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Review

Supplementation Across the Chronic Kidney Disease Journey: From Early Disease to Dialysis and Kidney Transplantation - An Evidence-Based Approach

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Abstract

Chronic kidney disease (CKD) represents a progressive systemic disorder characterized by complex metabolic, inflammatory and nutritional abnormalities that evolve throughout the course of disease. Beyond declining kidney function, CKD is associated with protein-energy wasting (PEW), sarcopenia, chronic inflammation, oxidative stress, anaemia, CKD-mineral and bone disorder (CKD-MBD), metabolic acidosis and multiple micronutrient disturbances. These abnormalities significantly contribute to frailty, cardiovascular complications, impaired quality of life and increased mortality.

Nutritional supplementation has therefore become an important component of comprehensive CKD management. However, contemporary evidence no longer supports empirical supplementation but emphasizes individualized interventions based on CKD stage, nutritional status, dietary intake, dialysis modality, biochemical parameters, functional capacity and transplant status. During early CKD, supplementation strategies focus primarily on correction of documented deficiencies, particularly vitamin D deficiency, while maintaining adequate nutritional intake and preventing malnutrition. In advanced CKD and dialysis, the prevention and treatment of PEW become central therapeutic goals, with oral nutritional supplements (ONS), adequate protein intake, iron therapy and correction of metabolic acidosis representing the interventions with the strongest evidence. Emerging approaches targeting inflammation, oxidative stress and the gut-kidney axis, including omega-3 fatty acids, probiotics, prebiotics, magnesium, vitamin K, β-hydroxy-β-methylbutyrate (HMB), coenzyme Q10 and other nutraceuticals, remain areas of active investigation.

Following kidney transplantation, nutritional priorities shift toward prevention of obesity, metabolic syndrome, post-transplant diabetes mellitus and cardiovascular disease while maintaining adequate micronutrient status and avoiding potentially harmful supplement-drug interactions.

This review summarizes current evidence regarding nutritional supplementation throughout the CKD continuum, distinguishing interventions supported by clinical evidence from those that remain promising but insufficiently validated.

Keywords: chronic kidney disease, medical nutrition therapy, protein-energy wasting, CKD-mineral and bone disorder, dialysis, kidney transplantation

Introduction

The changing nutritional phenotype throughout CKD

Chronic kidney disease (CKD) is not only a disorder of filtration but a systemic metabolic condition associated with profound alterations in protein metabolism, inflammation, hormonal regulation, and body composition. As kidney function declines, patients may develop a range of metabolic and nutritional disturbances, including reduced appetite, metabolic acidosis, increased oxidative stress, and chronic inflammatory activation [1].

One of the most important consequences of these abnormalities is protein-energy wasting (PEW), characterized by loss of body protein mass and energy reserves, reduced muscle mass, and inadequate protein and energy intake [2]. PEW is associated with increased morbidity and mortality, particularly among patients with advanced CKD and those receiving dialysis therapy.

The nutritional challenges of CKD change throughout the disease trajectory. In early stages, the main objective is preservation of kidney function while preventing nutritional deficiencies. In advanced CKD and dialysis, the focus shifts toward preventing catabolism and maintaining muscle mass. After transplantation,

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the nutritional phenotype changes again, with increased risk of obesity, metabolic syndrome, post-transplant diabetes mellitus, and cardiovascular complications.
Therefore, supplementation strategies should follow the concept of a CKD journey, where the right intervention is selected for the right patient at the right stage of disease.
The KDOQI Clinical Practice Guideline for Nutrition in CKD recommends regular nutritional assessment and individualized nutritional therapy, including supplementation when dietary counselling alone cannot achieve nutritional targets [1].

CKD G1-G5

Prevention of deficiency and preservation of nutritional status

Vitamin D supplementation: correction of deficiency

Vitamin D abnormalities are common in CKD and may occur early in the disease course. Vitamin D deficiency or insufficiency may contribute to disturbances in mineral metabolism and secondary hyperparathyroidism.
Current recommendations support measurement of serum 25-hydroxyvitamin D [25(OH)D] concentrations and correction of documented vitamin D deficiency or insufficiency using treatment strategies recommended for the general population [3]. However, routine vitamin D supplementation has not been shown to improve clinically relevant CKD outcomes. Therefore, nutritional vitamin D should primarily be used to correct documented deficiency or insufficiency rather than as routine nephroprotective therapy [3].
In adults with CKD G3a–G5 not on dialysis, calcitriol and vitamin D analogues should not be routinely used. Their use may be reserved for patients with CKD G4–G5 with severe and progressive secondary hyperparathyroidism [3].

Vitamin D–Vitamin K axis: emerging importance in CKD-MBD and vascular calcification

The interaction between vitamin D and vitamin K has gained increasing attention in the context of CKD-mineral and bone disorder (CKD-MBD), as both nutrients contribute to calcium homeostasis and bone–vascular metabolism. Vitamin D plays a central role in the intestinal calcium absorption, regulation of parathyroid hormone secretion and maintenance of bone mineral metabolism [3].
Vitamin K is required for the γ-carboxylation and activation of vitamin K-dependent proteins, including osteocalcin and matrix Gla protein (MGP). MGP is an important endogenous inhibitor of vascular calcification. Patients with CKD, particularly those receiving dialysis, frequently exhibit impaired vitamin K status, reflected by increased concentrations of inactive dephosphorylated-uncarboxylated MGP (dp-ucMGP), which have been associated with markers of vascular calcification and adverse cardiovascular outcomes [4].
Clinical trials of vitamin K supplementation, particularly vitamin K2 (menaquinone-7), have demonstrated improvements in vitamin K status and reductions in dp-ucMGP concentrations. However, evidence that vitamin K supplementation reduces progression of vascular calcification or improves cardiovascular outcomes remains insufficient [4,5].

Magnesium supplementation and CKD-mineral metabolism

Magnesium has attracted attention as a potential modulator of CKD progression and vascular calcification. Potential mechanisms include inhibition of calcium-phosphate crystal formation and suppression of phosphate-induced vascular calcification. Observational studies have suggested associations between lower magnesium concentrations and increased risk of CKD progression; however, these findings cannot establish causality [6].
The MAGiCAL-CKD randomized clinical trial demonstrated that magnesium supplementation increased plasma magnesium concentrations but did not significantly reduce the progression of coronary artery calcification in patients with predialysis CKD [7].
Current clinical interpretation comprise: the correction of documented hypomagnesemia is appropriate; magnesium supplementation may be considered in selected patients; and the routine magnesium supplementation specifically for prevention of vascular calcification is not currently supported by sufficient clinical evidence.

Progressive CKD (G3b–G5): Prevention of protein-energy wasting

As CKD progresses, metabolic and nutritional disturbances become increasingly pronounced. Patients may develop anorexia, metabolic acidosis, chronic inflammation and impaired anabolic metabolism, contributing to protein-energy wasting (PEW) and progressive loss of skeletal muscle mass [1,2].

Oral nutritional supplements

Oral nutritional supplements (ONS) are an established nutritional intervention for patients with CKD who are unable to meet their nutritional requirements through dietary counselling alone. According to the KDOQI Clinical Practice Guideline for Nutrition in CKD, ONS should be considered in adults with CKD 3-5D who are at risk of or have protein-energy wasting when dietary counselling alone does not achieve sufficient energy and protein intake [1].
Potential clinical indications for ONS include: inadequate dietary intake; protein-energy wasting or risk

of PEW; unintended weight loss or declining nutri–tional status; and a reduced muscle mass or other evidence of nutritional deterioration.
Hence, the renal-specific ONS are often formulated to provide: concentrated energy density; adequate high-quality protein; low or controlled electrolyte content; a formulation adapted to fluid and electrolyte restric–tions in CKD.
Clinical studies suggest that ONS can improve: the total energy and protein intake; body weight and se–lected nutritional parameters; and nutritional status, par–ticularly in patients with PEW or inadequate nutritional intake [1].

Protein restriction, ketoacid supplementation and nutritional preservation in CKD

Protein metabolism undergoes profound alterations during CKD progression. Although dietary protein restriction may reduce nitrogenous waste and poten–tially slow CKD progression, excessive dietary restric–tion may increase the risk of protein-energy wasting (PEW), particularly in patients with reduced appetite or increased nutritional risk.
Current recommendations emphasize individualized pro–tein prescription according to CKD stage, metabolic stability, diabetes status, nutritional status and thera–peutic goals. Adequate energy intake should accom–pany protein restriction to help maintain nutritional status and prevent loss of lean body mass [1].
In metabolically stable adults with non-dialysis CKD G3-G5 without diabetes, KDOQI recommends, under close clinical supervision, either a low-protein diet providing 0.55-0.60 g/kg/day or a very-low-protein diet providing 0.28–0.43 g/kg/day with additional ketoacid/amino acid analogues to meet protein requirements of 0.55–0.60 g/kg/day [1].
Potential benefits of ketoacid/amino acid supplementa–tion include reduction of nitrogenous waste and su–pport of nutritional adequacy while allowing a lower dietary protein intake. However, implementation is li–mited by adherence, availability and the need for ca–reful patient selection and clinical monitoring. There–fore, ketoacid supplementation should be considered as part of structured dietary management under spe–cialist supervision [1].

Leucine-enriched protein, whey protein and β-hydroxy-β-methylbutyrate (HMB)

Loss of skeletal muscle mass and function is strongly associated with adverse outcomes in patients with CKD. Nutritional optimization combined with resis–tance exercise is considered an important component of strategies aimed at preventing and managing sar–copenia in CKD [9].
Leucine and leucine-enriched protein supplements have attracted interest because leucine stimulates muscle protein synthesis through activation of anabolic sig–nalling pathways, including the mTOR pathway. Ho–wever, evidence from randomized clinical trials (RCTs) in older adults remains inconsistent. A systematic re–view and meta-analysis of 17 RCTs found that isolated leucine supplementation did not significantly improve total lean mass or muscle strength, whereas some combined nutritional interventions showed benefits in selected functional outcomes [8].
Thus, potential nutritional strategies include: leucine-enriched protein supplements; whey protein prepara–tions; and essential amino acid mixtures.
β-hydroxy-β-methylbutyrate (HMB), a metabolite of leucine, has also been investigated as a potential stra–tegy to attenuate muscle loss. However, CKD-specific evidence remains limited, and available studies in he–modialysis patients have not demonstrated consistent improvements in body composition or other clinically relevant outcomes [9].
The current clinical approach: prioritize adequate energy and protein intake according to CKD stage, metabolic status and nutritional risk; combine nutritional inter–ventions with resistance exercise whenever feasible; consider amino acid or leucine-enriched protein supp–lementation only in selected patients within indivi–dualized nutritional strategies; HMB supplementation should not be routinely recommended in CKD because of insufficient CKD-specific evidence [9].

Metabolic acidosis and sodium bicarbonate supplementation

Metabolic acidosis is a frequent complication of ad–vanced CKD, resulting from impaired renal acid ex–cretion and reduced capacity for bicarbonate regene–ration. Persistent metabolic acidosis is associated with several metabolic disturbances, including increased protein catabolism, loss of skeletal muscle mass, in–creased bone resorption, insulin resistance and poten–tial acceleration of CKD progression [10,11].
Oral sodium bicarbonate supplementation has been investigated as a therapeutic strategy to correct meta–bolic acidosis and attenuate its adverse metabolic con–sequences. A randomized controlled trial by de Brito-Ashurst *et al*., demonstrated that bicarbonate supp–lementation in patients with CKD and metabolic aci–dosis slowed decline in kidney function and improved nutritional parameters compared with standard care [10].
Subsequent randomized trials and systematic reviews have demonstrated that bicarbonate therapy effectively increases serum bicarbonate concentrations. A syste–matic review and meta-analysis of 15 RCTs found that sodium bicarbonate may slow decline in kidney fun–ction and reduce the risk of kidney failure although, the certainty of evidence was low, and effects on mor–

tality and other clinically relevant outcomes remained uncertain [11].

From a nutritional perspective, correction of metabolic acidosis may help reduce protein catabolism and su–pport preservation of nutritional status. However, the clinical significance of these effects remains uncertain, and sodium bicarbonate should be considered a tar–geted intervention in patients with persistent metabolic acidosis confirmed by biochemical assessment [10,11].

Current clinical considerations: sodium bicarbonate supplementation should be guided by repeated measu–rement of serum bicarbonate concentration; treatment should take into account sodium load, blood pressure and the risk of fluid retention; patients with hyper–tension, edema or heart failure require careful moni–toring; and the correction of metabolic acidosis should be integrated with individualized nutritional manage–ment and strategies aimed at preventing PEW and sarcopenia.

Therefore, sodium bicarbonate may provide benefits beyond correction of serum bicarbonate concentra–tions, including potential effects on nutritional status and kidney function. However, the certainty of evi–dence remains limited, and further adequately powered randomized trials are required to determine its long-term effects on clinically relevant outcomes [10,11].

Iron Supplementation in CKD-Associated Anaemia

Anaemia is one of the most frequent complications of CKD and results from multiple mechanisms, including reduced erythropoietin production, iron deficiency or iron-restricted erythropoiesis, chronic inflammation and increased hepcidin concentrations. Hepcidin decreases intestinal iron absorption and limits iron release from storage sites, contributing to iron-restricted erythropoiesis.

Iron therapy remains a cornerstone of CKD-associated anaemia management. Available strategies include oral and intravenous (i.v.) iron.

Oral iron advantages are simple administration, lower cost and no requirement for i.v. access.

Limitations of oral iron are: impaired gastrointestinal absorption, particularly in the presence of inflammation, gastrointestinal adverse effects and slower increases in haemoglobin and iron indices compared with i.v. iron.

Intravenous iron advantages are: bypasses gastrointes–tinal absorption, more rapid increase in haemoglobin and iron indices and particularly important in patients receiving haemodialysis, in whom KDIGO 2026 su–ggests a proactive i.v. iron strategy when iron therapy is initiated [12].

The choice of iron therapy should be individualized according to the degree of anaemia and iron defi–ciency, haemoglobin, ferritin and transferrin saturation (TSAT), treatment with erythropoiesis-stimulating agents (ESAs) or HIF-PHIs, dialysis status, tolerability, availa–bility, cost and patient preferences [12].

The updated KDIGO 2026 Clinical Practice Guideline emphasizes individualized iron management rather than reliance on a single fixed laboratory threshold. For patients with CKD not receiving haemodialysis or with CKD G5 receiving peritoneal dialysis, KDIGO su–ggests initiating iron when ferritin is <100 ng/ml and TSAT <40%, or when ferritin is 100–<300 ng/ml with TSAT <25% [12]. Routine iron should generally be with–held when ferritin is >700 ng/ml or TSAT ≥40% [12].

Dialysis phase: replacing losses and preventing protein-energy wasting

Patients receiving dialysis are at particularly high risk of nutritional deterioration and PEW due to multiple interacting factors, including dialysis-related losses of amino acids and other nutrients, chronic inflammation, oxidative stress, metabolic acidosis, reduced appetite and increased protein requirements [1].

The goals of nutritional supplementation during dialy–sis include maintaining adequate energy and protein intake, preserving muscle mass, preventing or treating PEW and supporting functional status. Nutritional in–terventions should be individualized according to nut–ritional status, dialysis modality, dietary intake, co–morbidities and metabolic requirements [1].

Oral nutritional supplements and intradialytic nutrition

Patients undergoing maintenance haemodialysis have higher protein requirements than patients with non-dialysis CKD because of amino acid losses during dialysis, chronic inflammatory activation and anabolic resistance. According to the KDOQI Clinical Practice Guideline for Nutrition in CKD, oral ONS should be considered in patients with CKD 3–5D who are at risk of or have protein-energy wasting when dietary coun–selling alone does not achieve sufficient energy and protein intake [1].

Renal-specific ONS may provide concentrated energy and protein while allowing adaptation of electrolyte and fluid content to CKD-related dietary restrictions.

Clinical studies suggest that ONS can improve energy and protein intake and may improve selected nutritional parameters, including serum albumin, particularly in patients with inadequate nutritional intake or PEW [1].

Intradialytic oral nutritional supplementation has emer–ged as a practical strategy for providing nutritional support during haemodialysis. RCTs in malnourished haemodialysis patients have demonstrated improvements in selected nutritional markers with intradialytic ONS com–pared with dietary counselling or usual care [13,14].

Recent evidence also suggests that combining intra–dialytic protein supplementation with neuromuscular electrical stimulation may provide additional benefits

for selected measures of muscle mass and physical function in haemodialysis patients [15].

Water-soluble vitamins during dialysis

Haemodialysis may contribute to losses of several water-soluble vitamins, including thiamine (vitamin B1), vitamin B6, folate, vitamin B12 and vitamin C. In addition to dialysis-related losses, inadequate dietary intake, dietary restrictions, impaired absorption and comorbid illness may contribute to micronutrient deficiencies in patients with CKD [1].
Therefore, in patients receiving dialysis who have sustained inadequate dietary intake, malnutrition or other evidence of micronutrient deficiency, supplementation with multivitamins containing water-soluble vitamins may be considered to prevent or treat deficiencies [1].
However, routine high-dose supplementation should be avoided. Vitamin C requires particular caution because excessive intake may increase serum oxalate concentrations and potentially contribute to calcium oxalate accumulation, particularly in patients with advanced kidney disease [1].
Current clinical practice should therefore favour individualized supplementation rather than routine high-dose administration of individual vitamins. Supplementation should be guided by nutritional assessment, dietary intake, clinical circumstances and, when appropriate, biochemical assessment [1].

Zinc supplementation

Zinc deficiency has been reported in patients with CKD, particularly among those receiving maintenance haemodialysis. Reduced zinc status in CKD may be related to inadequate dietary intake, inflammation, altered metabolism and dialysis-related factors. Low zinc status has been associated with impaired taste perception, reduced appetite and poorer nutritional status in some CKD populations [16].
Several RCTs and meta-analyses have evaluated the effects of zinc supplementation in patients with CKD, including those receiving haemodialysis. Zinc supplementation consistently increases serum zinc concentrations and may improve selected nutritional parameters. A 2026 systematic review and meta-analysis found increases in body weight, serum zinc, serum albumin and dietary energy intake, however, the overall certainty of evidence was low [16]. Earlier evidence in maintenance haemodialysis patients similarly demonstrated increases in serum zinc and dietary protein intake, together with reductions in selected inflammatory and oxidative stress markers [17].
Evidence regarding clinically important outcomes, including hospitalization, cardiovascular events and mortality, remains insufficient. Therefore, current evidence does not support routine zinc supplementation in all patients with CKD.
Zinc replacement may be considered in patients with documented deficiency or a high clinical suspicion of deficiency, particularly those with poor nutritional intake, anorexia, taste disturbances or malnutrition. Supplementation should be individualized and monitored to avoid unnecessary or excessive intake [16,17].
Current clinical approach considers: assess zinc status in selected high-risk patients; correct documented zinc deficiency; consider supplementation in selected patients with poor nutritional intake or clinical features suggestive of deficiency; and avoid universal supplementation because evidence for effects on hard clinical outcomes remains limited [16,17].

Gut–kidney axis: fibre, probiotics and synbiotics

The interaction between intestinal microbiota and kidney disease has become an increasingly investigated area in nephrology. CKD is associated with alterations of the gut-kidney axis, including changes in microbial composition and diversity, impaired intestinal barrier function and increased production of gut-derived uraemic toxins.
Nutritional interventions targeting the gut microbiome include dietary fibre, prebiotics, probiotics and synbiotics.

Dietary fibre and prebiotics

Potential mechanisms include: an increased production of short-chain fatty acids; modulation of microbial composition and diversity; enhancement of intestinal barrier function; and potential reduction in intestinal generation and systemic exposure to uraemic toxins.
Potential sources include resistant starch, inulin, psyllium and other fermentable fibres. Although experimental and small clinical studies suggest favourable effects on microbiome composition and selected metabolic markers, evidence for clinically relevant outcomes remains limited.

Probiotics and synbiotics

Recent systematic review and meta-analysis evidence suggests that probiotic and synbiotic supplementation may reduce blood urea nitrogen (BUN) and C-reactive protein (CRP) concentrations in patients with CKD. However, effects on serum creatinine and eGFR have not been consistently demonstrated, and evidence for effects on uraemic toxins and other clinical outcomes remains limited [18].
Therefore, microbiota-targeted supplementation should currently be considered an emerging supportive strategy rather than standard therapy for all patients with CKD. Larger, adequately powered RCTs are required

to determine whether modulation of the gut micro–biome can translate into meaningful clinical benefits [18].

Emerging nutritional supplements targeting oxidative stress and inflammation

Beyond established nutritional interventions, increasing interest has focused on nutritional supplements targe–ting oxidative stress and chronic inflammation, both of which are important pathophysiological mechanisms in CKD progression and its complications [20].
Several compounds, including polyphenols, curcumin-based preparations, vitamin E and other antioxidant supplements, have demonstrated biological effects in experimental studies and clinical trials. Some studies have reported improvements in selected inflammatory or oxidative stress biomarkers; however, evidence for consistent clinically meaningful renal outcomes re–mains limited [20,21]. Therefore, these supplements should currently be considered emerging or adjunctive interventions rather than established renoprotective therapies, and routine use cannot be recommended on the basis of current evidence [20,21].

Coenzyme Q10 (CoQ10) and alpha-lipoic acid (ALA)

CKD is associated with increased oxidative stress, alterations in mitochondrial function and disturbances in cellular energy metabolism. These processes may contribute to endothelial dysfunction, chronic infla–mmation and progressive tissue injury [19,20].
Coenzyme Q10 is an essential component of the mitochondrial electron transport chain and functions as a lipid-soluble antioxidant. Alpha-lipoic acid acts as a mitochondrial cofactor and redox regulator with anti–oxidant properties.
Potential mechanisms of action include: reduction of reactive oxygen species production, modulation of mi–tochondrial energy metabolism, modulation of infla–mmatory signalling pathways and reduction of oxi–dative damage.
Small clinical studies of antioxidant interventions have reported effects on selected biomarkers of oxidative stress and inflammation in patients with CKD. However, evidence remains insufficient to establish that CoQ10 or alpha-lipoic acid slows CKD progression, improves cardiovascular outcomes or reduces mortality [19,20].
Therefore, we should consider: CoQ10 and ALA re–main biologically plausible but insufficiently validated interventions; their use should currently be considered investigational rather than established CKD nutritional therapy; routine supplementation cannot currently be recommended.
Further adequately powered RCTs are required before these interventions can be incorporated into standard CKD nutritional management [19,20].

Curcumin and other nutraceuticals

Chronic inflammation and oxidative stress are impor–tant pathophysiological features of CKD and may con–tribute to disease progression, endothelial dysfunction and PEW [19,20]. Curcumin, the principal bioactive compound derived from *Curcuma longa* (turmeric), has attracted interest because of its anti-inflammatory and antioxidant properties [21].
Potential mechanisms include modulation of NF-κB signalling, regulation of pro-inflammatory cytokine produc–tion and modulation of oxidative stress pathways [21].
Experimental studies and small clinical trials suggest potential biological and renoprotective effects, however, human evidence in CKD remains limited and hetero–geneous. Important limitations include variable bio–availability, differences between curcumin formula–tions and limited long-term clinical safety data [21].
Therefore, curcumin should currently be considered an investigational nutraceutical rather than an established CKD therapy**,** and routine supplementation cannot currently be recommended.

L-carnitine supplementation

Carnitine plays an important role in mitochondrial fatty acid transport and cellular energy metabolism. In patients undergoing haemodialysis, plasma and tissue carnitine concentrations may decrease because of dia–lysis-associated losses, reduced dietary intake and im–paired endogenous synthesis.
Potential clinical effects of L-carnitine supplementa–tion include: improvement of muscle energy meta–bolism; possible reduction of muscle cramps; potential improvement in erythropoiesis-stimulating agent (ESA)-resistant anaemia.
Several clinical trials and systematic reviews have investigated L-carnitine supplementation in haemodialy–sis patients. Although some studies have suggested po–tential benefits, particularly for muscle symptoms and selected haematological parameters, evidence remains inconsistent, and clinically meaningful effects on ma–jor patient-centred outcomes have not been conclu–sively demonstrated [22].
Current clinical approach comprehense: L-carnitine supplementation is not routinely recommended for all dialysis patients; but it may be considered in selected patients with documented carnitine deficiency and per–sistent symptoms or clinical problems that remain ina–dequately controlled with standard management [22].
Further well-designed RCTs are needed to clarify the clinical role of L-carnitine supplementation in haemo–dialysis patients.

Vitamin D after transplantation

Vitamin D deficiency remains common after kidney transplantation. Several factors may contribute to reduced vitamin D status in transplant recipients, including limited sunlight exposure, corticosteroid therapy, persistent CKD-related mineral and bone abnormalities, and alterations in vitamin D metabolism.
Low vitamin D status after transplantation has been associated with: impaired bone health; increased fracture risk; persistent abnormalities of mineral metabolism; potential effects on immune regulation.
Recent expert consensus recommendations support monitoring and correction of vitamin D deficiency in patients with CKD, including kidney transplant recipients, while avoiding excessive dosing and maintaining appropriate biochemical monitoring. Vitamin D supplementation should therefore be individualized according to serum 25-hydroxyvitamin D concentration and relevant biochemical parameters, including calcium, phosphate and parathyroid hormone levels, rather than prescribed routinely at high doses without an indication [23].
Monitoring should include: serum 25-hydroxyvitamin D [25(OH)D]; serum calcium; serum phosphate; and parathyroid hormone (PTH).
Although low vitamin D status has been associated with several adverse outcomes after kidney transplantation, evidence that vitamin D supplementation improves graft survival or other major transplant outcomes remains insufficient. Further RCTs are required to determine whether correction of vitamin D deficiency translates into clinically meaningful benefits in transplant recipients [23].

Magnesium and calcineurin inhibitors

Hypomagnesemia is a frequent metabolic complication after kidney transplantation, particularly among patients receiving calcineurin inhibitors (CNIs) such as tacrolimus and cyclosporine.
Calcineurin inhibitors can promote renal magnesium wasting through effects on tubular magnesium transport. Tacrolimus has been associated with increased urinary magnesium loss and reduced serum magnesium concentrations due to alterations in renal tubular magnesium handling [24,25].
Low magnesium concentrations after kidney transplantation have been associated with several metabolic and cardiovascular risk factors, including: an increased risk of post-transplant diabetes mellitus (PTDM); adverse metabolic profiles; and cardiovascular risk factors [25,26].
Correction of documented hypomagnesemia is appropriate, particularly in patients with significant biochemical abnormalities or symptoms. However, current evidence remains insufficient to recommend routine magnesium supplementation for all kidney transplant recipients or to demonstrate improvement in graft survival or other major transplant outcomes [25].
Therefore, magnesium management after transplantation should be individualized according to: the immunosuppressive regimen; serum magnesium concentration; kidney function; risk of post-transplant diabetes; and the cardiovascular and metabolic risk profile [25,26].

Avoiding uncontrolled supplementation after transplantation

Kidney transplant recipients require particular caution regarding dietary supplements because of the potential for interactions with immunosuppressive therapy, particularly calcineurin inhibitors such as tacrolimus and cyclosporine.
Potential concerns include: an altered tacrolimus or cyclosporine exposure; the modulation of cytochrome P450 (CYP3A4/CYP3A5) enzymes and drug transport pathways; unpredictable pharmacological effects of herbal products; and variable composition and uncertain pharmacological effects of commercially available herbal and nutraceutical products [27,28].
Particular caution is required with: herbal products; concentrated nutraceutical combinations; and a high-dose antioxidant preparations.
Because immunosuppressive drugs have a narrow therapeutic window, any supplementation strategy after kidney transplantation should be discussed with the transplant care team and accompanied by appropriate monitoring of immunosuppressant drug levels and relevant clinical parameters [27,28].

Evidence-based classification of nutritional interventions across the CKD journey

The evidence-based classification of nutritional interventions according to current clinical evidence is summarized in Table 1.

Table 1. Evidence-based classification of nutritional interventions across the CKD journey

Intervention	Evidence level	Current clinical position
Medical nutrition therapy (MNT)	Strong	Recommended throughout CKD as the foundation of individualized nutritional managemen
Oral nutritional supplements (ONS) in patients at nutritional risk	Low / limited	Recommended as a trial when dietary counselling alone does not achieve adequate energy and protein intake
Protein supplementation in	Moderate / individualized	Individualized according to CKD stage,

PEW/sarcopenia risk		metabolic status and nutritional risk
Iron supplementation	Strong / established	Recommended for CKD-associated anaemia according to haemoglobin, ferritin, TSAT and clinical context
Correction of vitamin D deficiency	Moderate	Recommended when deficiency is documented, with biochemical monitoring
Sodium bicarbonate in metabolic acidosis	Moderate / evolving	May be considered in selected patients with persistent metabolic acidosis; long-term clinical benefit remains uncertain
Exercise combined with nutritional therapy	Increasing evidence	Important adjunctive strategy for prevention and management of sarcopenia and functional decline
Water-soluble vitamin/B-complex supplementation in dialysis	Targeted / deficiency-based	Consider in patients with inadequate intake or documented/suspected deficiency; routine high-dose supplementation is not establishe
Omega-3 fatty acids	Limited–moderate	Not routinely recommended as nephroprotective or cardiovascular preventive therapy in CKD/dialysis
Magnesium supplementation	Emerging	Correction of documented deficiency is appropriate; routine supplementation is not established
Vitamin K2	Emerging	Improves vitamin K status and surrogate markers such as dp-ucMGP; cardiovascular outcome benefits remain unproven
Fibre/prebiotics	Emerging	Promising gut–kidney axis strategy; clinical outcome data remain limited
Probiotics/synbiotics	Emerging	May improve selected uraemic and inflammatory biomarkers; effects on clinical outcomes remain uncertain
HMB	Emerging	Potential role in muscle preservation; insufficient evidence for routine CKD use
L-carnitine	Limited	May be considered in selected dialysis patients; routine supplementation is not recommended
Coenzyme Q10 / alpha-lipoic acid	Experimental	Biological plausibility exists, but clinical evidence is insufficient for routine use
Curcumin/nutraceuticals	Experimental	Investigational; insufficient evidence for routine clinical application
High-dose antioxidant supplementation	Not routinely recommended	No established clinical benefit sufficient to support routine use; potential for inappropriate or excessive supplementation

Abbreviations: CKD, chronic kidney disease; ONS, oral nutritional supplements; PEW, protein-energy wasting; HMB, β-hydroxy-β-methylbutyrate; dp-ucMGP, dephosphorylated-uncarboxylated matrix Gla protein.

Table 2. Supplementation strategies across CKD stages

Supplement/intervention	Early CKD G1–G3	Advanced CKD G3b–G5	Dialysis	Transplantation
Vitamin D	Correct documented deficiency with nutritional vitamin D; monitor CKD-MBD parameters	Consider active vitamin D analogues reserved for selected patients with severe/progressive secondary hyperparathyroidism	Correct deficiency and monitor calcium, phosphate and PTH	Correct deficiency; monitor vitamin D status and bone health
Vitamin K	Investigational; possible role in vascular calcification pathways	Investigational; evidence mainly based on vitamin K status and surrogate markers	Deficiency may occur; clinical benefit of supplementation remains unproven	Consider potential interactions, particularly with vitamin K–antagonist anticoagulants
Magnesium	Correct documented deficiency; monitor according to kidney function	Use cautiously because of reduced renal magnesium excretion	Consider in selected patients with documented deficiency	Monitor frequently because calcineurin inhibitors may promote magnesium wasting
Oral nutritional supplements (ONS)	Consider when dietary intake is	Important in patients at risk of PEW or	Recommended/considered in patients with	Usually not routine; consider according

	inadequate	sarcopenia	malnutrition or inability to meet nutritional targets despite dietary counselling	to nutritional status
Protein supplementation	Individualized according to CKD stage and nutritional risk	Individualized; balance nutritional adequacy with avoidance of excessive protein intake	Increased protein requirements; frequently required in PEW risk	Focus on adequate protein intake, healthy body composition and metabolic control
Ketoacid analogues	Selected patients receiving very-low-protein diets	May be considered within structured dietary programs	Not routinely used	Not standard therapy
Sodium bicarbonate	Consider if metabolic acidosis develops	Evidence-supported in selected patients with persistent low bicarbonate	Individualized; depends on acid-base status.persistent metabolic acidosis	Rarely required unless metabolic acidosis persists
Iron supplementation	According to iron status and anaemia parameters	According to Hb, ferritin, TSAT and clinical context	Frequently requires intravenous iron according to laboratory findings and clinical context	According to anaemia status
B vitamins	Usually adequate intake	Consider in selected patients with poor intake or deficiency risk	Consider in patients with inadequate intake, malnutrition or deficiency risk	Individualized
Omega-3 fatty acids	Cardiovascular/lipid indications; not established as nephroprotective therapy	Selected patients according to cardiovascular risk profile	Consider mainly for cardiovascular/lipid indications	Cardiovascular risk management
Fibre/probiotics	Research area	Promising gut–kidney axis strategy; clinical outcome data remain limited	Adjunctive only; clinical outcomes uncertain	Use cautiously, particularly early after transplantation
HMB/amino acids	Investigational	May be considered in selected patients at risk of sarcopenia	Investigational; insufficient evidence for routine use	Not routinely recommended.
CoQ10/ALA	Experimental	Experimental	Experimental	Consider potential drug interactions; not routinely recommended,
Curcumin/nutraceuticals	Experimental	Experimental	Not routinely recommended	Avoid uncontrolled use because of potential interactions with immunosuppressive therapy

Abbreviations: CKD, chronic kidney disease; PEW, protein-energy wasting; ONS, oral nutritional supplements; CKD-MBD, chronic kidney disease–mineral and bone disorder; PTH, parathyroid hormone; HMB, β-hydroxy-β-methylbutyrate; CoQ10, coenzyme Q10; ALA, alpha-lipoic acid.

Summary table: Supplementation across CKD stages

The recommended supplementation strategies accor–ding to CKD stage are summarized in Table 2.

Conclusions

Nutritional supplementation in CKD has evolved from a generalized supplementation approach toward indi–vidualized and evidence-based nutritional strategies guided by disease stage, nutritional phenotype and specific clinical needs.

The best-established components of nutritional mana–gement currently include: individualized medical nut–rition therapy, oral nutritional supplements in patients at nutritional risk, appropriate protein management according to CKD stage and nutritional status, iron therapy according to CKD-associated anaemia guide–lines, correction of documented vitamin D deficiency, and treatment of metabolic acidosis when present.

Several emerging interventions, including magnesium supplementation, vitamin K strategies, fibre-based the–rapies, probiotics and synbiotics, HMB, amino acid supp–lementation and antioxidant or mitochondrial-targeted strategies such as CoQ10 and alpha-lipoic acid, rep–resent promising areas of investigation. Ho–wever, cu–rrent evidence remains insufficient to support routine im–plementation of these interventions in all CKD patients.

The future of supplementation in CKD is not the prescription of more supplements, but the selection of the right intervention for the right patient at the right stage of kidney disease. This approach should be guided by nutritional assessment, biochemical evaluation and clinically meaningful outcomes rather than surrogate markers alone.

Conflict of interest statement. None declared.

References

1. Ikizler TA, Burrowes JD, Byham-Gray LD, *et al.* KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update. *American Journal of Kidney Diseases* 2020; 76(3 Suppl 1): S1-S107.
2. Fouque D, Kalantar-Zadeh K, Kopple J, *et al*. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney International* 2008; 73(4): 391-398.
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). *Kidney International Supplements* 2017; 7(1): 1-59.
4. Caluwé R, Verbeke F, De Vriese AS. Evaluation of vitamin K status and rationale for vitamin K supplementation in dialysis patients. *Nephrology Dialysis Transplantation* 2020; 35(1): 23-33.
5. Kurnatowska I, Grzelak P, Masajtis-Zagajewska A, *et al*. Effect of vitamin K2 on progression of atherosclerosis and vascular calcification in nondialyzed patients with chronic kidney disease stages 3-5. *Pol Arch Intern Med* 2015; 125(9): 631-640.
6. Sakaguchi Y, Hamano T, Isaka Y. Magnesium and Progression of Chronic Kidney Disease: Benefits Beyond Cardiovascular Protection? *Advances in Chronic Kidney Disease* 2018; 25(3): 274-280.
7. Bressendorff I, Hansen D, Schou M, *et al.* The Effect of Magnesium Supplementation on Vascular Calcification in CKD: A Randomized Clinical Trial (MAGiCAL-CKD). *J Am Soc Nephrol* 2023; 34(5): 886-894.
8. Guo Y, Fu X, Hu Q, *et al*. The Effect of Leucine Supplementation on Sarcopenia-Related Measures in Older Adults: A Systematic Review and Meta-Analysis of 17 Randomized Controlled Trials. *Front Nutr* 2022; 9: 929891.
9. Sabatino A, Cuppari L, Stenvinkel P, *et al.* Sarcopenia in chronic kidney disease: what have we learned so far? *J Nephrol* 2021; 34: 1347-1372.
10. de Brito-Ashurst I, Varagunam M, Raftery MJ, Yaqoob MM. Bicarbonate supplementation slows progression of CKD and improves nutritional status. *J Am Soc Nephrol* 2009; 20: 2075-2084.
11. Hultin S, Hood C, Campbell KL, *et al*. A Systematic Review and Meta-Analysis on Effects of Bicarbonate Therapy on Kidney Outcomes. *Kidney International Reports* 2021; 6(3): 695-705.
12. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO 2026 Clinical Practice Guideline for the Management of Anemia in Chronic Kidney Disease (CKD). *Kidney International* 2026; 109(1S): S1-S99.
13. Gharib MS, Nazeih MS, El Said TW. Effect of intradialytic oral nutritional supplementation on nutritional markers in malnourished chronic hemodialysis patients: prospective randomized trial. *BMC Nephrology* 2023; 24: 125.
14. Satirapoj B, Apiyangkool T, Thimachai P, *et al.* Intradialytic oral nutrition effects on malnourished hemodialysis patients: a randomized trial. *Scientific Reports* 2024; 14: 21400.
15. Park JH, Park JY, Lee GS, Cha RH. Efficacy of intradialytic neuromuscular electrical stimulation and oral nutritional supplementation in hemodialysis patients: a multicenter, randomized controlled trial. *Kidney Research and Clinical Practice* 2025; 44(2): 288-298.
16. Tan NLX, Young M, Lambert K, Dawson J. Impact of Zinc Supplementation in Adults With Chronic Kidney Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Nutrition Reviews* 2026; Feb 6: nuaf285. doi: 10.1093/nutrit/nuaf285. Online ahead of print.
17. Wang LJ, Wang MQ, Hu R, *et al*. Effect of Zinc Supplementation on Maintenance Hemodialysis Patients: A Systematic Review and Meta-Analysis of 15 Randomized Controlled Trials. *BioMed Research International* 2017; 2017: 1024769.
18. Liu C, Yang L, Wei W, Fu P. Efficacy of probiotics/ synbiotics supplementation in patients with chronic kidney disease: a systematic review and meta-analysis of randomized controlled trials. *Front Nutr* 2024; 11: 1434613.
19. Cachofeiro V, Goicochea M, de Vinuesa SG, *et al*. Oxidative stress and inflammation, a link between chronic kidney disease and cardiovascular disease. *Kidney International Supplements* 2008; 74: S4-S9.
20. Small DM, Coombes JS, Bennett N, *et al*. Oxidative stress, anti-oxidant therapies and chronic kidney disease. *Nephrology (Carlton)* 2012; 17(4): 311-321.
21. Hewlings SJ, Kalman DS. Curcumin: A Review of Its Effects on Human Health. *Foods* 2017; 6(10): 92.
22. Hurot JM, Cucherat M, Haugh M, Fouque D. Effects of L-carnitine supplementation in maintenance hemodialysis patients: a systematic review. *Journal of the American Society of Nephrology* 2002; 13(3): 708-714.
23. Jorgensen HS, Vervloet M, Cavalier E, *et al.* The role of nutritional vitamin D in chronic kidney disease-mineral and bone disorder in children and adults with chronic kidney disease, on dialysis, and after kidney transplantation-a European consensus statement. *Nephrol Dial Transplant* 2025; 40(4): 797-822.
24. Hoorn EJ, Walsh SB, McCormick JA, *et al*. The calcineurin inhibitor tacrolimus activates the renal sodium chloride cotransporter to cause hypertension. *Nature Medicine* 2011; 17(10): 1304-1309.
25. Stefanelli LF, Alessi M, Bertoldi G, *et al.* Calcineurin Inhibitor-Induced Hypomagnesemia in Kidney Transplant Patients: A Monocentric Comparative Study between Sucrosomial Magnesium and Magnesium Pidolate Supplementation. *Journal of Clinical Medicine* 2023; 12(3): 752.
26. van der Burgh AC, Moes A, Kieboom BCT, *et al.* Serum magnesium, hepatocyte nuclear factor 1β genotype and post-transplant diabetes mellitus: a prospective study. *Nephrology Dialysis Transplantation* 2020; 35(1): 176-183.
27. Nowack R, Schmitt W. Cytochrome P450 enzyme, and transport protein mediated herb–drug interactions in renal transplant patients: Grapefruit juice, St John's Wort-and beyond! *Nephrology* 2008; 13(4): 337-347.
28. Miedziaszczyk M, Bajon A, Jakielska E, *et al.* Controversial Interactions of Tacrolimus with Dietary Supplements, Herbs and Food. *Pharmaceutics* 2022; 14(10): 2154.