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Plant-based diets for prevention and management of chronic kidney disease

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Purpose of review
Plant-based diets have been used with growing popularity for the treatment of a wide range of lifestyle-related diseases, including diabetes, hypertension, and obesity. With the reinvigoration of the dietary management of chronic kidney disease (CKD) and the use of low protein diets for secondary prevention of CKD to delay or prevent dialysis therapy, there is an increasing interest in the potential role of plant-based diets for these patients.

Recent findings
Recently, a body of evidence related to the role of plant-based diets in preventing CKD has reemerged. Several observational studies have shown that red and processed meat have been associated with increased risk of CKD as well as faster progression in those with preexisting CKD. In several substitution analyses, replacement of one serving of red and/or processed meat has been linked with sizable reductions in CKD risk. Although limited, experimental trials for the treatment of metabolic acidosis in CKD with fruits and vegetables show outcomes comparable to oral bicarbonate. The use of plant-based diets in CKD may have other benefits in the areas of hypertension, weight, hyperphosphatemia, reductions in hyperfiltration, and, possibly, mortality. The risk of potassium overload from plant-based diets appears overstated, mostly opinion-based, and not supported by the evidence. Plant-based diets are generally well tolerated and provide adequate protein intake, including essential amino acids as long as the diet is correctly implemented.

Summary
Plant-based diets should be recommended for both primary and secondary prevention of CKD. Concerns of hyperkalemia and protein inadequacy related to plant-based diets may be outdated and unsupported by the current body of literature. Healthcare providers in general medicine and nephrology can consider plant-based diets as an important tool for prevention and management of CKD.

Keywords
acidosis, chronic kidney disease, hyperkalemia, plant-based diets, protein, vegan, vegetarian

INTRODUCTION

Plant-based diets have recently received growing attention for their potential to mitigate the consequences of a Western diet. Recently, plant-based diets have demonstrated significant utility for the prevention and treatment of diabetes, hypertension, and obesity, all of which have become modern-day scourges of society [1,2▪▪,3]. Their utility for the treatment of other diseases has led to a growing interest in their applicability for the prevention and treatment of chronic kidney disease (CKD), that is, primary and secondary prevention of CKD, respectively [4,5▪,6]. Herein we provide a narrative review of the evidence on this subject.

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KEY POINTS

- Animal protein, specifically red meat and processed meat, have been repeatedly linked to CKD in several observational studies.
- Interventional trials have shown the benefit of fruits and vegetables in the treatment of metabolic acidosis of CKD and in reducing CKD progression.
- Plant-based diets may have pleiotropic benefits in CKD, including improving blood pressure, reducing serum phosphate levels, and improving survival.
- Issues related to hyperkalemia and protein deficiency are not supported by the current body of literature.

OBSERVATIONAL EVIDENCE OF PLANT-BASED DIETS ON CHRONIC KIDNEY DISEASE

Several observational studies have suggested benefit for renal health by increasing the consumption of plant-based foods or, by proxy, reducing the intake of animal-based foods. Three cross-sectional studies worth noting are the Multiethnic Study of Atherosclerosis (MESA), the Tehran Lipid and Glucose Study (TLGS), and the Dutch DIAbetes and LifEstyle Cohort Twente-1 (DIALECT-1) study [7–9].

In the MESA study, Nettleton *et al.* [7] studied the associations of various food groups on spot urine albumin-to-creatinine ratio (UACR). Among 5042 participants aged 45–84 years, researchers found that eating high amounts of whole grains, fruits, vegetables, and low-fat dairy foods were associated with a 20% lower UACR across quintiles of consumption, whereas those consuming higher amounts of nondairy animal food were associated with a 11% higher UACR across quintiles. Some of the associations of nondairy animal foods with UACR were explained by a combination of higher waist circumferences, systolic blood pressure, and need for hypertensive medications, all of which may serve as potential mechanisms.

In contrast, both the TLGS and DIALECT-1 studies specifically examined the associations of animal versus plant foods on the risk of CKD. In TLGS, researchers characterized plant and animal food consumption according to the source of protein among 5316 adults [8]. Those consuming the highest quartile (compared with the lowest quartile) of plant protein had a 30% lower odds ratio (OR 0.70, 0.51–0.97) of CKD after adjusting for serum triglycerides, cholesterol, BMI, and hypertension. Along the same lines, those consuming the highest quartile of animal protein had a 37% higher OR (1.37, 1.05–1.79) of CKD.

Both the TLGS and MESA studies excluded people with diabetes. The Dutch DIALECT-1 study, however, only included people with diabetes [9]. Although it looked at only 420 patients, the study characterized plant and animal food consumption according to tertiles of protein intake. Among those consuming the highest tertile of vegetable protein, the relative risk of CKD decreased by 53% (prevalence ratio 0.47, 0.23–0.98). However, in this study, animal protein consumption did not increase the risk of CKD, which may have been related to the inclusion of both dairy and red meat into the same category despite their possible differences in risk. Although red meat consumption was associated with a higher risk of CKD, the differences did not reach statistical significance (Q3 versus Q1 prevalence ratio 1.41, 0.83–2.41, $P = 0.21$), which may have been related to small intergroup differences in red meat intake and small group sizes. Nonetheless, replacing 3% of energy intake from animal protein with vegetable protein was associated with an 80% lower prevalence ratio of CKD (0.20, 0.06–0.63).

Several prospective studies have also revealed similar findings. Some of the earliest evidence has come from the Nurses' Health Study, which followed nearly 3300 women for an average of 11 years. Researchers found that those consuming the highest quartile of animal fat (compared with the lowest quartile) had a higher odds ratio (1.72, 1.12–2.64) of having microalbuminuria [10]. Further, those consuming two or more servings of red meat per week also had a higher risk (OR 1.51, 1.01–2.26) of microalbuminuria. Further analyses revealed that higher sodium consumption was directly associated with renal function decline, whereas β-carotene, a plant-based antioxidant, appeared protective, which may suggest possible a mechanism for the differences observed between plant and animal foods and their risk on kidney disease. A related subgroup analysis of middle-aged women using Nurses' Health Study data found similar trends among dietary patterns [11]; those consuming Western-style diets including red and processed meats and saturated fats had associations with albuminuria and rapid estimated GFR (eGFR) decline (>3 ml/min/1.73 m^2/year), whereas those consuming a dietary pattern that included fruits, vegetables, and whole grains had a lower risk of rapid eGFR decline.

Larger observational studies with longer follow-up, like atherosclerosis risk in communities (ARIC) and Singapore Chinese Health Study (SCHS) have supported these findings. In the ARIC study, nearly 12 000 middle-aged adults were followed for 23 years. This study showed that those consuming the highest quintile (versus lowest) of nuts, legumes, and low-fat dairy were associated with a lower risk of

CKD (HR 0.81, 0.72–0.92), whereas red and processed meat consumption was linked with a higher risk of CKD (HR 1.23, 1.06–1.42). In a substitution analysis, the authors noted that replacing one serving of red or processed meat with one serving of legumes was associated with a 31% reduced risk of CKD (HR 0.69, 0.57–0.83). Other observational studies have shown similar findings in substitution analyses. For example, prospective data from TLGS showed that replacing one serving of processed and unprocessed red meat for whole grains was associated with a 21% lower risk of CKD (OR 0.79, 0.73–0.86) and one serving of processed meat for legumes with a 31% lower risk [12]. Substitution analyses like this may be helpful in contextualizing potential risk as diet is a zero-sum game; food choices to include one food are made at the expense of excluding others.

Finally, the SCHS is the largest observational study on this subject with a total size of more than 63,000 individuals [13]. In this study, Lew *et al.*[13] examined data from a mean of 15.5 years of follow-up and showed that those in the highest quartile of red meat consumption had an increased risk of developing end-stage renal disease (ESRD) (1.40, 1.15–1.71), which was dose dependent. Again, substitution analysis revealed that replacing one serving of red meat with soy and legumes was associated with a 50.4% reduced risk of ESRD.

EXPERIMENTAL EVIDENCE OF PLANT-BASED DIETS ON CHRONIC KIDNEY DISEASE

Experimental data regarding plant-based diets and their effects on CKD are sparse except for a few key areas. Several trials were done with the inclusion of fruits and vegetables for the treatment of metabolic acidosis and resultant kidney function. These trials offer insight into the effects of limited quantities of plant-based foods in CKD and allow us to extrapolate further.

Goraya *et al.* [14] published the first of the three seminal trials in 2012 on the effects of fruits and vegetables (F + V) or oral bicarbonate after 30 days on indices of renal injury among patients with CKD stages I and II. Researchers found that both F + V and sodium bicarbonate reduced UACR and indices of renal injury. However, the F + V group also had additional benefits not seen in the oral bicarbonate group like reductions in systolic blood pressure and weight.

The second trial by Goraya *et al.* [15] was randomized, longer (1 year), and included patients with more advanced kidney disease (stage IV CKD). In this trial, 71 patients with untreated metabolic acidosis were randomly assigned to oral bicarbonate (dosed to 1.0 mEq/kg/day) or F + V (dosed to reduce dietary acid by half). Although both groups had improvements in serum bicarbonate after one year, the F + V group did have slightly lower levels of bicarbonate (19.9 versus 21.2 mM). Despite this difference in serum bicarbonate, no significant differences were noted in glomerular filtration rate (GFR) at the end of the study between groups. Further, those in the F + V group again had additional benefits, like a reduction in systolic blood pressure, weight, and UACR.

Finally, the third trial Goraya *et al.* [16] in this domain randomized 108 patients with CKD stage III to either oral bicarbonate, F + V for a duration of three years, or no intervention (usual care). Both intervention groups again had increases in serum bicarbonate at the end of the study without a statistically significant difference in bicarbonate between both groups, whereas the usual care group had a decline in serum bicarbonate. Regarding GFR loss, the usual care experienced greater GFR loss than either of the alkali-based intervention groups. There was no difference in GFR at three years between groups treated with oral bicarbonate or F + V, suggesting that F + V was equivalent to oral bicarbonate in this regard. However, again, F + V demonstrated additional benefits with reductions in systolic blood pressure, UACR, and weight.

In sum, these trials show the reproducibility and sustainability of F + V for the treatment of metabolic acidosis in CKD – even in advanced stages – with the added benefit of reductions in weight, blood pressure, and UACR. Surprisingly, only two to four servings of F + V were required to show benefit [17]. It is hypothesized that a larger amount of plant-based foods would have even greater benefit.

PLEIOTROPIC BENEFITS OF PLANT-BASED DIETS IN CHRONIC KIDNEY DISEASE

In addition to the utility of plant-based diets for metabolic acidosis, hypertension, and weight as mentioned previously, these diets have also been shown to reduce serum phosphate levels. In a crossover trial of eight patients with CKD stage III and IV, Moe *et al.* [18] showed that those on a vegetarian diet (compared with a meat-based diet) had lower levels of plasma phosphorus and FGF-23. Despite popular opinion, plant-based foods are actually lower in phosphorus content than many other food sources when accounting for their reduced bioavailability. Plant-based foods contain phytate which binds to phosphate and prevents absorption as humans lack the enzyme phytase necessary to digest phytate. As such, the bioavailability of plant-based

foods is typically between 10 and 30% [19]. However, phytate can be disrupted with industrial processing, that is, bread baking, and can increase the bioavailability of phosphate [20].

Another common benefit of plant-based diets is that they may help avoid the risks of hyperfiltration associated with excess protein intake. The lower protein content of plant-based diets has also been incorrectly perceived as a disadvantage lest they may lead to protein deficiencies. However, several studies have shown that those consuming plant-based diets in CKD and even in dialysis-dependent ESRD were able to obtain adequate quantity and quality of protein [21▪]. For example, those with CKD on unrestricted vegan diets have been observed to consume 0.7–0.9 g/kg/day of protein [22–24]. This range of protein of consumption fortuitously coincides with the range recommended in low protein diets for the preservation of renal function via avoiding hyperfiltration [25]. In essence, plant-based diets may help to avoid protein excess that is common to typical Western diets (average protein intake 1.2–1.5 g/kg/day) while still meeting basic nutritional requirements [21▪].

Vegetarian diets have also been shown to be feasible for those on dialysis with patients attaining 1.2–1.25 g/kg/day of protein without compromise [26,27]. Another benefit for those consuming plant-based diets has been the reduced generation of uremic toxins, which may be related to the higher fiber content and lower protein content of those diets [26,28,29]. In one study of patients with CKD stage III and IV, researchers noted that dietary compliance was actually improved in those on vegetarian diets compared with those on animal-based diets, which may be related to reduced uremic toxin generation from these diets [23].

Another important and perhaps overlooked potential benefit of these diets may be the reduction in mortality associated with increasing consumption of these foods. In a meta-analysis of nearly 14 000 patients with CKD from six prospective studies, researchers found that a healthy dietary pattern higher in fruits, vegetables, fish, legumes, cereals, whole grains, and fiber and lower in red meat, salt, and refined sugars was associated with a lower risk of mortality (RR 0.73, 0.63–0.83). Similarly, in another prospective study of approximately 8000 patients with ESRD on dialysis over 2.7 years researchers showed that even a small increase in F + V consumption was associated with a reduction in mortality [30]. Those consuming the lowest tertile of F + V consumption (median 2 servings/week) compared with the highest tertile (median 17 servings/week) were linked with a 20% reduction in all-cause mortality (hazard ratio [HR] 0.80, 0.71–0.91) and a 23% reduction in non-cardiovascular mortality (HR 0.77, 0.66–0.91). The findings of this study are impressive when considering the size of the associated reduction in mortality, the high rate of mortality typically seen among patients with ESRD, and the relatively small amount of F + V consumed in the highest tertile of the study (a median of 2.4 servings/day) that was associated with the reduction. Further research in the form of experimental trials will be needed to corroborate these findings.

Clinical reversal of a glomerulopathy has also been documented while on a plant-based diet. One case comes from a patient who made changes to a plant-based diet, along with adoption of an exercise program, which led to complete and permanent remission of minimal change disease [31]. In brief, the patient had biopsy-proven minimal change disease with nephrotic range proteinuria that appeared to not respond to prednisone, cyclosporine, or mycophenolate mofetil. Curiously though, upon making lifestyle changes more than a decade ago, the patient continues to be in clinical remission of his disease [31,32]. Although the possibility of spontaneous remission certainly exists, this case report is thought provoking in terms of the potential of plant-based diet to augment chance of remission [33]. Finally, case reports have also been published patients with lupus nephritis having clinical improvement after trying a plant-based diet [34].

POTASSIUM AND PLANT-BASED DIETS

An enduring concern of many health care providers is hyperkalemia from plant-based foods. This deserves reconsideration. Indeed, case reports do exist of hyperkalemia but are often attributed to juices, sauces, excess dried fruit consumption, or the use of potassium-containing supplements [35]. All these substances should be avoided or restricted in patients with advanced kidney disease given the inherent characteristics of these specific substances that increase the amount of potassium ingested per unit time and, perhaps, their bioavailability. However, we are unaware of any trials documenting hyperkalemia from a whole, plant-based food except for a singular case of a patient with a preexisting hyperkalemic renal tubular acidosis [36]. For example, of the aforementioned clinical trials of F + V administration to patients with CKD stages I–IV for metabolic acidosis, no instances of hyperkalemia were seen in any of the studies although patients were carefully monitored and advised throughout the trials [14–16]. Additional data including patients with nondialysis CKD stage also did not show hyperkalemia [24].

The lack of hyperkalemia seen in those eating plant-based diets may be multifactorial [37]. Eating plant foods increases fiber consumption, which increases stool quantity and frequency. This facilitates gastrointestinal elimination of potassium. Up to 80% of ingested dietary potassium can be eliminated via feces in patients on hemodialysis [38]. In addition, the presence of cell walls in plant-based foods likely mitigates complete absorption of potassium. No more than 60% of potassium from unprocessed fruits and vegetables is absorbed [39▪▪]. Other related factors that prevent increases in serum potassium level include improved metabolic acidosis and improved insulin sensitivity. The historical avoidance of plant-based foods for fear of hyperkalemia has prevented patients from having beneficial substances like fiber, vitamins, minerals, and antioxidants.

CONCLUSION

Plant-based diets have a growing body of evidence for several diseases, including CKD. Although trial evidence is limited to primarily metabolic acidosis, observational evidences suggest harm with red and processed meats and benefit with even small amounts of plant-food consumption in all stages of CKD. Concerns regarding hyperkalemia and protein inadequacy may be outdated and may have prevented patients and physicians from utilizing the pleiotropic benefits of plant-based foods. Healthcare providers in nephrology may consider plant-based diets as an additional tool in the prevention and management of CKD patients.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
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