovenous fistulae or grafts in both upper extremities. To prevent the loss of available veins for dialysis access, cannulation of veins above the wrist in either upper extremity should be avoided.[42] Every effort should be made to limit phlebotomy and intravenous catheters to veins in the hand. Peripherally inserted central catheters (commonly known as PICC lines) are particularly problematic as they can cause thrombosis of the upper arm veins in up to 38% of patients precluding future vascular access in the entire ipsilateral upper extremity;[43] avoiding these catheters in patients with CKD from early in the disease course is, therefore, of paramount importance.

Step three: CKD education

Although a paucity of clinical trials exists, a preponderance of other evidence demonstrates tangible benefits of CKD education.[44–50] Early patient education in those with CKD is shown to be highly effective when focused on health promotion, shared decision-making, and discussion of treatment options.[45] In the only randomized, controlled trial on patient education that we are aware of, a one-on-one educational session followed by phone calls every 3 weeks significantly extended the time to requiring dialysis.[47] *Post hoc* analyses from this clinical trial, as well as findings from other observational studies, demonstrate a variety of additional benefits from patient education, including the following: reduced patient anxiety; delay in dialysis need; reduced number of hospitalizations; reduced numbers of emergency room and physician visits; increased likelihood that the patient will remain employed in work and be more adherent to therapy; and reduced mortality.[46,48,49] Furthermore, results from several studies have demonstrated a substantially reduced need for CVCs following patient education.[49,50] Consequently, it is important to maximize these benefits by engaging patients in CKD education prior to planning dialysis access placement (Table 1).

Patient education involves messengers, messages, receivers and a process. Before patient education can begin, the physician must initiate the discussion of what is often called breaking the bad news.[40,41] Patients do not want insensitive truth-telling but prefer for the truth to be told with support to assist them in decision-making.[51] It is estimated that it takes an average of five encounters before individuals actually understand the message; therefore, patient education on CKD should be iterative.[52] The initial message should be delivered in a private room that is free of interruptions, and preferably when the patient has a supportive friend or relative with them.[52–54] Communication of the bad news should be followed by formal CKD education, for which reimbursement is now available in the USA for Medicare beneficiaries.[55]

The curriculum for predialysis education should include psychosocial aspects and coping skills.[56] Components of successful CKD education programs have also included individualized and ongoing education throughout the course of the disease, tours of dialysis facilities, meeting patients who are undergoing treatment with different dialysis modalities, use of videos and written materials, and behavior-changing protocols with small-group problem-solving activities.[46,57,58] These and other strategies can be incorporated into any CKD education program (Table 1). The educator needs to possess skills in patient communication and to understand the nature of the patient's barriers to receiving the information.

Presenting treatment options to the patient is a major undertaking for the educator, and offering decision support is an important goal of successful CKD education. There is a large variability in the uptake of home dialysis options (peritoneal dialysis or hemodialysis) between centers, regions, and different countries.[1] Data from the USA indicate that the low uptake of peritoneal dialysis in the country does not reflect patient choice but is instead more often a reflection of the choice not being offered to patients by health-care providers.[3,4,59] Findings from numerous surveys show that most patients have no medical or psychosocial contraindications to in-center

Table 1 | An approach to developing a successful CKD education program

Core aspects	Details
Program initiation	Begin early in the course of CKD (eGFR <30 ml/min/1.73 m^2) but also involve all late-referred patients including those who have recently started dialysis with no prior nephrology care
Program leader	Designated CKD Educator*, preferably assisted by a dietitian and social worker
Target audience	Patients and their family members and/or care-givers; one-on-one or in a class setting
Program content	Discussion of CKD and interpretation of tests of kidney function; complications of CKD; interventions to slow loss of kidney function; importance of preserving upper extremity veins for future dialysis access; different options for dialysis and their impact on the individual's lifestyle; renal transplantation; dietary changes necessitated by disease state; timing of placement of dialysis access; insurance coverage and other financial considerations; advance directives
Frequency	Generally 3–6 sessions required
Use community resources	Involve current or former dialysis and transplant patients; include tours of dialysis facilities
Offer decision support	Help patients choose the dialysis modality that best fits their lifestyle and overcome fears of dialysis; discussion of treatment options should include home dialysis and nondialytic maximum conservative care

*The Medicare program in the USA offers reimbursement for CKD education if provided by a physician, nurse practitioner, physician assistant, or certified nurse specialist.[102] Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

or home dialysis.[3,60–63] Moreover, results from recent studies indicate that the 4-year, 5-year, and 10-year survival rates of patients treated with in-center hemodialysis are equivalent to survival rates with peritoneal dialysis.[64] Accordingly, for the vast majority of patients with CKD, decisions about dialysis modality should be based on what fits best with their lifestyle—a decision which individuals and their families must make for themselves.[65] Widespread, comprehensive CKD education will also empower patients to assume responsibility for their dialysis care, thereby increasing the uptake of home dialysis options. Expansion of home dialysis therapy is likely to be safe as the equivalency of outcomes of home peritoneal dialysis with in-center hemodialysis are maintained even when much larger proportions of patients are treated with the former therapy.[64] This therapy is also potentially more cost-effective given the lower societal costs for providing peritoneal dialysis, compared with in-center hemodialysis, in many countries.[66]

The discussion about treatment options should begin with open-ended questions and can be followed by introducing the two choices available to patients, dialysis or MCM. If the patient's preference is for dialysis, the choice of home dialysis versus in-center dialysis should be discussed next. Notably, fear and/or lack of knowledge of home dialysis has been shown to dissuade many patients from selecting this option.[67] One of the goals of patient education should be to offer patient support and help overcome such fear. Logical decision-making can be enhanced if the patient completes a 4-part grid listing their perceived advantages and disadvantages of dialysis therapies. Regular contact between the educator and the patient over the weeks to months after starting education is important in the process of decision-making. However, it is should be noted that the patient's choice of dialysis modality is simply the treatment with which they begin RRT, as many patients will actually transition between different therapies (for example, changing dialysis modalities, or from dialysis to transplantation and possibly back to dialysis again).

Step four: timely dialysis access

Hemodialysis

Patients who have made an initial decision to have hemodialysis can be referred for timely placement of a permanent vascular access (arteriovenous fistula or graft) to minimize use of CVCs. CVCs are often used as a bridge to a permanent vascular access, either because the patient starts dialysis without a mature fistula or graft, or because an existing permanent access has failed. CVCs are easy to place and can be used immediately for hemodialysis, but they are prone to causing recurrent bacteremia and thrombosis, and can also lead to central vein stenosis.[6,7]

Each type of vascular access has advantages and disadvantages. Fistulae have a high likelihood of failing to mature (20–60%), and 1–4 months is often required after their creation before fistulae can be cannulated.[68,69] Nevertheless, once the fistula matures it can last for many years with relatively few interventions.[68] Arteriovenous grafts have a lower early failure rate than do fistulae (10–20%), and can usually be cannulated for dialysis within 2–3 weeks of placement; however, grafts only last for an average of 2–3 years and require more frequent interventions to maintain long-term patency than do fistulae.[69] A mature fistula is, therefore, the preferred access type.[42] Advanced planning is required to ensure that patients have mature fistulae suitable for hemodialysis prior to the need for treatment. To achieve this goal, predialysis surgical creation of a permanent vascular access needs to be sufficiently early in the course of CKD to allow for potential surgical or percutaneous interventions to promote maturation of immature fistulae.[69] In addition, preoperative vascular mapping will assist the surgeon in planning the optimal site for vascular access placement.[70]

In the past 10 years, the importance of patient-specific factors in planning placement of vascular access has become increasingly recognized.[71] In certain patient subpopulations, there might be a subset of patients in whom a graft is a superior choice.[72] For example, in patients who have initiated dialysis prior to vascular access placement, failure of a fistula would result in prolonged CVC

dependence along with the complications associated with CVC use. Furthermore, if the patient is elderly with limited life expectancy, a compelling case might be made in favor of graft placement over a fistula creation.[73] The case for graft placement is stronger still if the patient has had a previous fistula that failed to mature.

Peritoneal dialysis

In patients who choose peritoneal dialysis, the considerations regarding access are somewhat different. The optimal interval between catheter placement and the start of peritoneal dialysis is approximately 2 weeks (known as the break-in period), which allows sufficient time for the catheter track to heal and minimizes the chance of a leak when dialysate is instilled in the peritoneal cavity.[74] However, placing the peritoneal dialysis catheter long before the need for dialysis would necessitate training the patient to perform daily catheter care, which is generally not possible outside of established peritoneal dialysis programs. Consequently, surgery for placement of a peritoneal dialysis catheter is generally deferred until the need for dialysis is imminent. Given the challenges in precisely timing the need for dialysis and in obtaining operating room access at short notice, many patients who have committed to peritoneal dialysis instead begin hemodialysis with a CVC. However, peritoneal dialysis catheters can be placed at any stage during the course of the disease—if a patient chooses to commit to the therapy and to preclude the need for prolonged catheter care prior to the start of dialysis, the external limb of the catheter can be embedded in the subcutaneous tissue.[75,76] The external limb can then be externalized in a physician's office and full-dose peritoneal dialysis can begin on the same day.[75]

Conversely, unlike hemodialysis, it is also feasible to begin peritoneal dialysis with a permanent dialysis access at short notice, precluding the need for CVCs. Although it is optimal to allow for a 2-week break-in period, peritoneal dialysis can begin on the same day as catheter placement, as long as care is taken to introduce only low volumes of fluid into the abdomen when the patient is supine.[77,78] This approach can be considered when the need for dialysis is imminent, for example in selected patients who have been referred late in the course of their disease or when catheter placement has been delayed.

In the context of minimizing long-term use of CVCs, it is also important to consider the challenges presented by patients on peritoneal dialysis who need to transfer to hemodialysis. It is estimated that 10–15% of patients on peritoneal dialysis may require transfer to hemodialysis treatment every year.[79,80] This situation might result in prolonged CVC dependence until a new vascular access is placed and achieves suitability for dialysis. This issue raises the question of whether a back-up arteriovenous fistula should be placed in every patient treated with peritoneal dialysis. In a UK dialysis center where back-up vascular access was placed in all patients undergoing peritoneal dialysis, 94% of fistulae were never used for hemodialysis and 70% of fistulae were not functioning when needed.[81] As such, routine placement of a vascular access in all patients who start treatment with peritoneal dialysis is not justified. However, nephrologists might consider placement of a back-up fistula in certain patients starting peritoneal dialysis, for example when peritoneal dialysis can only be performed for as long as residual renal function is present, or in patients with progressive difficulty in achieving adequate peritoneal ultrafiltration.[79]

Step 5: timely initiation of dialysis

In the 1990s, expert groups recommended that initiation of dialysis be considered when renal function declines to a predetermined level (mean of urea and creatinine clearance of ≤10.5 ml/min/1.73 m^2).[82] Over the past 10 years, however, the mean eGFR of patients starting dialysis in the USA has progressively increased.[1,83] Notwithstanding this change over time, there is no relationship between the duration of predialysis nephrology care and eGFR at the time of starting dialysis.[84] Furthermore, patients who start dialysis with a high eGFR are as likely as patients with a lower eGFR to use CVCs as the first dialysis access.[84] These observations suggest that nephrologists might be recommending patients for dialysis for the same general reasons, irrespective of eGFR. For example, individuals with low levels of serum creatinine (and a high eGFR) might need to start dialysis if they are likely to have poor tolerance for the consequences of renal function decline. Findings from several observational studies demonstrate that patients who start dialysis with a high eGFR are substantially more likely to have characteristics associated with an increased mortality (such as older age, male sex, white ethnicity, diabetes mellitus and other cardiovascular comorbidities).[84–94] Concerns about the rising trend of starting dialysis in patients with a high eGFR have been raised, particularly since many studies now show a direct association between a high eGFR at the time of dialysis initiation and subsequent risk of death.[84–94] This risk persists even after statistical adjustment for potential confounders and also when analyses are restricted to the healthiest subgroup; however, there is always the issue of residual confounding in observational studies.[87,88] Furthermore, there are data to suggest that with decreasing renal function, muscle mass becomes a more important determinant of serum creatinine level than is GFR.[95] It follows then that the association between high eGFR and an increased risk of death might, in part, be a reflection of the effect of cachexia (muscle loss causing lower levels of serum creatinine at any given level of eGFR) on mortality.[86] Given the limitations of observational studies, it is fortuitous that the importance of renal function at dialysis initiation has been tested in a randomized controlled clinical trial. In the only such trial that we are aware of, the IDEAL study, there was no difference in survival between patients randomly assigned to begin dialysis early (at a creatinine clearance of 10–14 ml/min) or late (at a creatinine clearance of 5–7 ml/min).[96] It is important to note that three-quarters of patients randomly assigned to starting dialysis late actually needed to begin

treatment earlier, primarily owing to the development of uremic symptoms.[96]

These data suggest that initiation of dialysis simply when renal function approaches a predetermined threshold, as measured by eGFR, is not appropriate. Indeed, it seems that dialysis can be safely delayed in otherwise asymptomatic individuals with advanced CKD. This is particularly important in patients in whom a permanent dialysis access is not ready for use, and deferring dialysis might mitigate the need for CVCs. However, findings from the IDEAL study also indicate that it might not be universally possible to defer initiation of dialysis until patients reach an eGFR <7 ml/min/1.73 m^2 as many patients with advanced CKD can develop uremic symptoms at high levels of renal function.[96] In addition to the indications for emergent dialysis (hyperkalemia, volume overload, pericarditis and encephalopathy), dialysis therapy has been shown to be effective in ameliorating uremic anorexia and is associated with improvement in measures of protein–energy wasting.[97–99] Hence, it is important to observe patients with advanced CKD for the early development of symptoms and/or uremic complications and begin dialysis at an appropriate time such that it precludes the development of complications that might require hospitalization or emergency intervention.

Conclusions

This step-by-step approach to the management of patients with CKD and ESRD outlines a strategy to bridge gaps in patient care with respect to the initiation of dialysis. Many of the recommendations presented in this Review are similar to those developed independently by a European workgroup.[100,101] The primary measures of success of this strategy would include minimizing the proportion of patients who start dialysis with CVCs, and maximizing the number of patients that actively participate in developing their care plan and who start dialysis with a permanent access. Challenges exist that might limit the implementation of this approach, such as the occurrence of ESRD after acute kidney injury or late patient presentation following an asymptomatic disease course. Educating these individuals about CKD might, nevertheless, facilitate their participation in selection of dialysis modality and might also result in an earlier transition to a permanent dialysis access.

Review criteria

No specific database searches were performed for this Review. Each section has been written by an author selected based on international recognition of their expertise in the area.

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Disclaimer
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