






ORIGINAL ARTICLE

Dietary Restriction, Socioeconomic Factors, Access to Kidney Transplantation, and Waitlist Mortality

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ABSTRACT

Introduction: Dietary restrictions for patients with end-stage kidney disease (ESKD) are burdensome. Kidney transplantation (KT) candidates who lack neighborhood resources and are burdened by dietary restrictions may have decreased access to KT.

Methods: In our two-center prospective cohort study (2014–2023), 2471 ESKD patients who were evaluated for KT (candidates) reported their perceived burden of dietary restrictions (not at all, somewhat/moderately, or extremely bothered). Neighborhood-level socioeconomic factors were derived from residential ZIP codes. We quantified the association of perceived burden of the dietary restrictions with a chance of listing using Cox models and risk of waitlist mortality using competing risks models. Then we tested whether these associations differed by neighborhood-level socioeconomic factors.

Results: At evaluation, 18% of KT candidates felt extremely bothered by dietary restrictions. Those who felt extremely bothered were less likely to be listed for KT (adjusted hazard ratio [aHR] = 0.75, 95% confidence interval [CI]: 0.64–0.87); this association did not differ by neighborhood-level socioeconomic factors. Overall, the burden of dietary restrictions was not associated with waitlist mortality ($p = 0.62$). However, among candidates living in high food insecurity neighborhoods, those who felt extremely bothered had higher waitlist mortality (adjusted subhazard ratio [aSHR] = 2.07, 95% CI: 1.14–3.75, $p_{\text{interaction}} = 0.02$). The association between dietary burden and waitlist mortality did not differ by neighborhood-level healthy food access.

Abbreviations: 3MS, Modified Mini-Mental State Examination; 95% CI, 95% confidence interval; aHR, adjusted hazard ratio; aSHR, adjusted subhazard ratio; BHLS, brief health literacy screen; BMI, body mass index; CCI, Charlson Comorbidity Index; ESKD, end-stage kidney disease; KDQOL-SF, Kidney Disease Quality of Life Short Form Health Survey; KT, kidney transplantation; NDI, Neighborhood Deprivation Index.

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Social Media: The perceived burden of dietary restrictions is associated with a reduced chance of listing for kidney transplant and an increased risk of waitlist mortality among those residing in high-food insecurity neighborhoods. Transplant centers should identify and support these vulnerable patients with nutrition education and food assistance.

Conclusion: The perceived burden of dietary restrictions is associated with a lower chance of listing for KT, and higher waitlist mortality only among candidates residing in neighborhoods with high food insecurity. Transplant centers should identify vulnerable patients and support them with nutrition education and access to food assistance programs.

1 | Introduction

Patients with end-stage kidney disease (ESKD) are counseled on dietary restrictions to help control uremic symptoms and comorbidities as well as reduce disease complications [1]. These restrictions are often complex and difficult to follow [1]. The burden of these dietary restrictions can lead to psychological distress, reduced quality of life [1, 2], and poor dietary adherence [2, 3], which can increase morbidity and mortality [4, 5]. Existing evidence suggests that ESKD patients undergoing hemodialysis (HD) are bothered by these dietary restrictions [6] resulting in lower health-related quality of life and increased mortality [7]. ESKD patients who have barriers to accessing healthy food and feel a higher burden of dietary restrictions may be less likely to gain access to kidney transplantation (KT) and be at an increased risk of mortality once listed.

Neighborhood deprivation, comprised neighborhood-level income, education, occupation, and housing conditions [8], impacts access to food and dietary intake [9]. This deprivation is especially concerning for patients with ESKD who are more likely to experience food insecurity than the general population [10]. Food insecurity may limit the ability of individuals with ESKD to adhere to dietary restrictions, as food may be financially or physically inaccessible. The burden of ESKD dietary restrictions is likely exacerbated by food insecurity and lack of access to healthy food [11, 12]. Diet quality may also suffer in the presence of food insecurity, which may impact uremic symptoms [10], and ultimately mortality.

Understanding whether the burden of dietary restrictions impacts access to KT overall, and among candidates who reside in high-risk neighborhoods, is a priority in nephrology. This study aimed to quantify the association between the perceived burden of dietary restrictions and the chance of listing and waitlist mortality. We also tested whether these associations differed by neighborhood-level factors among KT candidates.

2 | Materials and Methods

2.1 | Study Design

We conducted a prospective cohort study of 2471 adults with ESKD who were evaluated for KT at Johns Hopkins Hospital and New York University (NYU) affiliated hospitals between May 2014 and January 2023. Eligibility criteria were English-speaking and age ≥ 18 years.

At the time of KT evaluation, candidates' characteristics were collected and calculated by self-report, medical records linkage, or direct measurement, including age, sex, race, education, body mass index (BMI), type of dialysis, years on dialysis, history

of diabetes, comorbidities (Charlson Comorbidity Index [CCI] adapted for ESKD) [13, 14], frailty (physical frailty phenotype: unintentional weight loss, grip strength, gait speed, physical activity, and exhaustion) [15], depressive symptoms (Center for Epidemiologic Studies Depression [CESD]) [16], cognitive function (Modified Mini-Mental State Examination [3MS] [17, 18], trail making test [TMT]) [19], and health literacy (the brief health literacy screen [BHLS]) [20, 21]. The cause of ESKD and candidate's health insurance status were later ascertained through medical records once the candidate was waitlisted. Participants' five-digit residential ZIP codes were also collected for evaluation.

All clinical and research activities being reported are consistent with the Declaration of Helsinki and the Declaration of Istanbul. This is a multi-center study with Johns Hopkins University and NYU Langone Health. The Johns Hopkins IRB has approved this study and an agreement has been executed to form a single IRB with Johns Hopkins providing oversight for NYU Langone Health. Written informed consent was obtained from all participants involved.

2.2 | Perceived Burden of Dietary Restrictions

The burden of dietary restrictions was self-reported in a question from the Kidney Disease Quality Of Life Short Form Health Survey (KDQOL-SF) [22–24]. We chose to focus on this patient-reported outcome because perceived health-related quality of life is an important predictor of morbidity and mortality among HD patients [25]. Furthermore, the assessment of quality of life is mandated by the Centers for Medicare and Medicaid Service and the National Quality Forum recommends the KDQOL tool for this assessment [26]. Participants answered the following question: “Some people are bothered by the effects of kidney disease on their daily life, while others are not. How much does kidney disease bother you in each of the following areas: Dietary restriction?” Response options ranged from “not at all bothered” to “extremely bothered” using a 5-point Likert scale. For ease of interpretation, we classified dietary burden into three categories: not at all bothered, somewhat/moderately bothered, and very much/extremely bothered.

2.3 | Neighborhood-Level Socioeconomic Factors

At evaluation, candidates' residential ZIP codes were collected by self-report. We utilized the following data, detailed below, at either the tract-level or ZIP code tabulation areas (ZCTAs) to compute the levels of neighborhood socioeconomic factors for each ZIP code. Subsequently, these computed scores were linked to the study cohort by ZIP code to determine each candidate's level of neighborhood socioeconomic factors.

2.3.1 | Neighborhood Deprivation

We utilized the Neighborhood Deprivation Index (NDI) from the National Cancer Institute (NCI) at the census tract level to assess the levels of neighborhood deprivation [8, 27]. To account for population distribution, we computed population-weighted NDI scores for each candidate's ZIP code, using data from the American Community Survey (ACS) 5-year estimates [27]. These scores were then merged with our cohort data, assigning each candidate a residential neighborhood NDI score. We then assessed the distribution of candidate neighborhood NDI scores and categorized NDI into tertiles: low (>-2.90 , <-0.71), medium (≥-0.71 , <0.06), and high (≥0.06 , <1.69) [28–30]. These tertiles represented the level of deprivation in the candidate's neighborhood and were used for further analysis. A higher score signifies a higher level of deprivation within a residential neighborhood at the ZIP code level [27].

2.3.2 | Neighborhood Food Insecurity

To measure neighborhood food insecurity, we utilized data from the ACS 5-year estimates to determine the percentage of housing units in each candidate's ZIP code receiving Supplemental Nutrition Assistance Program (SNAP) benefits and then merged them with the cohort data [27]. SNAP is a federal government program that provides food benefits to low-income families and its utilization may indicate neighborhood-level food insecurity [31]. Participant neighborhood SNAP utilization percentages were categorized into tertiles: low (0, <7.00), medium (≥7.00 , <13.40), and high (≥13.40 , <52.70) categories, with the high-food insecurity (3rd tertile) category representing neighborhoods with the highest percentage of households utilizing SNAP benefits [32–34].

2.3.3 | Healthy Food Access

To evaluate access to healthy food, we measured the percentage of the census tract population consisting of low-income individuals living beyond 1 mile from the nearest grocery store. These data were sourced from the US Department of Agriculture 2019 Food Access Research Atlas (FARA), with low income defined as annual family income at or below 200% of the federal poverty threshold for family size [35]. We calculated population-weighted access to healthy food percentages for each candidate ZIP code using the US Department of Housing and Urban Development's ZIP Code Crosswalk Files [36] which were merged with the cohort data. The lack of access to healthy food percentages was categorized into tertiles: low (≥0 , <3.08), medium (≥3.08 , <8.03), and high (≥8.03 , <53.00), with the high category (3rd tertile) representing neighborhoods with the highest percentages of low-income candidates who lived beyond 1 mile from the nearest grocery store [32–34].

2.3.4 | Collinearity Between Neighborhood-Level Socioeconomic Factors

We quantified the collinearity, how much they are measuring the same construct, between the neighborhood-level

factors and dietary burden, through the variance inflation factor (VIF). Low collinearity was observed (neighborhood deprivation, VIF = 2.03; food insecurity, VIF = 1.99; healthy food inaccessibility, VIF = 1.08), suggesting the independence of these neighborhood-level factors.

2.4 | Statistical Analyses

2.4.1 | Descriptive Statistics

We reported distributions of characteristics overall and by dietary burden, generating percentages for categorical variables, and medians and interquartile ranges (IQRs) for non-normally distributed continuous variables. We then compared the characteristics between dietary burden categories, using Pearson's Chi-square test for categorical variables, and the Kruskal–Wallis test for non-normally distributed continuous variables.

2.4.2 | Dietary Burden, Socioeconomic Factors, and Chance of Listing

Among 2442 candidates who were evaluated for KT, we compared the chance of listing by dietary burden using Cox proportional hazards models. Time to listing was defined as the time from KT evaluation to the date of listing or administrative censoring (January 4, 2023). To assess whether this association between dietary burden and listing differed by neighborhood characteristics, we tested the interaction between dietary burden and each of the three characteristics (neighborhood deprivation, neighborhood food insecurity, and access to healthy food) separately using a Wald test. Models were adjusted for age, sex, race, education, BMI, and diabetes, based on existing literature pertaining to chance of listing [37–39].

2.4.3 | Dietary Burden, Socioeconomic Factors, and Waitlist Mortality

Among 1380 candidates who were listed for KT, we compared the risk of waitlist mortality by dietary burden using Fine and Gray competing risk models, with KT treated as a competing event. Time at risk was defined as the time from the date of listing to the date of KT, death, or administrative censoring (January 4, 2023). Similarly, to assess whether this association differed by neighborhood characteristics, we tested the interaction between dietary burden and each of the three characteristics (neighborhood deprivation, neighborhood food insecurity, and access to healthy food) separately using a Wald test. Models were adjusted for age, sex, race, education, BMI, diabetes, cause of ESKD, and insurance type. We ensured that all relevant and standard factors were included in the models by basing our selection on existing literature related to waitlist mortality [40, 41].

2.4.4 | Mediation by Unintentional Weight Loss

Unintentional weight loss is a marker of malnutrition, which is related to dietary burden and outcomes in ESKD [42, 43] and could play a role in the causal mechanism between perceived

dietary burden, chance of listing, and waitlist mortality. Therefore, we conducted a mediation analysis among a subgroup of 2329 candidates with data on weight loss intentionality. Unintentional weight loss was defined as unintentionally losing ≥ 10 lb of weight in the year before evaluation [15]. We estimated the indirect effect of unintentional weight loss on perceived dietary burden (feeling any levels of being bothered by dietary restriction vs. feeling not at all bothered by dietary restriction) on the chance of listing and waitlist mortality. We used the causal inference method of inverse odds ratio weighting (IORW) and performed 500 bootstraps. Details of this method have been published elsewhere [44–46].

2.4.5 | Sensitivity Analysis

To assess the robustness of our findings, we performed a sensitivity analysis limiting the study sample to only among candidates undergoing HD. This approach was chosen because individuals undergoing peritoneal dialysis (PD) may follow different dietary restrictions because they are dialyzed more frequently [47]. Studies suggest that ESKD patients initiating PD have greater perceived quality of life [48] or less perceived effects of kidney disease on daily life compared to those on HD [49]. Therefore, it was deemed important to assess HD patients separately.

We categorized neighborhood factors as low (lower 50%) versus high (higher 50%) to explore different cutoffs (neighborhood deprivation [NDI]: low (> -2.90 , < -0.352) and high (> -0.351 , < 1.69); neighborhood food insecurity (SNAP utilization percentages): low (≥ 0 , ≤ 9.30) and high (≥ 9.40 , ≤ 52.70); health food inaccessibility: low (≥ 0 , ≤ 5.151) and high (> 5.16 , < 53.00)). We then performed complete case analysis to account for missingness. We also included a full model presenting the association of each covariate including interaction terms with the outcomes.

Additionally, we quantified the association between the perceived burden of dietary restrictions, chance of listing, and waitlist mortality further adjusting for the following covariates: depression, health literacy, cardiovascular diseases (myocardial infarction, peripheral vascular disease, cerebral vascular disease, and congestive heart failure), and insurance type (non-private vs. private). We also stratified by insurance type in the association between perceived dietary burden and chance of listing. Finally, we stratified by BMI ≥ 35 kg/m² in the association between perceived burden of dietary restrictions, chance of listing, and waitlist mortality.

2.4.6 | Missing Data

Missing race, BMI, diabetes, cause of ESKD (among listed candidates), and insurance type (among listed candidates) accounted for $< 0.8\%$ of the cohort. We imputed these missing variables using multiple imputation methods with 10 iterations for all adjusted models [50]. Missing data for neighborhood deprivation (4.5%), neighborhood food insecurity (6.2%), and healthy food access (10.9%) were excluded when stratifying by these neighborhood factors.

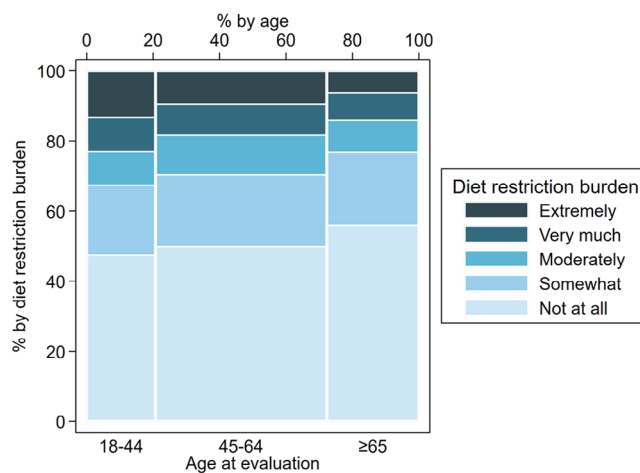


FIGURE 1 | Prevalence of dietary burden and age at evaluation ($N = 2471$). Areas of tiles represent the frequencies for each cross-combination of age and dietary burden. Dietary burden was defined as self-reported extent of feeling bothered by kidney disease regarding dietary restrictions.

All analyses were performed using Stata versions 16 and 17 (StataCorp, College Station, TX, USA). Two-sided p values < 0.05 were considered statistically significant.

3 | Results

3.1 | Study Population

Among 2471 adult KT candidates, the median age at evaluation was 57.3 years (IQR: 47.0–65.9), 39.5% of candidates were female, 44.5% were White, 39.1% had obesity, 43.4% had diabetes, and 18.8% experienced unintentional weight loss over the past year. The median time on dialysis was 0.6 years (IQR: 0.0–2.4) with 53.4% of candidates on HD (Table 1). Seven hundred and sixty-three (31%) candidates reported feeling somewhat/moderately bothered, and 443 (18%) reported feeling very much/extremely bothered by dietary restrictions. Younger candidates (18–44) reported a higher dietary burden (Figure 1). Candidates who resided in neighborhoods with high deprivation and candidates who resided in neighborhoods with high food insecurity were more likely to report feeling extremely bothered by dietary restrictions (Figure S1).

3.2 | Chance of Listing

Overall, the 3-year unadjusted cumulative incidence for chance of listing was 59.0% among candidates who did not feel bothered, 61.2% among candidates who felt somewhat/moderately bothered, and 49.8% among candidates who felt very much/extremely bothered (Figure 2a, log-rank $p < 0.001$). After adjustments, candidates who reported feeling very much/extremely bothered by dietary restrictions had a 25% (adjusted hazard ratio [aHR] = 0.75, 95% confidence interval [95% CI]: 0.64–0.87) lower likelihood of being listed for KT compared to those with no reported dietary burden (Table 2, Figure S2). This association did not differ

TABLE 1 | Characteristics of kidney transplant candidates by self-reported extent of feeling bothered by kidney disease dietary restrictions (N = 2471).

Characteristics	Total	Extent of feeling bothered by dietary restrictions					p value ^a
		Not at all	Somewhat	Moderately	Very much	Extremely	
N	2471	1265	507	256	216	227	
Age at evaluation, median (IQR)	57.3 (47.0–65.9)	58.7 (48.2–66.8)	57.3 (47.1–66.9)	55.9 (47.4–64.7)	55.8 (45.8–64.7)	52.8 (42.0–62.4)	<0.001
Female, %	39.5	38.3	39.4	39.1	39.8	46.3	0.27
Race, %							0.04
White/Caucasian	44.5	43.2	47.0	50.2	44.0	40.5	
Black/African American	46.4	48.3	44.1	38.8	48.2	48.0	
Asian/Asian American	3.8	3.7	4.2	4.3	4.6	2.2	
Native Hawaiian/Other Pacific Island and Other	5.3	4.8	4.7	6.7	3.2	9.3	
Education, %							0.67
Below high school	5.9	6.7	5.7	3.9	5.1	5.3	
High school	33.7	33.4	34.3	31.3	34.3	36.6	
Above high school	60.3	59.9	60.0	64.8	60.6	58.1	
BMI at evaluation, %							0.61
Underweight	2.6	2.4	2.2	4.7	2.3	3.1	
Normal weight	28.9	28.8	30.2	25.0	29.6	30.1	
Overweight	29.3	29.6	28.8	27.0	29.1	31.9	
Obese	39.1	39.2	38.8	43.4	39.0	35.0	
Type of dialysis, %							0.38
Not on dialysis	33.5	34.4	33.5	29.5	35.8	30.0	
Hemodialysis	53.4	52.2	52.2	58.3	55.3	56.1	
Peritoneal dialysis	13.1	13.4	14.3	12.2	8.8	13.9	
Years on dialysis, median (IQR)	0.6 (0.0–2.4)	0.6 (0.0–2.3)	0.5 (0.0–2.3)	0.7 (0.0–3.0)	0.8 (0.0–2.7)	0.7 (0.0–2.7)	0.33
Diabetes, %	43.4	42.2	45.6	48.4	40.5	42.9	0.27
Weight change ratio in previous year ^b , mean (SD)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.28
Frailty, %	19.4	18.5	19.2	20.5	19.0	24.1	0.48
Frailty components, %							
Unintentional weight loss	18.8	18.2	19.6	15.9	18.8	24.3	0.20
Low grip strength	48.0	48.5	47.7	49.8	44.9	46.2	0.89
Low gait speed	15.7	16.2	15.0	16.1	18.5	12.1	0.57
Low physical activity	39.1	38.5	39.8	41.7	37.9	39.2	0.93
Exhaustion	42.2	37.8	39.4	42.6	48.1	67.0	<0.001
Composite frailty score ^c , median (IQR)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.0–2.0)	1.0 (1.0–2.0)	2.0 (1.0–2.0)	0.003
Depressive symptoms ^d , %	24.2	18.1	25.0	27.0	28.0	50.0	<0.001
Global cognitive impairment ^e , %	9.8	10.9	9.6	7.1	7.3	10.1	0.38

(Continues)

TABLE 1 | (Continued)

Characteristics	Extent of feeling bothered by dietary restrictions						<i>p</i> value ^a
	Total	Not at all	Somewhat	Moderately	Very much	Extremely	
Executive function impairment ^f , %	8.2	8.9	9.0	6.0	5.7	6.9	0.39
Limited health literacy ^g , %	15.5	15.2	16.0	12.5	13.9	21.0	0.11

Note: Dietary burden was defined as self-reported extent of feeling bothered by kidney disease regarding dietary restrictions.

Abbreviation: IQR, interquartile range.

Statistically significant *p* values (<0.05) are in **bold**.

^a*p* values were obtained by Chi-squared test for categorical variables, and Kruskal–Wallis test for non-normally distributed continuous variables.

^bDefined as ([current weight–weight in the previous year]/weight in the previous year).

^cDefined by physical frailty phenotype.

^dDefined as Center for Epidemiologic Studies Depression (CESD) score ≥ 16 .

^eDefined as modified mini-mental state examination (3MS) score < 80.

^fDefined as using a time 1.5 SD above the mean for completing trail making test Part B minus Part A (TMTB–TMTA).

^gDefined as brief health literacy screen (BHLS) score ≤ 5 .

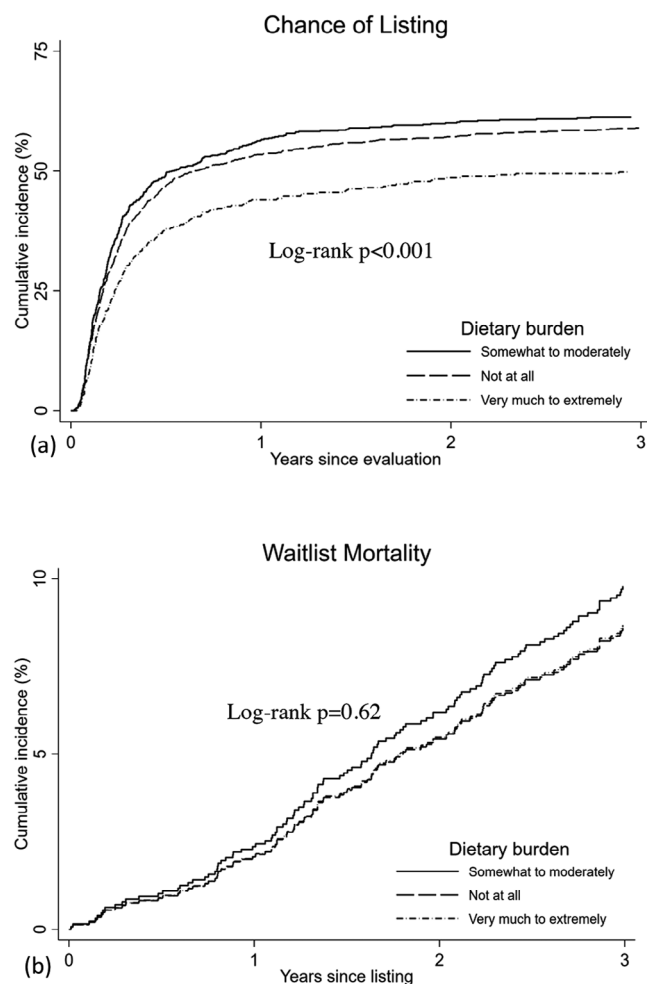


FIGURE 2 | Cumulative incidence of (a) chance of listing by dietary burden ($N = 2471$), and (b) waitlist mortality by dietary burden ($N = 1398$). Dietary burden was defined as self-reported extent of feeling bothered by kidney disease regarding dietary restrictions. Listing was obtained within the first 3 years since evaluation. Mortality was ascertained within the first 3 years since listing, with transplantation treated as a competing outcome.

by neighborhood deprivation, food insecurity, or healthy food inaccessibility (all $p_{\text{interactions}} > 0.05$).

3.3 | Waitlist Mortality

3.3.1 | Dietary Burden

Overall, the 3-year unadjusted cumulative incidence for waitlist mortality was 8.2% among candidates who did not feel bothered, 9.4% among those who felt somewhat/moderately bothered, and 8.3% among those who felt very much/extremely bothered. The cumulative incidence for waitlist mortality was not significantly different between dietary burden levels (Figure 2b, log-rank $p = 0.62$). After adjustments, being very much/extremely bothered by dietary restrictions was not associated with waitlist mortality (adjusted subhazard ratio [aSHR] = 1.17, 95% CI: 0.81–1.68) (Table 2). However, this association of dietary burden and waitlist mortality differed by neighborhood deprivation and food insecurity.

3.3.2 | Neighborhood Deprivation

The association of dietary burden and waitlist mortality significantly differed by neighborhood deprivation ($p_{\text{interaction}} = 0.03$). Specifically, among candidates residing in high-deprivation neighborhoods, those who were somewhat/moderately bothered by dietary restrictions had a 1.64-fold (aSHR = 1.64, 95% CI: 1.00–1.68) higher likelihood of waitlist mortality compared to those with no reported dietary burden; those who were very much/extremely bothered by dietary restrictions did not have a significantly higher likelihood (aSHR = 1.60, 95% CI: 0.87–2.95) of waitlist mortality. This association was not observed in low-deprivation neighborhoods (Table 2, Figure S2).

TABLE 2 | Association between dietary restriction burden and chance of listing and waitlist mortality, overall and stratified by neighborhood deprivation, neighborhood food insecurity, and healthy food access.

	Extent bothered by dietary restrictions			<i>P</i> _[interaction]
	Not at all	Somewhat /Moderately	Very much/Extremely	
Chance of listing^a, aHR (95% CI)				
Overall, <i>N</i> = 2471	1 (Ref)	1.07 (0.95, 1.20)	0.75 (0.64, 0.87)	
Neighborhood deprivation, <i>N</i> = 2361				
Low (1st tertile)	1 (Ref)	1.18 (0.97, 1.44)	0.84 (0.64, 1.09)	
Medium (2nd tertile)	1 (Ref)	1.00 (0.81, 1.23)	0.75 (0.57, 0.97)	0.49
High (3rd tertile)	1 (Ref)	1.00 (0.80, 1.24)	0.65 (0.49, 0.87)	0.33
Neighborhood food insecurity, <i>N</i> = 2319				
Low (1st tertile)	1 (Ref)	0.99 (0.81, 1.20)	0.86 (0.67, 1.10)	
Medium (2nd tertile)	1 (Ref)	1.03 (0.84, 1.27)	0.76 (0.58, 0.99)	0.68
High (3rd tertile)	1 (Ref)	1.08 (0.86, 1.35)	0.67 (0.50, 0.88)	0.25
Healthy food inaccessibility, <i>N</i> = 2203				
Low (1st tertile)	1 (Ref)	1.04 (0.83, 1.30)	0.78 (0.60, 1.02)	
Medium (2nd tertile)	1 (Ref)	0.99 (0.80, 1.21)	0.64 (0.48, 0.86)	0.61
High (3rd tertile)	1 (Ref)	1.11 (0.89, 1.37)	0.76 (0.58, 1.01)	0.90
Waitlist mortality^b, aSHR (95% CI)				
Overall, <i>N</i> = 1398	1 (Ref)	1.10 (0.83, 1.47)	1.17 (0.81, 1.68)	
Neighborhood deprivation, <i>N</i> = 1343				
Low (1st tertile)	1 (Ref)	0.64 (0.38, 1.07)	0.90 (0.48, 1.67)	
Medium (2nd tertile)	1 (Ref)	1.35 (0.80, 2.27)	1.26 (0.65, 2.44)	0.13
High (3rd tertile)	1 (Ref)	1.64 (1.00, 2.68)	1.60 (0.87, 2.95)	0.03
Neighborhood food insecurity, <i>N</i> = 1342				
Low (1st tertile)	1 (Ref)	0.78 (0.47, 1.28)	0.78 (0.39, 1.58)	
Medium (2nd tertile)	1 (Ref)	1.00 (0.60, 1.67)	1.01 (0.53, 1.91)	0.75
High (3rd tertile)	1 (Ref)	1.84 (1.08, 3.12)	2.07 (1.14, 3.76)	0.02
Healthy food inaccessibility, <i>N</i> = 1272				
Low (1st tertile)	1 (Ref)	0.85 (0.50, 1.44)	0.75 (0.41, 1.38)	
Medium (2nd tertile)	1 (Ref)	1.16 (0.68, 1.98)	1.31 (0.63, 2.73)	0.45
High (3rd tertile)	1 (Ref)	1.32 (0.78, 2.24)	1.68 (0.91, 3.11)	0.16

Note: Dietary burden was defined as self-reported extent of feeling bothered by kidney disease regarding dietary restrictions. Neighborhood deprivation was evenly distributed into three tertiles, with highest 3rd tertile representing greatest level of neighborhood deprivation. Neighborhood food insecurity was measured by percentage of housing units receiving SNAP benefits by ZIP code (evenly distributed into three tertiles), with the high food insecurity neighborhood (3rd tertile) category representing neighborhoods with the highest percentage of households utilizing SNAP benefits. Healthy food inaccessibility was measured by share of tract population with low income and low access to grocery (evenly distributed into three tertiles), with the high healthy food insecurity (3rd tertile) category representing neighborhoods with the highest percentage of low-income candidates who lived beyond 1 mile from the nearest grocery store.

Abbreviations: aHR, adjusted hazard ratio; aSHR, adjusted sub-hazard ratio.

Statistically significant *p* values and confidence intervals (*p* < 0.05) are in **bold**.

^aEstimated by Cox proportional hazards model, adjusted for age at evaluation, sex, race, education, BMI at evaluation, diabetes.

^bEstimated by competing-risks regression with transplantation as a competing outcome, and adjusted for age at evaluation, sex, race, education, BMI at evaluation, diabetes, cause of ESKD, insurance type.

TABLE 3 | Testing of mediation of unintentional weight loss on chance of listing ($N = 2329$) or waitlist mortality ($N = 1322$) between candidates with and without dietary burden.

	Chance of listing Proportion of association attributed to mediator (95% CI) ^a	Waitlist mortality Proportion of association attributed to mediator (95% CI) ^a
Base model (no potential mediator)	—	—
Model with unintentional weight loss (mediator)	0 (−1, 1)	11 (−22, 23)

Note: The base model is the association of dietary burden (feeling any level of bothered vs. not feeling at all bothered by dietary restrictions) on outcome without accounting for unintentional weight loss. The subsequent model shows the residual burden on the outcome after accounting for the mediator unintentional weight loss. Models are unadjusted.

Abbreviations: cHR, crude hazard ratio; cSHR, crude sub-hazard ratio.

^aEstimated by $([HR - 1] - [HR^* - 1]) / (HR - 1)$; HR, total burden effect; HR*, residual burden effect.

3.3.3 | Neighborhood Food Insecurity

The association of dietary burden and waitlist mortality also differed by neighborhood food insecurity ($p_{\text{interaction}} = 0.02$). In high food insecurity neighborhoods, candidates who were very much/extremely bothered by their dietary restrictions had a 2.07-fold (aSHR = 2.07, 95% CI: 1.14–3.76) higher likelihood of waitlist mortality compared to candidates who reported no dietary burden. Furthermore, candidates who were somewhat/moderately bothered by their dietary restrictions had a 1.84-fold (aSHR = 1.84, 95% CI: 1.08–3.12) higher likelihood of waitlist mortality. In low food insecurity neighborhoods, no association was observed (Table 2, Figure S2).

3.3.4 | Healthy Food Access

The association between feeling bothered by dietary restrictions and waitlist mortality did not differ by neighborhood healthy food inaccessibility ($p_{\text{interactions}} > 0.05$) (Table 2).

3.4 | Mediation Effect of Unintentional Weight Loss

Accounting for unintentional weight loss did not significantly attenuate the association between perceived dietary burden and chance of listing (proportion of association attributed to unintentional weight loss = 0%, 95% CI: −1% to 1%) (Table 3). Additionally, accounting for unintentional weight loss did not attenuate the association between perceived dietary burden and waitlist mortality (proportion of association attributed to unintentional weight loss = 11%; 95% CI: −22% to 23%).

3.5 | Sensitivity Analysis

Our inference remained consistent after we assessed the dietary burden with the chance of listing and waitlist mortality among candidates undergoing HD (Table S1). The findings were robust to categorizing neighborhood factors into higher

50% versus lower 50% (Table S2), and adjusting separately for depression, health literacy, and cardiovascular diseases (Table S3). After adjusting for insurance type, candidates reporting feeling somewhat/moderately bothered by dietary restrictions had a 1.22-fold higher chance of listing (aHR = 1.22, 95% CI: 1.04–1.42) compared to candidates who did not feel bothered; candidates reporting very much/extremely bothered by dietary restrictions had a 24% (aHR = 0.76, 95% CI: 0.62–0.93) lower likelihood of listing compared to those who did not feel bothered (Table S3).

When stratifying by BMI, no significant difference was observed for the association between perceived burden of dietary restrictions, chance of listing ($p = 0.81$), and waitlist mortality ($p = 0.56$) (Table S4). Similarly, no significant difference by insurance type was observed for the association between dietary burden and chance of listing ($p = 0.52$) (Table S5).

In the full model, age ≥ 65 years was associated with a lower chance of listing and higher waitlist mortality (Tables S6–S8). The findings remained robust in the complete case analysis (Table S9).

4 | Discussion

In this prospective cohort study of 2471 KT candidates, 31% reported feeling somewhat/moderately bothered, and 18% reported feeling very much/extremely bothered by dietary restrictions. Candidates who reported feeling very much/extremely bothered by dietary restrictions had a 25% lower likelihood of being listed for KT compared to those with no reported dietary burden. Although being bothered by dietary restrictions was not associated with waitlist mortality overall, it was significantly associated with important and vulnerable subgroups. Candidates residing in high-deprivation neighborhoods who were somewhat/moderately bothered by dietary restrictions had a 1.64-fold higher likelihood of waitlist mortality, an association that was not seen in low-deprivation neighborhoods. Also, among candidates living in neighborhoods with high levels of food insecurity, those who felt extremely bothered had 2.07-fold higher waitlist mortality.

In our study, candidates who reported feeling very much/extremely bothered by dietary restrictions had a 25% lower likelihood of being listed for KT than those with no reported dietary burden. To date, there is little existing research on the perceived burden of dietary restrictions and the chance of listing for KT [51]. A 2020 study of the Chronic Renal Insufficiency Cohort (CRIC) measured the KDQOL effect domain, which is a composite of eight items on the extent of feeling bothered by restrictions of CKD, including dietary restrictions [52]. This study reported that better KDQOL domain scores (feeling less bothered) were associated with decreased chance of listing, but did not assess dietary restrictions individually. The adverse association between dietary burden and chance of listing may be partially explained by dietary adherence. Prior work has shown that non-adherence to ESKD self-management, including poor adherence to diet or fluid restrictions and inconsistent intake of phosphate binders, is associated with increased hospitalizations, medical expenditures, and mortality [2, 3]. Medicare mandates that transplant centers and dialysis centers make dietitian services available to patients. Patients on the waitlist undergo a full transplant evaluation, which includes a nutrition assessment, but after that and before activation, they are not routinely seen by transplant center dietitians [53]. Few diagnoses receive mandated nutrition services or nutrition benefits through Medicare, but ESKD does, which highlight the importance of dietary restrictions, and the complex nature of these restrictions that require ongoing support. However, the number and frequency of visits, length of time spent with dietitians, topics covered, and other support for patients with nutrition risk or food insecurity are not mandated or consistent across centers. Our findings suggest while the support provided meets mandatory evaluation standards, it may not provide the ongoing support needed to improve the health-related quality of life or nutrition risk of vulnerable patients. Utilizing a question from the KDQoL that is routinely administered at HD centers to identify patients who are struggling with dietary restrictions could be a low-cost opportunity to screen for diet risk and provide earlier intervention. This screener does not require expertise to administer or interpret, as diet quality assessments do, and would not further burden patients or providers with additional tests. Further studies are warranted to investigate the underlying mechanism, and quantify the role of dietary adherence in this association.

Additionally, we did not observe a significant association between feeling bothered by dietary restrictions and waitlist mortality overall. However, after stratifying by neighborhood-level factors, dietary burden was associated with an increased risk of waitlist mortality among those who were somewhat/moderately bothered by dietary restrictions and residing in high-deprivation neighborhoods. Further, in neighborhoods with high levels of food insecurity, candidates who were somewhat/moderately bothered or very much/extremely bothered by their dietary restrictions had a higher likelihood of waitlist mortality compared to candidates who reported no dietary burden, and this association was not observed in neighborhoods with low levels of food insecurity. It has been reported in previous research that higher food insecurity was associated with a higher risk of mortality [54]. Food insecurity, closely linked with poverty [55], can worsen with unemployment [56], placing strain on food budgets and ultimately contributing to higher mortality rates. Additionally,

food insecurity may be associated with increased mortality by indirectly influencing health-related behaviors such as smoking and exercise [54, 55, 57–61], thereby exacerbating the impact of dietary burden on mortality. Future studies should explore additional built environment factors that interact with dietary burden, neighborhood-level factors, and mortality.

Strengths of this study include the large sample size with follow-up data on key pre-KT outcomes. The study population is made up of individuals from two different KT centers, allowing for the recruitment of a relatively diverse population. We included socioeconomic measures derived from the ACS, NCI, and FARA with specific markers of food accessibility and food insecurity to identify factors that are likely to lead to difficulty in following dietary restrictions. Our study also has limitations. Dietary burden is subjective and was only assessed at evaluation for KT. However, this is part of the validated KDQOL which has been associated with morbidity and mortality outcomes and is a widely used measure of health-related quality of life [25]. Although health-related quality of life may change after evaluation and the survey may be offered annually to patients, many studies rely on the data from a single administration of the KDQOL tool among HD patients [25, 26]. Information regarding candidates' nutritional status (with or at risk for malnutrition), dietary intake, or frequency of counseling by a registered dietitian nutrition (RDN) was not obtained. However, we completed a mediation analysis using unintentional weight loss as a proxy for malnutrition, as nearly 19% of our study sample reported unintentional weight loss, to estimate the indirect effect of unintentional weight loss on perceived dietary burden. Although accounting for unintentional weight loss did not significantly attenuate the association between perceived dietary burden, chance of listing, and waitlist mortality, understanding the cause of this perceived burden of dietary restrictions and would be useful in planning future interventions. Although dietary restrictions differ by dialysis vintage, laboratory values (potassium, phosphorus) comorbidities, and patient preferences [1], nearly half of all respondents reported feeling at least somewhat burdened by restrictions, suggesting this is an area in need of intervention. Ongoing RDN support can help improve nutritional status and compliance with dietary restrictions and is therefore recommended for patients with ESKD [62, 63]. Lastly, we used neighborhood-level variables to estimate key social constructs because the study did not collect individual-level measures of food insecurity or inaccessibility.

In conclusion, the perceived burden of dietary restrictions is associated with a decreased chance of being listed for KT. A high perceived burden of dietary restrictions is also associated with an increased risk of waitlist mortality among candidates residing in deprived neighborhoods with high rates of food insecurity. The question of the perceived burden of dietary restrictions could be used as a screener to identify those in need of nutrition or food security interventions to support adherence to evidence-based dietary recommendations which could improve outcomes. Frequent follow-ups for candidates with an RDN, social worker interventions, and connections with food assistance programs, should be a major focus of payers, dialysis and KT centers, and healthcare providers. Transplant providers should understand the challenges KT candidates face in adhering to dietary restrictions and the impact on both access to KT and waitlist mortality.

Author Contributions

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Nan-Su Huang, MHS, contributed to statistical analysis, interpretation of the data, and revision of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available upon request from the corresponding author with a proposal that is approved by the study team.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.