

# Nutritional status, hyperkalaemia and attainment of energy/protein intake targets in haemodialysis patients following plant-based diets: a longitudinal cohort study

Ailema González-Ortiz<sup>1,2</sup>, Hong Xu<sup>1,3</sup>, Samuel Ramos-Acevedo<sup>2</sup>, Carla M. Avesani<sup>4</sup>, Bengt Lindholm<sup>4</sup>, Ricardo Correa-Rotter<sup>2</sup>, Ángeles Espinosa-Cuevas<sup>2</sup> and Juan Jesús Carrero<sup>1</sup>

<sup>1</sup>Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden, <sup>2</sup>Department of Nephrology and Mineral Metabolism, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, <sup>3</sup>Department of Neurobiology, Care Sciences and Society, Division of Clinical Geriatrics, Karolinska Institutet, Stockholm, Sweden and <sup>4</sup>Department of Clinical Science, Intervention and Technology, Division of Renal Medicine and Baxter Novum, Karolinska Institutet, Stockholm, Sweden

Correspondence to: Juan Jesús Carrero; E-mail: [juan.jesus.carrero@ki.se](mailto:juan.jesus.carrero@ki.se)

## ABSTRACT

**Background.** Patients undergoing haemodialysis (HD) are often discouraged from eating fruits and vegetables because of fears of hyperkalaemia and undernutrition, yet evidence to support these claims is scarce. We here explore the association between adherence to a healthy plant-based diet with serum potassium, surrogates of nutritional status and attainment of energy/protein intake targets in HD patients.

**Methods.** We performed an observational single-centre study of stable patients undergoing HD with repeated dietary assessment every 3 months. Patients were provided with personalized nutritional counselling according to current guidelines. The diet was evaluated by 3-day food records and characterized by a healthy plant-based diet score (HPDS), which scores positively the intake of plant foods and negatively animal foods and sugar. The malnutrition inflammation score (MIS) and serum potassium were also assessed at each visit. We used mixed-effects models to evaluate the association of the HPDS with markers of nutritional status, serum potassium levels and attainment of energy/protein intake targets.

**Results.** After applying inclusion and exclusion criteria, a total of 150 patients contributing to 470 trimestral observations were included. Their mean age was 42 years [standard deviation (SD) 18] and 59% were women. In multivariable models, a higher HPDS was not associated with serum potassium levels or odds of hyperkalaemia {potassium >5.5 mEq/L; odds ratio [OR] 1.00 [95% confidence interval (CI) 0.94–1.07] per HPDS unit higher}. Patients with a higher HPDS did not differ in terms of energy intake [OR for consuming <30 kcal/kg day 1.05 (95% CI

0.97–1.13)] but were at risk of low protein intake [OR for consuming <1.1 g of protein/kg/day 1.11 (95% CI 1.04–1.19)]. A higher HPDS was associated with a lower MIS, indicating better nutritional status.

**Conclusions.** In patients undergoing HD, adherence to a healthy plant-based diet was not associated with serum potassium, hyperkalaemia or differences in energy intake. Although these patients were less likely to reach daily protein intake targets, they appeared to associate with better nutritional status over time.

**Keywords:** dietary intake, haemodialysis, hyperkalaemia, nutritional status, plant-based diets

## INTRODUCTION

People with chronic kidney disease undergoing maintenance haemodialysis (HD) are advised to change their diet in order to avoid complications linked to their inability to excrete and metabolize some specific nutrients. These recommendations involve restrictions of phosphorus, potassium, sodium and fluid intake, while providing sufficient energy and protein intake to prevent undernutrition [1–3]. Adherence to these recommendations typically results in a low intake of plant foods [4–6], and in a recent survey of ~8000 prevalent patients on HD from Europe, only 4% reached the minimum recommended consumption of four or more daily servings of fruits and vegetables for healthy eating [7]. The main reason for discouraging the intake of fruits and vegetables in these patients traditionally involves fears for hyperkalaemia due to dietary potassium load

## KEY LEARNING POINTS

### What is already known about this subject?

- Plant-based diets are currently gaining popularity in society and may be preferred by many patients on dialysis, especially if transitioning from a plant-based low-protein diet during their pre-dialysis care.
- Patients undergoing dialysis are often discouraged from eating fruits and vegetables because of fears of hyperkalaemia and undernutrition, yet evidence to support these claims is scarce.

### What this study adds?

- Patients on haemodialysis (HD) adhering to a healthy plant-based dietary pattern had a similar daily energy intake and serum potassium levels compared with patients not adhering to this diet.
- Patients on HD adhering to a healthy plant-based dietary pattern had a lower probability of reaching daily protein targets, but no differences were observed with regards to nutritional indicators. Instead, these patients appeared to have higher malnutrition inflammation scores.

### What impact this may have on practice or policy?

- This observational study challenges our dogmas of routinely recommending patients on dialysis avoid fruits and vegetables and emphasize the importance of performing interventional studies that explore possible benefits and harms of liberalizing the diet of dialysis patients with regards to the consumption of plant foods.

and for undernutrition, as plant-protein has been judged to have low biological value [8]. However, evidence to support these claims is scarce and graded as expert opinion recommendations [9, 10]. Recent studies indicate instead that such well-meaning guidance may deprive HD patients of potential benefits from consuming plant foods; for instance, observational studies suggest that while serum potassium in dialysis patients correlates poorly with dietary estimations of potassium intake [11, 12], higher fibre intake is associated with less constipation, resulting in lower intestinal potassium absorption [13] with less inflammation, less myocardial hypertrophy and injury and lower risk of cardiovascular events [14], and that increased consumption of fruits and vegetables associates with lower risk of death [7]. The term plant-based diet refers to a diverse family of dietary patterns generally characterized by a higher frequency of consumption of plant foods and minimal to no consumption of animal foods [15]. These diets are usually lower in fat and animal protein and higher in fibre and plant protein [16]. Plant-based diets are currently gaining popularity in society and may be preferred by many patients on dialysis, especially if transitioning from a plant-based low-protein diet during their pre-dialysis care [17]. However, there is virtually no information on

the risks and benefits of adhering to such diets in this population. In this study, we explore the likelihood of undernutrition and hyperkalaemia among routine-care patients on HD adhering to a plant-based dietary pattern.

## MATERIALS AND METHODS

### Study population

This is an observational single-centre cohort study of prevalent patients undergoing HD at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (Mexico City, Mexico). All patients received routine consultation with a renal dietitian approximately every 3 months. At each renal dietitian consultation, we collected information on the patient's dietary intake, nutritional status, sociodemographics, comorbidities, pre-dialysis routine laboratory measurements and medications consumed. Between 2014 and 2018, a total of 178 patients were recruited into the cohort. For this study we excluded patients with <3 months on HD ( $n=19$ ), with incomplete 3-day food records ( $n=3$ ), without nutritional assessment ( $n=5$ ) and those requiring tube feeding ( $n=1$ ), leaving a total of 150 patients for analysis. Patients were then followed up for 1 year, recording a maximum of five trimestral visits per patient. The study was conducted according to the Declaration of Helsinki and patient informed consent was not deemed necessary because the information analysed is part of our routine evaluations and care.

### Dietary assessment

At every renal dietitian consultation, patients were provided (verbally and in written form) with personalized nutritional counselling according to current guidelines [1, 2]. Dietary intake was evaluated by 3-day food records, asking the patient to record his/her food intake on an HD day, a non-HD mid-week day and a weekend day. For this purpose, patients received training from a trained dietitian on how to record their food consumption. Records were reviewed at each visit together with the patient and corrected (regarding the report of sizes and portions) with the help of standardized tridimensional and flat food replicas. Food records were introduced into the software Nutrikcal VO version 1 (Consinfo, Alvaro Obregon, Mexico), which determines the energy and macronutrients provided by each food group according to Mexican guidelines and food composition of typical Mexican foods. From this food composition analysis, we calculated average daily energy intake (DEI; kcal/kg/day), daily protein intake (DPI; g/kg/day) as well as macro and micronutrients consumption. Consumption of foods and nutrients was expressed as a percentage of intake (g/day or 1000 kcal/day, as appropriate).

### Study exposure: healthy plant-based diet score (HPDS)

Adherence to a healthy plant-based diet (HPD) was estimated from 3-day food records as previously described [18]. The HPDS is built by scoring the collective intake of plant and animal foods. The intake (servings/day) of four plant food groups—cereals (including potatoes, pasta, oat, rice and bread), fruit, vegetable and legumes—was transformed into quintiles of

**Table 1. Classification of food items for creation of an HPD**

Food groups	Food items	Plant-based diet index
Plant foods		
Cereals and tubers	Potatoes, pasta, oat, rice, bread, corn products and bakery	Positive
Fruits	Apples, pears, oranges and pineapples	Positive
Vegetables	Squash, broccoli, zucchini, carrots, cauliflower and cactus	Positive
Legumes	Beans, lentils and chickpeas	Positive
Sugar	Low-calorie soft drinks, regular soft drinks, fruit-flavoured beverages, chocolate bars or pieces of candy with and without chocolate, jams and jellies	Negative
Animal foods		
Dairy products	Low-fat milk, whole milk, yogurt and ice cream	Negative
Meats and eggs	Chicken, turkey, fish, beef, pork, cheese, eggs, processed meats (sausage, ham) and liver	Negative

Adapted to foods and servings recommended by the Mexican equivalent food system for the general population [21], following a similar methodology to previous publications [18].

distribution. The sum of the quintile values across these four food groups was scored positively (assigning a value of 1 for the first quintile, 2 for the second quintile, 3 for the third quintile, 4 for the fourth quintile and 5 for the fifth quintile). Because sugars have been associated with obesity, metabolic syndrome, type 2 diabetes and inflammatory diseases [19, 20], the intake of sugar was scored negatively, along with the intake (servings/day) of two animal food groups—meats (eggs, chicken and fish) and dairy products (ice cream, milk and yogurt)—in a similar manner as plant foods. The sum of quintile values across these food groups were scored negatively (assigning a value of 5 for the first quintile, 4 for the second quintile, 3 for the third quintile, 2 for the fourth quintile and 1 for the fifth quintile). The collective sum of these quintiles reflects the adherence to a healthy plant-based dietary pattern with final scores ranging from 7 (lowest adherence) to 35 (highest adherence). Because fatty foods in Mexican guidelines [21] include a mix of plant and animal sources together (nuts, animal fats and vegetable oils), we decided to exclude them from the scoring but to adjust for them in the multivariable analyses. The energy-adjusted estimates (residuals) were ranked according to their sex-specific quintiles, calculated and adjusted per visit (Table 1).

### Study outcomes

Study outcomes were assessed at each patient visit. The first study outcome was serum potassium and the presence of hyperkalaemia (potassium >5.5 mEq/L) at each patient visit, determined through routine measurements at our hospital laboratory and from blood samples drawn in fasting conditions before the start of the first HD session of the week. The second study outcome was the attainment of daily recommended energy and protein intake targets for HD patients [2]. These were defined as DPI  $\geq 1.1$  g/kg/day and DEI  $\geq 30$  kcal/kg/day and were estimated from 3-day food records. The third study outcome comprised surrogates of nutritional status as estimated by body mass index (BMI), calculated as weight in kilograms divided by the square of height in metres; standard skinfold triceps (%), obtained at the triceps skinfold measured using the Lange skinfold caliper and following current guidelines [1, 22]; and the malnutrition inflammation score (MIS), a nutritional assessment tool specific for HD patients

that consists of 10 dimensions of the patient's nutritional status that are scored and summed, providing a total score ranging from 0 (normal) to 30 (severely malnourished) points. A higher score reflects a more severe degree of malnutrition [23, 24].

### Study covariates

Other study covariates were collected under standardized methods and included demographics, self-reported civil status, employment, comorbidities and medications. Comorbidity history and ongoing medications were obtained from review of the patient's clinical files.  $K_t/V$  as a measurement of dialysis adequacy ( $K$  = dialyser urea clearance,  $t$  = time on dialysis and  $V$  = total body water) was extracted from the medical records. Hypertension was defined as the use of antihypertensive medications or by diagnosis as recorded in the medical records [25]. Diabetes was defined as fasting plasma glucose  $\geq 126.0$  mg/dL, the use of oral hypoglycaemic agents or insulin or by diagnosis in the medical records [26].

### Statistical analysis

We report baseline characteristics by increasing tertiles of HPDS distribution, with the first tertile as 'low adherence', second as 'moderate adherence' and third tertile as 'high adherence' to the HPD. We used the Jonckheere–Terpstra test to assess linear trends across these groups. Values are reported as mean and standard deviation (SD) for continuous variables with normal distribution, median [interquartile range (IQR)] for non-normally distributed continuous variables and number of cases and percentages for categorical variables.

We used one mixed-effects linear regression model with an unstructured variance–covariance matrix to evaluate associations between the HPDS and study outcomes through evaluation of all consecutive patient visits. In this model, consecutive data points are clustered if they belong to the same patient. Because of skewed data distribution, BMI and skinfold triceps were log-transformed before entering in the regression. We used multilevel mixed-effects logistic regression to explore the risk between adherence to the HPD and the attainment of energy/protein targets or the presence of hyperkalaemia. Data are expressed as regression coefficients ( $\beta$ ) and/or odds ratio (OR)

**Table 2. Baseline characteristics of HD patients according to increasing adherence (tertiles of distribution) to an HPD**

Characteristic	Low adherence (n = 43)	Moderate adherence (n = 53)	High adherence (n = 54)	P-value for trend
HPDS	16 (11–18)	21 (19–22)	24 (23–32)	
Age (years)	36 (22–54)	40 (26–62)	39 (25–57)	0.6
Sex (female), n %	24 (56)	28 (53)	37 (69)	0.2
Civil status, n (%)				
Single	22 (51)	31 (59)	28 (52)	0.8
Married	16 (37)	17 (32)	17 (31)	
Occupation, n (%)				
Unemployed	9 (21)	11 (21)	8 (15)	0.27
Employed	18 (42)	21 (40)	19 (35)	
Non-remunerated <sup>a</sup>	14 (32)	17 (32)	26 (48)	
Retired	2 (5)	4 (7)	1 (2)	
Cardiovascular disease, n %	11 (26)	16 (30)	12 (22)	0.7
Diabetes mellitus, n (%)	18 (42)	23 (43)	29 (54)	0.3
Hypertension, n (%)	25 (58)	30 (57)	31 (57)	0.9
Loop diuretics, n (%)	30 (70)	35 (66)	33 (61)	0.4
RAS blockers, n (%)	18 (42)	30 (57)	18 (33)	0.3
Dialysis characteristics				
Dialysis vintage (months)	4 (3–9)	4 (3–7)	4 (3–6)	0.9
K <sub>t</sub> /V	1.6 (1.3–1.9)	1.6 (1.3–1.8)	1.9 (1.4–2.0)	0.7
Venous catheters, n (%)	40 (93)	49 (92)	52 (96)	0.5
Biochemical measurements (serum)				
Albumin (g/dL), mean ± SD	3.6 ± 0.6	3.5 ± 0.6	3.5 ± 0.6	0.2
Haemoglobin (g/dL), mean ± SD	10.0 ± 1.5	9.3 ± 1.7	9.7 ± 1.5	0.6
Creatinine (mg/dL)	8.8 (5.0–12.2)	8.2 (4.5–10.6)	8.6 (4.5–10.9)	0.3
Calcium (mg/dL)	8.6 (8.2–9.3)	8.6 (8.3–9.3)	9 (8.4–9.2)	0.4
Phosphorus (mg/dL)	4.7 (3.5–6.1)	5.0 (3.6–6.3)	5.1 (3.7–6.1)	0.9
Potassium, mmol/L	4.9 (4.1–5.4)	5.1 (4.4–6)	4.7 (4.2–5.6)	1.0
Hyperkalaemia (>5.5 mmol/L), n (%)	10 (23)	21 (40)	15 (28)	0.7
Bicarbonate (mEq/L)	19.6 (17.8–26.7)	19.6 (17.4–22.2)	21.6 (20.4–23.8)	0.8
Nutritional status				
Weight (kg), mean ± SD	62 ± 17.7	60.4 ± 14.3	62.6 ± 17.2	0.9
BMI (kg/m <sup>2</sup> )	24 (19–26)	21 (20–25)	23(20–27)	0.8
MIS	8 (5–12)	8 (6–11)	7 (6–10)	0.8
Standard skinfold triceps (%)	67 (50–92)	71 ( 58–100)	71 (56–92)	0.6

<sup>a</sup>Housewife, student, volunteer.

Data are presented as median (25th–75th centile) unless stated otherwise.

and 95% confidence interval (CI). The selection of covariates for multivariable adjustment was done on the basis of biological plausibility and included age, sex, dialysis vintage, occupation, diabetes mellitus, hypertension, cardiovascular disease (CVD), use of renin–angiotensin system (RAS) blockers, loop diuretics, dietary energy intake and servings per day of fat. All statistical analysis was performed using Stata software version 15.1 (StataCorp, College Station, TX, USA).

## RESULTS

A total of 150 patients on HD were enrolled in the study with a median of three visits per patient (range 1–5) and 470 repeated patient visits. As many as 42 patients did not have all five visits during observation because of death ( $n = 7$ ), kidney transplantation ( $n = 12$ ) or a change in dialysis unit or therapy ( $n = 23$ ). At inclusion, their mean age was 42 years (SD 18), with a median dialysis vintage of 4 months. The majority were women [ $n = 89$  (59%)] and the most common comorbidities were hypertension (57%) and diabetes mellitus (47%).

The HPDS ranged from 11 to 32, with a median of 21. **Table 2** shows baseline patient characteristics across tertiles of HPD adherence. No major differences were observed across increasing HPD adherence with regards to demographics, comorbidities, laboratory values or nutritional status. **Table 3** shows food nutrients and group servings across tertiles of HPD adherence. In general, the intake of plant foods was higher and the intake of animal foods lower across higher HPDS tertiles. As expected, the intake of plant protein, carbohydrates and fibre was greater with higher HPD adherence. Notably, there was a linear trend towards lower dietary protein intake, but the estimated intake of potassium and phosphorus did not vary across tertiles.

We explored the association between the HPDS (as a continuous variable) and study outcomes throughout all recorded patient visits and clustering for visits of the same patient. After adjustment for identified confounders, we observed lower dietary protein intake for every unit higher in the HPDS. Conversely, no association was found between the HPDS and dietary energy intake or serum levels of potassium (**Table 4**). Markers of nutritional status did not associate with the HPDS



**Table 3. Food nutrients and group servings according to increasing tertiles of the HPDS**

Variable	Low adherence (n = 43)	Moderate adherence (n = 53)	High adherence (n = 54)	P-value for trend
Nutrient intake				
Energy (kcal/g/day)	25 (19–30)	21 (17–27)	23 (17–26)	0.06
Total protein (g/kg/day)	1.1 (0.8–1.3)	0.9 (0.8–1.1)	0.9 (0.7–1.1)	<0.01
Animal protein (g/day)	46 (5–64)	37 (27–49)	29 (21–40)	<0.01
Plant protein (g/day)	19 (16–24)	21 (16–25)	23 (18–30)	<0.01
Fat (% of energy)	32 (27–38)	29 (23– 33)	26 (21–31)	<0.01
Carbohydrates (% of energy)	51 (44–55)	56 (52–60)	59 (54–65)	<0.01
Fibre (g/1000 kcal/day)	7 (5–10)	9 (7–11)	12 (10–14)	<0.01
Potassium (mg/1000 kcal/day)	993 (885–1166)	1039 (839–1418)	1094 (913–1308)	0.11
Phosphorus (mg/1000 kcal/day)	325 (264–434)	322 (269–469)	340 (253–449)	0.9
Food groups (servings per 1000 kcal/day)				
Cereals	4.4 (3.5–5.4)	5.1 (4.5–6.1)	6.3 (5.3–7.0)	<0.01
Fruit	0.7 (0.4–1.2)	1.1 (0.5–2.0)	1.4 (1.1–1.9)	<0.01
Vegetable	0.9 (0.6–1.5)	1.2 (0.8–1.9)	1.8 (1.1–2.7)	0.01
Legumes	0.0 (0.0–0.2)	0 (0–0.2)	0.16 (0.0–0.3)	0.01
Sugar	1.8 (1.2–2.7)	1.0 (0.4–1.9)	0.4 (0.0–0.9)	<0.01
Meat	4.0 (2.9–4.5)	3.3 (2.6–4.6)	2.8 (2.2–3.9)	<0.01
Fat	2.3 (1.6–3.6)	2.1 (1.4–3.2)	1.8 (1.2–2.7)	<0.05
Milk	0.3 (0–0.6)	0.2 (0–0.6)	0.0 (0.0–0.14)	<0.01

Data are presented as median (25th–75th centile).

**Table 4. Linear mixed model exploring associations between the HPDS (per unit of increase) and study outcomes**

Variable	Estimate β (95% CI)	P-value
Dietary protein intake (457 observations in 150 patients), g/kg/day		
Model 1	−0.017 (−0.024 to −0.009)	<0.01
Model 2	−0.015 (−0.021 to −0.009)	<0.01
Dietary energy intake (457 observations in 150 patients), kcal/kg/day		
Model 1	−0.002 (−0.008–0.005)	0.5
MIS score (436 observations in 145 patients)		
Model 1	−0.075 (−0.146 to −0.004)	0.04
Model 2	−0.079 (−0.153 to −0.005)	0.03
BMI (443 observations in 149 patients), kg/m <sup>2</sup>		
Model 1	0.001 (−0.001–0.002)	0.30
Model 2	0.001 (−0.001–0.002)	0.43
Standard skinfolds triceps (421 observations in 141 patients), %		
Model 1	0.004 (−0.004–0.012)	0.37
Model 2	0.005 (−0.003–0.13)	0.26
Serum potassium (420 observations in 146 patients), mmol/L		
Model 1	−0.001 (−0.020–0.018)	0.89
Model 2	−0.002 (−0.022–0.018)	0.85

BMI and standard skinfold triceps were log transformed before entering in the models. Model 1: adjusted by age, sex, dialysis vintage, occupation, diabetes, hypertension, CVD history, RAS blockers and loop diuretics use.

Model 2: further adjusted by dietary energy intake and servings of fat.

(BMI or standard skinfold triceps). However, a higher HPDS was associated with a lower MIS, indicating better nutritional status (Table 4). The single components of MIS that mostly carried this association were recent changes (within the last 3 months) in body weight and signs of muscle wasting (Supplementary data, Table S1).

Attainment of energy and protein targets as well as the odds of hyperkalaemia were investigated by repeated measures categorical analyses (Table 5). Higher HPD adherence was not associated with the odds of hyperkalaemia [OR 1.00 (95% CI 0.94–1.07)]. Patients with a higher HPDS did not differ in terms of

reaching energy intake targets [OR for consuming <30 kcal/kg day 1.05 (95% CI 0.97–1.13)] but were at risk of low protein intake [OR for consuming <1.1 g of protein/kg/day 1.11 (95% CI 1.04–1.19)].

## DISCUSSION

Discouraging the intake of fruits and vegetables in patients on maintenance dialysis is common [4–7], in part because of fears of hyperkalaemia and undernutrition. Our study evaluated patients on HD following a healthy plant-based diet and observed no associations with serum potassium or the odds of hyperkalaemia. Although these patients were less likely to reach DPI targets, they did not differ as regards various markers of nutritional status and, if anything, adherence to an HPD appeared to associate with better MISs over time.

In our study, adherence to an HPD meant a progressively higher intake of fruits and vegetables and a lower intake of animal foods. Patients adhering to this diet showed similar serum potassium levels and odds of hyperkalaemia as patients with poor HPD adherence. This finding agrees with previous reports of a weak or no association between estimates of dietary potassium intake and serum potassium levels in patients on HD [11, 12]. It is possible that inaccuracies in the food records may explain the lack of association. For example, food records may miss potassium additives. Another explanation is that demineralization of foods by different cooking methods, like boiling, can lead to variable potassium absorption. However, it is often unrecognized that many animal foods are also high in potassium content and, for instance, the top sources of potassium in a cross-sectional evaluation of dietary recalls in US patients on HD from California were meat products (beef, chicken, ‘Mexican food’ and hamburgers, followed by legumes in fifth place) [11]. In our study, dietary potassium density marginally increased across tertiles of HPD adherence; however, these increases did not reach statistical significance. In addition, the

**Table 5. Multilevel mixed-effects logistic regression exploring associations between the HPDS (per unit increase) and the risk hyperkalaemia or not reaching energy/protein intake targets**

Variable	Estimate OR (95% CI)	P-value
Dietary protein intake <1.1 g/kg/day (457 observations in 150 patients) Adjusted model	1.11 (1.04–1.19)	0.002
Dietary energy intake <30 kcal/kg/day (457 observations in 150 patients) Adjusted model	1.05 (0.97–1.13)	0.250
Hyperkalaemia, potassium >5.5 mmol/L (442 observations in 149 patients) Adjusted model <sup>a</sup>	1.00 (0.94–1.07)	0.858

Model adjusted by age, sex, dialysis vintage, occupation, diabetes, hypertension, CVD history, RAS blockers, loop diuretics use and servings of fat.

<sup>a</sup>Further adjusted for energy intake.

absorption of potassium in the gastrointestinal tract is diminished if potassium is consumed together with fibre and alkali [8, 27, 28], and other conditions, such as RAS inhibitor medication, potassium levels in the dialysate, and comorbidities, may more strongly determine serum potassium levels than potassium intake in these patients. As recently discussed [29], feeding trials in healthy people suggest the 24-h urine potassium recovery from animal-based diets is ~80% and from plant-based diets is ~50–60% [30, 31]. While we recognize that the absence of evidence is not evidence of absence, carefully designed interventions to quantify the potential hyperkalaemia risks of encouraging the intake of plant foods in these patients are warranted.

We observed that adherence to an HPD allowed a similar energy intake as compared with non-adherence, which agrees with the notion that the dietary mean energy intake is not fundamentally different through the range of plant consumption, including that of vegans [32]. However, patients following this diet consistently consumed less protein and were less likely to attain current protein intake targets in our study. This observation agrees with a previous report from Taiwan, where vegetarian patients on HD (19 of 318 patients) had a slightly lower normalized protein catabolic rate than non-vegetarians [33]. The consequences of lower protein intake in these patients are unknown, as well as whether possible benefits from plant food consumption may outweigh purported undernutrition risks. In our analysis, while we observed no differences in most nutritional indicators evaluated (BMI and standard skinfold triceps), there was a consistent association between the HPDS and a lower MIS, denoting better nutritional status for patients adhering to plant-based diets. In previous studies, vegetarians on HD had a lower BMI, but grip strength, subjective global assessment and activities of daily living were similar to non-vegetarians [33]. Strict vegetarian patients on haemodiafiltration in the UK (16 of 138 patients) had slightly lower muscle mass indexed by height, but also a lower concentration of protein-bound uraemic toxins [34]. Finally, vegetarians on HD have been reported to have lower levels of systemic inflammation markers and less severe symptoms of uraemic pruritus [35]. All of this evidence

is observational and included patients in our study have been given dietary recommendations in line with current dietary guidelines for dialysis patients. Although it is possible that the intake of plant foods is low overall in our cohort due to these recommendations, here we score and compare those with the highest versus lowest plant food intake. It is possible to have a plant-based diet that complies with chronic kidney disease requirements, but this requires an adequate amount of knowledge on plant food options, something that we do not currently emphasize in our practice. For example, dietary protein consumption may be increased by consuming more legumes. We hypothesize that with adequate dietetic counselling and supervision, possible undernutrition risks can be adequately prevented. In the general population, although there are differences in the amino acid profile, digestibility and availability between plant and animal protein foods [36], these differences appear to be not clinically relevant in the context of a varied diet [37–41].

The use of repeated dietary food records over a year is a strength of our study, as it increases the power and consistency of our analysis. However, our study is observational and precludes inferences of causality. In this sense, adherence to a plant-based diet may represent increased interest in healthy lifestyles, including exercise, less smoking and less alcohol consumption. In socially deprived populations, adherence to a plant-based diet may also represent the inability to afford to buy more expensive animal foods. Although we tried to adjust for some socio-economic and lifestyle indicators, residual confounding exists in this and in any observational study. Our population is of Mexican origin from a single centre, relatively young and with a high proportion of diabetes. This limits generalizability and extrapolations of our results to other countries, races or diets should be done with caution.

In conclusion, adherence to a HPD in patients undergoing HD was not associated with serum potassium levels, including risk for hyperkalaemia, or differences in energy intake. Although these patients were less likely to reach DPI targets, a higher HPDS was associated with a lower MIS over time, indicating better nutritional status. There is currently scarce evidence on the long-term consequences of plant-based diets in patients on HD. An observational study showed that a higher intake of fruits and vegetables (>5.5 servings per week) was associated with a lower risk of mortality [7], but other dietary patterns consistent with plant-based diets, such as Dietary Approaches to Stop Hypertension or Mediterranean diets were not [42, 43]. In spite of our results, we recognize that individualized decisions in terms of prescribed diets are needed for HD patients, as some may require significant dietary potassium restriction due to individual responses and behaviours, in particular when pre-dialysis hyperkalaemia is consistently documented.

Acknowledging that there are other complications in these polymorbid complex patients that may more strongly determine adverse outcomes than a dietary pattern, studies should evaluate the impact of this lifestyle intervention on patient's quality of life and satisfaction, as well as the impact of this diet on clinical endpoints, such as potassium and phosphorus

control, inflammation, constipation, nutritional status and uraemic toxin levels, that may mediate clinical outcomes.

## SUPPLEMENTARY DATA

Supplementary data are available at [ndt](https://www.nature.com/ndt) online.

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## AUTHORS' CONTRIBUTIONS

A.G.O., H.X., A.E.C. and J.J.C. participated in study conception and design, data analysis and writing the article. C.M.A., B.L. and R.C.R. participated in interpretation of the data and/or critical revision of the manuscript to its final form. All authors read and approved the final manuscript.

## CONFLICT OF INTEREST STATEMENT

J.J.C. reports grant funding from AstraZeneca, Vifor Pharma and Astellas; consulting fees from Baxter and AstraZeneca and speaker fees for Abbott, Nutricia, AstraZeneca and Vifor Pharma, all outside the submitted work. B.L. is affiliated with Baxter Healthcare Corporation, outside the submitted work. A.E.C. acknowledges speaker honoraria from Abbott Laboratories and AbbVie. None of the other authors declare any conflicts of interest.

(See related article by St-Jules and Fouque. Is it time to abandon the nutrient-based renal diet model? *Nephrol Dial Transplant* 2021; 36: 574–577)

## REFERENCES

1. Koppole JD. National Kidney Foundation K/DOQI clinical practice guidelines for nutrition in chronic renal failure. *Am J Kidney Dis* 2001; 37(1 Suppl 2): S66–S70
2. Fouque D, Vennegoor M, ter Wee P *et al*. EBPG guideline on nutrition. *Nephrol Dial Transplant* 2007; 22(Suppl 2): ii45–ii87
3. Cupisti A, Brunori G, Di Iorio BR *et al*. Nutritional treatment of advanced CKD: twenty consensus statements. *J Nephrol* 2018; 31: 457–473
4. Fernandes AS, Ramos CI, Nerbass FB *et al*. Diet quality of chronic kidney disease patients and the impact of nutritional counseling. *J Ren Nutr* 2018; 28: 403–410
5. Martins AM, Bello Moreira AS, Canella DS *et al*. Elderly patients on hemodialysis have worse dietary quality and higher consumption of ultra-processed food than elderly without chronic kidney disease. *Nutrition* 2017; 41: 73–79
6. Luis D, Zlatkis K, Comenge B *et al*. Dietary quality and adherence to dietary recommendations in patients undergoing hemodialysis. *J Ren Nutr* 2016; 26: 190–195
7. Saglimbene VM, Wong G, Ruospo M *et al*. Fruit and vegetable intake and mortality in adults undergoing maintenance hemodialysis. *Clin J Am Soc Nephrol* 2019; 14: 250–260



8. Cupisti A, Kovesdy C, D'Alessandro C *et al*. Dietary approach to recurrent or chronic hyperkalemia in patients with decreased kidney function. *Nutrients* 2018; 10: 261
9. Clase CM, Carrero JJ, Ellison DH *et al*. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int* 2020; 97: 42–61
10. Carrero JJ, González-Ortiz A, Avesani CM *et al*. Plant-based diets to manage the risks and complications of chronic kidney disease. *Nat Rev Nephrol* 2020; 10.1038/s41581-020-0297-2
11. Noori N, Kalantar-Zadeh K, Kovesdy CP *et al*. Dietary potassium intake and mortality in long-term hemodialysis patients. *Am J Kidney Dis* 2010; 56: 338–347
12. St-Jules DE, Woolf K, Pompeii ML *et al*. Exploring problems in following the hemodialysis diet and their relation to energy and nutrient intakes: the balance wise study. *J Ren Nutr* 2016; 26: 118–124
13. Chauveau P, Koppe L, Combe C *et al*. Vegetarian diets and chronic kidney disease. *Nephrol Dial Transplant* 2019; 34: 199–207
14. Wang AY, Sea MM, Ng K *et al*. Dietary fiber intake, myocardial injury, and major adverse cardiovascular events among end-stage kidney disease patients: a prospective cohort study. *Kidney Int Rep* 2019; 4: 814–823
15. Freeman AM, Morris PB, Barnard N *et al*. Trending cardiovascular nutrition controversies. *J Am Coll Cardiol* 2017; 69: 1172–1187
16. González-Ortiz A, Xu H, Avesani CM *et al*. Plant-based diets, insulin sensitivity and inflammation in elderly men with chronic kidney disease. *J Nephrol* 2020; <https://doi.org/10.1007/s40620-020-00765-6>
17. Rhee CM, Ahmadi SF, Kovesdy CP *et al*. Low-protein diet for conservative management of chronic kidney disease: a systematic review and meta-analysis of controlled trials. *J Cachexia Sarcopenia Muscle* 2018; 9: 235–245
18. Satija A, Bhupathiraju SN, Rimm EB *et al*. Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. *PLoS Med* 2016; 13: e1002039
19. Karalius VP, Shoham DA. Dietary sugar and artificial sweetener intake and chronic kidney disease: a review. *Adv Chronic Kidney Dis* 2013; 20: 157–164
20. Malik VS, Popkin BM, Bray GA *et al*. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. *Diabetes Care* 2010; 33: 2477–2483
21. Pérez-Lizaur AB. Sistema Mexicano de Alimentos Equivalentes, 4th edn. Cuauhtémoc, Mexico: Fomento de Nutrición y Salud, 2014
22. Rodrigues J, Santin F, Brito F *et al*. Nutritional status of older patients on hemodialysis: which nutritional markers can best predict clinical outcomes? *Nutrition* 2019; 65: 113–119
23. Rambod M, Bross R, Zitterkoph J *et al*. Association of malnutrition-inflammation score with quality of life and mortality in hemodialysis patients: a 5-year prospective cohort study. *Am J Kidney Dis* 2009; 53: 298–309
24. Carrero JJ, Thomas F, Nagy K *et al*. Global prevalence of protein-energy wasting in kidney disease: a meta-analysis of contemporary observational studies from the international society of renal nutrition and metabolism. *J Ren Nutr* 2018; 28: 380–392
25. Whelton PK, Carey RM, Aronow WS *et al*. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. *J Am Coll Cardiol* 2018; 71: e127–e248
26. American Diabetes Association. 2. Classification and diagnosis of diabetes. *Diabetes Care* 2015; 38(Suppl 1): S8–S16
27. St-Jules DE, Goldfarb DS, Sevick MA. Nutrient non-equivalence: does restricting high-potassium plant foods help to prevent hyperkalemia in hemodialysis patients? *J Ren Nutr* 2016; 26: 282–287
28. Carlisle EJ, Donnelly SM, Ethier JH *et al*. Modulation of the secretion of potassium by accompanying anions in humans. *Kidney Int* 1991; 39: 1206–1212
29. Picard K. Potassium additives and bioavailability: are we missing something in hyperkalemia management? *J Ren Nutr* 2019; 29: 350–353
30. Appel LJ, Moore TJ, Obarzanek E *et al*. A clinical trial of the effects of dietary patterns on blood pressure. DASH collaborative research group. *N Engl J Med* 1997; 336: 1117–1124
31. Naismith DJ, Braschi A. An investigation into the bioaccessibility of potassium in unprocessed fruits and vegetables. *Int J Food Sci Nutr* 2008; 59: 438–450
32. Rizzo NS, Jaceldo-Siegl K, Sabate J *et al*. Nutrient profiles of vegetarian and nonvegetarian dietary patterns. *J Acad Nutr Diet* 2013; 113: 1610–1619

33. Wu TT, Chang CY, Hsu WM *et al.* Nutritional status of vegetarians on maintenance haemodialysis. *Nephrology (Carlton)* 2011; 16: 582–587
34. Kandouz S, Mohamed AS, Zheng Y *et al.* Reduced protein bound uraemic toxins in vegetarian kidney failure patients treated by haemodiafiltration. *Hemodial Int* 2016; 20: 610–617
35. Tseng CY, Wu TT, Lai CW *et al.* Vegetarian diet may ameliorate uremic pruritus in hemodialysis patients. *Ren Fail* 2018; 40: 514–519
36. Chan M, Kelly J, Tapsell L. Dietary modeling of foods for advanced CKD based on general healthy eating guidelines: what should be on the plate? *Am J Kidney Dis* 2017; 69: 436–450
37. Millward DJ. Identifying recommended dietary allowances for protein and amino acids: a critique of the 2007 WHO/FAO/UNU report. *Br J Nutr* 2012; 108(Suppl 2): S3–S21
38. Rand WM, Pellett PL, Young VR. Meta-analysis of nitrogen balance studies for estimating protein requirements in healthy adults. *Am J Clin Nutr* 2003; 77: 109–127
39. Millward DJ. The nutritional value of plant-based diets in relation to human amino acid and protein requirements. *Proc Nutr Soc* 1999; 58: 249–260
40. Young VR, Pellett PL. Plant proteins in relation to human protein and amino acid nutrition. *Am J Clin Nutr* 1994; 59: 1203S–1212S
41. Joshi S, Shah S, Kalantar-Zadeh K. Adequacy of plant-based proteins in chronic kidney disease. *J Ren Nutr* 2019; 29: 112–117
42. Saglimbene VM, Wong G, Craig JC *et al.* The association of Mediterranean and DASH diets with mortality in adults on hemodialysis: the DIET-HD multinational cohort study. *J Am Soc Nephrol* 2018; 29: 1741–1751
43. Saglimbene VM, Wong G, Teixeira-Pinto A *et al.* Dietary patterns and mortality in a multinational cohort of adults receiving hemodialysis. *Am J Kidney Dis* 2019; 75: 361–372

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## Effect of comorbidities on survival in patients >80 years of age at onset of renal replacement therapy: data from the ERA-EDTA Registry

Jaakko Helve<sup>1,2</sup>, Anneke Kramer <sup>3</sup>, Jose Maria Abad Diez<sup>4</sup>, Nuria Aresté-Fosalba<sup>5,6</sup>, Mustafa Arici<sup>7</sup>, Aleix Cases <sup>8,9</sup>, Frederic Collart<sup>10</sup>, James Heaf<sup>11</sup>, Johan De Meester<sup>12</sup>, Maurizio Nordio<sup>13,14</sup>, Runolfur Palsson<sup>15,16</sup>, Alfonso Pobes<sup>17</sup>, Helena Rydell<sup>18,19</sup>, Anna Varberg Reisæter<sup>20</sup>, Ziad A. Massy<sup>21,22</sup>, Kitty J. Jager<sup>3</sup> and Patrik Finne<sup>1,2</sup>

<sup>1</sup>Finnish Registry for Kidney Diseases, Helsinki, Finland, <sup>2</sup>Abdominal Center Nephrology, University of Helsinki, Helsinki University Hospital, Helsinki, Finland, <sup>3</sup>Department of Medical Informatics, ERA-EDTA Registry, Academic Medical Center, University of Amsterdam, Amsterdam Public Health Research Institute, Amsterdam, The Netherlands, <sup>4</sup>Renal Registry of Aragon, Aragon Health Service, Zaragoza, Spain, <sup>5</sup>Department of Nephrology, University Hospital Virgen Macarena, Seville, Spain, <sup>6</sup>Information System of the Autonomic Transplant Coordination of Andalucía (SICATA), Andalucía, Spain, <sup>7</sup>Department of Nephrology, Faculty of Medicine, Hacettepe University, Ankara, Turkey, <sup>8</sup>Department of Nephrology, Hospital Clinic, Universitat de Barcelona, IDIBAPS, Barcelona, Spain, <sup>9</sup>Registre de Malalts Renals de Catalunya, Barcelona, Spain <sup>10</sup>French-Belgian ESRD Registry (GNFB), Brussels, Belgium, <sup>11</sup>Department of Medicine, Zealand University Hospital, Roskilde, Denmark, <sup>12</sup>Department of Nephrology, Dialysis and Hypertension, Dutch-speaking Belgian Renal Registry (NBVN), Sint-Niklaas, Belgium, <sup>13</sup>Veneto Dialysis and Transplantation Registry, Regional Epidemiology System, Padua, Italy, <sup>14</sup>Nephrology Dialysis Unit, Padua, Italy, <sup>15</sup>Division of Nephrology, Landspítali-The National University Hospital of Iceland, Reykjavik, Iceland, <sup>16</sup>Faculty of Medicine, School of Health Sciences, University of Iceland, Reykjavik, Iceland, <sup>17</sup>Area Gestation Clinica Nefrología VII-VIII Asturias, Spain, <sup>18</sup>Department of Clinical Sciences Intervention and Technology, Karolinska Institutet, Huddinge, Sweden, <sup>19</sup>Department of Internal Medicine, Swedish Renal Registry, Ryhoy County Hospital, Jönköping, Sweden, <sup>20</sup>Department of Transplantation Medicine, Oslo University Hospital, Rikshospitalet, Oslo, Norway, <sup>21</sup>Division of Nephrology, Amboise Paré University Hospital, APHP, Boulogne-Billancourt, Paris, France and <sup>22</sup>Institut National de la Santé et de la Recherche Médicale (INSERM) Unit 1018 team5, Research Centre in Epidemiology and Population Health (CESP), University of Paris Ouest-Versailles-St Quentin-en-Yveline, Villejuif, France

Correspondence to: Jaakko Helve; E-mail: Jaakko.Helve@Helsinki.fi; Twitter handle: @EraEdtaRegistry

### ABSTRACT

**Background.** The number of elderly patients on renal replacement therapy (RRT) is increasing. The survival and quality of life of these patients may be lower if they have

multiple comorbidities at the onset of RRT. The aim of this study was to explore whether the effect of comorbidities on survival is similar in elderly RRT patients compared with younger ones.