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Dietary energy intake predicts mortality in Chinese patients with peritoneal dialysis: a single-center 18 years' follow-up study

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Abstract

Background Lower dietary energy intake (DEI) may be associated with increased mortality risk. This study aims to analyze the influence of baseline DEI, time average DEI, and other factors on survival in peritoneal dialysis (PD) patients.

Method It was a single-center retrospective cohort study. Patients who started PD from January 2006 to June 2021 were included in this study and followed up until June 2023. Their baseline (six months after the beginning of PD) demographic, dietary intake, laboratory data, and time varying dietary intake data were collected and analyzed. The relationships between these data and survival were examined using Cox model to estimate death hazard ratios.

Result A total of 794 patients were included in this study, 424 males and 370 females, with a mean age of 58.87 ± 16.02 years. Their mean normalize baseline dietary energy intake (nDEI) was 25.46 ± 6.72 kcal/kg/day, time average nDEI was 24.87 ± 4.74 kcal/kg/day. The median follow-up duration was 46.58 (27.38, 78.52) months in the overall cohort. Based on multivariate Cox proportional hazard analysis, age (HR = 1.056, 95% CI = 1.047–1.065, $p < 0.001$), diabetes (HR = 1.364, 95% CI = 1.114–1.671, $p = 0.003$), serum albumin (HR = 0.945, 95% CI = 0.923–0.967, $p < 0.001$), blood sodium (HR = 0.973, 95% CI = 0.954–0.992, $p = 0.002$), serum urea (HR = 0.974, 95% CI = 0.953–0.994, $p = 0.025$), and baseline nDEI (HR = 0.980, 95% CI = 0.964–0.996, $p = 0.017$) were significantly associated with mortality. Baseline DPI, BMI and time average nDEI were not related to PD patients' survival. When classified baseline nDEI into 4 groups (< 25 kcal/kg/day, 25-29.99 kcal/kg/day, 30-34.99 kcal/kg/day, and ≥ 35 kcal/kg/day), the univariate and multivariate Cox proportional hazard analysis showed that the patients with nDEI 30-34.99 kcal/kg/day had the lowest mortality risk (using the DEI < 25 kcal/kg/day group as reference, $p < 0.05$).

Conclusion Our study revealed that DEI 30-34.99 kcal/kg/day might be beneficial to the long-term outcome for the Chinese PD population.

Clinical trial number Not applicable.

Keywords Peritoneal dialysis, Mortality, Dietary energy intake, Cohort study

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Introduction

Chronic kidney disease (CKD) is a major burden throughout the world. In China, although studies in recent years found that the prevalence of CKD showed a minor downward trend with effective intervention and examination [1], the number of CKD patients may still reach 150 million [2]. For patients with end-stage renal disease (ESRD), if kidney transplantation is not available, dialysis becomes the necessary option to maintain their life. Although the percentage of peritoneal dialysis (PD) was much lower than hemodialysis (HD) all over the world [3], the number of patients receiving PD were still gradually increasing in China, the United States, Singapore and other places [3, 4]. The latest data from Chinese National Renal Data System (CNRDS) reported that there were more than 150 thousand patients on PD in Mainland China until the end of 2023 [5].

Nutritional status was a key factor affecting the survival of PD patients [6, 7]. Previous studies reported that the prevalence of protein-energy wasting (PEW) in patients with continuous ambulatory peritoneal dialysis (CAPD) was about 45-52.9% [6, 7]. PEW was common in dialysis patients and had become an important risk factor for mortality [8–10]. Adequate dietary energy and protein intake are essential for maintaining good nutritional status. The relationship between dietary protein intake (DPI) and survival of PD patients had been explored in several previous studies [11–13]. However, the influence of dietary energy intake (DEI) on survival of PD patients remains inconclusive.

In the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guidelines for nutrition in CKD (2020 update), guideline 3 states that, " In adults with CKD 1-5D (1 C) or post-transplantation (OPINION) who are metabolically stable, we recommend prescribing an energy intake of 25–35 kcal/kg body weight per day based on age, sex, level of physical activity, body composition, weight status goals, CKD stage, and concurrent illness or presence of inflammation to maintain normal nutritional status [14]. Although the evidence level for this point was acceptable (1c), most data came from non-dialysis or hemodialysis patients, so whether it is applicable to PD patients remains questionable. Although PD and HD have similar patient populations, the energy metabolism of patients on PD or HD will be different due to the different dialysate components and treatment mechanism. In addition, most of the relevant evidence in K/DOQI came from western populations, and there were few studies in Chinese populations [14]. The conclusions given by K/DOQI may not be appropriate to the Chinese population. According to Chinese Clinical Practice Guidelines for Nutrition in CKD (2021 edition), the DEI of PD patients should be 35 kcal/kg/d, which is quite different from the recommendation raised by K/DOQI guideline, but the evidence level is still relatively low (2D) [15]. More high-quality studies are needed to explore the DEI recommendation in Chinese PD patients. Therefore, we conducted this study to analyze the relationship between DEI and patients' outcome and explore the appropriate DEI level in PD patients through a single center long-term follow-up cohort.

Methods

Subjects and follow-up

It was a retrospective cohort study. The patients who started peritoneal dialysis at Peking University Third Hospital from January 2006 to June 2021 were included in this study, and all participants were followed up until June 2023. The inclusion criteria were: patients (1) had been on PD for more than 6 months; (2) were 18 years or above. Patients with multiple organ failure or malignancy were excluded. The demographic data, including gender, age, primary disease of ESRD, body weight, height, presence of diabetes mellitus (DM), and Charlson index were collected [16]. All subjects were followed up until death, transfer to HD, kidney transplantation, or the end of the study. All-cause mortality was recorded as outcome events. The study was approved by the Medical Ethical Committee of Peking University Third Hospital (approval number: IRB 2024-096-03). Individual informed consent was waived by IRB given the study was a retrospective, non-interventional design and using a deidentified dataset.

Dietary variables

We suggested at least 0.8 g/kg of dietary protein and 25 kcal/kg of dietary energy based on previous study and European Best Practice Guideline [14, 17]. During the follow-up, all patients visited the PD clinic monthly. Three-day dietary records were collected at the sixth month of dialysis as baseline dietary intake data and subsequently every one to three months. The dietary intake collection process was the same as our previous study described [13]. Daily baseline DPI and DEI were normalized as nDPI & nDEI by ideal body weight (IBW), which was defined as body height (cm) minus 105 (modified Broca method) [18].

The time-averaged calculations of nDEI were conducted based on the measurements taken over a 6-month period. The detailed methodology can be described as follows. Patients' follow-up records were segmented into intervals of 6 months. Within each 6-month interval, the data for all patient visits were averaged to create a single average record for that 6-month period. Depending on the varying follow-up times, there might be multiple "6-month average" follow-up records available, represented as 'n' records. To obtain the overall average follow-up record, the data from these 'n' records were averaged together. When calculating the average, any corresponding records with missing data were excluded from the calculation.

Dialysis adequacy and nitrogen balance at baseline

Patients' 24-hour urine and dialysate samples were collected to measure urea and creatinine levels one day before the clinic visit. Using standard methods, we calculated weekly total Kt/V urea, creatinine clearance, and residual renal function (RRF). The urea nitrogen appearance (UNA) was defined as the urea nitrogen output in urine and dialysate, and then the total nitrogen appearance (TNA, the nitrogen output in urine, feces, and dialysate) was calculated using the Bergstrom formula [19] or new formulae which was reported in our previous study [20]. NB (nitrogen balance) = NI -TNA = DPI/6.25-TNA.

Blood chemistries

The blood test results were also collected at baseline, such as blood urea nitrogen, creatinine, hemoglobin, albumin, phosphate, potassium, and sodium etc.

Statistical analyses

Continuous variables were reported as either mean ± standard deviation (SD) or median (interquartile range, IQR) based on their distribution. Categorical data were presented as proportions. Patient follow-up time was computed as the time of starting PD to the date of outcome events (all-cause mortality) appeared, or being censored (transplantation, transfer to HD or other centers, or the end of the study). The one-way ANOVA, non-parametric test or Chi-square test were used to analyze the baseline parameter difference among different baseline nDEI groups based on different variable categories.

The Cox proportional hazards model of univariate and multivariate analysis was used to evaluate the association between baseline nDEI, time average nDEI and survival as well as to estimate the Hazard ratios (HR) with 95% Confidence Interval (CI). Multivariate Cox's regression analysis (using Backward Wald method to select variable) included all the significant variables from the univariate analysis ($p < 0.1$) and the variables concerned by the literature (like Kt/V and eGFR) [21, 22]. For variables which had obvious collinearity, the one with lower p value was included in the multivariate analysis. Potential confounders included patients' baseline demographic data, data of dietary intake, dialysis adequacy, residual kidney function, laboratory tests and nitrogen balance.

The hypotheses of proportional risk models of the baseline nDEI groups (nDEI < 25 kcal/kg/day; 25-29.99 kcal/kg/day; 30-34.99 kcal/kg/day; ≥35 kcal/kg/day) and serum sodium groups (≤ 137 mmol/L, 137.1–139 mmol/L, 139.1–141 mmol/L and ≥ 141.1 mmo/L) on mortality were tested by Graphical analysis using a log minus log plot (LML plot) [23]. The Kaplan-Meier analysis was used to generate survival curves. The log-rank test was used to evaluate the difference in survival rate according to baseline nDEI and serum sodium groups. Multivariate Cox's regression analysis was used to analyze the independent risk of baseline nDEI groups on mortality adjusting the variables which were distributed differently among the four nDEI groups. As sensitivity analysis, the same multivariate Cox's regression analysis process was implemented to test the influence of baseline nDEI groups on other outcomes, such as transfer to HD, and combination of mortality & transfer to HD.

All of the reported p-values were two-tailed, and statistical significance was set at 0.05. Statistical analyses were performed using the SPSS software package (IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp).

Results

Characteristics of the study population

A total of 1257 patients who started PD therapy in our center from January 2006 to June 2021 were initially followed up. Within half a year of dialysis, 136 dialysis patients withdrew from PD. Three patients had complete recovery of kidney function, 324 patients could not be followed-up regularly due to living far away from the PD center, suffering from cancer or other reasons. Finally, 794 patients were included in this analysis (see Fig. 1), 424 males and 370 females, with a mean age of 58.87 ± 16.02 years, 45 receiving automated peritoneal dialysis (APD) and 749 on CAPD. According to the etiology of kidney disease, the percentage of diabetic kidney disease (DKD), chronic glomerulonephritis (CGN), hypertensive nephropathy (HTN), chronic interstitial nephritis (CIN), polycystic kidney disease and other causes was 35%, 31.1%, 13.4%, 8.9%, 3.5%, and 8.1%, respectively. There were 343 patients (43.2%) who had diabetes.

The median follow-up duration was 46.58 (27.38, 78.52) months in the overall cohort. The 1-year, 2-year, 3-year, 5-year survival rates were 96.7%, 87.3%, 78.6% and 66.0%, respectively. At the end of the study as of June 2023, 148 patients were still on PD, 412 died, 91 had transferred to HD, 44 had undergone kidney transplantation, 99 had transferred to other hospitals, and the causes of death were cardiovascular diseases (159 cases, 38.6%), systemic infections (105 cases, 25.5%), multiple organ failure (55 cases, 13.3%), malignant tumors (22 cases, 5.3%) and other causes (71 cases, 17.2%).

The baseline dietary intake, nutritional status, and nitrogen balance of the patients were shown in Table 1. The time average nDEI was 24.87 ± 4.74 kcal/kg/day.

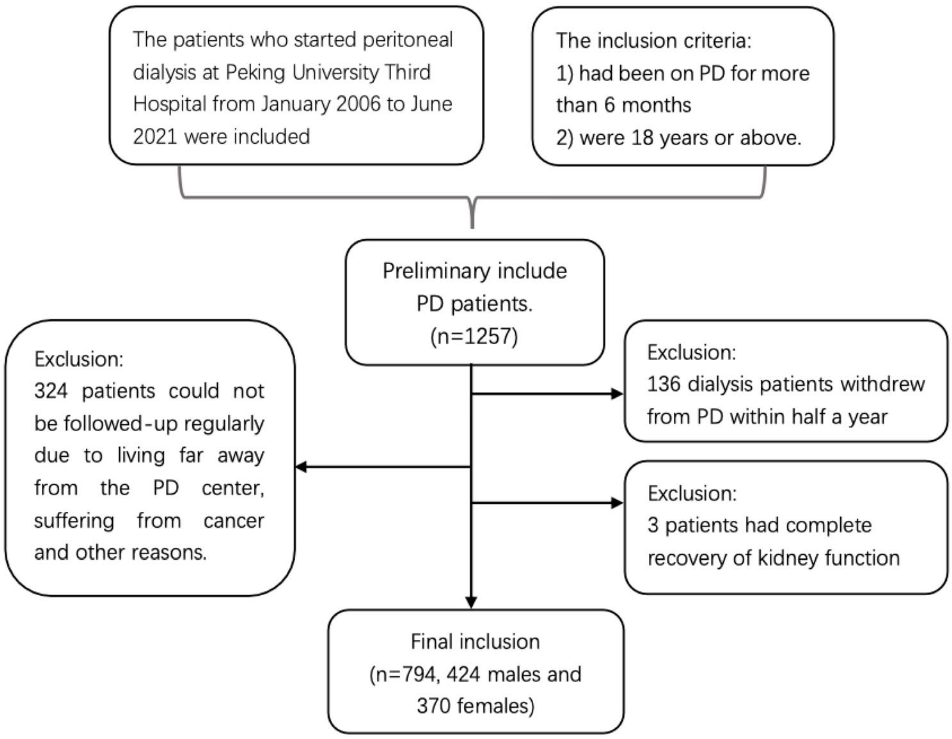


Fig. 1 Flow chart of patients screened and excluded

The effect of parameters on survival

In the univariate Cox regression model, age, Charlson index, diabetes, urine volume, ultrafiltration, total fluid removal, serum urea, serum creatinine, serum potassium, serum sodium, albumin, fat intake, carbohydrate intake, DPI, DEI, baseline and time average nDEI, TNA and NB were all associated with mortality (see Table 2). Considering collinearity between variables as well as variables concerned in the literature, age, diabetes, urine volume, ultrafiltration, Kt/V, serum urea, serum creatinine, serum phosphate, serum potassium, serum sodium, albumin, fat intake, DPI, baseline nDEI, time average nDEI, and TNA were included in the multivariate Cox proportional hazard analysis. Charlson index, total fluid removal, eGFR, carbohydrate intake and DEI were excluded from the analysis. After multivariate Cox proportional hazard analysis, age, diabetes, serum urea, serum albumin, serum sodium and baseline nDEI were independently associated with patients' mortality, see Table 2 for detail information. Baseline DPI and BMI were not related to PD patients' mortality.

If patients were divided into four quartiles based on blood sodium level (≤ 137 mmol/L, 137.1–139 mmol/L, 139.1–141 mmol/L and ≥ 141.1 mmo/L), only patients having the lowest blood sodium (≤ 137 mmol/l) had poorer outcome as compared with the others (see Fig. 2).

The effect of longitudinal nDEI on survival

In the univariate Cox regression model, time average nDEI was associated with mortality (HR = 0.950, 95%CI 0.929–0.971, $P < 0.001$). Since the correlation between time average nDEI and baseline nDEI was low ($r = 0.38$), we placed both time average nDEI and baseline nDEI into multivariate Cox proportional hazard analysis. And the time average nDEI was removed from the model after adjusting other covariates (Table 2).

Baseline nDEI level as a categorical variable

All the subjects were classified into four groups according to baseline nDEI, i.e., < 25 kcal/kg/day, 25-29.99 kcal/kg/day, 30-34.99 kcal/kg/day and ≥ 35 kcal/kg/day. There were differences in age, diabetes percentage, nDPI, fat intake, carbohydrate intake, nitrogen intake, NB and albumin among the patients in the four groups ($p < 0.05$). Only patients with nDEI ≥ 35 kcal/kg/day could achieve positive nitrogen balance if using the Bergstrom formula to estimate TNA. However, if using the new formula, the patients in three groups (25-29.99 kcal/kg/day, 30-34.99 kcal/kg/day and ≥ 35 kcal/kg/day) could get positive nitrogen balance. Detail information is shown in Table 3.

As shown in Fig. 3; Table 4, compared with the two groups with higher nDEI (30-34.99 kcal/kg/day and ≥ 35 kcal/kg/day), the two groups with lower nDEI (< 25 kcal/kg/day and 25-29.99 kcal/kg/day) had inferior

Table 1 Baseline dietary energy intake, nutritional parameters, and dialysis adequacy of PD patients

Variables	Data*
height, cm	164.04 ± 8.57
body weight, kg	63.41 ± 12.41
BMI, kg/m^2	23.20 ± 3.64
Charlson index	6(4,7)
nDPI, g/kg/day	0.86 ± 0.25
nDEI, kcal/kg/day	25.46 ± 6.72
Fat intake, g/d	54.85(43.49,68.77)
Carbohydrate intake, g/d	195.72(156.58,237.44)
Alb, g/l	37.17 ± 4.65
Dialysis dose, ml	6000(6000,8000)
ultrafiltration, ml	350(102.5,649)
urine volume, ml	550(250,992.5)
total fluid removal, ml	971(700,1305)
Kt/V	1.98(1.63,2.41)
Tccr, (L/w)	60.31(48.29,76.61)
eGFR, ml/min	2.45(1.12,3.99)
Nitrogen intake, g/d	8.05 ± 2.45
TNA, g/d (Bergstrom)	9.58 ± 2.11
TNA, g/d (New formula)	8.05 ± 2.17
NB, g/d (Bergstrom)	-1.52 ± 2.67
NB, g/d (New formula)	0.01 ± 2.71
Hb, g/l	116.07 ± 19.25
Serum urea, mmol/l	20.37 ± 5.82
Serum, creatinine, μ mmol/l	721.38 ± 255.13
Serum calcium, mmol/l	2.26 ± 0.28
Serum phosphate, mmol/l	1.52 ± 0.40
Serum potassium, mmol/l	4.31 ± 0.73
Serum sodium, mmol/l	139.99 ± 5.40
CO_2CP, mmol/l	26.58 ± 3.65

*: mean ± sd for normalized distribution parameters, median(P25, P75) for non-normalized distribution parameters

PD: peritoneal dialysis; BMI: body mass index; nDPI: normalized dietary protein intake; nDEI: normalized dietary energy intake; Alb: albumin; Tccr: total clearance rate of creatinine; eGFR: estimated Glomerular filtration rate; TNA: total nitrogen appearance; NB: nitrogen balance; Hb: hemoglobin; CO_2CP: carbon dioxide combining power

survival ($p < 0.05$). There was no significant difference between the two groups with relatively higher nDEI (30-34.99 kcal/kg/day compared with ≥ 35 kcal/kg/day, $p > 0.05$) and relatively lower nDEI (< 25 kcal/kg/day versus 25-29.99 kcal/kg/day, $p > 0.05$).

As shown in Table 3, there were differences on age, diabetes, BMI, nDPI, fat intake, albumin, ultrafiltration, Kt/V, and eGFR among the four nDEI groups. After adjusting these covariates, the baseline nDEI group was still associated with mortality ($p = 0.038$). Table 4 shows that the third group of patients with nDEI 30-34.99 kcal/kg/day had the lowest risk in both univariate and multivariate Cox proportional risk models (HR = 0.567 vs. 0.632, respectively). However, if using other outcome events, such as transfer to HD, and combination of mortality & transfer to HD, the associations between baseline nDEI group and these outcomes were not significant (Table 5).

Discussion

In this single-center long-term follow-up PD cohort, we found a higher baseline level of nDEI was significantly associated with a lower risk of death (HR = 0.980; 95% CI = 0.964–0.996, $p = 0.017$) even after adjusted by age, diabetes, urine volume, ultrafiltration, Kt/V, serum urea, serum creatinine,serum phosphate, serum potassium, serum sodium, albumin and DPI by multivariate Cox proportional hazard analysis. According to the multivariate Cox regression analysis, old age, having diabetes, hypoalbuminemia, a lower level of blood sodium and urea were also significantly associated with inferior survival. Baseline BMI was not related to PD patients' survival. Higher longitudinal time average nDEI was also related to better survival in univariate Cox proportional hazard analysis, but the association disappeared after adjusting other parameters in multivariate Cox proportional hazard analysis. It indicated that the time average nDEI was less sensitive than baseline one to predict mortality. In this study, the baseline data was collected at the sixth month of dialysis when most of the patients had improved from uremia, while the time-average dietary intake may be influenced by decreased residual renal function or new complication(s) over time, all of these factors may explain why the baseline nDEI was associated with mortality rather than time-average nDEI.

The influence of DEI on PD patients' all-cause mortality was found in our previous longitudinal study which also reported that DEI rather than DPI was an independent risk factor for mortality of patients having PD [13], it indicated the importance of adequate energy intake for PD patients to maintain the nutritional status and achieve good outcome. Additionally, the present study further analyzed the optimal nDEI level in Chinese PD population. In univariate analysis, patients whose nDEI was higher than 30 kcal/kg/day had better prognosis. After adjusting other confounding factors, patients with nDEI of 30-34.99 kcal/kg/day had the lowest mortality risk among the four groups. In the sensitivity analysis, the baseline nDEI group was not associated with other outcome events, such as transfer to HD or the combination of mortality & transfer to HD. In present study, most of the causes for transfer to HD were catheter-related infection, catheter malfunction, hernia, and surgical operation. The competing risk was small since dietary intake had limited influence on these events.

On the other hand, in our study, the calculation of nDEI did not take into account the energy absorption from the dialysate (usually 250–300 kcal/d, about equals to 5 kcal/kg/d for a patient with 60 kg normalized body weight) [24]. If considering this part of energy intake, it

Table 2 Univariate Cox regression analysis of the impact of data on mortality

Variables	Univariate Cox regression analysis		Multivariate Cox regression analysis*	
	HR(95%CI)	*P* value	HR(95%CI)#	*P* value
Age, years	1.062[1.053–1.071]	< 0.001	1.056[1.047,1.065]	< 0.001
Gender	1.012[0.834–1.229]	0.902		
Charlson index, points	1.580[1.489–1.677]	< 0.001	not included	
Diabetes	1.721[1.416–2.092]	< 0.001	1.364[1.114,1.671]	0.003
BMI	0.984[0.958–1.010]	0.225		
urine volume, ml	1.000[0.999-1.000]	0.001	1.000[1.0001.000]	0.747
Dialysis dose, ml	1.000[1.000–1.000]	0.864		
ultrafiltration, ml	1.278[1.006–1.625]	0.045	1.000[1.000,1.000]	0.363
total fluid removal, ml	1.000[1.000–1.000]	0.085	not included	
Kt/V	1.061[0.898–1.252]	0.487	0.872[0.717,1.060]	0.169
Tccr, L/w	0.999[0.995–1.003]	0.541		
eGFR, ml/min	1.007[0.966–1.049]	0.757	not included	
Hb, g/l	1.000[0.995–1.006]	0.952		
Serum urea, mmol/l	0.952[0.935–0.970]	< 0.001	0.974[0.953,0.994]	0.012
Serum creatinine, umol/l	0.998[0.998–0.999]	< 0.001	1.000[0.999,1.000]	0.223
Serum calcium, mmol/l	0.994[0.711–1.391]	0.973		
Serum phosphate, mmol/l	0.798[0.618–1.031]	0.084	1.309[0.983,1.743]	0.065
Serum potassium, mmol/l	0.729[0.631–0.842]	< 0.001	0.918[0.792,1.065]	0.260
Serum sodium, mmol/l	0.977[0.966–0.988]	< 0.001	0.973[0.954,0.992]	0.005
CO_2CP, mmol/l	0.997[0.969–1.024]	0.807		
Alb, g/l	0.913[0.895–0.931]	< 0.001	0.945[0.923,0.967]	< 0.001
Fat intake, g/d	0.995[0.990-1.000]	0.048	0.999[0.992,1.007]	0.886
Carbohydrate intake, g/d	0.995[0.993–0.997]	< 0.001	not included	
DPI, g/day	0.992[0.985–0.998]	0.017	1.002[0.992,1.012]	0.689
nDPI, g/kg/day	0.721[0.474–1.097]	0.127		
DEI, kcal/day	0.999[0.999-1.000]	< 0.001	not included	
nDEI, kcal/kg/day	0.966[0.951–0.981]	< 0.001	0.980[0.964,0.996]	0.017
Time average nDEI, kcal/kg/day	0.950[0.929,0.971]	< 0.001	0.990[0.966,1.014]	0.410
TNA, g/d (Bergstrom)	0.874[0.831–0.918]	< 0.001	0.984[0.892,1.085]	0.745
TNA, g/d (New formula)	0.877[0.836–0.920]	< 0.001	not included	
NB, g/d (Bergstrom)	1.042[1.005–1.081]	0.027	not included	
NB, g/d (New formula)	1.044[1.007–1.082]	0.020	not included	

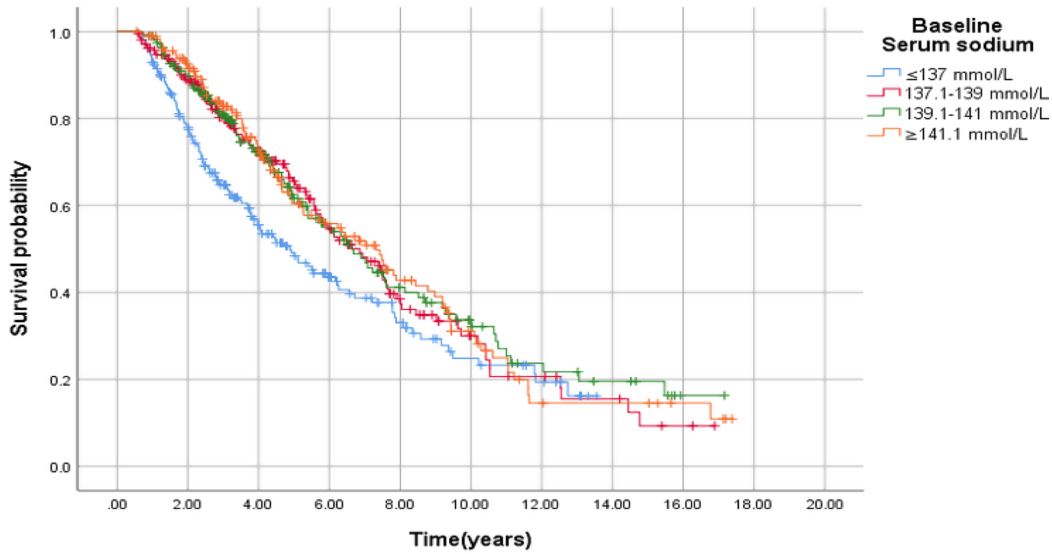
Note BMI, body mass index; Tccr: total clearance rate of creatinine; eGFR: estimated Glomerular filtration rate; Hb: hemoglobin; CO_2CP: carbon dioxide combining power; Alb: albumin; DPI: dietary protein intake; nDPI: normalized dietary protein intake; DEI: dietary energy intake; nDEI: normalized dietary energy intake; TNA: total nitrogen appearance; NB, nitrogen balance

*Multivariate Cox's regression analysis (using Backward Wald method to select variable) included all the variables which showed significance [$p < 0.1$, including age, diabetes, urine volume, ultrafiltration, serum urea, serum creatinine, serum phosphate, serum potassium, serum sodium, Alb, DPI, nDEI, fat intake, and TNA(Bergstrom)] from the univariate analysis. For variables which had obvious collinearity, the one with lower P value was included in the multivariate analysis

#For the variable removed from the model, the P value and HR of the last step were reported

may mean that the nDEI of our patients on PD should be more than 35 kcal/kg/day to ensure better survival. The result exceeds the recommendations (25–35 kcal/kg/day) provided by the K/DOQI guidelines [14, 25], and is consistent with the Chinese Clinical Practice Guidelines for Nutrition in CKD (2021 edition) [15].

Why do our Chinese PD patients have higher energy requirements? The increased energy expenditure was one of the main reasons. To maintain the patient's energy balance, their energy intake should be equal to their energy expenditure when at a stable metabolic condition. The total energy expenditure (TEE) of the human body mainly includes three parts, named resting energy expenditure (REE), thermic effect of food and activities induced energy expenditure (AEE). In these three parts, REE can account for 60–75% of TEE in normal population [26]. Therefore, REE plays an important role in evaluating energy expenditure in patients with CKD. For the patients with CKD, many studies have found that REE generally increased [27, 28]. Although the cause of increased REE in CKD patients has not been clearly determined, many possible causes exist. For example, chronic inflammation can lead to increased REE [29], and the incidence of chronic inflammation was higher in CKD patients [30]. The excitation of the sympathetic nervous system may also be one of the reasons for the



baseline SNa+	number at risk										
≤137mmol/L	210	153	84	48	29	16	10	0	0	0	0
137.1-139mmol/L	208	166	106	63	32	16	10	6	2	0	0
139.1-141mmol/L	192	161	95	56	35	22	12	8	1	0	0
≥141.1mmo/L	183	155	99	58	36	21	8	7	4	0	0
	0	2	4	6	8	10	12	14	16	18	20

Time(years)

Fig. 2 The Kaplan–Meier survival curves in PD patients according to the baseline Serum sodium level. PD: peritoneal dialysis. All the subjects were classified into four groups according to baseline Serum sodium, i.e., ≤ 137mmol/L, 137.1-139mmol/L, 139.1-141mmol/L and ≥ 141.1mmo/L. As shown in Fig. 2, patients with lowest Serum sodium (≤ 137mmol/L) had lower survival compared with patients in the other three groups ($p < 0.05$). There was no significant difference in survival among the other 3 groups (Serum sodium 137.1–139, 139.1–141, ≥ 141.1 mmol/l; $p > 0.05$)

increase of REE in the dialysis patients [31]. In addition, the comorbidity of CKD patients, such as diabetes, may also be the cause of their increased REE [27, 28]. Thus, dialysis patients may need higher DEI to maintain energy balance. In present study, patients with nDEI ≥ 30 kcal/kg/day could also achieve positive nitrogen balance if using new formula (which may be more suitable for Chinese PD patients) [20] rather than the Bergstrom formula to estimate TNA. Some nutritional studies involving hemodialysis patients or non-dialysis ESRD patients also showed that DEI 35 kcal/kg/day and above was beneficial to maintain patients' nutritional status [32, 33].

Except the higher REE level, the BMI characteristic of our study population may also be a reason for their higher energy requirements. Patients' BMI levels in this study were lower than patients from Western countries in other studies [34]. More than 60% percent of the study population were in the normal range or underweight status in spite of using the BMI stratification criteria for Chinese population [35]. It is obvious that underweight or normal weight people need more energy intake than the overweight or obese ones.

In addition, in present study, we found that lower serum albumin levels, as well as lower serum sodium levels, were associated with poor prognosis in patients having PD. Serum albumin, a popular-used nutritional & inflammatory marker for dialysis patients, its correlation with survival of patients on PD had been fully described in previous studies [36–38]. As for blood sodium levels, Ravel VA et al. also reported that lower baseline serum sodium levels had been associated with a poorer prognosis in PD patients, although the exact sodium threshold below which higher mortality risk was observed varied across different analyses (134–140 mmol/L) [39]. The results of the present study added a flavor on this phenomenon, we found patients with serum sodium ≤ 137mmol/L had poorer outcomes as compared with the others. Hyponatremia may lead to poor prognosis of PD patients in a number of ways. Some studies have shown that low serum sodium levels may be associated with higher cardiovascular risk, central system adverse reactions, and higher risk of infection [40–42]. Additionally, low serum sodium in dialysis patients can also aggravate PEW, which leads to poor prognosis in

Table 3 Comparison of baseline parameters among patients in different nDEI groups

Variables	Baseline nDEI level				F/Z/x^2	*p*
	< 25 kcal /kg/day* (*n* = 404)	25-29.99 kcal/kg/day* (*n* = 217)	30-34.99 kcal/kg/day* (*n* = 107)	≥ 35 kcal /kg/day* (*n* = 66)		
age, years	58.56 ± 16.48	61.86 ± 15.15[#]	56.57 ± 15.67[&]	54.65 ± 16.21[&]	4.784	0.003
Male(%)	223(55.2%)	119(54.8%)	50(46.7%)	32(48.5%)	3.253	0.354
Diabetes(%)	197(48.8%)	84(38.7%)	44(41.1%)	18(27.3%)	14.21	0.003
Charlson index	6(4,7)	6(4,7)	5(3,7)	4(3,7)	2.074	0.557
BMI	23.72 ± 3.79	23.10 ± 3.57	23.04 ± 3.27	23.88 ± 3.46	2.149	0.093
nDPI, g/kg/day	0.72 ± 0.18	0.91 ± 0.16[#]	1.05 ± 0.18[#&]	1.23 ± 0.24[#&^]	232.435	< 0.001
Fat intake, g/d	47.04(36.69,55.51)	60.18(51.16,71.66) [#]	69.30(57.57,83.92) [#&]	78.40(58.20,100.37) [#&]	158.516	< 0.001
Carbohydrate intake, g/d	165.32(135.56,196.48)	212.08(175.67,246.47) [#]	244.21(211.00,289.56) [#&]	288.99(236.86,368.42) [#&^]	222.752	< 0.001
Alb, g/l	36.98 ± 4.61	36.80 ± 4.43	37.29 ± 4.58	39.27 ± 5.26[#&^]	5.243	0.001
Dialysis dose, ml	6000(6000,8000)	6060(6000,8000)	6000(6000,8000)	6000(5000,8000)	1.073	0.784
ultrafiltration, ml	350(102.5,650)	350(100,605)	300(100,600)	425(200,740)	6.255	0.100
urine volume, ml	500(200,925)	550(255,1000)	575(350,900)	650(210,1000)	2.120	0.548
total fluid removal, ml	950(700,1296.5)	1000(687.5,1350)	968(700,1299)	1115(840,1450)	2.384	0.497
Kt/V	1.93(1.55,2.35)	1.96(1.66,2.41)	2.02(1.66,2.53)	2.06(1.79,2.47)	7.459	0.059
TCcr, (L/w)	59.03(47.50,74.88)	60.90(49.42,75.75)	62.47(49.27,82.67)	66.20(49.56,83.00)	5.901	0.117
eGFR, ml/min	2.36(0.97,3.84)	2.46(1.20,4.04)	2.40(1.24,4.53)	3.11(1.37,4.93)	4.526	0.210
Nitrogen intake, g/d	6.91 ± 1.99	8.57 ± 1.82[#]	9.67 ± 2.34[#&]	10.80 ± 2.85[#&^]	105.157	< 0.001
TNA, g/d (Bergstrom)	9.44 ± 2.05	9.61 ± 2.18	9.78 ± 2.25	9.94 ± 2.08	1.532	0.205
TNA, g/d (New formula)	7.90 ± 2.12	8.08 ± 2.25	8.25 ± 2.32	8.42 ± 2.15	1.532	0.205
NB, g/d (Bergstrom)	-2.53 ± 2.24	-1.05 ± 2.43[#]	-0.11 ± 2.75[#&]	0.86 ± 2.94[#&^]	59.107	< 0.001
NB, g/d (New formula)	-1.00 ± 2.28	0.48 ± 2.48[#]	1.42 ± 2.79[#&]	2.38 ± 2.96[#&^]	59.769	< 0.001
Hb, g/l	115.68 ± 20.29	117.55 ± 18.95	114.95 ± 17.31	115.52 ± 15.98	0.622	0.601
Serum urea, mmol/l	20.13 ± 6.08	20.45 ± 5.64	21.13 ± 5.57	20.38 ± 5.03	0.858	0.463
Serum creatinine, μ mmol/l	735.12 ± 262.83	707.49 ± 239.55	717.50 ± 275.34	697.05 ± 218.91	0.812	0.487
Serum calcium, mmol/l	2.25 ± 0.28	2.28 ± 0.28	2.26 ± 0.24	2.25 ± 0.34	0.536	0.658
Serum phosphate, mmol/l	1.53 ± 0.41	1.52 ± 0.39	1.51 ± 0.43	1.51 ± 0.40	0.068	0.977
Serum potassium, mmol/l	4.27 ± 0.77	4.36 ± 0.71	4.37 ± 0.72	4.28 ± 0.62	0.986	0.399
Serum sodium, mmol/l	138.90 ± 3.08	138.82 ± 8.98	139.42 ± 3.20	139.48 ± 3.24	0.513	0.673
CO_2CP, mmol/l	26.72 ± 3.51	26.64 ± 3.70	26.10 ± 3.99	26.30 ± 3.77	0.979	0.402

*: mean ± sd for normalized distribution parameters, median(P25, P75) for non-normalized distribution parameters

[#]: there is a significant difference compared with the first group (nDEI < 25 kcal/kg/day; $p < 0.05$)

[&]: there is a significant difference compared with the second group (nDEI 25-29.99 kcal/kg/day; $p < 0.05$)

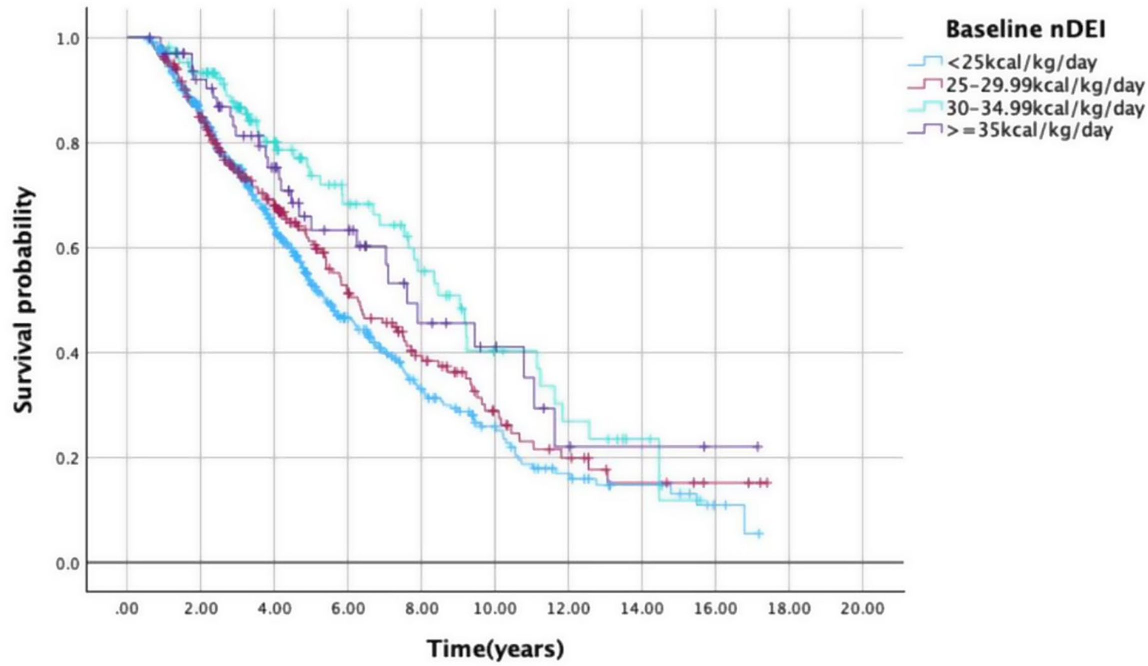
[^]: there is a significant difference compared with the third group (nDEI 30-34.99 kcal/kg/day; $p < 0.05$)

nDEI: normalized dietary energy intake; BMI: body mass index; nDPI: normalized dietary protein intake; Alb: albumin; TCcr: total clearance rate of creatinine; eGFR: estimated Glomerular filtration rate; TNA: total nitrogen appearance; NB: nitrogen balance; Hb: hemoglobin; CO_2CP: carbon dioxide combining power

dialysis patients [43]. However, a most recent study from a provincial HD cohort from China reported a U-shaped relationship between serum sodium and all-cause mortality in HD patients, with serum sodium ≤ 137.5 mmol/L or > 142.5 mmol/L being related to a higher risk of death [44]. The exact serum sodium range which could lead to better survival in dialysis patients still needs further studies.

Limitations

There are some limitations of this study. First, the three-day dietary recall data may underestimate the dietary intake, even though we gave all the patients and their caregivers sufficient education. However, the study used the guidelines' recommending 3-day diet record to assess diet, which is currently a reliable assessment method with both high reliability and validity. In addition, this does not affect the conclusion of this study. If there is an underestimation of dietary intake, then PD patients may need a higher DEI to ensure a good survival than the results of the present study. Second, the study was conducted in a single center, and the results were more internally validated, which might have some limitations in terms of generalizability. Third, some potential confounding factors (including both baseline and longitudinal factors) which may affect the outcomes could not be completely excluded or analyzed. The last, the selection bias may exist due to many patients lost follow-up or withdrew from PD.



Baseline nDEI	number at risk										
<25kcal/kg/day	404	315	181	100	55	33	17	10	3	0	0
25-29.99kcal/kg/day	217	174	112	65	40	21	12	6	3	0	0
30-34.99kcal/kg/day	107	93	55	37	25	13	8	3	0	0	0
>=35 kcal/kg/day	66	54	36	23	12	8	3	2	1	0	0
	0	2	4	6	8	10	12	14	16	18	20

Time(years)

Fig. 3 The Kaplan–Meier survival curves in PD patients according to the baseline nDEI level PD: peritoneal dialysis; nDEI: normalized dietary energy intake. Compared with the two groups with higher DEI (30-34.99 kcal/kg/day and ≥ 35 kcal/kg/day), the two groups with lower DEI (< 25 kcal/kg/day and 25-29.99 kcal/kg/day) had lower survival ($p < 0.05$). There was no significant difference between the two groups with relatively high (30-34.99 kcal/kg/day versus ≥ 35 kcal/kg/day, $p > 0.05$) and relatively low DEI (< 25 kcal/kg/day versus 25-29.99 kcal/kg/day, $p > 0.05$)

Table 4 Association between baseline nDEI groups and mortality in proportional hazards models ($N = 749$)

	No. of participants	No. of events	univariable model		Multivariable model	
			HR	*p*	HR	*p*
nDEI group				0.003		0.038
< 25 kcal/kg/day	404	222	1.00(ref)		1.00(ref)	
25-29.99 kcal/kg/day	217	119	0.870[0.696,1.087]	0.221	0.839[0.669,1.052]	0.128
30-34.99 kcal/kg/day	107	42	0.567[0.408,0.789]	< 0.001	0.632[0.455,0.877]	0.006
≥ 35 kcal/kg/day	66	29	0.655[0.445,0.965]	0.032	0.956[0.642,1.424]	0.826

Note Multivariable model was adjusted for age, diabetes, BMI, nDPI, fat intake, Alb, ultrafiltration, Kt/V, eGFR. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) were calculated by proportional hazards model

Conclusion

Our study revealed that baseline nDEI 30-34.99 kcal/kg/day was beneficial to the long-term outcome of our PD population based on the results of survival analysis. If considering the glucose absorption from the dialysate, the total nDEI may need to achieve 35 kcal/kg/day to ensure the optimal long-term outcome for our Chinese PD patients.

Table 5 Association between baseline nDEI groups and different ending in proportional hazards models ($N=749$)

baseline nDEI groups	proportional hazards model of death		proportional hazards model of transfer to HD		proportional hazards model of death and transfer to HD	
	No. of events	Multivariable model	No. of events	Multivariable model	No. of events	Multivariable model
< 25 kcal/kg/day	222	1.00(ref)	49	1.00(ref)	271	1.00(ref)
25-29.99 kcal/kg/day	119	0.839[0.669,1.052]	16	0.672[0.370,1.219]	135	0.855[0.677,1.080]
30-34.99 kcal/kg/day	42	0.632[0.455,0.877]	16	1.268[0.653,2.465]	58	0.793[0.573,1.098]
≥ 35 kcal/kg/day	29	0.956[0.642,1.424]	10	1.512[0.600,3.809]	39	1.177[0.767,1.807]

[*]Multivariable model was fully adjusted for the same covariates in the Table 4

[#]Hazard ratios (HRs) and 95% confidence intervals (95% CIs) were calculated by proportional hazards model

Abbreviations

AEE Activities induced energy expenditure
Alb Albumin
BMI Body mass index
CAPD Continuous ambulatory peritoneal dialysis
CI Confidence Interval
CGN Chronic glomerulonephritis
CKD Chronic kidney disease
CNRDS Chinese National Renal Data System
CO_2CP Carbon dioxide combining power
DEI Dietary energy intake
DKD Diabetic kidney disease
DM Diabetes mellitus
DPI Dietary protein intake
eGFR Estimated Glomerular filtration rate
ESRD End-stage renal disease
Hb Hemoglobin
HD Hemodialysis
HR Hazard ratios
HTN Hypertensive nephropathy
IBW Ideal body weight
IQR Interquartile range
K/DOQI The National Kidney Foundation Kidney Disease Outcomes Quality Initiative
NB Nitrogen balance
nDEI Normalized dietary energy intake
nDPI Normalized dietary protein intake
PD Peritoneal dialysis
PEW Protein-energy wasting
REE Resting energy expenditure
RKF Residual kidney function
SD Standard deviation
Tccr Total clearance rate of creatinine
TEE Total energy expenditure
TNA Total nitrogen appearance
UNA Urea nitrogen appearance

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not applicable.

Author contributions
L SX contributed to the conception and design of the study, data analysis, and drafting of the manuscript. XK Z XQ and made significant contributions to the data collection and analysis. L MY and Z XQ revised the manuscript. S CY and TW, as the corresponding authors, made substantial contributions to the conception and design, and critically important intellectual content revisions of the manuscript. All authors have read and approved the final version of the manuscript and agree with the order of the authors' presentation.

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Data availability
The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Medical Ethical Committee of Peking University Third Hospital with approval number IRB 2024-096-03. Individual informed consent was waived by the IRB since the study was a retrospective, non-interventional design and using a deidentified dataset. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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