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Rationale & Objective: Clinical practice guidelines for dietary intake in hemodialysis focus on individual nutrients. Little is known about associations of dietary patterns with survival. We evaluated the associations of dietary patterns with cardiovascular and all-cause mortality among adults treated by hemodialysis.

Study Design: Prospective cohort study.

Setting & Participants: 8,110 of 9,757 consecutive adults on hemodialysis (January 2014 to June 2017) treated in a multinational private dialysis network and with analyzable dietary data.

Exposures: Data-driven dietary patterns based on the GA²LEN food frequency questionnaire. Participants received a score for each identified pattern, with higher scores indicating closer resemblance of their diet to the identified pattern. Quartiles of standardized pattern scores were used as primary exposures.

Outcomes: Cardiovascular and all-cause mortality.

Analytical Approach: Principal components analysis with varimax rotation to identify common dietary patterns. Adjusted proportional hazards regression analyses with country as a random effect to estimate the associations between dietary pattern scores and mortality. Associations were expressed as adjusted HRs with 95% CIs, using the lowest quartile score as reference.

Results: During a median follow-up of 2.7 years (18,666 person-years), there were 2,087 deaths (958 cardiovascular). 2 dietary patterns, "fruit and vegetable" and "Western," were identified. For the fruit and vegetable dietary pattern score, adjusted HRs, in ascending quartiles, were 0.94 (95% CI, 0.76-1.15), 0.83 (95% CI, 0.66-1.06), and 0.91 (95% CI, 0.69-1.21) for cardiovascular mortality and 0.95 (95% CI, 0.83-1.09), 0.84 (95% CI, 0.71-0.99), and 0.87 (95% CI, 0.72-1.05) for all-cause mortality. For the Western dietary pattern score, the corresponding estimates were 1.10 (95% CI, 0.90-1.35), 1.11 (95% CI, 0.87-1.41), and 1.09 (95% CI, 0.80-1.49) for cardiovascular mortality and 1.01 (95% CI, 0.88-1.16), 1.00 (95% CI, 0.85-1.18), and 1.14 (95% CI, 0.93-1.41) for all-cause mortality.

Limitations: Self-reported food frequency questionnaire, data-driven approach.

Conclusions: These findings did not confirm an association between mortality among patients receiving long-term hemodialysis and the extent to which dietary patterns were either high in fruit and vegetables or consistent with a Western diet.

The risk for premature death among patients with end-stage kidney disease is high. People who commence long-term hemodialysis therapy can expect to live for only 3 to 4 years on average,[1] with cardiovascular disease responsible for ∼40% of these deaths.[2] In contrast to findings from the general population, interventions directed at lowering lipid levels, controlling blood pressure and glucose levels, and preventing thrombosis have shown minimal or no survival benefits in this at-risk population.[3-6] Identification of strategies that prevent cardiovascular death is a research priority for hemodialysis patients, caregivers, and clinicians.[7]

Dietary and other lifestyle choices, such as smoking and physical activity, are potentially modifiable determinants of health with substantial public health benefit. Dietary patterns, such as the Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets, are associated with a 10% to 30% reduction in cardiovascular events and mortality.[8-10] However, these dietary patterns have not been shown to be associated with improved survival in hemodialysis patients.[11]

Dietary guidelines suggest modifying the intake of individual nutrients in dialysis patients to control serum phosphate and potassium levels and fluid overload while maintaining a high protein and energy intake.[12-14] However, there is limited high-certainty evidence showing that targeting single nutrients improves clinical outcomes.[15-17] Assessments of dietary patterns overcome the limitations of an individual nutrient or food approach by accounting for correlations and interactions between nutrients and foods.

In addition, whole dietary patterns are readily understandable to patients and policy makers and therefore are suitable candidate interventions.

In a previous analysis of the DIET-HD study, we examined the association between existing dietary patterns (Mediterranean and DASH diets) and survival among hemodialysis patients in a multinational setting.[11] In the present analysis, principal component analysis has been conducted in the same cohort to generate data-driven patterns reflecting the eating behavior of the DIET-HD hemodialysis population. This approach can support greater understanding of the prognosis associated with real-world dietary practices in hemodialysis patients.[18,19] The aim of this analysis was to evaluate the association of commonly practiced dietary patterns with cardiovascular and all-cause mortality among adults treated with hemodialysis.

Methods

Study Design

This analysis is based on data from the Dietary Intake, Death and Hospitalization in Adults With End-Stage Kidney Disease Treated With Hemodialysis (DIET-HD) study, which has been described previously.[20] In brief, it is a multinational prospective cohort study of food frequency intake among adults treated with long-term outpatient hemodialysis in 11 countries in Europe (France, Germany, Italy, Hungary, Poland, Portugal, Romania, Spain, Sweden, and Turkey) and South America (Argentina). This analysis is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[21]

Study Population

Adults with kidney failure treated with long-term hemodialysis (at least 90 days) were eligible for inclusion in
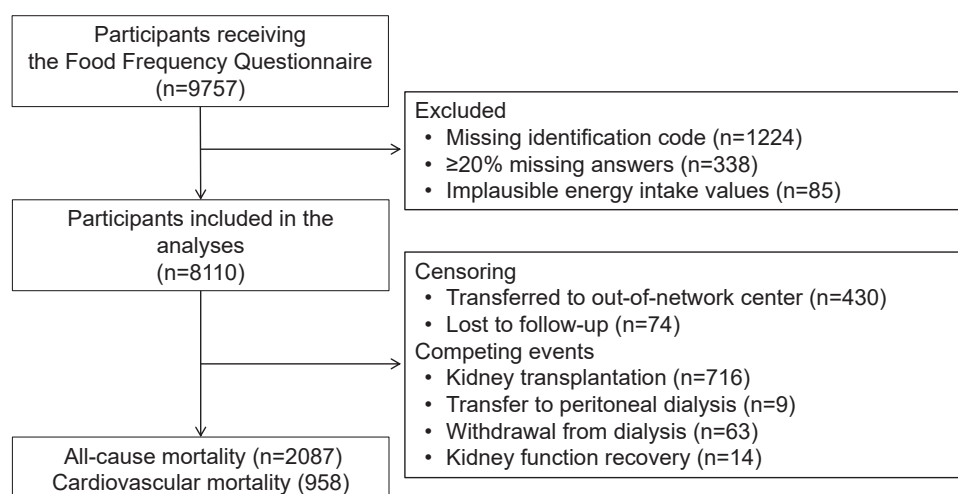
DIET-HD. Patients were excluded if they were unable to complete the food frequency questionnaire (FFQ), had life expectancy less than 6 months, or anticipated kidney transplantation within 6 months of recruitment according to their treating clinician. All participants gave written informed consent. The study was conducted in accordance with the Declaration of Helsinki and was approved by the relevant institutional ethics committees.

Dietary Intake Assessment

Participants completed the Global Allergy and Asthma European Network (GA²LEN) FFQ during a routine hemodialysis treatment, either independently or assisted by an interviewer (in case of severe clinical conditions or limited literacy).[20] The FFQ was designed as a single, standardized, and internationally validated instrument to ascertain dietary intake facilitating international comparisons.[22] It records the consumption of 210 foods during the previous 12 months as frequencies from never to 4 or more times per day. Responses to the FFQ were converted into average servings per week.[23] Total energy intake was estimated from food intakes considering standard portion size and using the latest available McCance & Widdowson's Food Composition Tables.[24,25] Patients with >20% missing answers or implausible responses (total energy intake not within 3 standard deviations [SDs] from the log-transformed mean) in the FFQ were excluded from the DIET-HD analyses (Fig 1).

Covariates

Baseline demographic and clinical characteristics were obtained within 1 month of enrollment using data linkage with a centralized routinely collected administrative database.[20] Data were provided by participants' treating clinicians using medical records for laboratory, clinical, and dialysis characteristics and participants' self-reported surveys for lifestyle characteristics.

```
┌─────────────────────────────┐
│ Participants receiving      │
│ the Food Frequency          │
│ Questionnaire               │
│ (n=9757)                    │
└─────────────────────────────┘
            │          ┌──────────────────────────────────────────────┐
            ├─────────→│ Excluded                                     │
            │          │ • Missing identification code (n=1224)       │
            │          │ • ≥20% missing answers (n=338)               │
            │          │ • Implausible energy intake values (n=85)    │
            ▼          └──────────────────────────────────────────────┘
┌─────────────────────────────┐
│ Participants included in the│
│ analyses                    │
│ (n=8110)                    │
└─────────────────────────────┘
            │          ┌──────────────────────────────────────────────┐
            │          │ Censoring                                    │
            ├─────────→│ • Transferred to out-of-network center (n=430)│
            │          │ • Lost to follow-up (n=74)                   │
            │          │ Competing events                             │
            │          │ • Kidney transplantation (n=716)             │
            │          │ • Transfer to peritoneal dialysis (n=9)      │
            │          │ • Withdrawal from dialysis (n=63)            │
            ▼          │ • Kidney function recovery (n=14)            │
┌─────────────────────────────┐ └──────────────────────────────────┘
│ All-cause mortality (n=2087)│
│ Cardiovascular mortality    │
│ (958)                       │
└─────────────────────────────┘
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Figure 1. Study flow chart.

Outcomes

Cardiovascular and all-cause mortality (while on maintenance hemodialysis) were identified through data linkage to a centralized administrative database. Causes of death were obtained from death certificates and recorded according to the US coding for the end-stage kidney disease population.[26,27] Cardiovascular mortality was defined as sudden death or death due to acute myocardial infarction, pericarditis, atherosclerotic heart disease, cardiomyopathy, cardiac arrhythmia, cardiac arrest, valvular heart disease, pulmonary edema, congestive cardiac failure, and cerebrovascular accident, including intracranial hemorrhage, ischemic brain damage/anoxic encephalopathy, or hemorrhage from ruptured vascular aneurysm. All-cause mortality was death from any cause.

Statistical Methods

Analyses were conducted using SAS, version 9.4 (SAS Institute), and STATA, version 14 (StataCorp).

Dietary Pattern Analysis

The common dietary patterns were characterized using principal component analysis. This was performed using data concerning food items reported to be consumed at least once per week by >5% of participants.[23] To account for the variability of food intake across countries and identify dietary patterns that were generalizable to all participating countries, we used a meta-analytical approach to calculate pooled Pearson correlation coefficients of foods listed in the FFQ.[23,28,29] First, food variables were standardized (by SD scaling) by country. Second, within each country, Pearson correlation coefficients were evaluated for each pair of food items. Third, country-specific correlation coefficients were converted into Fisher z scores to improve normality. Fourth, Fisher z scores were given a weight proportional to the sample size of the country of interest (for each pair of food items, the associated Fisher z score was multiplied by the number of observations for that pair of foods within the country of interest and divided by the total number of observations for the same pair of foods in the entire cohort). An inverse Fisher transformation was applied to obtain a pooled matrix of Pearson correlation coefficients[29] (Item S1). Finally, principal component analysis with varimax rotation was applied to the pooled matrix of Pearson correlation coefficients identifying dietary patterns that were applicable to the data drawn from all countries. The number of patterns to be retained was chosen based on examination of the scree plot (Fig S1) and interpretability. Food items with absolute factor loadings (equivalent to Pearson correlation coefficients with the pattern) ≥0.30 were considered as main constituents of a dietary pattern.

Participants received a score for each identified dietary pattern reflecting how closely their diet resembled that pattern, with higher scores indicating closer resemblance. Dietary pattern scores were standardized variables (mean equal to zero and SD equal to 1) calculated by summing standardized intake of the food items weighted by their factor loadings on the relevant pattern. When computing dietary pattern scores, missing intakes of individual food items (ranging from 0.3%-3.3%) were imputed using single imputation by chained equations with predictive mean matching.[30,31] Dietary pattern scores and their quartiles were considered as the primary exposure for survival analysis.

Survival Analysis

Fractional polynomials were used to test for a linear association between dietary pattern scores and mortality (no deviation from linearity was found). Survival time for each participant was defined as days from FFQ administration to the date of death (cardiovascular or all-cause), kidney transplantation, withdrawal from dialysis, recovery of kidney function, transfer outside the network, transfer to peritoneal dialysis, loss to follow-up, or end of the follow-up period. For both cardiovascular and all-cause mortality (while on hemodialysis), competing events were kidney transplantation, withdrawal from dialysis, recovery of kidney function, and transfer to peritoneal dialysis, whereas transfer outside the network, loss to follow-up, and end of the follow-up period were censoring events. For cardiovascular mortality, noncardiovascular mortality was also a competing event. For analyses of cardiovascular mortality, patients who had died from noncardiovascular causes were treated as censoring using cause-specific hazards models.

Univariable mortality associations between mortality and quartiles of dietary pattern scores were examined in cumulative probability plots. In the presence of competing events, cumulative probabilities were estimated using cumulative incidence functions and compared using Gray test. Univariable and multivariable cause-specific hazards models were fitted with a frailty, a random effect to account for countries as clusters. Dietary pattern scores were modeled both as continuous variables and as quartiles. Results were presented per each 1-SD greater and as hazard ratio (HR) with the associated 95% confidence interval (CI), respectively. The lowest quartile was used as the reference category. Backwards elimination was used to select covariates for inclusion in the multivariable models retaining those (aside from energy intake, sex, physical activity, education, and diabetes, which were clinically relevant variables specified a priori) associated with mortality ($P < 0.05$) or with a clinically meaningful impact on the HR for the outcome of the dietary pattern scores (≥10%).

Analyses of cardiovascular mortality were adjusted for age, sex, daily physical activity, education (secondary vs none/primary), diabetes, smoking (current or former vs never), myocardial infarction, stroke, vascular access type (fistula vs graft/catheter), body mass index (categories according to World Health Organization), albumin (tertiles), Charlson comorbidity index score (quartiles),

serum phosphorus level, serum calcium level, hemoglobin level, urea clearance (Kt/V), and total energy intake (per 1,000-kcal/d increase). Analyses of all-cause mortality were adjusted for the same variables with the exception of stroke and the additions of being wait-listed for a transplant and time on dialysis.

All analyses of the fruit and vegetable dietary pattern's score were adjusted for the Western dietary pattern's score and vice versa. We imputed missing covariates (while outcomes data were complete for all patients), using multiple imputation by chained equations (20 rounds). Interactions terms between dietary pattern scores (modeled as continuous) and age, sex, and body mass index were tested in the multivariable model (none was eligible for retention). The proportional hazards assumption was assessed by fitting time-dependent covariates in the multivariable model, for which a violation of proportionality was considered if P values of the time-dependent covariates were <0.01 (no violation was found).

Sensitivity Analysis

In sensitivity analysis of principal component analysis, oblique (promax) rotation was applied for the interpretation of dietary patterns. In survival analysis, a complete-case analysis was conducted including only patients with complete data for covariates.

Results

Participant Characteristics

Overall, 9,757 hemodialysis patients completed the FFQ between January 2014 and January 2015. Of these, 8,110 (83%) had complete and plausible dietary data and were followed up through June 27, 2017 (Fig 1). Baseline characteristics of the cohort are shown in Table 1.
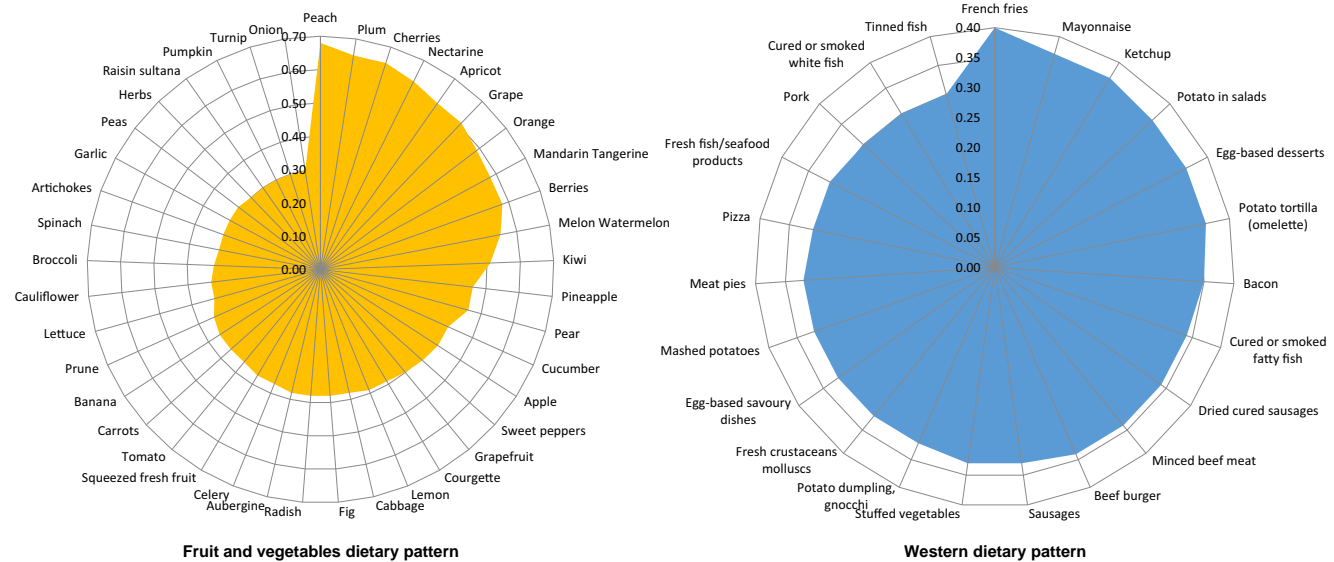
Dietary Patterns

From the 210 available in the FFQ, 179 food items were included in the principal component analysis; 31 foods were excluded based on infrequent consumption. From the principal component analysis, the first 2 principal components, explaining 10% of the total variance in the dietary intake, were chosen (based on interpretability of the dietary patterns composition and the scree plot in Fig S1 showing an "elbow," indicating that after 2 components, each single additional component would explain little more of the variance) for dietary patterns. The same patterns were obtained when applying either varimax or promax rotation. Figure 2 and Table 2 report correlation coefficients (factor loadings from the principal component analysis) between individual food items and the identified dietary patterns showing which foods were the main constituents of each pattern. Intake of foods with low factor loadings (<0.30) was similar between the 2 dietary patterns and therefore considered nondiscriminatory of the 2 identified patterns

Table 1. Baseline Characteristics of Participants

Variable	No. of Participants With Data	Overall
Sociodemographic Characteristics		
Age, y	8,110	63 ± 15
Male sex	8,110	4,691 (58%)
Life partner	6,095	4,127 (68%)
Secondary education	6,090	2,699 (44%)
Daily physical activity	6,199	934 (15%)
Wait-listed for transplant	8,094	1,496 (18%)
Clinical Characteristics		
Current or former smoker	6,280	2,068 (33%)
Body mass index	7,872	
Underweight (<18.5 kg/m²)		365 (5%)
Normal range (18.5-24.9 kg/m²)		3,309 (42%)
Preobese (25.0-29.9 kg/m²)		2,659 (34%)
Obese (≥30.0 kg/m²)		1,539 (20%)
Hypertension	7,320	6,219 (85%)
Diabetes	7,283	2,332 (32%)
Myocardial infarction	7,239	838 (12%)
Stroke	7,233	634 (9%)
Charlson comorbidity score	8,110	6 [4, 8]
Laboratory Variables		
Albumin, g/dL	6,167	4.0 ± 0.4
Phosphorus, mg/dL	7,869	4.7 ± 1.4
Calcium, mg/dL	7,870	8.9 ± 0.7
Hemoglobin, g/dL	7,869	11.1 ± 1.3
Potassium, mEq/L	2,357	5.0 ± 0.7
Dialysis Characteristics		
Arteriovenous fistula	8,051	64,81 (80%)
Time on dialysis, y	8,108	4 [2, 7]
Kt/V urea	7,818	1.7 ± 0.3
Food Group, servings/wk		
Stone fruit	8,105	2.0 [0.5, 6.0]
Citrus fruit	8,103	2.5 [1.0, 7.0]
Pome fruit	8,096	6.0 [1.5, 8.0]
Leafy green vegetables	8,097	1.5 [0.5, 3.5]
Cruciferous vegetables	8,105	1.0 [0.5, 2.0]
Red and orange vegetables	8,109	6.0 [3.0, 9.5]
Potatoes	8,104	2.0 [1.0, 3.5]
Eggs	8,100	0.5 [0.0, 1.0]
Red and processed meat	8,110	1.5 [0.5, 4.0]
Pork	8,085	0.5 [0.0, 1.0]
Fish (cured, smoked, tinned)	8,104	0.5 [0.0, 1.0]

Note: Data are expressed as mean ± standard deviation, median [interquartile range], or number (percentage). Body mass index categories are defined according to the World Health Organization. Food groups are based on selected food components of the identified patterns (Fig 2). Stone fruit: peach, plum, cherries, nectarine, and apricot; citrus fruit: orange, mandarin/tangerine, grapefruit, and lemon; pome fruit: apple and pear; leafy green vegetables: spinach and lettuce; cruciferous vegetables: cabbage, cauliflower, and broccoli; red and orange vegetables: sweet peppers, tomato, carrots, and pumpkin; potatoes: French fries, potato in salads, potato tortilla (omelette), potato dumpling, gnocchi, and mashed potatoes; eggs: egg-based desserts and egg-based savory dishes; red and processed meat: bacon, dried cured sausages, minced beef meat, beef burger, sausages, and meat pies; pork: cutlet, chop, steak, fillet, loin, pork ribs, and minced; fish (cured, smoked, and tinned): cured smoked fatty fish, cured smoked white fish, and tinned fish.

Figure 2. Food composition of the identified dietary patterns. Food items with a Pearson correlation coefficient > 0.30 were considered main constituents of the dietary pattern and were included in the graphs.

The first dietary pattern was characterized by higher intake of fruit (including stone, citrus, and pome [pears and apples] fruit) and vegetables (including cruciferous and green leafy vegetables). The second pattern was characterized by higher intake of Western style foods, such as French fries, other potato meals, eggs, desserts, red and processed meat (including bacon, sausages, beef burger, and meat pie), fish (mostly cured, smoked, or tinned), and pizza. Consumption of the main food groups representative of the identified dietary patterns by quartiles of score is shown in Table S1. Higher levels of both dietary pattern scores in quartiles were associated with higher total energy intake (Table 3). Overall, both identified dietary patterns were consistently observed across the 11 countries (Tables S2 and S3). Based on their food compositions, the common dietary patterns were labeled as "fruit and vegetables" and "Western."

Dietary Patterns and Cardiovascular Mortality

During a median follow-up of 2.7 years (18,666 person-years), there were 2,087 (26%) deaths, of which 958 (46%) were attributable to cardiovascular diseases. The cumulative incidence function plots showing survival associated with dietary scores are shown in Figs S2 and S3.

In multivariable analyses, compared with patients in the lowest quartile of the fruit and vegetable dietary pattern score, adjusted HRs for cardiovascular mortality in the other quartiles, in ascending order, were 0.94 (95% CI, 0.76-1.15), 0.83 (95% CI, 0.66-1.06), and 0.91 (95% CI, 0.69-1.21; Fig 3). For the Western dietary pattern, the corresponding estimates were 1.10 (95% CI, 0.90-1.35), 1.11 (95% CI, 0.87-1.41), and 1.09 (95% CI, 0.80-1.49; Fig 4). Similar findings were observed in case-complete

analyses. Results of continuous dietary patterns scores agreed with those of quartiles (Figs 3 and 4).

Dietary Patterns and All-Cause Mortality

Compared with patients in the lowest quartile of the fruit and vegetable dietary pattern score, adjusted HRs for all-cause mortality among those in the other quartiles, in ascending order, were 0.95 (95% CI, 0.83-1.09), 0.84 (95% CI, 0.71-0.99), and 0.87 (95% CI, 0.72-1.05; Fig 3). For the Western dietary pattern, the corresponding estimates were 1.01 (95% CI, 0.88-1.16), 1.00 (95% CI, 0.85-1.18), and 1.14 (95% CI, 0.93-1.41; Fig 4). Similar findings were observed in case-complete analyses. Results of continuous dietary patterns scores agreed with those of quartiles except for a signal of a significant association between higher fruit and vegetables dietary pattern score and lower all-cause mortality in case-complete analyses (Figs 3 and 4).

Discussion

In this study of 8,110 adults treated with hemodialysis, 2 common dietary patterns were observed: a fruit and vegetable diet, typically based on fruit and vegetables of low potassium content (such as pears and apples), and a Western diet favoring consumption of potatoes, eggs, and red and processed meat. These patterns were consistent across 10 European countries and Argentina. Over 3 years, with 2,087 deaths (958 cardiovascular related), there was no evidence of association between fruit and vegetable–based or a Western dietary pattern and cardiovascular and all-cause mortality.

The lack of association between the 2 identified dietary patterns and mortality may have several potential explanations. First, the influence of end-stage kidney disease (and

Table 2. Pearson Correlation Coefficients Between Food Items and the Identified Dietary Patterns

	Fruit and Vegetable Dietary Pattern	Western Dietary Pattern
Peach	0.68	−0.08
Plum	0.65	−0.11
Cherries	0.65	−0.07
Nectarine	0.63	−0.06
Apricot	0.61	−0.06
Grape	0.61	−0.02
Orange	0.59	−0.02
Mandarin/tangerine	0.58	−0.05
Berries	0.58	−0.07
Melon or watermelon	0.55	−0.01
Kiwi	0.51	0.03
Pineapple	0.46	0.14
Pear	0.46	0.00
Cucumber	0.42	0.17
Apple	0.42	−0.02
Sweet peppers	0.41	0.23
Grapefruit	0.40	0.08
Courgette	0.39	0.19
Lemon	0.39	0.08
Cabbage	0.38	0.25
Fig	0.38	0.01
Radish	0.38	0.17
Aubergine	0.38	0.26
Celery	0.37	0.20
Fresh squeezed fruit juice	0.37	0.19
Tomato	0.36	0.20
Carrots	0.36	0.21
Banana	0.36	0.11
Prune	0.35	0.03
Lettuce	0.33	0.18
Cauliflower	0.33	0.25
Broccoli	0.32	0.23
Spinach	0.31	0.24
Artichokes	0.31	0.16
Garlic	0.31	0.16
Peas	0.31	0.28
Herbs	0.30	0.13
Raisin (sultana)	0.30	0.12
Pumpkin	0.30	0.23
Turnip or swede	0.30	0.16
Onion	0.30	0.16
French fries	0.12	0.40
Mayonnaise	0.04	0.37
Ketchup	0.08	0.37
Potato in salads	0.17	0.36
Egg-based desserts	0.09	0.36
Potato tortilla (omelette)	0.10	0.36
Bacon	0.05	0.35
Cured or smoked fatty fish	0.11	0.34
Dried cured sausages	0.04	0.34
Minced beef meat	0.11	0.34
Beef burger	0.04	0.34

(Continued)

Table 2 (Cont'd). Pearson Correlation Coefficients Between Food Items and the Identified Dietary Patterns

	Fruit and Vegetable Dietary Pattern	Western Dietary Pattern
Sausages	0.05	0.33
Stuffed vegetables	0.17	0.33
Potato dumpling, gnocchi	0.09	0.32
Fresh crustaceans or mollusks	0.12	0.32
Egg-based savory dishes	0.10	0.32
Mashed potatoes	0.12	0.32
Meat pies	0.08	0.32
Pizza	0.06	0.31
Other fresh fish/seafood products (eg, taramasalata)	0.08	0.31
Pork (cutlet, chop, steak, fillet, loin, pork ribs, minced)	0.11	0.30
Cured or smoked white fish	0.10	0.30
Tinned fish	0.10	0.30

Note: Food items with an absolute Pearson correlation coefficient ≥ 0.30 were considered main constituents of the dietary pattern and therefore were included in the table.

its comorbid conditions) on health could be so profound that factors such as diet, which had been shown to be beneficial for survival in the general population[8-10,32,33] and patients with early- to moderate-stage chronic kidney disease,[34] may have substantially smaller absolute effects on mortality in dialysis patients. This hypothesis is supported by results of another substudy of the DIET-HD study, which also showed little or no association between mortality and a priori dietary patterns considered healthy for the general population, namely the Mediterranean and DASH diets.[11] Second, the relatively short follow-up may have precluded the detection of any significant association between mortality and these dietary patterns. Third, residual confounding from unmeasured factors (such as frailty or socioeconomic factors different from education [for which the analyses were adjusted]) may have masked any associations between the identified dietary patterns and mortality. Finally, the self-reported and single dietary assessment may have led to measurement error that may have biased results toward the null.

Although in univariable analysis and multivariable case-complete analysis, there was a significant association between higher fruit and vegetables dietary patterns score, treated as continuous variables, and lower all-cause mortality, this association was not confirmed in the primary analyses. These findings are to some extent in contrast with our previous hypothesis-driven analysis examining the role of fruit and vegetables as a specific food group in the same cohort, which consistently showed an association between higher intake of these foods and lower all-cause mortality.[35] This inconsistency may be due to the different methodological approaches in defining the exposures of interest (data-driven patterns derived from intake of all the individual food items of the administered FFQ vs intake of fruit and vegetables measured from the

Table 3. Daily Nutrients Intake by Quartiles of the Identified Dietary Pattern Scores

	Score Quartile 1	Score Quartile 2	Score Quartile 3	Score Quartile 4
Fruit and Vegetable Dietary Pattern				
Total energy, kcal	1,274 (962-1,610)	1,718 (1,387-2,075)	2,088 (1,718-2,538)	2,841 (2,271-3,599)
Protein, g	62 (45-83)	85 (65-110)	104 (81-133)	138 (105-182)
Carbohydrates, g	137 (99-183)	186 (144-237)	229 (182-290)	319 (249-426)
Fiber, g	7 (5-10)	10 (8-13)	14 (11-17)	20 (15-27)
Total fat, g	50 (35-66)	67 (51-85)	82 (64-104)	111 (84-144)
Sugar, g	56 (38-82)	84 (61-116)	112 (83-150)	171 (126-240)
Phosphorus, mg	880 (646-1,269)	1,211 (923-1,587)	1,519 (1,175-2,008)	2,103 (1,604-2,823)
Sodium, mg	857 (608-1,198)	1,157 (867-1,513)	1,421 (1,057-1,900)	2,019 (1,480-2,811)
Potassium, mg	2,107 (1,569-2,864)	3,001 (2,403-3,732)	3,891 (3,172-4,890)	5,891 (4,655-7,629)
Western Dietary Pattern				
Total energy, kcal	1,205 (925-1,502)	1,673 (1,397-1,979)	2,117 (1,813-2,459)	2,972 (2,460-3,681)
Protein, g	58 (43-77)	82 (64-104)	105 (84-127)	149 (118-190)
Carbohydrates, g	134 (97-178)	184 (143-232)	232 (187-286)	323 (256-421)
Fiber, g	7 (5-10)	10 (8-14)	13 (10-17)	20 (15-26)
Total fat, g	45 (33-59)	64 (52-79)	83 (69-101)	121 (97-153)
Sugar, g	59 (39-89)	84 (61-119)	111 (80-151)	163 (117-225)
Phosphorus, mg	838 (624-1,182)	1,161 (922-1,525)	1,493 (1,214-1,884)	2,225 (1,719-2,907)
Sodium, mg	789 (569-1,058)	1,101 (858-1,412)	1,448 (1,168-1,820)	2,222 (1,695-2,959)
Potassium, mg	2,119 (1,571-2,929)	2,992 (2,395-3,803)	3,835 (3,149-4,817)	5,796 (4,585-7,523)

responses to 2 general questions about the overall fruit and vegetable consumption). However, inconsistency in the prognosis of fruit and vegetable intake between 2 differing measurement approaches may also suggest that any relationship between fruit and vegetable intake and survival, if any, may be of low magnitude.

We are not aware of previous research that has examined dietary patterns using principal component analysis in the hemodialysis population. However, the 2 dietary patterns identified in our study, fruit and vegetable–based and Western, are consistent with those generally identified in studies of data-driven dietary patterns in the general population.[18,36-38] These findings suggest that although hemodialysis patients are advised to modify components of their diet, their overall dietary intake may not differ substantively from that of the general population. Identification of a Western dietary pattern is also in agreement with previous research reporting high consumption of fast and processed food among patients on hemodialysis.[39,40] This may reflect the challenges (including financial) of adhering to dietary modifications, time or energy limitations preventing shopping and preparation of food, or may be consistent with the widespread consumption of convenience foods observed in the contemporary society.[41,42]

This study has several strengths. The analysis investigated dietary patterns in patients receiving hemodialysis by embracing a whole dietary intake approach compared with the existing research in this setting, which is centered on individual nutrients (such as protein, phosphate, and potassium). The study assessed empirical dietary patterns, recognizing that dietary intake among hemodialysis patients may be systematically different than the wider community due to altered appetite, lower socioeconomic status, and dietary modification advice. As such, this analysis integrates our previous analysis of a priori dietary patterns for a comprehensive evaluation of the relationship between overall diet quality and survival, using different methodological approaches. The study applied a meta-analytic principal component analysis to a large variety of foods deriving dietary patterns common to many countries.

There are also potential limitations due to the observational nature of the study, challenges inherent in the assessment of a complex exposure such as diet (in general and in the specific setting of hemodialysis), and the applied method of ascertaining dietary patterns. The study relied on an FFQ, which used standard food portion sizes and has been validated against plasma phospholipid fatty acids, but not with other dietary assessment methods and not in the setting of hemodialysis. Participants completed the FFQ during the hemodialysis procedure, when they may have experienced adverse events, such as intradialytic hypotension, which may hamper the accuracy of the reporting. Due to the self-reported nature of the FFQ, social desirability bias was also possible. Collectively, these limitations may have led to measurement error and misclassification of the exposures. The direction and magnitude of potential measurement error are difficult to predict with certainty and may have led to under- or overestimation of the observed association between dietary patterns and clinical outcomes.[43,44]
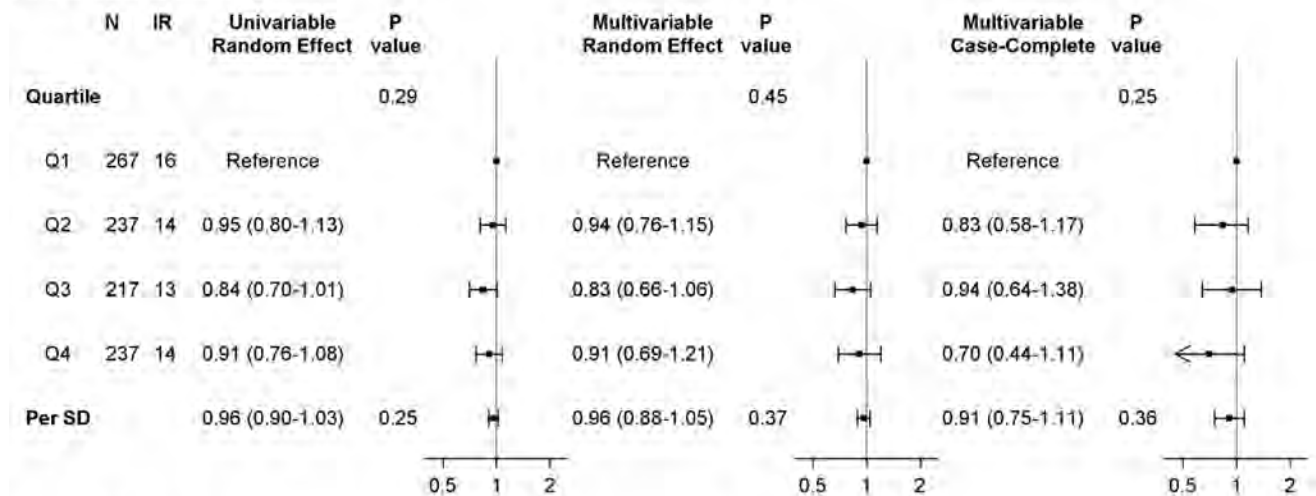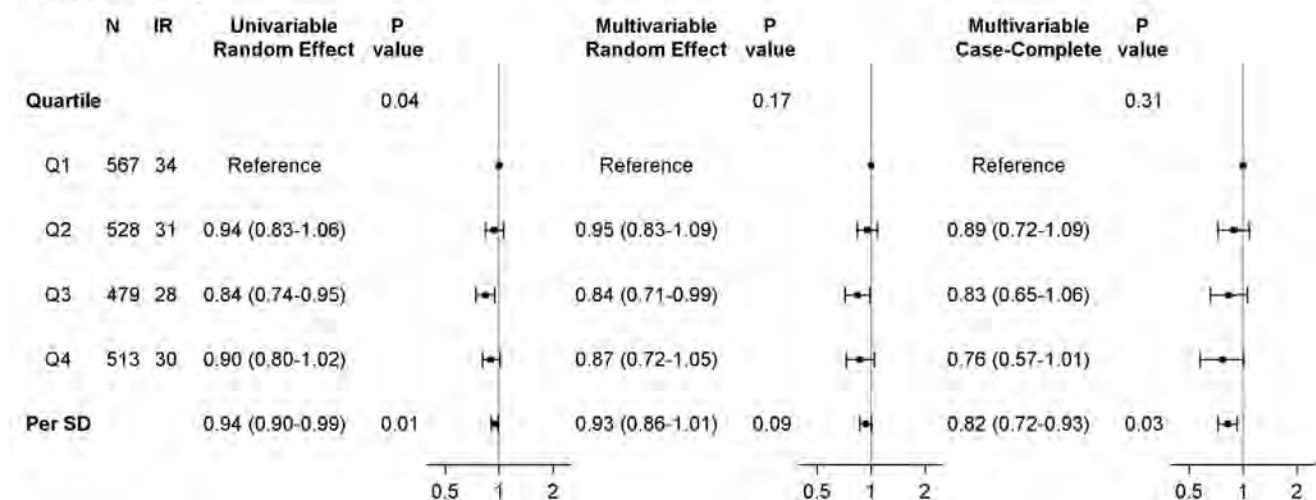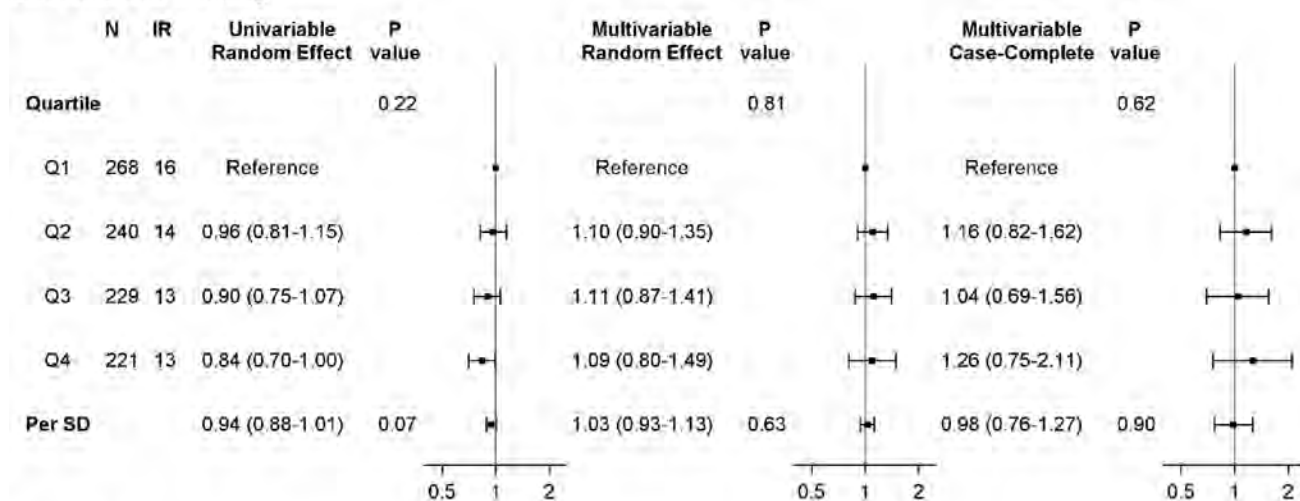
Figure 3. Mortality incidences and hazard ratios (95% confidence interval) by quartiles of the fruit and vegetable dietary pattern score. Multivariable analyses for cardiovascular mortality were adjusted for country (fixed effect in competing-risk analysis and random effect in all others), sex, daily physical activity, education (secondary vs none/primary), diabetes, smoking (current or former vs never), myocardial infarction, stroke, vascular access type (fistula vs graft/catheter), body mass index (categories according to World Health Organization), albumin (tertiles), Charlson comorbidity score (quartiles [Q]), age, phosphorus level, calcium level, hemoglobin level, Kt/V, and energy intake (1,000 kcal/d increase). Multivariable analyses for all-cause mortality were adjusted for the same variables with the exception of stroke, and the addition of time on dialysis and being wait-listed for transplantation. Analyses of each pattern were adjusted for the other one. Abbreviations: IR, incidence rate; N, number of events; per SD, per standard deviation increase.

In addition, the single dietary assessment did not allow detection of any potential change in dietary habits and patterns over time, particularly in relation to the health decline that can occur in an individual on hemodialysis. Selection bias was also possible due to exclusion of 17% of patients with incomplete or implausible dietary data. Principal component analysis was able to explain 10% of the variance in dietary exposure, indicating that there likely were other aspects of dietary intake that were not captured by the best-fit patterns of fruit and vegetables and Western dietary scores. However, a small amount of

explained variance is not uncommon in studies of principal component analysis.[23,28,36,41,45] The data-driven approach could limit the generalizability of our findings, which may not be applicable to patients living outside Europe and Argentina.

These findings of little or no association of dietary patterns with mortality outcomes added to the uncertain benefits of restricting single dietary components[12,15-17] leads to the conclusion that further investigation of dietary recommendations in hemodialysis is warranted. This is especially relevant given the substantial adverse
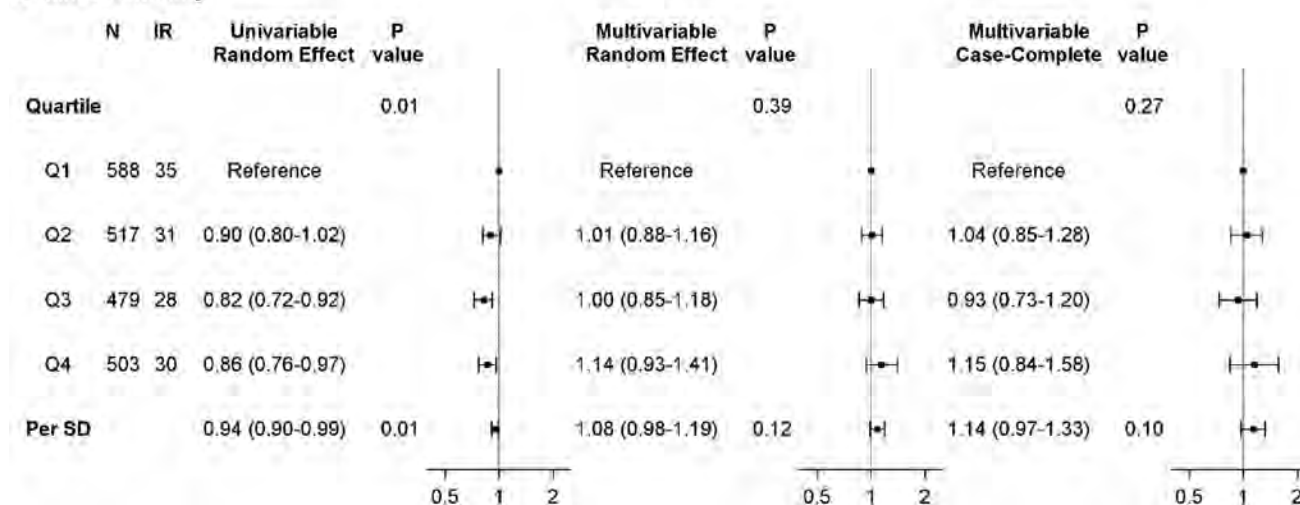
Figure 4. Mortality incidences and hazard ratios (95% confidence interval) by quartiles (Q) of the Western dietary pattern score. Multivariable analyses for cardiovascular mortality were adjusted for country (fixed effect in competing-risk analysis and random effect in all others), sex, daily physical activity, education (secondary vs none/primary), diabetes, smoking (current or former vs never), myocardial infarction, stroke, vascular access type (fistula vs graft/catheter), body mass index (categories according to World Health Organization), albumin (tertiles), Charlson comorbidity score (quartiles), age, phosphorus level, calcium level, hemoglobin level, Kt/V, and energy intake (1,000 kcal/d increase). Multivariable analyses for all-cause mortality were adjusted for the same variables with the exception of stroke and the addition of time on dialysis and being wait-listed for transplantation. Analyses of each pattern were adjusted for the other one. Abbreviations: IR, incidence rate; N, number of events; per SD, per standard deviation increase.

impact that dietary restrictions have on quality of life.[46,47] This call for further evaluation is supported by other studies.[42,48] For instance, recent observational studies of either dietary phosphorus restrictions or phosphate binders found better indexes of nutritional status and greater survival associated with less stringent dietary control.[49,50] Based on these collective data, future trials should investigate whether a more liberal approach to the intake of fruit and vegetables or dietary control can offer similar survival and improved quality of life for patients treated with long-term hemodialysis.

In conclusion, our findings did not confirm an association between mortality among patients receiving long-term hemodialysis and the extent to which dietary patterns were either high in fruit and vegetables or consistent with a Western diet. Trials investigating the benefits and harms of more inclusive diets are warranted.

Supplementary Material

Supplementary File (PDF)

Figure S1: Results from the principal component analysis with the varimax rotation

Figure S2: Cumulative incidence function plots for cardiovascular and all-cause mortality by quartiles of the fruit and vegetable dietary pattern score.

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