Review

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Chronic kidney disease in the elderly: evaluation and management

Chronic kidney disease (CKD) is a very common clinical problem in elderly patients and is associated with increased morbidity and mortality. As life expectancy continues to improve worldwide, there is a rising prevalence of comorbidities and risk factors such as hypertension and diabetes predisposing to a high burden of CKD in this population. The body of knowledge on the approach to elderly patient with CKD is still evolving. Thus, this review seeks to explore the epidemiology and to discuss current understanding of challenges in the diagnosis and management of elderly patients CKD.

Keywords: chronic kidney disease • CKD • elderly • GFR • MDRD • old age • risk factors • US

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Although considerable interest continues to mount on diseases of the elderly, there is no universally accepted definition of elderly particularly in patients with chronic kidney disease (CKD). In 1935, the USA passed the first Social Security Act, using age 65 years as the age of retirement and the age at which a person became eligible for government welfare benefits [1]. Since then, being above 65 years old is largely accepted as being elderly. The proportion of the US population over the age of 65 years has increased from 4% (approximately 3 million in a population of 65 million) in 1900, to 12% (35 million in a population of 280 million) in the year 2000 [2]. The proportion of the elderly is predicted to further rise to 20% by the year 2030 [3]. Worldwide the median age of the world's population has increased, due to a decline in fertility with fewer births and a 20-year increase in the average life span in the second half of the 20th century [4]. Overall the demographic change from a pattern of high birth rates and high mortality to low birth rates and delayed mortality has contributed to the rise in the elderly population [5]. Given the rise of the aging population, and implications on diagnosis and management of the elderly with CKD, as of 2005 the Accreditation Council for Graduate Medical Education included geriatric nephrology training in the core curriculum for nephrology fellowship [6].

Prevalence of CKD in the elderly

There is a high prevalence of CKD in the elderly. This is attributable mainly to increasing prevalence of traditional risk factors for CKD such as diabetes, [7] hypertension and cardiovascular disease (CVD) as well as due to new definitions that have expanded the estimated glomerular filtration rate (eGFR) range for CKD. These new definitions for CKD are kidney damage evidenced by abnormal renal markers or a reduction of the absolute eGFR to less than 60 ml/min/1.73 m^2 for at least 3 months. Abnormal renal markers are proteinuria, abnormal radiology, abnormal cells in the urine or renal pathology on biopsy. In addition, a history of renal transplantation is included in the definition [8]. These definitions were derived from studies of the Third National Health and Nutrition Examination Survey data in the United States. The prevalence of CKD in the US adult population was noted to be 11%. The

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prevalence in the US elderly was much higher at about 39.4% of persons aged 60+ years have been noted to have CKD versus 12.6 and 8.5% of persons aged 40–59 years and 20–39 years, respectively [9]. These numbers could have been overestimated but are higher than the percentage of people with diabetes alone (9.3%) or just CVD (8.5%) making CKD a significant public health problem.

Based on Medicare (age >65 years) claims data for 2011 prevalent US population, CKD was noted to be about 10% in contrast to 1.5% of the younger employed population [10], suggesting that the elderly carried the overall burden of CKD. Indeed, the older one is, the higher the likelihood for CKD. The odds ratio (OR) of CKD for Medicare patients between ages 75 and 79 is 40% higher (OR: 1.4) than patients 65–74 years. In those people over age 80 the OR is 1.75. Men have more CKD than women and African-Americans are also much more likely to have CKD than whites. Claims data give us the number of CKD people ascertained by medical personnel. Because CKD is largely a silent disease, many people will meet the technical criteria but not be observed in the clinic setting and therefore these claims data may underestimate CKD prevalence.

Classification of CKD

Based on new definition of CKD noted above [11], guidelines were developed that classify kidney disease into five stages, from kidney disease with a preserved GFR to end-stage kidney failure. In stage 1, there is evidence of kidney damage but glomerular filtration rate (GFR) is preserved (>90 ml/min); stage 2 is mild kidney damage with GFR 60–90 ml/min; stage 3 is moderate kidney damage with GFR 30–59 ml/min; stage 4 is severe kidney damage with GFR 15–29 ml/min; while stage 5 is end-stage renal failure (ESRD) with GFR <15 ml/min. This classification serves as a means of alerting health care providers when complications of CKD occur, and to give guidelines as to when to initiate various interventions (Table 1) [12]. For instance, stage 3 requires initiating management of complications alongside controlling risk factors to retard disease progression while stage 5 requires that patient be adequately prepared to initiate renal replacement therapy.

Accurate determinations of GFR require the use of inulin clearance or a radiolabeled compound (e.g., iothalamate), which are expensive and not commonly used. In practice, precise knowledge of the GFR is not required, and the disease process usually can be adequately monitored by obtaining a 24-h urine collection for calculation of creatinine clearance. However, there is a significant variability of test results due to inaccurate 24-h urine collection, patient compliance with instructions on the collection technique and normal variation from day to day [13]. Estimating equations (Table 2), such as the modification of diet in renal disease (MDRD) or CKD-epidemiology (CKD-EPI) formulas [14], for their ease of use have now largely replaced creatinine clearance measurement. Software for estimating GFR are available on the internet and can be accessed using personal digital assistants.

Difficulty of eGFR

Recognizing CKD increasingly as a disease of elderly individuals there are concerns that this standardization of eGFR has led to an increase in the number of older individuals labeled as having CKD [15]. An important question that must be addressed is whether elderly patients classified as having CKD are done so based on a single reduced eGFR value without other evidence of kidney damage [16]. The difficulty in calculating the eGFR in the elderly is further compounded by the various equations that can be used while there is conflicting data about which one is best. Ferhman and others used the iohexol clearance to determine GFR and compared the results to estimating equations in normal elderly subjects between the ages 70 and 110 years, and found that the GFR had a strong correlation with age ($p = 0.0002$), with an annual decline of 1.05 ml/min [17]. In addition, they found that using the MDRD formula performed better in the elderly while Cockroft–Gault, underestimated clearance. On the other hand, Dowling and others found that the MDRD and CKD-EPI equations significantly overestimated creatinine clearance in elderly individuals, which could lead to dose calculation errors for many drugs, particularly in individuals with severe renal impairment and suggested that the Cockcroft Gault equation be used in older adults for the purpose of renal dosage adjustments [18]. Koppe and others, compared the Berlin Initiative Study (BIS-1) equation that was recently developed to improve the precision and accuracy of GFR estimation in older people and compared it to the simplified MDRD and the CKD-EPI equations in a study of 224 Caucasian patients over the age of 70 years. Simultaneous measurements of plasma creatinine and renal clearance of inulin were used. They found that BIS-1 was the most accurate: the percentage of GFR estimates that fell within the range of measured GFR was 75.56% compared with 70.67% with MDRD and 72% with CKD-EPI. In addition BIS-1 had the lowest median bias and the highest precision. As disease progressed, in people with CKD stages 4 and 5, the CKD-EPI equation had the highest accuracy, the lowest median bias and the highest precision. They concluded that

Table 1. Classification and estimated prevalence of chronic kidney disease.

Stage	GFR status	eGFR (ml/min/1.73 m²)	Intervention
1	Kidney disease with normal GFR	>90	Control comorbidities, slow progression, CVD risk reduction
2	Mildly impaired GFR	60–89	Estimating rate of progression
3	Moderately impaired GFR	30–59	Treat complications
4	Severely impaired GFR	15–29	Preparation for dialysis or transplant
5	Kidney failure	<15	Dialysis or transplant

The estimates for the prevalence of patients with stages 1–4 are derived using microalbuminuria (stage 1 has 6 million, stage 2 has 5 million, stage 3 has 8 million and stage 4 has 400,000 patients). Stage 5 is the actual number of patients treated with dialysis or kidney transplant and does not include untreated CKD stage 5. Therefore, the overall prevalence of eGFR <15 is much higher in elderly patients given that most elderly patients with eGFR <15 are untreated.
CKD: Chronic kidney disease; CVD: Cardiovascular disease; eGFR: Estimated glomerular filtration rate; GFR: Glomerular filtration rate.
Data taken from [12].

age and CKD stage determines the best equation for calculating GFR and that BIS-1 was reliable for use in the elderly with stage 1–3 CKD and CKD-EPI be used in stages CKD 4–5. [19].

Risk factors for CKD in the elderly

Box 1 summarizes modifiable and nonmodifiable risk factors for CKD and those directly related to aging are discussed in detail here [12]. Older age is a key predictor of CKD, and 11% of individuals older than 65 years without hypertension or diabetes have creatinine levels that falls in stage 3 or worse CKD. Whether this is due to intrinsic kidney disease, normal process of aging or just a function of the type of equation used is unclear. Nonetheless, due to the overall increased prevalence of CKD, particularly in the elderly, Kidney Disease: Improving Global Outcomes (KDIGO) in 2006 suggested that CKD screening should be offered to patients with risk factors and those over the age of 60 years [20].

Diabetes

Microvascular disease resulting from diabetes can cause CKD in about 40–50% of patients with diabetes, a process called diabetic nephropathy. In one large population study, the authors estimated the prevalence of diabetes for all age-groups worldwide to be 2.8% in the year 2000 and this is projected to increase to 4.4% by the year 2030. The total number of people with diabetes is projected to rise from 171 million in the year 2000 to 366 million by 2030. The most important demographic change to diabetes prevalence across the world appears to be the increase in the proportion of people >65 years of age. Concomitant increase in both the aging and diabetic population has resulted in increased prevalence of elderly diabetics at risk for CKD [21].

In the United States, the number of people who have diabetes has increased especially in the elderly population. The CDC reported that among adults aged 65–79 years, incidence of diagnosed diabetes has significantly increased from 6.9 per 1000 in 1980 to 15.4 per 1000 in 2011 [22].

Obesity

Data from National Health and Nutrition Examination Survey between 2007 and 2010 revealed that more than a third of adults aged 65 and above were obese. In addition, obesity prevalence was higher among those aged 65–74 years compared with those aged 75 years and above in both men and women. Further, the prevalence of obesity in women aged 65–74 years was higher than in women aged over 75 years in all racial and ethnic groups except non-Hispanic black women, where approximately one in two were obese among both age groups. Between 1999–2002 and 2007–2010, the prevalence of obesity among older men over the age of 65 years increased [23].

Foster and others noted that the association between BMI and CKD in a logistic regression model using baseline BMI to predict incident stage 3 CKD and incident dipstick proteinuria in the Framingham Offspring participants in 2676 subjects. After adjusting for age, sex, diabetes, systolic blood pressure, hypertension treatment, smoking status and high-density lipoprotein cholesterol level they found that while obesity was associated with increased risk of developing stage 3 CKD, it was no longer significant after adjustment for known CVD risk factors. They concluded that the relationship between obesity and stage 3 CKD may be mediated through CVD risk factors [7].

Hypertension & CVD

The association between CKD and CVD emerged over three decades ago and more data continue to accumulate supporting the association. The Hyper-

Table 2. Formulas used to estimate glomerular filtration rate.

Name of equation	Comments
MDRD study	Less accurate at eGFR >60 ml/min/1.73 m^2 and older age
CockroftGault	Decreased accuracy at lower levels of CKD
CKD-EPI Scr	Overestimates CKD in older individuals
CKD-EPI cystatin C	Better for older individuals and those with reduced muscle mass
CKD-EPI Cr-cystatin C	Performs better than all above in estimating GFR. Better in elderly
Berlin initiative study (BIS-1)	Reliable for use in the elderly with stage 1–3 CKD, CKD-EPI be used in stages CKD 4–5

CKD: Chronic kidney disease; CKD-EPI: Chronic kidney disease epidemiology collaboration; eGFR: Estimated glomerular filtration rate; MDRD: Modification of diet in renal disease; Scr: Serum creatinine.

tension Detection and Follow-up Program followed 10,940 persons for 5 years in a community-based, randomized, controlled trial of treatment for hypertension the primary end point of the study was all-cause mortality, with morbid events involving the heart, brain and kidney as secondary end points. Progression of kidney failure determined by changes in serum creatinine was among these secondary events. Baseline serum creatinine concentration had a significant prognostic value for 8-year mortality with those who had a baseline serum creatinine greater than or equal to 1.7 mg/dl, 8-year mortality including cardiovascular mortality was more than three-times that of all other participants. The decline in renal function was greater in men, blacks and older adults, as well as in those with higher entry diastolic blood pressure. In addition in the CKD group, mortality due to CVD was frequently associated such that it was more likely that patients with CKD would die of CVD than to progress to kidney failure [24]. Furthermore, there was high prevalence of CVD in dialysis patients and that mortality due to CVD in this population was ten- to 30-times higher than in the general population [25].

Older age seems to be a risk factor for mortality in ESRD patients with congestive heart failure (CHF), which is common in the dialysis population. A prospective multicenter study of 432 dialysis patients for 41 months looked at mortality and development of morbid cardiovascular events. 133 (31%) subjects had CHF at the time of initiation of dialysis therapy. Multivariate analysis showed that the risk factors including systolic dysfunction, older age, diabetes mellitus and ischemic heart diseases were significantly and independently associated with CHF at baseline. Over the course of dialysis 76 subjects (25%) who did not have baseline CHF subsequently developed CHF. The median survival of subjects with CHF at baseline was 36 months compared with 62 months in subjects without CHF [26]. The elderly with CKD had more CVD burden than the non-CKD population in the USRDS 2013 annual data report. CHF was noted in 43% of CKD patients, compared with just 18.5% in the non-CKD patients.

Aging & CKD

Data from the Baltimore Longitudinal Study of Aging looked at repeated serial creatinine clearances, between 5 and 14 studies in 446 normal volunteers between 1958 and 1981. Subjects with renal or urinary tract disease or those on diuretics or antihypertensives were excluded. The residual group consisted of 254 normal subjects, and revealed a mean decrease in creatinine clearance as 0.75 ml/min/year, which could be estimated as 10 ml/min/decade in those over the age of 40 years. A third of all subjects followed had no absolute decrease in renal function and there was a small group of patients who showed a statistically significant increase ($p < 0.05$) in creatinine clearance with age [27]. The nephrology society is still divided about whether the decline in GFR noted with aging is part of the normal aging process versus CKD [28]. Nonetheless, preservation of the kidneys hormonal function, electrolyte and acid base balance as well as normal urinalysis in elderly patients with GFR <60 ml/min/1.73 m^2 is indicative of a kidney aging normally rather than a kidney with CKD.

Acute kidney injury with CKD in the elderly

Pascual and others reviewed data from 13 hospitals in Madrid for acute kidney injury (AKI) based on age. Those over 80 years were compared with aged 65–79 years and a group younger than age 65. The authors found old age was not a particularly poor prognostic sign in AKI and suggested that dialysis not be withheld just on the basis of age alone [29]. In the three groups, the group over 80 had less acute tubular necrosis of 39 versus 48% and 55% in the other groups, respectively. The 2013 USRDS annual data report describes the incidence of AKI in Medicare patients age 66 and older to vary considerably

by race in 2011, reaching 45.3 per 1000 patient years in blacks/African–Americans compared with 25.8 and 23.9, respectively, in whites and individuals of other races. Despite having AKI follow-up with a nephrologist was inadequate. After an initial hospitalization with AKI, only 13% saw a nephrologist after discharge. In patients with CKD stages 1–2 prior to the hospitalization, 45% were later classified as having stage 3–5 CKD and in those with stage 3–5 CKD prior to hospitalization, 11.5% reached ESRD, suggesting the contribution of AKI to progression of CKD.

Common pathway for progression of CKD

Regardless of the etiology, the final common pathway for irreversible kidney damage has been hypothesized to be increased intraglomerular hypertension which is cause by loss of glomeruli resulting in hypertrophy and hyperfiltration of the remaining nephrons [30]. The remaining nephrons continue to deteriorate setting up a vicious cycle where loss of additional nephrons culminates in hypertrophy and hyperfiltration further leading to nephron loss until the kidney fails. Additional insults are contributed by various hormones and cytokines such as angiotensin II, which causes vasoconstriction of the efferent arteriole exacerbating intraglomerular hypertension and TGF-β, which results in fibrosis [31].

Management of CKD

There is limited information for evidence-based guidelines and recommendations for managing CKD in the elderly. Geriatric issues such as frailty, quality of life, life expectancy, end of life issues, pharmacokinetics and pharmacodynamics of drugs and treatment complications must be addressed when planning the management of CKD in the elderly. AKI may be precipitated by nephrotoxic antibiotics, radio-contrast exposure, combinations of ACEI and angiotensin receptor blockers (ARB), NSAID diuretics and must be recognized and avoided [32].

Using the general approach to CKD management, the unique issues of CKD management in the elderly are emphasized. The goal of CKD management is to halt or retard disease progression. As shown in Table 1, interventions, which become additive as disease progresses, have been designed for each stage of CKD. In stages 1 and 2, the strategy requires strict control of comorbidities including CVD and as complications emerge, they are addressed in stages 3–5. Preparation for renal replacement therapy is imminent in stage 4 leading to renal replacement in stage 5. The management of CKD can be summarized by the acronym BE ACTIVE (Box 1).

Box 1. Risk factors for chronic kidney disease.

Modifiable traditional risk factors
- Hypertension
- Diabetes
- Obesity
- Proteinuria
- Hyperlipidemia
- Cardiovascular disease
- Glomerular and tubulointerstitial disease
- Metabolic acidosis
- Smoking
- High-protein diet

Modifiable nontraditional risk factors
- Anemia
- Hyperuricemia
- Radiological contrast
- Nephrotoxic herbs
- NSAIDs
- Antibiotics
- Elevated FGF-23 levels
- Interstitial calcium phosphate deposition
- Hyperphosphatemia
- Hypercalcemia

Nonmodifiable risk factors
- Old age
- Race/ethnicity
- Gender
- Low birth weight
- Family history

Data taken from [12].

Blood pressure

The general management of hypertension and considerations in the elderly has been addressed elsewhere [33]. It has long been recognized that control of blood pressure is extremely important in efforts to slow the progression of CKD. The use of an angiotensin converting enzyme inhibitor (ACEI) or an ARB seems to have theoretical advantage because of the role of angiotensin in progression of CKD, and their proven beneficial effects on proteinuria. One of the earlier papers to demonstrated retardation of CKD progression using ACEI in patients with Type 1 diabetes was by Lewis *et al.* [34]. In that study, Type 1 diabetics were treated with Captopril or placebo and other blood pressure medication so that both groups had virtually equivalent blood pressure control. Lewis found that patients on Captopril were significantly less likely, $p < 0.007$, to have a doubling of serum creatinine, and concluded that "Captopril protects against deterioration in renal function in insulin-dependent diabetic nephropathy and is significantly more effective than blood-pressure control alone." Similar observations were later conformed in nondiabetic renal disease [35,36]. What the ideal blood pressure is for such patients is not clear. The original targets for BP

control were less that 125/75 mmHg for patients with diabetic nephropathy and less than 130/80 mmHg for nondiabetic CKD [37]; however, Upadhyay [38] found in a systemic review of over 2000 patients, that there was no evidence that those values were any better that 140/90 mmHg, except in patients with proteinuria.

More recently, a large cohort study of mortality of veterans (mean age 73.8 ± 9.7 years) with CKD showed that at low blood pressure levels, mortality actual rose [39]. They concluded that the ideal BP for CKD patients seemed to be between 130–159 mmHg systolic and 70–89 mmHg diastolic. The current 2013 KDIGO (Kidney Disease Outcome Global Imitative) guidelines recommend blood pressure less than or equal to 140/90 mmHg if albuminuria is less than <30 mg/day and BP less than or equal to 130/80 mmHg if albuminuria is more than >30 mg/day. The guidelines also recommend the use of ACEI or ARB in diabetics if albuminuria >30 mg/day, and nondiabetics if albuminuria >300 mg/day.

Erythropoiesis-stimulating agents

The recommended dose for the use of erythropoiesis-stimulating agents (ESAs) for the treatment of the anemia of renal disease is also in flux. Anemia usually develops in stage 3 CKD, and the availability of erythropoietin and its analogs has made an important improvement in many aspects of patients with CKD, including less need for blood transfusion, better quality of life and improvement in left ventricular hypertrophy. The target hemoglobin for dialysis patients was between 11 and 12 g/dl. However, two studies, the CHOIR [40] and the TREAT [41] study (median age: 68 years) revealed an increased risk of cardiovascular events at hemoglobin levels greater than 13 g/dl. Therefore, the 2012 KDIGO guidelines recommend to not start ESA in CKD patients with Hgb >10 g/dl.

Acidosis

Because of impaired ammonia excretion in CKD, patients develop acidosis, beginning in stage 3. A recent study by deBrito-Ashurst treating 134 stage 3–4 patients with metabolic acidosis randomized to either usual care or replacement with oral sodium bicarbonate for 2 years showed that patients receiving the drug had a significantly slower progression of CKD and better nutritional parameters [42]. Even in early CKD stage 2 patients, the use of bicarbonate was associated with retarding progression compared with controls [43].

Cardiovascular risk assessment

Patients with CKD have many of the traditional risk factors for CVD including diabetes mellitus and hypertension, and cardiac disease is very prevalent in that population. CKD patients are more likely to have the metabolic syndrome, elevated C-reactive protein levels and abnormal mineral metabolism, especially calcium. CKD and proteinuria are considered independent risk factors of CAD and cardiovascular mortality is increased in patients with CKD. The Rotterdam study investigated whether the level of renal function, estimated by GFR, was associated with the risk of incident myocardial infarction among 4484 apparently healthy subjects (mean age: 69.6 years). The study showed that a 10 $ml.min^{-1}/1.73\ m^2$ decrease in glomerular filtration rate was associated with a 32% increased risk of myocardial infarction ($p < 0.001$), and that renal function is a graded and independent predictor of the development of myocardial infarction in an elderly population [44]. The KDIGO recommendations for CVD risk reduction in CKD include interventions to slow the loss of GFR regardless of age, therapeutic lifestyle change (such as smoking cessation, weight loss, increased physical activity), specific use of ACEI or ARBs in combination with other agents to control blood pressure and management of diabetes and other cardiovascular risk factors. It should however be noted that the use of ACEI and ARB in older patients (age: >55 years) with diabetes and high cardiovascular risk may result in complications such as worsening renal function, dialysis, hyperkalemia or death and therefore the combination should be avoided in the group [45].

Timing

In CKD patients who are clearly progressing, discussion about options in renal replacement therapy should start in late stage 3, depending on the individual patient. Referral to a transplant program is considered for those who are surgical candidates. In stage 4, for those electing dialysis, access for either hemodialysis or peritoneal dialysis should be discussed, and vein mapping done for those electing hemodialysis. Vascular access should usually be placed at that stage. There is no clear consensus as to when to actually start dialytic therapy. KDOQI suggests starting when eGFR is less than 14 $ml/min/m^2$ in patients who have symptoms. In those who are symptom free, start at an eGFR of less than 6 $ml/min/m^2$. Cooper *et al.* conducted a randomized control study of 828 stage 5 patients. There was an 'early start' group, eGFR 10–15 $ml/min/m^2$, and a late start group, eGFR 5–7 $ml/min/m^2$. There was no difference in survival or adverse outcomes, although many of the 'late start' group started earlier because of fluid overload and other complications [46].

Iron

When iron deficiency is diagnosed in CKD, a search must be initiated for any sources of blood loss. Unlike

in hemodialysis patients, there is no clear advantage shown with intravenous versus oral administration in CKD patients therefore both routes of administration are options. CKD population differs from hemodialysis patients in the extent of blood loss, with hemodialysis patients losing much more blood during the procedure. Oral iron therapy may be a more reasonable option [47] unless oral therapy previously failed given the difficulty with parenteral injections in CKD patients. Iron should be considered in all patients with iron deficiency and in patients receiving ESAs. The goal of therapy is to have an iron saturation of more than 25%, and a serum ferritin of between 300 and 500 ng/ml.

Insulin & glucose control with oral agents

Several studies suggest controlling blood sugar to goal retards progression of microvascular complications including diabetic CKD. The United Kingdom Prospective Diabetes Study Group, showed a risk reduction of 11% in all diabetic end points including renal failure over a 10-year period in patients who had 'tight' control, HgbA1c 7.0% compared with those with conventional control HgbA1c 7.9% [48]. Similarly, The VADT study showed that intensive glucose control in patients with poorly controlled Type 2 diabetes had no significant effect on the rates of major cardiovascular events, death or microvascular complications, with the exception of progression of albuminuria ($p = 0.01$) [49]. Finally, the ACCORD study in 2010 looked at 10,251 patients either treated intensively HgbA1c less that 6%, versus a group with a mean HgbA1c of 7.0–7.9%. While the tight control delayed the onset of albuminuria, the study was ended early because of high mortality in the intensively treated group [50].

Vitamin D & bone disease

Bone disease in CKD is extensive, and a full review is beyond the scope of this article. However, bone disease usually starts to become evident in stage 3 and 4 and serum levels of calcium, phosphorus and intact parathyroid hormone (PTH) should be measured at these stages. Abnormalities in these levels can lead to vascular and other soft tissue calcification, renal osteodystrophy, increased fractures, cardiovascular events, increased mortality and calciphylaxis. Recommendations for treatment include use of oral phosphate binders to control serum phosphorus and the use of vitamin D or analogs or calcimimetic to suppress PTH levels and to replace vitamin D deficiency.

Eat (diet)

Whether or not a low protein diet is beneficial in slowing the progression of CKD remains to be proven. There was some suggestion that a low-protein diet, which is 0.50 g protein/kg of body weight, had a minimal effect on slowing the progression of CKD in the MDRD, Modification of Diet in Renal Disease Study [51]. A more recent study in which 423 patients were assigned to two diets, 0.5 or 0.8 g/kg of protein found that the BUN increased significantly in the higher protein diet, and serum phosphate and PTH levels remained the same. Those patients on the lower protein diet needed less phosphate binders, less diuretics and less sodium bicarbonate replacement. There was no difference in adverse effects between the two groups [52].

Renal replacement therapy in the elderly

The onset of CKD stage 5, with an eGFR of less than 15 ml/min is fatal if untreated. Stage 5 CKD patients have clinically documentable physical and psychological signs and symptoms during their last month of life that are similar to or more severe than those in advanced cancer patients [53]. Untreated kidney failure (eGFR <15 ml/min/1.73 m^2) is more prevalent in the elder, particularly in those over age 75 years old [54]. This is particularly important in the aged population where eGFR progression may be slow enough for a patient to die of other causes without having to endure dialysis. Several large meta-analyses have also found that the associations between eGFR and adverse events such as end-stage renal disease (ESRD) and death did not vary substantially with advancing age [55]. One meta-analysis of approximately 1.5 million individuals from multiple cohorts according to level of retained eGFR, noted that associations between lower levels of eGFR with the incidence of death, CVD, ESRD and progression of kidney disease were similar among those older and younger than 65 years [56]. Thus, it was presumed that progressive renal disease as judged by CKD stages was similar in older and young adults. A consequence of this presumption was the national policy that elderly patients with progressive CKD should have a forearm Brescia–Cimino arteriovenous fistula as the preferred means of vascular access for maintenance hemodialysis, a view advanced by the 'Fistula First' initiative. Transplantation remains and option in patients who are surgical candidates though rarely transplantation is recorded in patents above 80 years of age.

Vascular access in very old dialysis patients

More recently, a focused review of vascular access related morbidity and mortality has reopened the issue of purported benefit of establishing an arteriovenous fistula over implanting a vein graft in very old dialysis patients. DeSillva *et al.* analyzed data from a cohort of 115,425 incident hemodialysis patients ≥67 years old derived from the USRDS with linked Medicare claims to iden-

tify the first predialysis access placed of whom 3472 had venous arteriovenous grafts, 21,436 had fistulas and 90,517 had catheters [57]. While patients dialyzed via a catheter had significantly inferior survival compared with those patients with a fistula, there was no significant mortality difference between those patients who are of age 80 or older dialyzed via a catheter and those dialyzed with a fistula, supporting the inference that a 'Fistula First' policy may not be superior for this age group [58].

Timing of dialysis in the elderly

Also bearing on the timing of when to begin dialysis in the very old is the growing belief that their relative risk for all-cause mortality associated with a reduction in eGFR may be somewhat smaller than in younger individuals, though the risks are similar for cardiovascular mortality and ESRD in both younger and older individuals. A detailed meta-analysis confirmed that the relative risks for all-cause mortality associated with a given eGFR were smaller among older individuals; however, the absolute risk of death associated with a given eGFR was higher among older individuals due to their elevated baseline risk of death [59]. This stark reality was underscored by Tamura *et al.*'s report of the dismal outcome of a cohort of 3702 elderly nursing home residents, of mean age 73.4 years, who after 1 year of hemodialysis sustained a 58% mortality with predialysis functional status maintained in only 13% [60]. The reality of a dismal prognosis for newly started dialysis patients older than 75 years (elderly) was characterized by Rosenthal as a 'Sad Truth' when begun at an eGFR of 10 ml/min per 1.73 m^2 or higher because of the greater probability of death from a comorbid condition while renal function persists than that of death in uremia [61].

Clinicians' acceptance of the absence of benefit and the potential for harm in following a policy of initiating 'early dialysis' in the therapy of both elderly and younger adults is reflected in the declining percentage of 'early dialysis starts' at an eGFR ≥ 10 ml/min per 1.73 m^2 which, in data from the USRDS, grew from 19 to 54% of all new starts between 1996 and 2009 but remained stable between 2009 and 2011 [62]. The largest increase in new dialysis starts was in those ≥75 years. In the opinion of authors, Rosansky and Clark, "later dialysis starts and greater use of conservative and palliative care, may improve quality of life for elderly patients with advanced renal failure, and may continue to attenuate the increase observed in previous years." Long-term follow-up is needed to confirm the value of 'later starts.'

From the forgoing, it is rational to advocate what O'Hare has termed an 'individualized approach' to planning care for elderly patients with deteriorating renal function who are being monitored by serial eGFR measurements [63]. While 38% of adults 70 years or older have an eGFR of less than 60 ml/min/1.73 m^2, most eGFR reductions are in the 30–59 ml/min/1.73 m^2 range [64]. Opinions differ as to whether such decreases reflect normal aging versus a high prevalence of unrecognized kidney disease. In a study of primary care practices across Britain, Roderick *et al.* conducted a multidimensional assessment of adults 75 years and older of whom more than half had an eGFR of less than 60 ml/min/1.73 m^2 with baseline characteristics that were no different than in those with an eGFR of 60 ml/min/1.73 m^2 or greater [65]. For both men and women with a depressed eGFR of 45–59 ml/min/1.73 m^2, death was not significantly more likely to occur than in those with an eGFR of 60 ml/min/1.73 m^2 or greater. In the elderly, the eGFR level below which mortality risk exceeds that in a reference category without known kidney disease has yet to be determined.

Table 3. Acronym and management of chronic kidney disease.

Acronym	Meaning
B	Blood pressure control
E	Erythropoitin-stimulating agents
A	Acidosis management
C	Cardiovascular management
T	Timing of Access
I	Iron, insulin (glucose management)
V	Vitamin D and bone disease
E	Eat (diet)

Conclusion & future perspective

For every decade above age 40 years, GFR declines by 10 ml/min such that by age 70 years, the GFR has declined by about 30 ml/min. The aging process compounded by risk factors as well as well as hemodynamic and nonhemodynamic consequences of activation of the renin angiotensin system make the elderly susceptible to CKD. Strategies to retard CKD progression must be comprehensive, encompassing management of both traditional and nontraditional risk factors to their respective target goals, as well as instituting renal replacement therapy as symptoms become manifest in stage 5. As transplantation is limited by surgical suitability and not widely available, the only realistic choice for renal replacement therapy is dialysis. Therefore early education is paramount to ensuring that patients are adequately informed to make the appropriate choices, including the choice to not initiate renal replacement therapy. Due to paucity of data in the treatment of CKD in the elderly, future studies should focus on identifying and evaluating the effec-

tiveness of specific antihypertensive therapies in slowing disease progression in this population (Table 3).

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Practice points

- Age is a significant risk factor for chronic kidney disease (CKD).
- The high prevalence of CKD in the US elderly population is the result of a combination of age and cardiovascular risk factors that accrue with age.
- Screening for CKD should be offered to patients with risk factors and in those over the age of 60 years and these risk factors should be managed to retard progression to end-stage renal disease.

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