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Authors
Narasaki, Yoko
Siu, Man
Nguyen, Matthew
et al.

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Personalized nutritional management in the transition from non-dialysis dependent chronic kidney disease to dialysis

Yoko Narasaki[1,2], Man Kit Siu[1,2], Matthew Nguyen[1], Kamyar Kalantar-Zadeh[1,2,3], Connie M. Rhee[1,2]

[1]*Division of Nephrology, Hypertension, and Kidney Transplantation, Department of Medicine, University of California Irvine, Orange, CA, USA*
[2]*Tibor Rubin Veterans Affairs Long Beach Healthcare System, Long Beach, CA, USA*
[3]*The Lundquist Institute at Harbor-UCLA Medical Center, Torrance, CA, USA*

Dialysis has been the dominant treatment regimen in end-stage kidney disease as a means to remove uremic waste products and to maintain electrolyte, acid base, and fluid balance. However, given that dialysis may not always provide a survival benefit nor improved quality of life in certain subpopulations, there is growing recognition of the need for conservative and preservative management as an alternative treatment strategy for advanced chronic kidney disease (CKD). Personalized nutritional management tailored to patient's sociodemographics, social needs, psychological status, health literacy level, and preferences is a key component of conservative and preservative care, as well as in the management of patients transitioning from non-dialysis dependent CKD to dialysis. In this review, we discuss the nutritional and metabolic alterations that ensue in CKD; the rationale for low-protein diets in the conservative and preservative management of advanced CKD; the role of plant-based diets in kidney health; emerging data on dietary potassium and sodium intake on CKD outcomes; and the practical implementation of dietary interventions in advanced kidney disease.

Keywords: Chronic kidney disease, Conservative management, Dietary protein intake, Nutrition, Plant-based diet

Introduction

Each year ~125,000 patients in the United States transition to end-stage kidney disease (ESKD), with the majority treated with in-center hemodialysis [1]. With respect to international comparisons, the highest incidence rates of treated ESKD have been observed in Taiwan, the United States, Singapore, the Republic of Korea, and Thailand (525,

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Correspondence: Connie M. Rhee
Division of Nephrology, Hypertension, and Kidney Transplantation, Department of Medicine, University of California Irvine, 333 The City Blvd West, Suite 400, Orange, CA 92868, USA. E-mail: crhee1@hs.uci.edu
ORCID: https://orcid.org/0000-0002-9703-6469

Yoko Narasaki's current affiliation: Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; Tibor Rubin Veterans Affairs Long Beach Healthcare System, Long Beach, CA, USA

Man Kit Siu's current affiliations: Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; Nephrology Section, Veterans Affairs Greater Los Angeles Healthcare, Los Angeles, CA, USA

Connie M. Rhee's current affiliations: Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; Nephrology Section, Veterans Affairs Greater Los Angeles Healthcare, Los Angeles, CA, USA; Division of Nephrology, Hypertension, and Kidney Transplantation, Department of Medicine, University of California Irvine, Orange, CA, USA

396, 366, 355, and 339 per million population, respectively) [1]. While there are widely varying recommendations with regard to the timing of transition to renal replacement therapy across clinical practice guidelines [1], many patients in the United States initiate dialysis with an estimated glomerular filtration rate (eGFR) of >15 mL/min/1.73 m^2 and as high as 25 mL/1.73 m^2 [1]. This may be in part due to ongoing uncertainty regarding the optimal timing of dialysis transition. Although the IDEAL (Initiating Dialysis Early and Late) Trial demonstrated no differences in survival nor secondary outcomes with "early-start" (dialysis transition at an eGFR of 10–15 mL/min/1.73 m^2) vs. "late-start" dialysis (dialysis transition at an eGFR of 5–7 mL/min/1.73 m^2) [1], interpretation of these data are limited given the high degree of crossover between the early-start vs. late-start arms, narrow eGFR separation at the time of dialysis initiation across the two groups, lack of racial/ethnic heterogeneity in the study population, and unclear generalizability of the cohort's case-mix to that of the broader global ESKD population (i.e., less cardiovascular disease and comorbidities) [2,3]. Furthermore, given the exceptionally higher mortality rates observed during the first several months of dialysis treatment, particularly amongst those of older age and higher comorbidity burden [4], there has been growing recognition of the importance of identifying strategies to delay or avoid the initiation of dialysis. With the advent of the 2019 Advancing American Kidney Health Initiative, in which one of the major priorities is to encourage treatments that prevent the development and/or progression of kidney disease [5], discussions of the critical need for conservative and preservative management as an alternative treatment strategy for advanced chronic kidney disease (CKD) have been brought to the forefront [6].

Conservative and preservative kidney care aims to provide active, comprehensive medical management of advanced CKD using non-dialytic strategies, while also focusing on the preservation of remaining kidney function [6]. The three major objectives of these treatment approaches are to 1) optimize patients' health-related quality of life (HRQOL), 2) mitigate the uremic complications and unpleasant symptoms of ESKD using non-dialytic approaches, and 3) maintain residual kidney function. To achieve these goals, a multidisciplinary approach is needed in conservative and preservative management, of which dietary interventions used to slow or avoid the need for renal replacement therapy are a major component. Personalized nutritional management tailored to patient's sociodemographics, social needs, psychological status, health literacy level, and preferences is a key aspect of conservative and preservative care, including the management of patients transitioning from non-dialysis dependent (NDD) CKD to dialysis [7]. In this review, we discuss alterations in nutrition and metabolic status that occur in CKD; the premise for low-protein diets (LPDs) in the conservative and preservative management of advanced CKD; the role of plant-based diets on CKD outcomes; emerging data on dietary potassium and sodium intake on kidney health; and practical implementation of dietary interventions in advanced kidney disease.

Alterations in metabolic and nutritional status and protein energy wasting in advanced chronic kidney disease

Protein energy wasting is a prevalent complication in ESKD patients that is associated with worse HRQOL, increased frequency of hospitalizations, and higher mortality risk [8]. Given various metabolic and nutritional changes that develop with declining kidney function, including 1) the accumulation of uremic toxins, such as catabolic by-products of protein metabolism and inflammatory cytokines, 2) reduced appetite and food intake, and 3) increased muscle catabolism in the setting of CKD-related metabolic acidosis and insulin resistance, patients with advanced CKD are at heightened risk of developing protein energy wasting [8]. Moreover, elderly CKD patients are at even higher risk for developing protein energy wasting due to age-related changes in body composition over time, namely increased body fat and decreased lean body mass, as well as the above CKD-associated metabolic and nutritional derangements [9].

Low-protein diets and kidney health

Impact on delaying dialysis initiation and/or survival

High dietary protein intake may contribute to progressive decline in kidney function through the dilation of afferent arterioles, aggravated glomerular hyperfiltration and intraglomerular hypertension, and upregulation of

proinflammatory gene expression [10,11]. Thus, clinical practice guidelines recommend the utilization of LPDs to reduce the risk of ESKD and/or mortality in the nutritional management of moderate-to-advanced NDD-CKD patients [12,13]. The recently updated 2020 National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines for nutrition in CKD recommend that adults with stages 3 to 5 NDD-CKD without diabetes who are metabolically stable should consume 1) an LPD of 0.55 to 0.60 g/kg body weight/day, or 2) a very low protein diet (VLPD) of 0.28 to 0.43 g/kg of body weight/day with additional ketoacid analogs in order to reduce the risk of ESKD and/or death and to improve HRQOL. The KDOQI guidelines also indicate that it is reasonable to prescribe a lower dietary protein intake of 0.6 to 0.8 g/kg/day among adults with stages 3 to 5 NDD-CKD and underlying diabetes. These recommendations have been endorsed by the International Society of Renal Nutrition and Metabolism, which has advised that it is also reasonable for clinicians to aim for the lower end of a streamlined target of 0.6 to 0.8 g/kg/day irrespective of the etiology of CKD, considering that lower dietary protein targets may be challenging to achieve without compromising energy intake or in settings without access to ketoacid supplements. Furthermore, among the clinical trials of LPDs, the actual amount of protein consumed was typically above 0.6 g/kg/day despite a prescribed target of 0.55 to 0.6 g/kg/day.

The kidney protective effect of dietary protein restriction has been demonstrated as far back as the 1960s, including a study of eight patients with chronic uremic symptoms among whom an LPD led to a reduction in nitrogen waste products and uremic symptoms [14]. Subsequent research has shown that LPDs reduce the progression of kidney disease by reducing the compensatory hemodynamic changes and glomerular hyperfiltration of CKD [15]. In addition to reducing glomerular hyperfiltration, intraglomerular hypertension, and cellular injury [11], LPDs and/or supplemented VLPDs may reduce mesangial proliferation, glomerulosclerosis, and kidney fibrosis vis-à-vis amelioration of kidney inflammation and oxidative stress [16]. Despite strong evidence supporting the benefits of LPDs on CKD outcomes, the efficacy and safety of this dietary intervention still remains widely debated. The main findings of the MDRD (Modification of Diet in Renal Disease) study concluded that there was no effect of an LPD (i.e., 0.58 g/kg/day) on reducing CKD progression and that a VLPD had a slightly but not clearly significant effect on reducing the decline in GFR levels vs. higher dietary protein intake (i.e., 1.3 g/kg/day). However, expert opinion/commentaries have indicated that these findings are not definitive [17] due to 1) the study cohort composition not being generalizable to the broader CKD population (i.e., under-representation of patients with diabetes and over-representation of patients with polycystic kidney disease), and 2) secondary analyses of the data examining GFR trajectories after 3 months showing significant reduction in CKD progression in the low-protein diet arm [18]. Other studies have demonstrated that LPDs slow the decline in GFR and delay requirements for renal replacement therapy in CKD patients with [19] and without diabetes [20]. For example, a meta-analysis of 16 randomized controlled trials of LPDs in NDD-CKD demonstrated that dietary protein restriction was associated with lower risk of ESKD, greater survival, higher serum bicarbonate levels, lower serum phosphorus levels, and less azotemia [21]. Another randomized controlled trial has shown that a ketoacid analog supplemented with VLPD (dietary protein intake of 0.3 g/kg/day) mitigated kidney function decline and reduced the number of patients requiring renal replacement therapy [22]. Emerging data also demonstrate the benefits of LPDs in kidney disease patients of older age, who comprise a large proportion of the CKD population [9]. Indeed, a growing body of literature has shown that LPDs have kidney protective effects in both older and younger patients with CKD [23]. In a recent study of 352 patients with stages 3 to 5 NDD-CKD from Japan who were stratified by age, after a median follow-up of 4.2 years, it was found that moderate dietary protein intake (i.e., >0.8 g/kg/ day) was associated with faster decline in eGFR among the overall cohort and in those of elder age (>65 years) as compared with low protein intake (i.e., 0.6–0.8 g/kg/day) and very low protein intake (i.e., <0.6 g/kg/day) [24]. In another study of 56 NDD-CKD patients from Italy that specifically examined the impact of LPDs in the elderly population (>70 years of age), a ketoacid analog supplemented very low protein vegan diet was shown to delay dialysis transition by approximately 1 year vs. non-restriction of dietary protein intake [25].

Plant-based diets and kidney health

Impact on incident chronic kidney disease and/or chronic kidney disease progression

In addition to the amount of dietary protein intake, the source of dietary protein (animal vs. plant-derived) may have an important bearing on CKD-related outcomes, including the incidence and/or progression of CKD, risk factors for developing CKD, and CKD-related complications. While there are a variety of plant-based diets (e.g., Mediterranean, dietary approaches to stop hypertension, flexitarian, vegetarian, and vegan diets), which are defined as eating patterns with a large proportion of plant-dominant foods, it is important to underscore that not all plant-based diets are *per se* LPDs. Hence, there are ongoing studies that are examining the efficacy of a plant-dominant LPD (PLADO), which is comprised of a lower dietary protein intake of 0.6 to 0.8 g/kg/day originating from >50% plant-based sources, that is also high in fiber (>25 g/day), low in sodium (<4 g/day), and with adequate caloric content (30–35 kcal/kg/day) [26], including a National Institutes of Health-funded clinical trial of the PLADO in patients with diabetic kidney disease (PLAFOND [Plant-Focused Nutrition in Patients With Diabetes and Chronic Kidney Disease] trial) [27]. To optimize the effectiveness, safety, and adherence of these dietary interventions, collaboration with specialty-trained kidney dietitians in administering the PLADO/PLAFOND diet and medical nutrition therapy is of paramount importance.

A growing number of studies have shown that plant-based diets may favorably impact kidney disease endpoints, including lowering of glomerular hyperfiltration [28], amelioration of incident CKD and/or CKD progression [29–31], and reduction of mortality risk [32]. For example, in a study of 11,952 participants from the ARIC (Atherosclerosis Risk in Communities) cohort who had normal underlying kidney function and underwent food frequency questionnaires, after a median follow-up of 23 years both red meat and processed meat consumption were associated with higher risk of developing CKD. In contrast, a higher dietary intake of nuts, legumes, and low-fat dairy was associated with a lower risk of incident CKD. In another study of 1,624 female participants from the Nurses' Health Study (including 1,135 and 489 participants with and without CKD, respectively), higher vegetable protein intake was associated with a lower risk of GFR decline compared to higher nondairy protein intake. Clinical trials examining the effects of plant-based diets on kidney disease markers are sparse but have shown promising outcomes. In a randomized controlled trial 41 patients with type 2 diabetes and CKD who were randomized to a soy protein (comprised of two-thirds soy/vegetable protein) vs. control diet (comprised of two-thirds animal protein), after a follow-up period of 4 years those in the soy protein group had significantly lower glucose, lipid, and inflammatory markers (i.e., C-reactive protein), as well as proteinuria [33]. In another clinical trial of 207 patients with stages 4 to 5 CKD without diabetes who were randomized to a supplemented vegetarian VLPD vs. a conventional LPD, those in the vegetarian LPD arm were less likely to experience the primary composite endpoint of renal replacement initiation and/or >50% reduction in eGFR (13%) vs. those in the LPD arm (42%).

Impact on chronic kidney disease-related complications

PLADOs may also favorably impact various CKD-related complications, including mineral bone disease, metabolic acidosis, uremic toxin generation, and mortality risk. The higher contents of nonadditive derived dietary potassium, nonadditive derived dietary phosphorus with lesser bioavailability, and dietary fiber in plant-derived foods (i.e., vegetables, fruits, legumes, nuts, and whole grains) might partly explain the favorable effects of plant-based proteins on kidney health. First, plant-based LPDs reduce dietary phosphorus load and hyperphosphatemia, resulting in a decrease of fibroblast growth factor 23 (FGF23) levels [34] as a risk factor for cardiovascular morbidity (i.e., left ventricular hypertrophy, cardiovascular events), death, and dialysis initiation [35,36]. In a crossover trial of nine CKD patients who underwent 1 week of a meat diet and 1 week of a vegetarian diet, during the vegetarian diet period patients demonstrated lower serum phosphorus levels, which resulted in a reduction of serum parathyroid hormone and FGF23 levels [37]. Second, whereas animal-based proteins and foods generate acid due to being comprised of sulfur-containing amino acids (i.e., methionine, cysteine) and cationic amino acids (i.e., lysine, arginine), plant-based proteins are base producing due to the presence of natural

dietary alkali (i.e., citrate, malate) that are converted to bicarbonate [38–40]. Hence, plant-based LPDs mitigate net acid generation, and two clinical trials in NDD-CKD patients have shown that increased fruit and vegetable intake had greater efficacy in improving acidemia than sodium bicarbonate therapy and/or usual care [41,42]. Third, PLADOs may modulate the gut microbiome's generation of various uremic toxins including trimethylamine *N*-oxide (TMAO), p-cresol sulfate, and indoxyl sulfate, which may relate to greater dietary fiber content [43]. In an experimental animal model of CKD, administration of fiber led to decreased production of p-cresol sulfate, increased production of short-chain fatty acids (i.e., which may have favorable effects on systemic hypertension, glucose and lipid metabolism, and cardiovascular health [44]), and kidney injury [45]. In a clinical study of 26 patients without CKD among whom 15 patients consumed a vegetarian diet whereas 11 patients consumed an unrestricted diet, vegetarians had lower production of both p-cresol sulfate and indoxyl sulfate, and it was found that the lower excretion of p-cresol sulfate and indoxyl sulfate among vegetarians was linked with greater fiber intake and lower protein intake [46]. In a clinical trial of 56 hemodialysis patients who were randomized to supplements with vs. without increased dietary fiber, those in the dietary fiber arm experienced a greater reduction in indoxyl sulfate and p-cresol sulfate vs. those in the control arm [47]. Other salutary effects of greater dietary fiber intake include improvements in blood pressure control, glycemic status, lipid levels, and gastrointestinal motility/constipation symptoms [48]. Finally, observational data suggest that greater plant-based and lesser animal-based protein consumption may favorably impact survival. In an observational study of 1994 participants with eGFRs of <60 mL/min/1.73 m^2 from the National Health and Nutrition Examination Survey, increasingly higher intake of protein from high biological value protein sources (which have an amino acid composition similar to human protein and are typically from animal sources) was associated with incrementally higher all-cause mortality risk [49].

Dietary potassium intake considerations

Although restriction of dietary potassium intake has been a longstanding paradigm in the nutritional management of advanced CKD patients given concerns about hyperkalemia and its complications (i.e., cardiac arrhythmias, accelerated initiation of renal replacement therapy), the efficacy and safety of this approach has not been informed by rigorous evidence. Furthermore, there is growing recognition that imposing excessive dietary potassium restriction may inadvertently lead to a missed opportunity among CKD patients to encourage greater consumption of plant-based heart-healthy foods which tend to be from potassium-rich sources [50]. Indeed, observational studies from participants with and without kidney dysfunction have revealed that lower dietary potassium intake is associated with higher mortality risk [51,52]. There are various plausible mechanisms by which higher dietary potassium intake may favorably impact kidney and cardiac health. First, a diet high in potassium can lower blood pressure and improve or protect kidney and/or cardiac function by reducing vascular resistance [53,54]. Second, high potassium intake may promote vasodilation and reduce the risk of glomerulosclerotic lesions and tubular injury by increasing renal kallikrein expression [55,56]. Third, increased endothelium-dependent nitric oxide production and decreased salt-induced transforming growth factor beta production induced by higher potassium intake may promote vascular protection against atherosclerosis, thereby further preventing kidney and cardiovascular complications [57]. Fourth, dietary patterns that are rich in potassium are generally comprised of healthy fruits and vegetables [58,59], which may further engender lowering of blood pressure and blunting the progression of renal dysfunction via antioxidant and anti-inflammatory effects [60]. Hence, concurrent use of potassium binders paired with PLADOs may reduce the risk of hyperkalemia while allowing patients to relax the dietary restrictions with respect to greater plant-based food intake [61,62]. Future studies are necessary to determine the long-term efficacy and safety of a plant-based potassium-liberalized diet paired with a potassium binder vs. a potassium-restricted diet.

Sodium intake and kidney health

Dietary sodium intake has been recognized as a modifiable factor and treatment target for hypertension in both CKD patients and the general population. In a randomized controlled trial of 115 patients with type 2 diabetes and macroalbuminuria who underwent 3 months of moder-

ate salt restriction (<100 mEq [2.4 g]/day) vs. high-sodium intake (>200 mEq [4.8 g]/day), those in the salt restriction arm demonstrated an enhanced antiproteinuric effect of angiotensin-receptor blockers [63]. *Post-hoc* analyses of 1,177 patients from the RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) and the IDNT (Irbesartan Diabetic Nephropathy Trial) trials also demonstrated that the risk of reaching the renal or cardiovascular endpoints was more than two-fold higher among patients in the highest tertile of 24-hour urine sodium excretion vs. those in the lowest tertile [64]. While these data suggest that dietary sodium intake affects the efficacy of hypertension treatment and that greater sodium consumption may be detrimental with respect to CKD progression via increased blood pressure and extracellular volume [65], further research is needed to determine the efficacy and safety of sodium restriction upon the endpoints of survival as well as patient-centered outcomes including HRQOL.

Dietary patterns and kidney health

In addition to plant-based LPDs, growing research studies have also explored the role of adherence to healthy dietary patterns in the prevention of CKD and its progression [66]. For example, while diets rich in vegetables, fruits, legumes, nuts, whole grains, fish, and low-fat dairy products have resulted in favorable CKD outcomes, higher intake of red and processed meats, sodium, and sugar-sweetened beverages has been associated with higher risk of CKD progression [31]. Although underlying mechanisms have not been fully elucidated, healthy dietary patterns may associated with improved CKD outcomes due to lower production of dietary acid loads and uremic toxins by the gut microbiota (i.e., TMAO, indoxyl sulfate, and p-cresyl sulfate) [67], as well as higher content of important nutrients (i.e., potassium, fiber, micronutrients, mono- and polyunsaturated fatty acid, lower saturated fats) [68–70], while also avoiding excessive amounts of phosphorus (particularly from sources of high bioavailability) and sodium [65,71,72].

Nutritional management and practical considerations in advanced kidney disease

The treatment goals for nutritional management in patients with advanced CKD include 1) slowing the rate of CKD progression, 2) controlling uremia and proteinuria, and 3) ensuring adequate dietary intake and optimal nutritional status. LPDs are generally recommended as a core component of the nutritional management of patients with stages 3B-5 NDD CKD (Fig. 1). There are two types of LPDs recommended by the 2020 KDOQI guidelines, namely non-supplemented vs. supplemented (Table 1). The first LPD (i.e., non-supplemented LPD) provides a dietary protein intake of 0.55 to 0.60 (in patients without diabetes) or 0.6 to 0.8 (in patients with diabetes) g/kg body weight/day, while the second LPD (i.e., supplemented LPD) is a VLPD which provides a dietary protein intake of 0.28 to 0.43 g/kg body weight/day accompanied by substitutes such as 7 to 15 g/day of keto acids or hydroxy acid analogs and essential amino acids to meet protein requirements (0.55 to 0.60 g/kg body weight/day in patients without diabetes). In addition to the amount of dietary protein intake, the source of dietary protein intake should also be taken into account, with an emphasis on plant-based protein sources such as in the PLADO/PLAFOND diets. Additionally, the 2020 KDOQI guidelines recommend that daily sodium intake should be restricted to less than 2.3 g/day (or less than 100 mmol/day) for CKD stages 3 to 5 patients (including stage 5 CKD patients on dialysis) to achieve blood pressure reduction, better volume control, and a decrease in proteinuria levels [13].

The potential risks of dietary protein and/or sodium restriction include decreased appetite and/or failure to achieve adequate dietary energy intake, which could result in malnutrition, protein energy wasting, and/or sarcopenia [73]. Thus, it is essential to maintain dietary energy intake at approximately 30 to 35 kcal/kg/day despite consuming a lower amount of protein in order to avoid impaired nutritional status and development of protein energy wasting [74]. Given the higher age-related requirements for protein intake in the elderly compared to their younger counterparts (i.e., due to anabolic differences) [75,76] and age and CKD-related reductions in appetite [77], using a personalized approach to achieve adequate dietary energy and protein intake should be emphasized particularly in the elderly CKD population.

Although LPDs and VLPDs with adequate energy intake have favorable effects on CKD outcomes, a potential challenge in the practical implementation of this treatment strategy is low adherence. Given that CKD diets may be

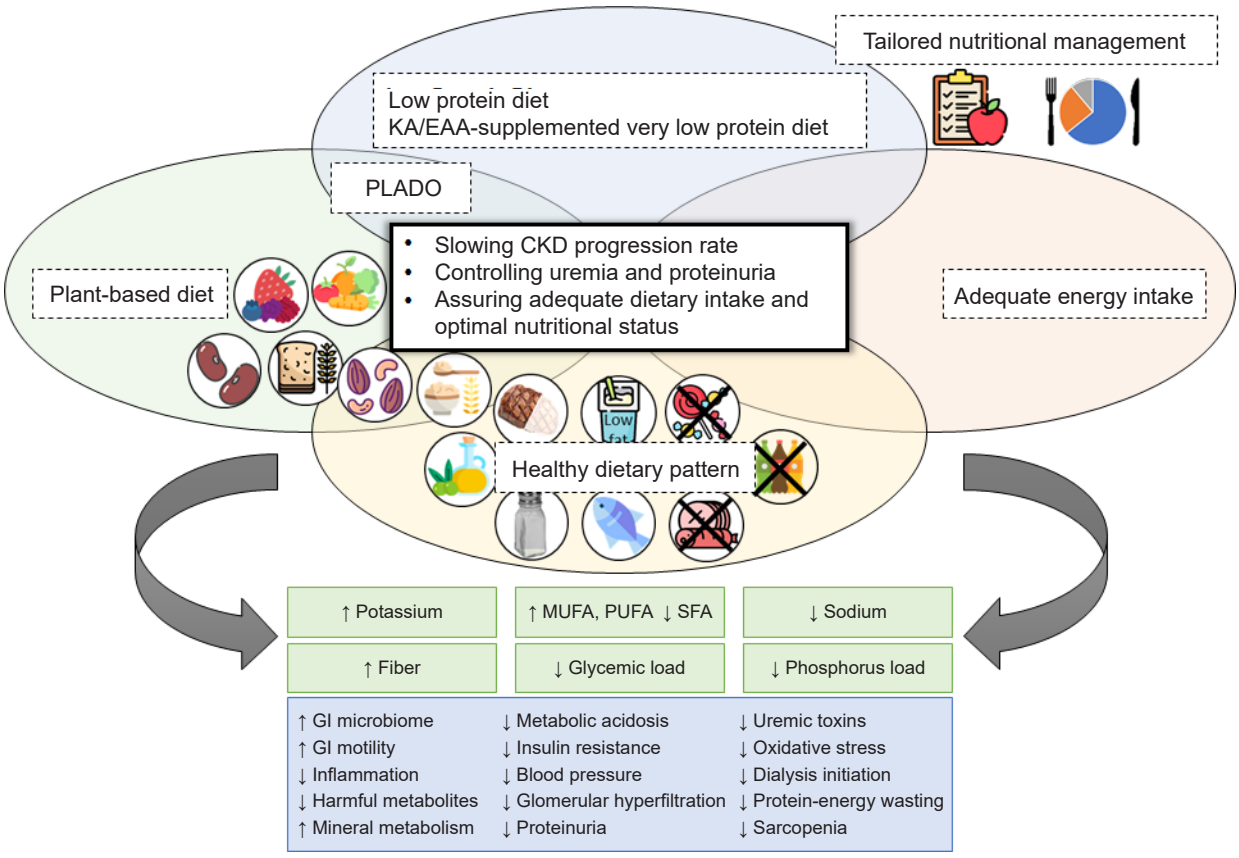

Figure 1. Nutritional management in advanced CKD.
CKD, chronic kidney disease; EAA, essential amino acids; GI, gastrointestinal; KA, ketogenic amino acids; MUFA, monounsaturated fatty acid; PLADO, plant-dominant low-protein diet; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids.

Table 1. Nutritional guidelines for patients with non-dialysis dependent CKD (i.e., stages 3 to 5 CKD) according to 2020 KDOQI guidelines

Nutrient	Recommendations
Energy[a]	25–35 kcal/kg ideal body weight/day
Protein[b]	Low-protein diet (0.55–0.60 or 0.6–0.8 g/kg body weight/day for patients without diabetes or with diabetes, respectively)
	Very low protein diet (0.28–0.43 g/kg body weight/day with additional keto acid/amino acid analogs to meet protein requirements)
Long-chain omega-3 PUFA	~2 g/day to lower serum triglyceride levels
Sodium	<2.3 g/day (<100 mmol/day)
Potassium	Adjust to maintain serum potassium levels in the normal range
	Dietary or supplemental potassium intake for patients with either hyperkalemia or hypokalemia should be based on a patient's individual needs and the clinician's judgment
Calcium[c,d]	800–1,000 mg/day
Phosphorus	Adjust to maintain serum phosphorus levels in the normal range
	Consider the bioavailability of phosphorus sources (e.g., animal, vegetable, additive)

CKD, chronic kidney disease; KDOQI, Kidney Disease Outcomes Quality Initiative; PUFA, polyunsaturated fatty acid.
[a]Energy intake should be prescribed based on age, sex, levels of physical activity, body composition, weight status goals, CKD stage, and concurrent illness or presence of inflammation to maintain normal nutritional status. [b]Insufficient evidence to recommend a particular protein type (plant vs. animal) in terms of the effects on nutritional status, calcium or phosphorus levels, or the blood lipid profile. [c]For patients without taking active vitamin D analogs. [d]Including dietary calcium, calcium supplementation, and calcium-based phosphorus binders.
Created using the information from Ikizler et al. (Am J Kidney Dis 2020;76:S1-S107) [13].

perceived as more restrictive than other chronic disease states [12], as well as concerns about the potential development of protein energy wasting in advanced CKD patients, using a personalized approach with intensive dietary counseling and ongoing close and frequent monitoring by specialty-trained kidney dietitians in collaboration with other specialists is of paramount importance in the nutritional management of CKD [78–80]. Other strategies used to enhance adherence to dietary interventions in CKD include 1) having the actual protein intake within a 20% difference from prescribed protein intake, 2) providing strong social support, 3) recommending a graduated adaptation from actual dietary protein intake to prescribed protein intake amount by reducing protein intake by 0.2 g/kg/day during each dietary counseling and consultation visit, and 4) allowing dietary "liberalization" for perhaps one meal per week [81,82].

Conclusion

In summary, using personalized nutrition management instead of a one-size-fits-all approach can enhance the effectiveness of dietary regimens for advanced CKD patients while preventing the progression of protein energy wasting and maintaining patients' nutritional status at optimal levels. Future studies are needed to determine the efficacy and safety of the PLADO/PLAFOND and other plant-based LPDs on kidney outcomes in order to support the conservative and preservative management of CKD patients.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Data sharing statement

The data presented in this study are available upon reasonable request from the corresponding author.

Authors' contributions

Conceptualization, Data curation, Funding acquisition, Formal analysis, Investigation, Methodology, Resources, Software: YN, KKZ, CMR
Writing–original draft: All authors
Writing–review & editing: All authors
All authors read and approved the final manuscript.

ORCID

Yoko Narasaki, https://orcid.org/0000-0002-2571-3803
Man Kit Siu, https://orcid.org/0009-0003-0288-4110
Matthew Nguyen, https://orcid.org/0000-0002-6517-041X
Kamyar Kalantar-Zadeh, https://orcid.org/0000-0002-8666-0725
Connie M. Rhee, https://orcid.org/0000-0002-9703-6469

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