receiving home dialysis, in priority risk groups for early vaccination against SARS-CoV-2.

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Is it time to abandon the nutrient-based renal diet model?

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The traditional renal diet is logical, but perhaps not biological. In this issue of *Nephrology Dialysis Transplantation*, Gonzalez-Ortiz *et al.* present findings from cross-sectional analyses that add to the growing body of literature [1]. The analysis fails to support the theory that diet-related complications in hemodialysis (HD) patients are caused by diet-derived nutrient imbalances [2–4]. In particular, the renal dietary pattern for HD is designed to be low potassium, low phosphorus and high protein, with the understanding that this would help to prevent and treat hyperkalemia, hyperphosphatemia and protein–energy wasting (PEW), respectively [5].

The approach used to develop the renal diet was similar to that used to prevent nutrient imbalances in the food guide [6]. First, prescriptions were established for key nutrients [7]. Then, the balance of food groups and variety of food choices within each food group were determined based on their nutrient composition [5]. The resultant HD diet restricts many high-potassium and high-phosphorus plant foods, and promotes animal-based protein foods. Regarding the latter, the 1993 National Renal Diet food guide produced by the American Dietetic Association Renal Practice Group advised dialysis patients to 'eat all the unsalted meats, fish, and poultry, or eggs you want' [8]. The study by Gonzalez-Ortiz *et al.* found that tertiles of the Healthy Plant-Based Diet Score, an index of plant intake, were not associated with serum potassium and phosphorus concentrations, or malnutrition inflammation score in HD patients.

As noted by Gonzalez-Ortiz *et al.*, it is possible that the nutrient-based renal diet is efficacious for managing these conditions, but cannot be detected in observational studies using standard dietary assessment methods because of measurement error related to misreporting, and the effects of food processing and preparation, which can concentrate, dilute, add and remove nutrients. However, another possibility is that the assumptions underlying the nutrient-based model are incorrect, in which case, dietary restrictions may be an unnecessary burden in HD patients that could contribute to poor health outcomes.

ASSUMPTIONS OF THE NUTRIENT-BASED MODEL

(i) Causality: One of the core assumptions of the nutrient-based model is that these metabolic conditions are primarily caused by nutrient imbalance, and that other dietary factors are relatively unimportant. This assumption appears to be mostly true for phosphorus and hyperphosphatemia [9]. However, although adequate protein intake is necessary to prevent PEW, and excess potassium intake can cause hyperkalemia in people with chronic kidney disease (CKD), other dietary factors may be more clinically relevant determinants of these conditions. For example, although protein requirements are often treated as fixed patient characteristics based on lean body mass, protein utilization in CKD depends on the metabolic state, which can be affected by diet (e.g. metabolic acidosis, uremia, inflammation, energy balance, insulin resistance) [4]. Similarly, the higher potassium load of plant-rich diets may be offset by biological factors affecting potassium metabolism (e.g. adaptation, metabolic acidosis, glucose/insulin response, stool output) [3].

(ii) Equivalence: Another major assumption of the nutrient-based model is equivalence, which is applied in the translation of nutrient prescriptions into dietary recommendations. Specifically, foods in the renal diet are classified based on their crude nutrient content. However, the bioavailable fraction and/or utilization of nutrients may differ by source. Studies examining differences in urinary phosphorus output, an indicator of excess phosphorus load, show that phosphorus from plants and dairy products may contribute relatively less to phosphorus load than animal-based protein foods and food additives [10]. Of note, while inorganic phosphorus is often claimed to be 90–100% bioavailable, this figure appears to be based on *in vitro* digestibility studies that do not account for limitations in phosphorus absorption [11–13]. Likewise, whole fruit and vegetables, and whole grains have been found in some studies to increase stool potassium output, a finding that may be due to reduced potassium absorption from dietary fiber [14–16].

Protein equivalence in PEW risk is more complicated, as protein requirements encompass absolute protein needs, as well as needs for essential amino acids (EAAs). With few exceptions (e.g. soybeans, quinoa), proteins from plants have lower biological value (quality) than proteins from animals due to lower bioavailability and limiting EAAs. However, amino acid scores are determined based on requirements established in healthy individuals, and fail to account for protein complementation that exists in the context of a mixed diet. Grain products provide ~3 g of protein per oz equivalent serving, which is incomplete because they are limited in lysine. Both plant- and animal-based protein foods contain adequate lysine, and therefore form a complete protein when paired with grain products. However, plant-based protein foods are limiting in sulfur-containing amino acids, whereas animal-based protein foods are not. As a result, the strict focus on animal-based protein foods in the traditional renal diet may contribute an unnecessary excess of sulfur-containing amino acids and corresponding dietary acid load when metabolized.

The lack of evidence surrounding the recommendation that HD patients consume at least half of their protein from high biological value (HBV) sources, generally interpreted as animal-based protein, has long been known. In his 1996 McCollum Award Lecture paper, Dr Kopple states, 'we have also recommended, although without testing this question experimentally, that about 50% of this protein should be of high biological value' [17]. Unfortunately, this nuance appears to have been lost in translation, as until recently, recommendations for 50% HBV were rarely accompanied by this disclaimer.

(iii) Acuity: An often-overlooked assumption in translating nutrient prescriptions into dietary recommendations is that the acute rather than chronic nutrient load causes nutrient imbalances, as foods are generally classified based on their nutrient richness (milligram/serving), not their nutrient density (milligram/kilocalorie) [5]. This approach may be suitable for potassium, as serum potassium values increase in response to a potassium bolus in people with CKD due to impaired dietary potassium tolerance [18–20]. However, it is worth noting that acute potassium exposure can be controlled without eliminating high-potassium foods (e.g. balanced meals, portion control), and chronic nutrient load may better represent the biological relationships linking dietary and serum phosphorus, and dietary protein and PEW in people with CKD. If the latter is true for hyperphosphatemia and PEW, factors other than nutrient richness (e.g. serving size, energy density) must also be considered when classifying foods as low or high phosphorus and protein. For example, high-fat milk is lower in phosphorus density than many lean meats [21].

(iv) Adherence and translation: Finally, as with all diet therapies, the overall health impacts of dietary guidelines depend on how they are adopted in practice, as well as the balance of secondary benefits and consequences. Studies in CKD populations have failed to consistently demonstrate that knowledge of the renal diet predicts adherence and outcomes [22]. The renal dietary pattern is largely inconsistent with dietary guidelines for the general population [23], as well as those with hypertension and diabetes mellitus [24, 25], the two main causes of CKD. In addition, to navigate the substantial information burden presented by the renal diet, some patients may adopt monotonous, mundane eating patterns that could compromise their nutrition status and health.

IMPLICATIONS

The finding from Gonzalez-Ortiz *et al.* reinforce the concept that, at least within the context of normal dietary intakes, restrictions imposed by the nutrient-based renal dietary pattern may not significantly lower the risk of diet-related complications in people with CKD. However, the authors note 'absence of evidence is not evidence of absence'. Unfortunately, many questions remain unanswered, and liberalized, plant-rich diets are not necessarily risk-free. For example, the lack of association between reported dietary potassium intakes, and fasting and predialysis serum potassium levels does not preclude the possibility that high-potassium meals cause unseen postprandial hyperkalemia between dialysis sessions [26]. In additional, although dietary fiber may help address the metabolic determinants of PEW (e.g. gut-derived uremic toxins), excess fiber may promote weight loss through satiation. Furthermore, plant-based diets contain less bioavailable iron, and therefore, may add to the problem of iron deficiency in people with CKD [27].

This is not to suggest that the findings should be ignored either, as they have important clinical implications. Indeed, if fasting and predialysis serum potassium concentrations are not valid biomarkers of dietary potassium intake in HD patients, they should not be used as a measure of adherence to the low-potassium diet. In fact, serum potassium appears to be a stronger indicator of protein intake than potassium intake in CKD patients [28, 29]. In a single-group pilot feeding study of CKD patients provided a DASH (Dietary Approaches to Stop Hypertension) diet, changes in 24-h urinary potassium output were not correlated with changes in serum potassium concentration ($r = 0.39$, $P = 0.30$), but changes in urine urea nitrogen output were ($r = 0.67$, $P = 0.046$) [29]. However, at the same time, hyperkalemia was a well-established consequence of the very low-protein Giordano–Giovanetti diets used to manage uremia, which were also low in potassium [30, 31]. Clearly, the dietary pattern impacts these relationships in complex ways.

A recent survey of renal dietitians in the US indicates a major schism in clinical practice, with many dietitians adhering to the traditional nutrient-based renal diet, and nearly an equal proportion recommending a more liberalized, plant-rich diet [32]. Standardized care is a major goal of evidence-based dietetic practice, and lack of thereof may generate confusion and expose patients to unknown risks. Randomized clinical trials of dietary patterns in people with CKD are needed to inform these fundamental questions to clinical practice. Until such time that these studies are conducted, caution on both sides of this debate is warranted.

CONFLICT OF INTEREST STATEMENT

None declared.

(See related article by González-Ortiz *et al.* Nutritional status, hyperkalaemia and attainment of energy/protein intake targets in haemodialysis patients following plant-based diets: a longitudinal cohort study. *Nephrol Dial Transplant* 2021; 36: xxx–xxx)

DATA AVAILABILITY STATEMENT

There are no new data associated with this article.

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Does the relationship between measured and prescribed dialysate sodium matter in the nephrology community?

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THE IMPORTANCE OF DIALYSATE SODIUM PRESCRIPTION

Dialysate composition is one of the most fascinating topics in nephrology. Learning about the art and science of haemodialysates (regarding sodium, potassium, calcium, magnesium and bicarbonates) is one of the best ways to further our understanding of the pathophysiologic processes underlying the myriad of acid–base, fluid, electrolyte and blood pressure abnormalities in end-stage kidney disease [1].

NDT is publishing in this issue a systematic review and meta-analysis aimed at assessing the agreement between prescribed and delivered dialysate sodium (DNa) and whether the relationship varies according to the prescribed DNa levels [2]. The study indicated the lack of an average difference between measured and prescribed DNa values. Individual dialysate sample analysis showed an ~1:1 monotonic relationship between the two variables. However, among individually reported samples measured DNa was lower by almost 2 mmol/L and the 95% limits of agreement ranged from ~−4 to ~+8 mmol/L, depending on the type of dialysis machine, type of dialysate preparation, type of concentrate etc. The authors concluded that informed DNa prescription requires more precision in the actual delivery of DNa [2]. The significant differences between prescribed and measured DNa concentrations may have beneficial or deleterious effects on clinical outcomes [3].

Sodium is the main extracellular ion and defines osmolality and the size of the extracellular volume; increased plasma sodium concentration results in an increase in osmolality, thirst

