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CURRENT OPINION

Prevention of Chronic Kidney Disease and Its Complications in Older Adults

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Abstract

In an era marked by a global demographic shift towards an aging society, there is a heightened prevalence of chronic kidney disease (CKD) among older adults. The burden of CKD spans from kidney-related complications to impacting psychological well-being, giving rise to depressive symptoms and caregiver burnout. This article delves into CKD prevention strategies within the context of aging, contributing to the discourse by exploring its multifaceted aspects. The prevention of CKD in the older adults necessitates a comprehensive approach. Primary prevention is centered on the modification of risk factors, acknowledging the intricate interplay of various comorbidities. Secondary prevention focuses on early CKD identification. Tertiary prevention aims to address factors contributing to CKD progression and complications, emphasizing the importance of timely interventions. This comprehensive strategy aims to enhance the quality of life for individuals affected by CKD, decelerating the deterioration of functional status. By addressing CKD at multiple levels, this approach seeks to effectively and compassionately care for the aging population.

Key Points

With a global demographic shift towards an aging society, there is an increased prevalence of CKD among older adults, leading to a range of complications from physical to psychological issues.

Preventing CKD in older adults requires a multifaceted approach. Primary prevention involves modifying risk factors and managing comorbidities. Secondary prevention focuses on early detection of CKD, while tertiary prevention addresses factors contributing to CKD progression and complications through timely interventions.

This comprehensive prevention strategy aims to improve the quality of life for older individuals with CKD by slowing the deterioration of functional status, ultimately providing comprehensive care.

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1 Introduction

The global demographic landscape is undergoing a transformative shift marked by an increasing mean age, a declining birth rate, and extended life expectancy propelled by advancements in high technologies [1]. This phenomenon is steering the world towards the challenges posed by an aging society. As populations age, the consequential rise in comorbidities and mortality becomes evident, with chronic kidney disease (CKD) emerging as a prominent concern, a condition in which aging itself plays a causative role.

A meta-analysis by Hill et al. [2] highlighted the linear correlation observed in the prevalence of CKD and advanced age, suggesting a substantial proportion of the overall CKD burden of aging. Insights from the Global Burden of Disease (GBD) studies [3] revealed an increased disability-adjusted life years associated with CKD. There is an early peak in low-income countries and a later peak in high-income countries, shedding light on the complex dynamics of CKD across different economic strata. Projections for the future point towards an upward trajectory in CKD cases, necessitating a proactive stance in addressing this growing health issue.

The recent US Renal Data System (USRDS) annual data report [4] provided a nuanced perspective on CKD prevalence, indicating a decline among individuals aged 65 and above. However, there was a consistent elevation

in prevalence among older adults compared with their younger counterparts in the past decades. Despite a reduction in CKD prevalence in all age groups in 2021 except for individuals aged 75 and above that was increased. This underscores the urgency for a comprehensive understanding of CKD prevention and detection strategies tailored to an aging demographic. Regarding these demographic shifts and epidemiological patterns, this article aims to contribute to the essential discourse on CKD prevention by delving into the multifaceted aspects of the disease within the context of an aging population.

2 Decline in eGFR in Older Adults

Even in the absence of comorbidities, renal mass experiences a decline with aging, contributing to the physiologically decrease in estimated glomerular filtration rate (eGFR), commonly referred to as kidney senescence [5]. Kidney senescence in healthy older individuals differs from CKD, as proximal tubular function, along with serum levels of calcium, phosphorus, magnesium, and erythropoietin production, may remain normal despite the eGFR decline [6, 7]. However, continuous activation of kidney inflammatory and fibrotic pathways that exceed the aging kidneys' ability to adapt can lead to persistent kidney injury, promoting the progression to true CKD [8]. The rate of creatinine clearance decline follows an inverse relationship with age, initiating at 40 years, with an approximate annual change of −0.87 ml/min, as reported in the study by Lindeman [9]. The impact of eGFR decline is heightened in the presence of other risk factors and comorbidities, as demonstrated by previous research indicating an accelerated rate of decline, especially after the age of 60 years [10]. Another observational study found that in healthy kidney donors under the age of 70 years, the GFR of a single kidney does not significantly change with age. [11]

Despite reaching a peak (> 400 g) between the ages of 30–40 years, kidney mass undergoes a subsequent decrease to < 300 g by the age of 90 years [12]. Mechanisms contributing to kidney senescence include upregulated senescence genes, oxidative stress, hormonal changes, and atherosclerotic alterations in vascular supply. After the age of 40 years, renal blood flow tends to decrease by 10% annually, compromising renal blood flow, leading to repetitive ischemic injuries, sclerotic changes, and reduced nephron mass [13]. Histopathological examination of kidney tissue from older individuals reveals common findings such as focal glomerulosclerosis, mesangial expansion, glomerular basement membrane thickening, podocyte foot process fusion and detachment, tubular atrophy, interstitial fibrosis, and vascular hyalinosis, providing confirmation of the proposed mechanisms [12].

Concomitant with other comorbidities contribute to faster decline in eGFR. Diabetes and hypertension, the two most common etiology of CKD, become more prevalent with age. While the prevalence of diabetes is increasing worldwide, the prevalence increases in the proportion of individuals aged > 65 years [14]. In older adults, factors such as insulin resistance and reduced physical activity contribute to the increased prevalence of these conditions. Additionally, arterial stiffness, dysregulation of neurohormonal pathways, and autonomic dysfunction further contribute to the development of hypertension [15]. Findings from the Framingham Heart Study highlight the significance of age-related hypertension, revealing that 60% of individuals reach the age of 60 years with high blood pressure, and approximately 65% of men and 75% of women acquire hypertension by the age of 70 years [16]. The escalating prevalence of glomerulopathies with aging, including minimal change disease, membranous nephropathy, IgA nephropathy, and pauci-immune glomerulonephritis, exacerbates the complexity of kidney health in older adults [17].

Another risk for CKD in the older adults is recurrent or prolonged acute kidney injury (AKI). The aging kidney's impaired autoregulatory mechanisms increase susceptibility to significant damage and hinder the reparative process, making older adults more prone to AKI and subsequent progression to CKD. Dehydration and exposure to nephrotoxic substances are frequent contributors to AKI [18, 19]. Another potential cause of AKI is postrenal AKI, which can stem from conditions ranging from benign prostatic hypertrophy to pelvic malignancy [20].

3 Burden of CKD in Older Adults

The burden of CKD encompasses various dimensions, including kidney-related issues, comorbidities, complications, and treatments implications. CKD is known as an independent risk factor of cardiovascular disease, increasing the risk of cardiovascular disease and heart failure [21]. This interaction forms a detrimental cycle known as cardiorenal syndrome, intensifying the risks of mortality and hospitalization. Concurrently, managing volume in CKD becomes more complex in the presence of heart disease. Additionally, CKD contributes to metabolic bone disease (CKD–MBD), exacerbating age-related osteoporosis and increasing the risk of fractures [22].

Older adults, often burdened by various comorbidities, commonly engage in the utilization of multiple medications. Notably, 91% of older adults typically rely on at least one medication, with more than half depending on a regimen of at least five daily medications [23]. This prevalence is

further exacerbated in patients with CKD, where medical complexity contributes to a higher incidence of polypharmacy and, consequently, an inappropriate drug prescription [24]. The older population, generally less tolerant to the development of adverse drug reactions, faces an elevated risk of drug interactions and overdose. This vulnerability also contributes to an increased incidence of drug-induced AKI within this population [25].

CKD-associated neurocognitive impairment consists of a spectrum of cognitive deficits, including dementia, attention deficit, executive function difficulties, and frailty [26, 27]. The complex interplay between renal dysfunction and neurocognitive decline is influenced by various factors, including vascular changes, inflammation, oxidative stress, and metabolic disturbances, including electrolyte imbalances and uremic toxins [28, 29]. CKD also affects psychological well-being, contributing to depressive symptoms and adjustment disorders. These mental issues further link to the loss of appetite, affecting nutritional status, and worsening frailty [30]. This burden extends beyond the cognitive realm, affecting daily functioning, quality of life, and independence. As CKD progress and functional decline occurs, the need for caregiving becomes more demanding. The responsibility of providing both physical and emotional support often leads to caregiver burnout, impacting their own health and well-being [31]. However, it is noteworthy that illness perceptions from patients' mindsets are influenced by life experiences, with older adults often having a more positive perception and acceptance of CKD as a chronic disease [32].

4 Primary Prevention: Risk Modification

Primary prevention of CKD entails a targeted approach to modifying risk factors, aiming to forestall the onset of renal complications (Fig. 1). By addressing the modifiable risk factors proactively, managing and controlling conditions that predispose individuals to CKD, such as hypertension, diabetes, obesity, and cardiovascular diseases, through pharmacological interventions and diligent monitoring, play pivotal roles in risk modification. Lifestyle interventions, such as adopting a balanced and low-sodium diet, engaging in regular physical activity, and maintaining a healthy weight, are also important. Factors contributing to susceptibility of CKD, generation of CKD, and aggravating CKD progression are shown in Fig. 2.

Additionally, preventing repetitive AKI in older adults is vital, particularly by addressing factors such as dehydration and drug toxicity. Both intravascular and extravascular volume status should be assessed regularly as changes in muscle and fat component can decrease intracellular component [33]. Some drugs with vasodilatory effects can also change the volume distribution. Noted that the physical indicators of dehydration may be unreliable in older adults, preventative measures against drug toxicity involve several strategies. These include conducting drug reconciliation to pinpoint potential nephrotoxic agents and interactions, modifying doses based on renal function, and routinely monitoring drug levels [19]. Adjusting the dosage of potential nephrotoxic medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), should be guided by kidney function and avoided during periods of hemodynamic instability. Additionally, given the increased vulnerability of older adults to changes in hemodynamic status and the heightened risk of acute kidney injury (AKI) during illness, it is advisable to institute a "sick-day rule." This protocol entails making adjustments or withdrawing certain medications, especially those that impact renal blood flow, such as angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs).

The role of anti-AGE/oxidant substances and vitamin supplements were studied, aiming to neutralizing ROS and minimizing oxidative damage to cellular components [34]. Pentoxyphylline, a phosphodiesterase inhibitor with antioxidant, antifibrogenic, and immunomodulatory properties, has demonstrated potential in slowing the decline of eGFR, suggesting a beneficial impact on renal function [34, 35]. In contrast, bardoxolone methyl, a semisynthetic triterpenoid, has shown promise in improving eGFR in certain studies. However, its use has been associated with an increase in albuminuria in some research findings [36, 37]. Other antioxidants and vitamins have failed to establish efficacy in CKD prevention [34]. A composite dietary antioxidant index, although positively associated with lower CKD prevalence, has no established evidence [38]. Further research and clinical scrutiny are warranted to better understand the nuanced effects of these compounds and their applicability in the context of renal health.

A novel and promising target for intervention in age-related kidney dysfunction is senescent cells, and this approach, known as senotherapy, has demonstrated positive outcomes in aging animal models, contributing to kidney recovery [39] and prolonging life span [40]. Senolytic interventions, which involve the removal of senescent cells, have shown efficacy. For instance, quercetin, a flavonoid found in produce, has been demonstrated to attenuate atherosclerosis by inducing apoptosis in senescent endothelial cells [41]. Another approach to eliminating senescent cells involves activating invariant natural killer (NK) T cells [42] or chimeric antigen receptor T cells [43]. An anti-aging vaccine, targeting CD153-expressing senescent T cells, has shown a reduction in atherosclerotic plaque in a mouse model [44]. Senotherapy also includes the use of senostatic or senomorphic drugs aimed at regulating the senescence-associated secretory phenotype (SASP). Senostatic drugs such as metformin [45], ruxolitinib (a JAK inhibitor) [46],

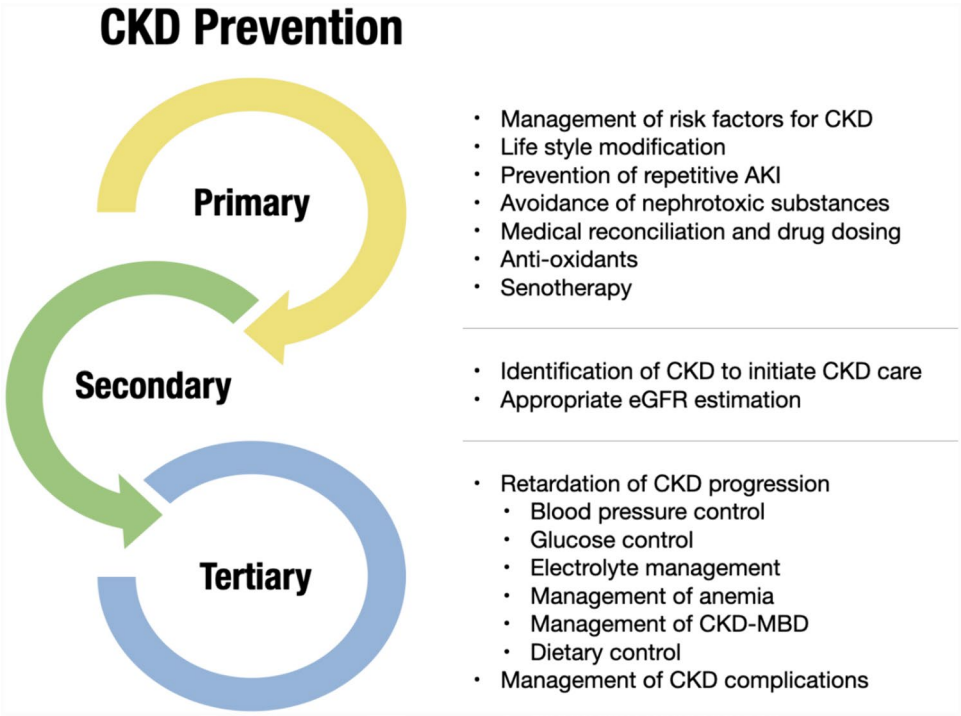

Fig. 1. Strategies for primary, secondary, and tertiary prevention for chronic kidney disease in older adults (*AKI* acute kidney injury, *CKD* chronic kidney disease, *eGFR* estimated glomerular filtration rate, *MBD* metabolic bone disease)

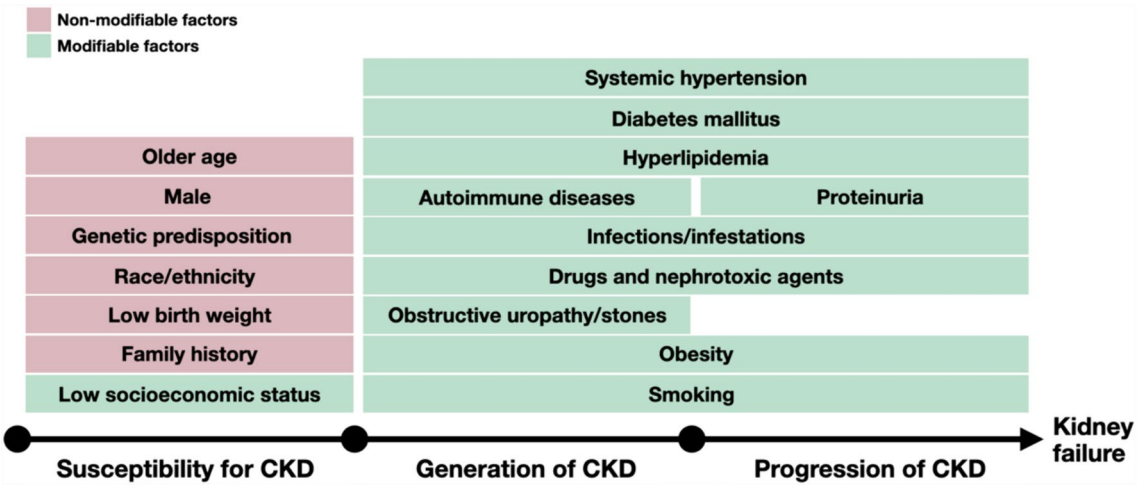

Fig. 2 Factors contributing to each step of chronic kidney disease (CKD) progression

and rapamycin (an mTOR inhibitor) [47], among others, have shown the ability to suppress SASP and inhibit cell senescence in in vitro studies. Additionally, the boost of senescence inhibitors, including Klotho [48] and sirtuins-activating compounds (STACs) [49] has demonstrated reno-protective effects. However, it is important to note that while these findings are promising in animal or in vitro studies, the translation of these strategies from preclinical models to human trials is a critical next step in fully understanding the potential benefits and risks associated with senotherapy in addressing age-related kidney issues and promoting longevity.

5 Secondary Prevention: Identification of CKD

Secondary prevention of chronic kidney disease (CKD) revolves around the timely and accurate identification of CKD to initiate interventions that can slow its progression

(Fig. 1). One common method for identification is the measurement of creatinine-based eGFR and albuminuria. [50]

5.1 eGFR Estimation in Older Adults and Implications for Clinical Practice

The Cockcroft–Gault equation was widely used to calculate creatinine clearance, especially for drug-dosing adjustment [51]. However, it was derived from a cohort of younger adults and does not account for body surface area, making it less accurate. The Modification of Diet in Renal Disease (MDRD) equation was also developed from a cohort of middle-aged adults [52], showing higher relevant to measured creatinine clearance than the Cockcroft–Gault equation and was adopted by the 2002 Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline (CPG) [53]. However, this relevance is less among those with higher eGFR (> 60 ml/min/m^2), making it less accurate when estimating in healthy individuals or those with mild renal impairment. A more recent creatinine-based equation is the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [54], which was adopted by the 2012 Kidney Disease Improving Global Outcomes (KDIGO) CPG for CKD [55]. In the developing cohort, 15% were older adults aged > 65 years. Although the overall bias of MDRD and CKD-EPI was comparable, CKD-EPI showed lower bias in predicting measured GFR in individuals aged > 65 years with eGFR of 60–89 ml/min/m^2) in the validation cohort [56]. However, these formulas rely on serum creatinine levels, which are subject to various influencing factors, including age, gender, muscle mass, and the use of medications that affect renal tubular secretion [57]. In older individuals with sarcopenia, serum creatinine levels may appear lower than typical. Notably, the Baltimore Longitudinal Study of Aging has demonstrated that both the MDRD and CKD-EPI equations tend to overestimate measured creatinine clearance [58]. For more accuracy, a cystatin-based equation may be used, if available [50]. Meta-analysis showed discrepancies in eGFR assessments based on creatinine and cystatin C highlight the potential for misclassification of kidney function in diverse cohorts [59]. Use of cystatin C alone or in combination with creatinine yields more accurate GFR estimation and CKD classification. Other equations have been developed to enhance the accuracy of estimating glomerular filtration rate (GFR) in older adults. The Full Age Spectrum (FAS) equation is designed for a wide age range, including individuals over 70 years old [60], while the Berlin Initiative Study (BIS) equation is specifically derived from individuals aged 70 and older [61, 62]. Despite the initial high performance of the BIS equation in older adults, it exhibited limited accuracy in individuals aged 65–74 years with a measured GFR below 45 ml/min/1.73 m^2 [63, 64]. Current evidence emphasizes that no single equation surpasses the others. Each equation has its own limitations, and their interpretation should be approached cautiously.

Age-related declines in eGFR may signify normal kidney functions rather than indicating pathological conditions and does not lead to clinical significance. To date, there is no age-specific recommendation for identification of CKD, including the criteria for diagnosis of CKD. A large population-based cohort showed that using a fixed eGFR threshold for all ages, compared with an age-adapted threshold, had 60% higher incidence of CKD [65]. About 75% of individuals diagnosed with CKD solely based on current eGFR criteria were aged 65 years or older, with an eGFR of 45–59 ml/min/1.73 m^2 and normal/mild albuminuria. Despite an increased relative risk of kidney failure and death in those under 75 years compared with non-CKD controls, their absolute risks were comparable, emphasizing the potential for overdiagnosis. These findings underscore the importance of considering age-adapted eGFR thresholds to avoid overdiagnosing CKD in individuals with normal-to-mild albuminuria.

5.2 CKD Screening Strategy in Older Adults

Older individuals face an increased risk of chronic kidney disease (CKD) [66]. While CKD is often overdiagnosed in this population, underdiagnosis can lead to serious complications. Therefore, it is crucial to screen and monitor older adults for CKD, especially those with diabetes, hypertension, or other CKD risk factors, as well as those showing signs such as salt and water retention, electrolyte imbalances, or unexplained anemia [6]. Beyond early detection, this is important because many older adults take medications that depend on kidney function or can harm the kidneys. When assessing kidney function, using tests such as eGFR and albuminuria in older adults, it is important to consider age-related muscle mass changes and sarcopenia [50]. CKD screening should be integrated in a comprehensive geriatric assessment, including a thorough review of medical history and medication usage, functional status, cognitive function and mental health, nutritional status, cancer screening, fall risk, quality of life, social support, and advance care planning. These screening strategies should be tailored to each individual, particularly those with limited life expectancy or frailty, taking into account their preferences and overall health status.

6 Tertiary Prevention: Retardation of CKD Progression and Management of CKD Complications

While CKD is not curable, its progression to kidney failure can be effectively treated. Tertiary prevention strategies focus on slowing CKD progression and treatment of associated complications (Fig. 1). Kidney functions, including serum creatinine, eGFR, albuminuria, serum electrolytes (sodium, potassium, chloride, and bicarbonate levels), serum albumin, CKD-MBD panel (calcium, phosphate, magnesium, and parathyroid hormone levels), hemoglobin, and iron profile should be regularly monitored in order to detect CKD progression and complications (Table 1) [55].

6.1 Blood Pressure Control

Age-related arterial stiffness is known to associated with major adverse cardiovascular outcomes and all-cause mortality [67]. These changes involve systolic hypertension, reduced diastolic blood pressure (BP), and a higher incidence of orthostatic hypotension, rendering BP lowering in older adults challenging due to elevated risks of stroke, myocardial infarction, and fall [68, 69]. Nevertheless, results from the Hypertension in the Very Elderly Trial (HYVET) [70] and the Systolic Blood Pressure Intervention Trial (SPRINT) [71] have demonstrated benefits in treating hypertension in advanced age on reduction of major cardiovascular events and death from any cause.

While the 2021 KDIGO CPG for BP management [72] recommended target systolic BP of < 120 mmHg when tolerated, caution of intensive blood pressure control is advised, especially in older adults with lower baseline diastolic BP or coronary arterial disease. The 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) Guideline [73] suggested systolic BP target in older adults at 130–140 mmHg and against target of 120 mmHg, while the 2017 American College of Cardiology/American Heart Association (ACC/AHA) Guideline [74] suggested the target of < 130/80 at the age of 65 years or older, while the.

In older adults, antihypertensive regimen should be initiated with monotherapy, particularly using ACEIs/ARBs for their renoprotective effects on reduction of albuminuria. However, careful monitoring of eGFR and serum potassium is essential, especially when exposure to nephrotoxic

Table 1 Summary of targets in CKD management

Parameters	Targets
Blood pressure [72–74]	2021 KDIGO: SBP < 120 mmHg[a] 2018 ESC/ESH: SBP < 130–140, avoid SBP < 120 mmHg 2017 ACC/AHA: BP < 130/80 mmHg Use of ACEI/ARB if no contraindication
Blood glucose [79]	Hemoglobin A1C < 8–8.5%
Albuminuria [55]	ACR < 30 mg/g
Electrolytes [55]	Serum potassium ≤ 5.5 mmol/l Correction of metabolic acidosis Serum bicarbonate 24–26 mmol/l
Anemia [110]	Hemoglobin 11–12 g/dl, avoid hemoglobin > 13 g/dl Iron supplements Iron saturation ≥ 25% Serum ferritin 300–500 ng/ml Considering erythropoiesis-stimulating agents if hemoglobin < 10 g/dl
CKD-MBD [111]	Avoid hypercalcemia Lowering serum phosphate to normal range Treatment of hyperparathyroidism if intact parathyroid hormone level is progressively rising and persistent above upper normal limit
Lipid [55]	Statin if age ≥ 50 and eGFR ≥ 60 ml/min/m^2 Statin ± ezetimibe if age ≥ 50 and eGFR < 60 ml/min/m^2
Diet [107]	Adequate protein intake ≥ 1 g/kg/day Adequate calory intake ≥ 30 kcal/kg/day Monitoring for malnutrition
Lifestyle [55]	Smoking cessation

[a]Requires individualized approach due to high comorbidity level with older age.

ACC/AHA American College of Cardiology/American Heart Association, *ACR* albumin-creatinine ratio, *BP* blood pressure, *eGFR* estimated glomerular filtration rate, *ESC/ESH* European Society of Cardiology/European Society of Hypertension, *KDIGO* Kidney Disease: Improving Global Outcomes, *MBD* metabolic bone disease, *SBP* systolic blood pressure

substances or dehydration. Consideration should be given to combining with thiazide diuretics or calcium channel blockers [72]. Recent randomized controlled trials that included older adults have indicated the efficacy of chlorthalidone in lowering blood pressure in advanced CKD [75], while Finerenone, despite demonstrating kidney and cardiac protective effects, has modest impacts on BP reduction and an increased risk of hyperkalemia [76].

6.2 Glucose Control

Hemoglobin A1C (HbA1C) is the gold standard for monitoring glucose level in CKD. However, the correlation between HbA1c and fasting glucose exhibited its strongest association in individuals without anemia. Poor associations of HbA1c, glycated albumin, and fructosamine with fasting glucose were observed in individuals with severe or very severe CKD irrespective of anemia status [77]. In such population, HbA1C might be replaced with continuous glucose monitoring (CGM) or self-monitoring of blood glucose (SMBG) [78]. As HbA1C levels and adverse clinical outcomes are related in an U-shape correlation As HbA1C levels and adverse clinical outcomes are related in an U-shape correlation, the 2022 KDIGO CPG for diabetes management in CKD [79] recommended individualized glycemic target with HbA1C ranging from < 6.5 to < 8%. The HbA1C target tends to be higher in individuals who are at higher risk of hypoglycemia, have lower hypoglycemic awareness, have more comorbidities, or have shorter life expectancy.

The current landscape of antihyperglycemic medications for glucose control in older adults with CKD, involves navigating a complex balance between glycemic control and potential complications. Metformin stands out as the first-line therapy due to its cost-effectiveness and low hypoglycemia risk [80]. However, caution is warranted in older adults with CKD, as it may increase the risk of lactic acidosis and gastrointestinal side effects. Sodium-glucose cotransporter 2 inhibitors (SGLT2i), while demonstrating promising effects on kidney and cardiovascular outcomes, have been the subject of only a limited number of randomized trials specifically investigating their efficacy and safety in older adults [81, 82]. The diuretic effects of SGLT2i can lead to hypotension, and the negative caloric balance may result in weight loss. Glucagon-like peptide-1 (GLP-1) receptor agonists present newer options for renoprotective effects with low hypoglycemia risk, but their tolerability, especially in terms of gastrointestinal upset and cost, needs consideration in older populations [83]. DPP-4 inhibitors also provide low hypoglycemic risk and tolerability in older adults [84]. Sulfonylureas, effective in lowering blood glucose, pose an increased hypoglycemia risk in older adults with CKD [85]. Thiazolidinediones, although avoiding hypoglycemia, come with concerns about weight gain, fluid retention, and cardiovascular issues, limiting their use in older patients with CKD [86]. Overall, the choice of antihyperglycemic agents for older adults with CKD demands a personalized, cautious approach, considering efficacy, safety, and individual patient characteristics.

6.3 Electrolyte Management

Older adults face a heightened risk of hyperkalemia, which is exacerbated by reduced eGFR, common use of ACEIs/ARBs, and constipation [87]. This population's susceptibility to arrhythmias underscores the importance of carefully managing potassium levels to prevent serious cardiovascular complications. Sodium polystyrene sulfonate (SPS), historically used for hyperkalemia, lacks robust clinical trial data and raises safety concerns, including the potential for intestinal necrosis [88]. Newly approved options such as patiromer, a potassium-binding polymer, effectively reduces serum potassium levels and has demonstrated safety and tolerability in older adults [89]. Another investigational option, sodium zirconium cyclosilicate, also shows efficacy in lowering serum potassium levels in hyperkalemic patients, but further research is needed to assess its long-term safety and tolerability, particularly in older adults. [90]

Managing dysnatremia in older adults with CKD requires careful consideration due to the complexity of fluid and electrolyte imbalances in this population, such as impaired water excretion, as well as syndrome of inappropriate antidiuretic hormone secretion, adrenal insufficiency, and medications affecting sodium levels [91, 92]. Both hyponatremia and hypernatremia can impact morbidity and mortality and should be corrected even if asymptomatic [93]. It is crucial to avoid rapid shifts in sodium levels to prevent neurological complications [94, 95]. Calcium supplementation also need careful consideration. Inadequate calcium intake increases risk of fracture, osteoporosis, and falls, while excessive supplementation can lead to vascular calcification [96, 97]. Maintaining adequate magnesium levels through sufficient dietary intake is advisable, as chronic magnesium deficiency potentially explains the link between inflammation, oxidative stress, and aging-related disorders. However, the benefit of magnesium supplements remains controversial [98, 99].

6.4 Management of Anemia

Anemia is a prevalent concern in older individuals with CKD, contributing to fatigue and exacerbating functional decline. Among older adults, malnutrition and impaired gut absorption often lead to iron-deficiency anemia, making iron supplementation a primary therapeutic approach. In advanced CKD cases, where erythropoietin deficiency is evident, the use of erythropoiesis-stimulating agents (ESAs)

may be considered [100]. Older individuals may have lower bone marrow erythropoietin response, requiring higher dose of ESA. However, it is crucial to note that targeting hemoglobin levels > 11 g/dl with these agents has been associated with an increased risk of stroke and thrombotic events [101]. Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs) represent a novel class of agents with efficacy in treating anemia comparable to ESAs. However, their use in older adults is associated with uncertainty due to a lack of comprehensive safety data and insights into long-term outcomes for this specific population [100]. The potential risks of thrombotic events and malignancy associated with HIF-PHIs emphasize the need for caution when considering their use in older adults [102]. Additionally, anemia in the older adults may be multifactorial, with other chronic illnesses such as cancer playing a role, emphasizing the importance of a comprehensive diagnostic approach.

6.5 Management of Metabolic Bone Disease

CKD-MBD is associated with various complications, including cardiovascular disease and fractures, which can significantly impact the health and quality of life of older adults [103]. Beyond phosphate diet restriction, phosphate binders are commonly used [104]. Sevelamer, lanthanum, iron, and calcium-based binders, on major outcomes are uncertain. Sevelamer in CKD G5D may reduce all-cause death and hypercalcemia compared with calcium-based binders. Adverse effects vary among binders, including constipation and vomiting. Older individuals often have osteoporosis and bone fragility. The use of antiresorptive agents, such as bisphosphonates or denosumab, may exacerbate these disturbances in individuals with CKD. This can potentially lead to complications, including disruptions in calcium and phosphate balance, increased risks of hypocalcemia, and impaired bone turnover [105].

Regarding multiple comorbidities and psychosocial burdens, treatment plans should be individualized, based on shared decision making with care givers and family members. The goal of care, especially in individuals with advanced age, should also account for quality of life, frailty, performance status, life expectancy, and end-of-life care plan.

6.6 Dietary Protein Intake

Older adults face a dilemma regarding protein intake as high protein diets can worsen CKD progression, yet they are at risk of malnutrition and protein-energy wasting [106]. Geriatric guideline suggest a protein intake of 1.0–1.2 g/kg body weight per day to prevent malnutrition and sarcopenia [107]. Decisions regarding protein restriction should be guided by both nutritional status and the risk of CKD progression [66]. It is important to avoid protein restriction in cases of malnutrition or protein-energy wasting, especially if kidney function is stable [106]. However, in instances of advanced or rapidly progressing CKD, restricted protein intake may be safe for stabilizing metabolic status [108, 109]. This should be done with careful nutritional assessment and monitoring.

7 Conclusions

CKD in older adults is a multifaceted challenge that stems from the intricate interplay of various comorbidities and frailty. Each condition and its treatments can interact with others, making it more complicated impacting both individuals and their caregivers. Preventing CKD in older adults requires a comprehensive approach encompassing primary prevention to modify risk factors, secondary prevention for early CKD identification, and tertiary prevention to address complications. This comprehensive strategy aims to enhance the quality of life for individuals affected by CKD and slow down the deterioration of functional status. By addressing CKD at multiple levels (primary, secondary, and tertiary), this approach seeks to mitigate the multifaceted nature of the condition, providing a more effective and patient-centered approach to care in the older adults.

Declarations

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Conflict of interest S.T. and A.K.B. declare that they have no conflicts of interest that might be relevant to the contents of this manuscript.

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Consent (participation and publication) Not applicable.

Data availability All data generated or analysed during this study are included in this published article.

Code availability Not applicable.

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