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REVIEW ARTICLE

Optimizing care for chronic kidney disease: Considerations from A to Z

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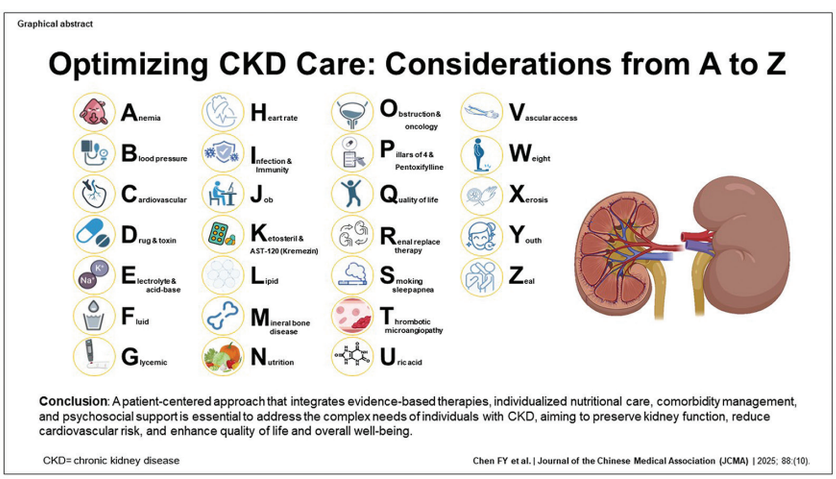
Abstract

Chronic kidney disease (CKD) management requires a comprehensive and multidisciplinary approach to optimize clinical outcomes. This review systematically outlines essential components of CKD care from A to Z, offering evidence-based guidance to enhance patient management. Anemia treatment emphasizes iron supplementation, erythropoiesis-stimulating agents, and novel hypoxia-inducible factor prolyl hydroxylase inhibitors. Achieving optimal blood pressure control through renin-angiotensin system inhibitors and calcium channel blockers reduces cardiovascular risk and delays CKD progression. Cardiovascular risk management includes statins combined with ezetimibe or proprotein convertase subtilisin/kexin type 9 inhibitors, along with appropriate anticoagulation therapy for atrial fibrillation. Individualized glycemic control strategies prioritize sodium–glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists for their cardiovascular and renal protective effects. Vigilance in avoiding nephrotoxic agents, such as non-steroidal anti-inflammatory drugs, proton pump inhibitors, aminoglycosides, and contrast media, is essential for preventing renal injury. Rigorous management of electrolytes and acid-base disturbances, involving dietary sodium and potassium restrictions, phosphate binders, and bicarbonate supplementation, reduces CKD progression and related complications. Appropriate fluid management through dietary sodium and water restriction with individualized diuretic therapy prevents volume overload and associated cardiovascular complications. Nutritional interventions, particularly low-protein diets supplemented with ketoanalogues of amino acids, effectively delay CKD progression and control metabolic disturbances. Therapies addressing CKD-related mineral and bone disorders, including phosphate binders, vitamin D analogues, and calcimimetics, reduce the risk of vascular calcification. In addition, lipid-lowering therapies, anticoagulation therapy, optimal vascular access management for dialysis, and early detection of arrhythmias and thrombotic microangiopathy significantly enhance patient outcomes. Attention to quality of life issues, such as alleviating xerosis symptoms, promoting optimal body mass index through weight management strategies, and providing psychosocial support, further enhances patient-centered care. This comprehensive review highlights the crucial importance of a multidisciplinary approach in CKD management.

Keywords: Cardiovascular protection; Chronic kidney disease; Multidisciplinary care; Quality of life; Renal outcomes



Lay summary: This comprehensive review introduces an A to Z framework for chronic kidney disease care, covering 26 essential topics ranging from anemia, blood pressure control, cardiovascular protection, and blood sugar management to fluid balance, nutritional therapy, and psychosocial support. It highlights current guideline-recommended treatments, including the four key medication classes: renin-angiotensin system inhibitors, sodium–glucose cotransporter-2 inhibitors, glucagon-like peptide-1 receptor agonists, and non-steroidal mineralocorticoid receptor antagonists. The article also discusses infection prevention, avoidance of kidney toxins, appropriate vascular access for dialysis, and symptom management such as itchiness and sleep disturbances. Emerging considerations, including occupational exposures, thrombotic microangiopathy, and anti-aging strategies, are also addressed. This review provides clinicians with a practical, patient-centered, and multidisciplinary roadmap to improve kidney function, reduce complications, and enhance the quality of life across the spectrum of chronic kidney disease.

1. INTRODUCTION

Chronic kidney disease (CKD), characterized by progressive and irreversible decline in kidney function, represents a major global health challenge with diverse etiologies, including diabetes mellitus, hypertension, glomerulonephritis, and exposure to environmental or occupational nephrotoxins. The clinical manifestations of CKD frequently include electrolyte disturbances, cardiovascular complications, anemia, and mineral-bone disorders, significantly impairing patients' well-being and prognosis. Progressive CKD can result in end-stage kidney disease (ESKD), necessitating dialysis or kidney transplantation, markedly increasing morbidity and mortality, and highlighting the need for comprehensive multidisciplinary care.[1] The global prevalence of CKD continues to rise, driven by aging populations and increased incidence of diabetes, hypertension, obesity, and nephrotoxin exposure. CKD currently affects approximately 10% to 15% of adults worldwide and accounts for nearly one million annual deaths, primarily due to cardiovascular complications. It represents a significant public health and economic issue, and results in increased healthcare utilization, medication costs, dialysis requirements, and associated complications. Furthermore, epidemiological evidence underscores pronounced regional disparities, with low- and middle-income countries disproportionately impacted by occupational and environmental nephrotoxins, inadequate healthcare infrastructure, and limited resources for effective CKD prevention and management.[2]

Optimized CKD management is critical for attenuating disease progression, reducing cardiovascular risks, and enhancing patient-centered outcomes. Comprehensive care encompasses pharmacological interventions, rigorous blood pressure and glycemic control, nutritional modifications, and avoidance of nephrotoxic exposures. Recent therapeutic advancements, including novel agents such as sodium–glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and non-steroidal mineralocorticoid receptor antagonists (MRAs), have demonstrated significant renoprotective and cardioprotective effects, reshaping clinical guidelines.[3] Multidisciplinary and patient-centered approaches integrating clinical, pharmacological agents, psychosocial, and nutritional care effectively address CKD's complexities. This review systematically highlights essential CKD management strategies from A to Z, offering clinicians evidence-based guidance to optimize patient outcomes and improve clinical practice.

2. A TO Z CONSIDERATIONS FOR CKD CARE

2.1. Anemia management

Anemia management in CKD encompasses iron supplementation, erythropoiesis-stimulating agents (ESAs), and hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs). Iron supplementation effectively corrects iron deficiency, improving hemoglobin levels and reducing ESA dosage requirements; however, vigilant monitoring is essential to avoid iron overload.[4] ESAs effectively increase hemoglobin levels and reduce transfusion dependence, but higher ESA doses or elevated hemoglobin targets may elevate cardiovascular risk.[5] Novel HIF-PHIs, such as daprodustat, stabilize hypoxia-inducible factors, stimulating endogenous erythropoietin production and enhancing iron metabolism, providing a promising alternative for anemia treatment.[6] Nevertheless, long-term safety, particularly regarding cardiovascular and malignancy risks, warrants further evaluation.[7]

2.2. Blood pressure control

Optimal blood pressure (BP) management is crucial in CKD management. The recent Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommend BP targets below 120 mm Hg to minimize cardiovascular events and slow CKD progression.[8] Renin-angiotensin-aldosterone system (RAAS) inhibitors are recommended as first-line therapy, especially in proteinuric CKD, due to their renoprotective effects.[9] Dihydropyridine calcium channel blockers (CCBs) complement angiotensin II receptor blockers effectively, assisting in achieving BP targets without adverse renal outcomes. Integrating diuretics further optimizes fluid and BP control. In addition, lifestyle modifications, including dietary salt restriction, regular physical activity, and weight management, enhance the efficacy of pharmacological interventions and improve overall patient outcomes.[10,11]

2.3. Cardiovascular disease prevention

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in CKD patients.[12] Statins, frequently combined with ezetimibe, significantly reduce cardiovascular events by effectively lowering low-density lipoprotein cholesterol (LDL-C) levels in this population.[13] Proprotein convertase subtilisin/kexin type 9 inhibitors further decrease LDL-C, demonstrating additional cardiovascular benefits.[14] While aspirin or purinergic receptor type Y, subtype 12 (P2Y12) inhibitors are recommended for secondary prevention, routine primary prophylaxis remains controversial due to limited benefits and increased bleeding risks.[15] Management strategies for heart failure involve individualized selection of RAAS inhibitors, beta-blockers, diuretics, MRAs, and SGLT2 inhibitors, which could improve clinical outcomes and reduce cardiovascular morbidity and mortality.[16]

2.4. Drugs and toxins

Nephrotoxic agents, both pharmacologic and environmental, play a significant role in the onset and progression of

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CKD. Among commonly used medications, non-steroidal anti-inflammatory drugs impair renal perfusion and increase the risk of acute kidney injury (AKI) and CKD progression.[17] Proton pump inhibitors have been linked to interstitial nephritis and long-term renal impairment,[18] while aminoglycosides are well-known for their dose-dependent tubular toxicity.[19] Iodinated contrast media carry a risk of contrast-induced nephropathy, particularly in patients with preexisting CKD or repeated exposures.[20,21] In oncology, chemotherapeutic agents such as cisplatin and immune checkpoint inhibitors may cause AKI, tubulointerstitial nephritis, or immune-mediated renal dysfunction.[22,23] Environmental nephrotoxins also contribute substantially to the CKD burden. Chronic exposure to heavy metals such as lead, cadmium, arsenic, and mercury has been associated with tubular injury and progressive renal fibrosis.[24] In addition, air pollution, particularly fine particulate matter (PM2.5), has been implicated in CKD development via systemic inflammation, oxidative stress, and endothelial dysfunction.[25]

2.5. Electrolyte balance and acid-base control

Effective management of electrolyte balance, particularly sodium, potassium, calcium, phosphorus, and magnesium, is essential to prevent CKD-related complications.[26] Sodium restriction controls hypertension and edema, whereas potassium management prevents hyperkalemia-related arrhythmias.[27] The regulation of calcium and phosphorus, including phosphate binders and vitamin D analogues, mitigates vascular calcification and mineral bone disorders.[28] Magnesium levels should be monitored due to associations with cardiovascular risk.[29] In addition, correcting metabolic acidosis through bicarbonate supplementation (target serum bicarbonate ≥22 mmol/L) reduces CKD progression, muscle wasting, and bone mineral disturbances.[30] Comprehensive electrolyte and acid-base control could improve patient outcomes.

2.6. Fluid management

Optimal fluid management in CKD prevents volume overload, reducing hypertension, heart failure risk, and disease progression.[31] Dietary sodium restriction (<2.3 g/d) is essential for minimizing fluid retention and maintaining euvolemia.[32] Loop diuretics effectively control extracellular volume, especially in advanced CKD, although careful titration is necessary to prevent electrolyte imbalance and ototoxicity. Contrary to previous assumptions, thiazide-type diuretics retain efficacy even at lower glomerular filtration rates and may complement loop diuretics.[33] In advanced CKD and dialysis patients, fluid intake must be restricted (~1-1.5 L/d), with ultrafiltration during dialysis individualized to achieve optimal volume status, preventing cardiovascular events and enhancing outcomes.[34]

2.7. Glycemic control

Tight glycemic control is crucial in CKD to slow the progression to ESKD and reduce complications.[35] Both the American Diabetes Association and KDIGO guidelines recommend individualized HbA_1c targets (~6.5%-8.0%) to maximize microvascular benefits and improve cardiovascular outcomes and survival while minimizing hypoglycemia risk.[36] Pharmacotherapy must be tailored to renal function. The SGLT2 inhibitors and GLP-1 receptor agonists are preferred for type 2 diabetes with CKD due to their glucose-lowering efficacy and evidence of slowing CKD progression and reducing cardiovascular events.[16] Dipeptidyl peptidase-4 inhibitors are often well-tolerated in CKD. For instance, linagliptin requires no dose adjustment even in advanced disease.[37] Insulin often becomes a mainstay in advanced CKD when oral agents are limited but requires careful titration and close monitoring to avoid hypoglycemia.

2.8. Heart rhythm management

Patients with CKD exhibit an elevated prevalence of arrhythmias, notably atrial fibrillation, increasing cardiovascular morbidity and mortality risk.[38] Beta-blockers remain first-line therapy for rate control but require cautious dosing due to altered drug metabolism and risks of bradycardia.[39] Antiarrhythmic drugs necessitate careful selection and renal dose adjustments to minimize toxicity and proarrhythmic effects.[40] Anticoagulation is critical for stroke prevention in CKD patients with atrial fibrillation; however, bleeding risk demands careful patient assessment, and dose-adjusted direct oral anticoagulants are typically preferred over warfarin.[41,42]

2.9. Infection and immunity

Patients with CKD have increased susceptibility to infections due to impaired innate and adaptive immunity.[43] Preventive vaccination, including annual influenza, pneumococcal conjugate and polysaccharide vaccines, and hepatitis B immunization, is strongly recommended, particularly in dialysis-dependent individuals.[44] Dialysis patients frequently experience catheter-related bloodstream infections or peritonitis, significantly increasing morbidity and mortality.[45] Kidney transplant recipients, subjected to lifelong immunosuppression, are particularly vulnerable to opportunistic infections (eg, cytomegalovirus, BK virus), necessitating regular surveillance and prophylactic therapies.[46] Immunosuppressive therapy must be individualized, balancing the risk of graft rejection with infection, requiring vigilant monitoring for early detection and treatment of infectious complications.[47]

2.10. Job (occupational disease)

Occupational exposures might contribute to CKD development. Chronic exposure to heavy metals, such as lead, cadmium, and mercury, prevalent in industries like mining, metallurgy, and battery manufacturing, is strongly linked to nephrotoxicity and CKD.[48] Organic solvents encountered in industrial processes also elevate CKD risk through chronic tubular damage and oxidative stress.[49] Agricultural workers frequently exposed to pesticides, particularly herbicides (eg, atrazine, pendimethalin), demonstrate higher CKD incidence due to chronic tubular-interstitial injury.[50] Mechanistically, these occupational nephrotoxicants induce chronic inflammation, oxidative stress, and progressive renal fibrosis, leading to accelerated CKD progression.[51]

2.11. Ketosteril and AST-120

Ketosteril (ketoanalogues of amino acids), combined with a low-protein diet, reduces nitrogenous waste, significantly delays renal decline, controls metabolic abnormalities such as hyperphosphatemia, and preserves nutritional status.[52,53] Its use is recommended for stable, non-dialysis CKD patients (stages 3-5) with close nutritional monitoring, demonstrating improved renal and metabolic outcomes (Table 1).[53] AST-120, an oral spherical carbon adsorbent, binds uremic toxins (eg, indoxyl sulfate) in the gastrointestinal tract, potentially slowing CKD progression by reducing oxidative stress and inflammation.[59] Although AST-120 is approved in Japan and several Asian countries, it is not approved by the United States Food and Drug Administration or the European Medicines Agency. Its efficacy was challenged by two large, multinational RCTs—Evaluating Prevention of Progression in Chronic Kidney Disease (EPPIC)-1 and EPPIC-2—which failed to demonstrate significant benefit in delaying CKD progression.[59,62] These findings limit its broader clinical adoption. Most clinical trial results remain inconsistent regarding renal benefits. However, in the post hoc subgroup analysis of the EPPIC trials, AST-120 has been demonstrated to decrease the composite renal endpoints of serum creatinine

Table 1

Comparative summary of clinical trials evaluating renal and cardiovascular outcomes in CKD patients

Medication name	Trial name	Patient number/ study duration	Inclusion criteria	Age, y	Sex (% male)	Baseline eGFR, mL/ min/1.73 m²	Primary endpoints	Secondary endpoints	Results of primary endpoints	eGFR change (annual decline)	Clinical considerations	Reference
Dapagliflozin	DAPA-CKD	4304/median 2.4 y	CKD, eGFR 25-75, UACR 200-5000 mg/g	62	66.9%	43	Sustained ≥50% eGFR decline, ESKD, renal/ CV death	Renal outcomes, HHF hospitalization, all-cause mortality	HR = 0.61, $p < 0.001$	−2.86 vs −3.79 (placebo), $p < 0.001$	Effective in diabetic and non-diabetic patients, good safety profile	[16]
Empagliflozin	EMPA-KIDNEY	6609/median 2.0 y	CKD, eGFR 20-90, UACR ≥200 mg/g	63.8	66.4%	37	Sustained ≥40% eGFR decline, ESKD, renal/ CV death	HHF, HF, or CV death, all-cause mortality	HR = 0.72, $p < 0.001$	−1.95 vs −2.70 (placebo), $p < 0.001$	Effective in diabetic and non-diabetic CKD patients, well-tolerated	[54]
Canagliflozin	CREDENCE	4401/median 2.6 y	T2DM with CKD, eGFR 30-90, UACR >300 mg/g	63	66.1%	56	Doubling of serum creatinine, ESKD, renal/ CV death	Renal-specific endpoints, MACE, HHF	HR = 0.70, $p < 0.001$	−1.85 vs −3.37 (placebo), $p < 0.001$	Effective in diabetic CKD patients, well-tolerated	[55]
Semaglutide (Ozempic)	FLOW	3533/median 3.4 y	T2DM with CKD, eGFR 25-75, UACR 100-5000 mg/g	66.6	70.0%	47	≥50% eGFR decline, ESKD, renal/CV death	Renal outcomes, MACE, all-cause mortality	HR = 0.76, $p = 0.0003$	−2.10 vs −3.26 (placebo), $p < 0.001$	First GLP-1 trial confirming renal benefit, GI side effects common	[56]
Dulaglutide (Trulicity)	AWARD-7	577/52 wk	T2DM, CKD stages 3-4, HbA1c 7.5-10.5%	65	52.0%	34	HbA1c change at week 26	eGFR and albuminuria at week 52	Non-inferior HbA1c control	−0.70 vs −3.30 (insulin), $p < 0.001$	Effective and safe in advanced CKD, significantly improved albuminuria	[57]
Finerenone	FIDELIO-DKD	5734/median 2.6 y	T2DM with CKD, eGFR 25-75, UACR 30-5000 mg/g	64	70.0%	44	≥40% eGFR decline, ESKD or renal death	CV composite (MACE, HF hospitalization)	HR=0.82, $p = 0.001$	−2.00 vs −2.96 (placebo), $p < 0.001$	Monitor hyperkalemia risk	[58]
AST-120	EPPIC-1 and EPPIC-2	2035/median 3.3 y	Advanced CKD (serum creatinine 2.0-5.0 mg/ dL), diabetic/ non-diabetic	55.5	59.2%	22	Doubling of serum creatinine, initiation of dialysis	eGFR decline rate, dialysis timing	HR = 0.74, $p = 0.029$ (USA post hoc subgroup analysis)	Estimated values: −2.2 vs −3.2 (placebo), $p = 0.004$	Mild gastrointestinal side effects	[59,60]
Ketosteril	Garneata	50/15 mo	Non-diabetic CKD stage 4 (eGFR <30), proteinuria <1 g/d	59	60.0%	18	Dialysis initiation or ≥50% eGFR decline	Nutritional status, biochemical parameters	HR = 0.31, $p < 0.001$	−0.40 vs −2.90 (control), $p < 0.001$	Requires strict dietary adherence and patient compliance	[53]
Pentoxifylline	PREDIAN	169/2 y	T2DM CKD stages 3-4, eGFR ~20-60	61	65.0%	37	Annual eGFR slope	≥25% eGFR decline, albuminuria, inflammatory markers	Significantly slowed eGFR decline, $p < 0.001$	−1.05 vs −3.25 (placebo), $p < 0.001$	Anti-inflammatory, anti-proteinuric effects, mild side effects	[61]

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; AWARD-7 = A Study Comparing Dulaglutide With Insulin Glargine on Glycemic Control in Participants With Type 2 Diabetes and Moderate or Severe Chronic Kidney Disease; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; CREDENCE = Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation; DAPA-CKD = Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease; CV = cardiovascular; EMPA-KIDNEY = Study of Heart and Kidney Protection with Empagliflozin; EPPIC-1 and EPPIC-2 = evaluating prevention of progression in CKD; ESKD = end-stage kidney disease; FIDELIO-DKD = Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease; FLOW = evaluate renal function with semaglutide once weekly; GLP-1 = Glucagon-like peptide-1; HbA1c = Glycated hemoglobin; HF: Heart Failure; HHF = Hospitalization for Heart Failure; HR = hazard ratio; MACE = major adverse cardiovascular events; PREDIAN = pentoxifylline for renoprotection in diabetic nephropathy; RAS = renin-angiotensin system; SGLT2 inhibitor = sodium–glucose cotransporter-2 inhibitor; T2DM = type 2 diabetes mellitus; UACR = urine albumin-to-creatinine ratio; USA = United States of America.

doubling, dialysis, or renal transplantation by 26% and the risk of dialysis or renal transplantation by 30% (Table 1).[60]

2.12. Lipid control

Dyslipidemia accelerates atherosclerosis and CVD in CKD patients and may also contribute to CKD progression.[63,64] Guidelines recommend intensive LDL-C targets under 100 mg/dL for non-dialysis CKD (stages 3b-4).[65] Moderate-intensity statins, often combined with ezetimibe, significantly reduce cardiovascular events and mortality in CKD patients not yet on dialysis.[13] However, initiating statins in dialysis-dependent patients is generally not advised due to limited cardiovascular benefits.[65] Proprotein convertase subtilisin/kexin type 9 inhibitors, offering potent LDL-C reduction, may benefit CKD patients inadequately controlled by statins and ezetimibe, although robust clinical trial data in advanced CKD remain limited.[66]

2.13. Mineral bone disease and vascular calcification

Chronic kidney disease–mineral bone disorder (CKD-MBD) involves disrupted metabolism of calcium, phosphate, parathyroid hormone, vitamin D, and fibroblast growth factor-23 (FGF-23), promoting renal osteodystrophy and vascular calcification.[66] Hyperphosphatemia and elevated FGF-23 levels accelerate arterial calcification, increasing cardiovascular risk.[67] Management includes dietary phosphate restriction, phosphate binders (eg, sevelamer), active vitamin D analogs, and calcimimetics (eg, cinacalcet).[68] Recent guidelines recommend individualized therapy targeting biochemical parameters to reduce the progression of CKD-MBD and cardiovascular complications.[66]

2.14. Nutrition and diet

Nutritional management is fundamental in CKD care. Major guidelines recommend low-protein diets (0.6-0.8 g/kg/d) to reduce uremic toxin generation and slow CKD progression, with very-low-protein diets (VLPD, 0.3-0.4 g/kg/d) supplemented with ketoanalogues considered in advanced CKD under close supervision.[69] The Kidney Disease Outcomes Quality Initiative (KDOQI) 2020 and KDIGO 2020 guidelines emphasize plant-dominant low-protein diets (PLADO), defined as ≥50% plant-based protein intake, for their added benefits in reducing acid load, modulating gut microbiota, and improving cardiometabolic profiles.[70] A randomized trial demonstrated that a VLPD with ketoanalogues delayed dialysis initiation while maintaining nutritional status.[53] Dietary patterns such as the Dietary Approaches to Stop Hypertension (DASH), Mediterranean, and vegetarian diets have also shown favorable effects on CKD progression, cardiovascular risk, and metabolic health.[71] In the Chronic Renal Insufficiency Cohort (CRIC) Study, greater adherence to DASH-style diets was associated with slower estimated glomerular filtration rate (eGFR) decline and reduced mortality.[72] Several Taiwanese cohort studies further report that vegetarian diets reduce CKD risk in patients with diabetes, hyperuricemia, or obesity.[73–77] Adequate energy intake (30-35 kcal/kg/d), micronutrient repletion (eg, vitamin B12), and monitoring of electrolytes such as potassium are essential to avoid malnutrition and complications associated with high fruit/vegetable intake. Individualized nutritional counseling remains crucial.

2.15. Obstruction and oncology

Chronic urinary tract obstructions, including kidney stones, benign prostatic hyperplasia (BPH), and ureteral strictures, significantly contribute to CKD progression by inducing hydronephrosis, increased intrarenal pressure, and progressive tubular injury.[78] Vascular obstructions, such as renal artery stenosis, reduce renal perfusion, causing ischemic nephropathy and renal function deterioration.[79] Unresolved obstructions result in hypertension, recurrent infections, and accelerated progression to ESKD.[80] Management emphasizes prompt resolution of obstructions via medical therapy, minimally invasive approaches (eg, ureteral stents, lithotripsy), or surgical interventions (eg, transurethral resection of the prostate for BPH, angioplasty or stenting for vascular obstruction). In addition, malignancy has emerged as a growing concern in CKD care. Patients with CKD have a higher risk of developing cancers, particularly involving the urinary tract, gastrointestinal system, and hematologic organs, due to chronic inflammation, immune dysregulation, and uremic toxin accumulation.[81] Conversely, cancer treatments, including chemotherapy, targeted therapies, and radiotherapy, can induce or worsen kidney injury. This bidirectional relationship highlights the need for integrated nephrology-oncology care, with emphasis on early screening, nephrotoxicity risk assessment, and renal function preservation throughout the cancer care continuum.

2.16. Four pillars and pentoxifylline in CKD treatment

Effective pharmacological management of CKD rests on four core pillars: RAAS inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, and non-steroidal MRAs, each supported by KDIGO 2024 recommendations.[3]

1. RAAS inhibitors (ACEi or ARB) remain foundational, reducing intraglomerular pressure, proteinuria, and CKD progression, particularly in patients with moderate-to-severe albuminuria; they are recommended for individuals with A2/A3 albuminuria with or without diabetes (GRADE 1B).
2. SGLT2 inhibitors significantly delay CKD progression by promoting natriuresis, mitigating glomerular hyperfiltration, and reducing heart failure risk, and are strongly recommended in adults with eGFR ≥20 and urine albumin-creatinine ratio (UACR) ≥200 mg/g or heart failure (GRADE 1A).
3. GLP-1 receptor agonists offer complementary glycemic control and cardiorenal protection, and are recommended for patients with type 2 diabetes and CKD when SGLT2 inhibitors are insufficient, not tolerated, or contraindicated (GRADE 1B).
4. Non-steroidal MRAs: Finerenone, a novel non-steroidal MRA, attenuates inflammation and fibrosis beyond RAAS blockade, showing significant renal and cardiovascular benefits in albuminuric diabetic CKD, and is conditionally recommended for individuals with eGFR >25 mL/min/1.73 m², normal serum potassium, and persistent albuminuria despite renin-angiotensin system inhibition (GRADE 2A).

Pentoxifylline, a nonselective phosphodiesterase inhibitor, has demonstrated potential in managing CKD through its anti-inflammatory and antifibrotic properties.[82,83] Although not approved specifically for CKD, it has been evaluated in trials such as the Pentoxifylline for Renoprotection in Diabetic Nephropathy (PREDIAN) study for its anti-proteinuric and anti-inflammatory effects.[61] Despite some favorable results, systematic reviews emphasize inconsistent outcomes and gastrointestinal side effects, limiting their recommendation as standard care.[84]

Optimal use of these therapies requires individualized treatment based on clinical characteristics, risk stratification, and regular monitoring for adverse effects to ensure efficacy and patient safety (Table 1).

2.17. Quality of life

Quality of life (QoL) is critically impaired in CKD patients due to symptoms (fatigue, pruritus, insomnia), treatment burden, psychological distress, and lifestyle restrictions. Reduced QoL

adversely affects clinical outcomes, increasing risks of hospitalization and mortality.[85] Improving QoL requires multidimensional strategies, including symptom management, psychosocial interventions (eg, counseling, cognitive-behavioral therapy), exercise programs, and nutritional support. Patient-centered care approaches, involving shared decision-making and patient-reported outcome monitoring, enhance adherence, improve QoL, and optimize clinical outcomes.

2.18. Renal replacement therapy

Renal replacement therapies in CKD include dialysis and kidney transplantation, each significantly impacting QoL and survival. Hemodialysis and peritoneal dialysis effectively manage renal failure but are associated with high symptom burden, reduced QoL, and increased morbidity.[86] Kidney transplantation remains the optimal treatment, providing superior outcomes, survival advantage, and improved QoL compared to dialysis.[87] For patients unsuitable for dialysis or transplantation, conservative kidney management emphasizing palliative and hospice care improves symptom control and QoL, particularly for elderly or frail patients, highlighting the importance of individualized care aligned with patient preferences and prognosis.

2.19. Smoking and sleep apnea

Smoking accelerates CKD progression, worsens proteinuria, increases cardiovascular risk, and reduces dialysis graft and fistula survival; thus, smoking cessation is strongly recommended in CKD patients.[88] Sleep apnea, particularly obstructive sleep apnea, is highly prevalent in CKD and is independently associated with hypertension, accelerated kidney disease progression, cardiovascular events, and mortality. Effective management of obstructive sleep apnea through lifestyle interventions, weight loss, and continuous positive airway pressure therapy improves BP control, sleep quality, and renal outcomes.

2.20. Thrombotic microangiopathy

Thrombotic microangiopathy (TMA) is characterized by endothelial injury, platelet activation, and microvascular thrombosis, causing AKI or CKD progression.[89] CKD-associated TMA commonly arises secondary to uncontrolled hypertension, malignant nephrosclerosis, autoimmune disorders, drug-induced etiologies (eg, calcineurin inhibitors), and complement dysregulation. Management requires prompt identification and removal of underlying triggers, BP optimization, and supportive care. Complement-targeted therapies, such as eculizumab, significantly improve renal outcomes in complement-mediated TMA.[90] Timely diagnosis through laboratory assessment (schistocytes, thrombocytopenia, elevated LDH) and kidney biopsy when appropriate can guide targeted treatment, thereby minimizing renal injury, stabilizing kidney function, and improving patient prognosis.[89]

2.21. Uric acid control

Hyperuricemia is common in CKD and may promote renal progression, CVD, and increased mortality through mechanisms involving oxidative stress and inflammation.[91] Current guidelines suggest a target serum uric acid level below 6.0 mg/dL (360 μmol/L) for CKD patients, with a stricter goal (<5.0 mg/dL or 300 μmol/L) recommended for severe gout (eg, frequent flares, tophi).[3] Achieving these targets involves dietary purine restriction and pharmacological therapies such as allopurinol or febuxostat. Allopurinol requires careful renal-dose adjustments, while febuxostat requires no renal-dose adjustment but necessitates cardiovascular monitoring.[92]

2.22. Vascular access

Optimal vascular access is vital in dialysis management. Arteriovenous fistulas are preferred due to lower infection rates, longer patency, and better clinical outcomes compared to arteriovenous grafts and catheters.[93] Arteriovenous grafts are considered to be the alternative choice when arteriovenous fistulas are not feasible, but they carry increased thrombosis and infection risks. Central venous catheters, while immediately usable, carry the highest infection risk and mortality, and they are thus recommended only temporarily. Complications like stenosis, thrombosis, and infection necessitate careful surveillance and intervention, including regular Doppler ultrasound, angioplasty, or surgical revision to maintain access patency.

2.23. Weight management

Weight management is essential in CKD, as obesity accelerates renal progression and cardiovascular risk. Recommended body weight goals include achieving and maintaining a body mass index of approximately 20 to 25 kg/m² in CKD patients.[69] Structured lifestyle interventions involving caloric restriction, aerobic exercise (≥150 min/wk moderate intensity), and behavioral modifications effectively reduce proteinuria, stabilize renal function, and decrease cardiovascular morbidity. Bariatric surgery is considered in severely obese patients (body mass index of ≥35 kg/m²) who fail conservative management, potentially reversing CKD progression.[94]

2.24. Xerosis

Xerosis (dry skin) frequently occurs in CKD, affecting up to 80% of dialysis patients due to chronic inflammation, altered lipid metabolism, uremic toxins, and impaired skin barrier function. Xerosis significantly impacts patient QoL, exacerbating pruritus, sleep disturbance, and psychological distress.[95] The regular use of topical emollients, ointments, and moisturizers (eg, glycerin, urea-based creams) effectively improves skin hydration, restoring barrier function and alleviating symptoms. The avoidance of excessive bathing, the use of mild cleansers, and gentle skincare routines are crucial adjunctive measures.

2.25. Youth and anti-aging (resveratrol)

Resveratrol, a polyphenol with potent antioxidant. Preclinical models suggest resveratrol's potential anti-inflammatory and antioxidant effects. However, human studies in CKD are sparse and heterogeneous. A 2023 meta-analysis reported modest improvements in eGFR and biomarkers, but with low certainty of evidence and substantial variability across trials.[96] Moreover, poor bioavailability further constrains its therapeutic utility.

2.26. Zeal (psychosocial support)

Psychosocial support enhances QoL, treatment adherence, and clinical outcomes in CKD patients. Depression, anxiety, and reduced social support negatively impact treatment compliance, exacerbating CKD progression and increasing mortality. Structured psychosocial interventions, including cognitive-behavioral therapy, peer support programs, and patient education, improve psychological well-being, coping strategies, and disease self-management. Promoting patient engagement, shared decision-making, and holistic care through multidisciplinary approaches has enhanced emotional well-being, treatment adherence, and overall outcomes, underscoring psychosocial support as essential in CKD management.[97]

In conclusion, effective management of CKD requires a multidisciplinary, patient-centered approach that addresses anemia, BP, cardiovascular risk, glycemic control, electrolyte balance, and fluid status. Key pharmacologic agents, including RAAS inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists,

and non-steroidal MRAs, offer robust renal and cardiovascular protection. Lifestyle modification, nutritional therapy, and psychosocial support further contribute to improved outcomes. Emerging insights into CKD pathophysiology have identified gut microbiota dysbiosis, chronic inflammation, and molecular heterogeneity as important therapeutic targets. Interventions such as probiotics, dietary fiber, and oral adsorbents aim to restore gut–kidney axis homeostasis. Anti-inflammatory agents and multi-omics technologies are also advancing the field of precision nephrology. Collectively, these established and emerging strategies underscore a growing shift toward holistic, personalized CKD care to better meet the complex and evolving needs of each patient.

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