Prognosis of Peritoneal Dialysis Patients with Different Peritoneal Transport Characteristics: A Retrospective Cohort Study

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Original Paper

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Introduction. We aimed to examine the clinical characteristics of peritoneal dialysis (PD) patients with different baseline peritoneal transport characteristics and the effect of peritoneal transport characteristics on the prognosis of PD patients.
Methods. Patients who received PD for more than 3 months were included. Clinical characteristics, risk factors for high peritoneal transport, and risk factors for death and technique failure were examined. All patients were treated with glucose-containing peritoneal dialysis solution, and the peritoneal dialysis protocol was either day ambulatory peritoneal dialysis (DAPD) or continuous ambulatory peritoneal dialysis (CAPD).
Results. A total of 351 patients were enrolled, comprising 70 in the low transport group, 149 in the low average transport group, 88 in the high average transport group, and 44 in the high transport group. Multivariate logistic regression analysis showed that a high Charlson's comorbidity index (CCI) and low albumin were risk factors for a high baseline transport status. In the nonhigh transport group, the proportion of patients with albumin less than 30 g/L, who developed high transport status, was higher than those with albumin more than 30 g/L (P = .029). The survival rate in the high transport group was significantly lower than that in the other three groups (P < .001). Multivariate Cox regression analysis showed that age, systolic blood pressure, CCI, C-reactive protein (CRP) and high transport were independent risk factors for all-cause mortality. Male sex, triglycerides and CRP were independent risk factors for technique failure.
Conclusion. High peritoneal transport status is an independent risk factor for death. High CCI and low albumin are determinants of baseline high peritoneal transport. To avoid development of a high transport state, serum albumin should be increased to more than 30 g/L.

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INTRODUCTION

As the number of patients with end-stage kidney disease (ESKD) is growing, peritoneal dialysis (PD) becomes an important and effective form of renal replacement therapy. The survival rate of PD is comparable to that of haemodialysis,[1] but PD

is less expensive and can provide better quality of life for ESKD patients.[2] In Asia, application of PD ranges from 3 to 73%, and China has a fairly high PD rate.[3-5] PD uses solute and fluid exchange across peritoneal capillary blood and the dialysis solution, and the flow rate can be adjusted to achieve maximum removal.[6] Through PD, wastes, toxins, water, and other substances in human blood can pass through the peritoneum into the dialysis fluid to remove excess substances from the body. At the same time, the dialysis fluid contains electrolytes and nutrients that can enter the patient's body through the peritoneum to meet the needs of normal metabolism.[7]

Peritoneal solute transport characteristics vary greatly among patients. Such differences in baseline peritoneal transport characteristics can have important clinical implications and form the basis for future changes in peritoneal transport characteristics during long-term PD therapy.[8] Previous studies have shown that patients with high peritoneal transport status have poor fluid clearance and poor prognosis;[9,10] however, recent studies have reported that baseline peritoneal transport status is not associated with prognosis.[11,12] There are many clinical studies to date showing that the peritoneal transport function of peritoneal dialysis patients is affected by a variety of factors, such as the inflammatory response, endocrine function, nutritional reserve, and cardiovascular events.[13,14] Yet, there are no standardized clinical guidelines, and the degree of influence of these factors is not consistent among patients of different sexes, ages, and regions.[15,16] These reasons contribute to the lack of clinical references for developing interventions to protect altered transit function.

Generally, as the duration of PD increases, both the function and morphology of the peritoneum will change. Therefore, we retrospectively examined the clinical characteristics and prognosis of PD patients with different basic peritoneal transport characteristics, as well as changes in peritoneal transport in long-term PD patients, to explore the impact of peritoneal transport characteristics on the prognosis of PD patients.

MATERIALS AND METHODS

Study Population

Patients who started PD treatment in the Nanjing Drum Tower Hospital between January 1, 2012, and September 30, 2020, and received PD treatment for at least three months were included in the study. All patients were treated with glucose-containing peritoneal dialysis solution (Guangzhou Baxter Medical Supplies Co., Ltd., Lactate-G 2.5%, H44025291); the peritoneal dialysis protocol was either day ambulatory peritoneal dialysis (DAPD) or continuous ambulatory peritoneal dialysis (CAPD). The exclusion criteria were: i) missing baseline peritoneal balance test data, ii) missing follow-up, and iii) having kidney transplantation. The end points were death, technical failure, or follow-up until September 30, 2022. Technical failure refers to transfer to haemodialysis due to inadequate peritoneal dialysis or refractory peritonitis. The protocol of the present study was approved by the Ethics Committee of Nanjing Drum Tower Hospital (NO.2020-278-01). In addition, all study participants signed an informed consent form. This study was conducted in strict compliance with the Declaration of Helsinki.

Data Collection

Basic clinical data, including sex, age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP) and presence or absence of diabetes, were collected before PD. Charlson's comorbidity index (CCI) was calculated. Laboratory indicators such as haemoglobin (Hb), serum creatinine (Scr), blood urea nitrogen (BUN), albumin (Alb), cholesterol (Chol), triglyceride (TG), calcium (Ca), phosphorus (P) and C-reactive protein (CRP) were recorded before PD. Dialysis adequacy indicators such as the urea clearance index (Kt/V) and creatinine clearance (CCr) were recorded within 3 months after PD initiation.

Peritoneal Equilibration Test and Study Groups

The baseline peritoneal equilibration test (PET) was completed within three months after PD initiation and every 6 to 12 months thereafter. i) One day in advance, 2 L of 2.5% LD solution was instilled into the peritoneal cavity. ii) The dialysis solution was drained out, and the patient was instructed to lie on his or her back. When every 400 ml was instilled, the patient was instructed to turn over from side to side once. iii) The time was counted when all the peritoneal dialysis fluid was instilled. Two hundred millilitres of dialysis fluid were drained out at 120 min: 10 mL of specimen

was retained, and the remainder was instilled back into the peritoneal cavity. An automatic biochemistry analyser (Myriad BS-2800M) was used to detect the concentrations of glucose, urea nitrogen, and creatinine. iv) A peripheral venous blood sample was collected at 120 min, and glucose, urea nitrogen and creatinine concentrations were detected. v) After four hours, the abdominal cavity was emptied in 20 min, the amount of drainage fluid was measured, the amount of ultrafiltration was calculated, and 10 ml specimens were retained to detect glucose, urea nitrogen and creatinine concentrations.

The patients were divided into the following four groups based on the D/Pcr ratio according to the Twardowski classification criteria (17): the high transport group (0.81 to 1.03), the high average transport group (0.65 to 0.80), the low average transport group (0.50 to 0.64), and the low transport group (0.34 to 0.49).

Statistical Analysis

Descriptive data are expressed as the mean ± standard deviation for normal distribution and median and interquartile range for a skewed distribution. Data that conformed to a normal distribution were analysed by one-way ANOVA with two-way comparisons between groups using the LSD test, and the data that did not conform to a normal distribution were analysed by using the Kruskal–Wallis H test. Categorical data are expressed as numbers and percentages, and comparisons were made by using the χ^2 test. Kaplan–Meier survival analysis was conducted to compare the survival rate and technical failure rate between groups. Logistic regression was used to analyse the influence of initial high peritoneal transport status, and Cox regression was used to analyse risk factors for death and technical failure. The risk ratio (HR) and 95% confidence interval (CI) were used to describe relative risks.

Statistical analyses were performed by using SPSS version 23.0. $P < .05$ was considered statistically significant.

RESULTS

General Data

Initially, 559 patients were included. Of these, 102 patients were excluded because baseline D/Pcr values were lacking, 60 patients were lost to follow-up or transferred to other centres, and 46 patients underwent renal transplantation. Finally, 351 patients were enrolled, with an average age of 53.31 ± 15.47 years, comprising 205 males and 146 females. In terms of primary disease, there were 187 cases of chronic glomerulonephritis, 96 cases of diabetes nephropathy, 18 cases of hypertensive nephropathy, and 50 cases of other diseases. The median follow-up time was 4.11 ± 2.06 years. At the end of the follow-up period, 53 patients died, and technical failure occurred in 77 cases.

Retrospective Data Analysis of Different Transport Groups

Of the 351 patients, there were 70 in the low transport group, 149 in the low-average transport group, 88 in the high-average transport group, and 44 in the high transport group. Differences in clinical baseline data, such as age, sex, and BMI, among the four groups were not significant ($P > .05$), indicating that they were comparable. There were differences in CCI score, diabetes, and serum albumin level among the four groups. CCI scores were higher in the high transport group than in the high-average transport, low-average transport, and low transport groups. The proportion of diabetes was higher in the high transport group than in the high average transport, low average transport and low transport groups. Albumin levels were lower in the high transport group than in the high-average transport, low-average transport, and low transport groups (Table 1).

Analysis of Risk of High Peritoneal Transport

Univariate logistic regression showed that diabetes mellitus (OR = 2.232, 95% CI: 1.178 to 4.226), CCI (OR = 1.300, 95% CI: 1.084 to 1.559), and albumin level (OR = 0.913, 95% CI: 0.855 to 0.975) correlated with high peritoneal transport status. Multivariate regression analysis showed that CCI (OR = 1.233, 95% CI: 1.016 to 1.495) and low albumin level (OR = 0.931, 95% CI: 0.869 to 0.998) were significantly associated with high peritoneal transport status at baseline (Table 2). In the nonhigh transport group, 202 patients had D/Pcr follow-up data. The group was divided into two groups according to serum albumin: less than 30 g/L and more than 30 g/L. The proportion of those who developed high peritoneal transport was 35.1% for serum albumin level below 30 g/L

Table 1. Baseline Data of Patients with Different Peritoneal Transport Characteristics

	Low Transport Group (n = 70)	Low-average Transport Group (n = 149)	High-average Transport Group (n = 88)	High Transport Group (n = 44)	*P*
Follow-up Time, y	4.01 ± 1.95	4.25 ± 2.02	3.79 ± 1.84	3.62 ± 0.98	.132
Age, y	50.17 ± 14.28	54.13 ± 16.44	52.73 ± 15.26	56.68 ± 13.71	.059
Male (n, %)	32 (45.7)	91 (61.1)	55 (62.5)	27 (61.4)	.119
BMI, kg/m^2	23.24 ± 4.53	23.12 ± 3.42	23.31 ± 3.69	23.25 ± 3.63	.997
SBP, mmHg	146.57 ± 24.36	143.32 ± 22.03	143.91 ± 24.61	146.57 ± 22.04	.717
DBP, mmHg	87.53 ± 13.31	85.88 ± 14.43	85.30 ± 16.74	88.41 ± 13.98	.422
CCI (points)	2 (2, 5)	3 (2, 4)	3 (2, 5)	4 (3, 5)	< .001
Diabetes (n, %)	20 (28.6)	42 (28.2)	33 (37.5)	22 (50.0)	.034
HB, g/L	79.80 ± 16.10	78.07 ± 15.51	78.11 ± 17.28	74.41 ± 14.72	.376
Scr, μmol/L	821.26 ± 336.56	893.03 ± 360.50	950.63 ± 442.32	887.30 ± 379.15	.332
BUN, mmol/L	29.27 ± 8.93	30.82 ± 9.78	31.67 ± 9.49	28.98 ± 8.84	.268
Alb, g/L	35.39 ± 4.99	34.88 ± 4.39	33.69 ± 4.37	32.54 ± 5.12	.002
Chol, mmol/L	4.14 ± 1.33	4.06 ± 1.21	4.35 ± 1.45	3.81 ± 1.81	.246
TG, mmol/L	1.81 ± 0.99	1.54 ± 0.81	1.62 ± 1.18	1.86 ± 1.19	.154
Ca, mmol/L	2.13 ± 0.32	2.08 ± 0.27	2.09 ± 0.32	2.04 ± 0.30	.682
P, mmol/L	1.79 ± 0.49	1.93 ± 0.61	1.99 ± 0.49	1.85 ± 0.57	.234
CRP, mg/L	4.10 (2.30, 8.53)	3.90 (2.05, 11.55)	3.95 (2.20, 12.85)	3.70 (2.25, 12.58)	.951
CCr, L/W/1.73 m^2	71.90 ± 25.89	78.30 ± 27.46	77.16 ± 25.94	70.82 ± 25.02	.294
Kt/V	2.15 ± 0.55	2.08 ± 0.53	2.09 ± 0.62	1.84 ± 0.64	.242

Table 2. Logistic Regression Analysis of Risk Factors for High Peritoneal Transport Characteristics

Variable	Univariate			Multivariate		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	1.017	0.996 to 1.038	.123			
Male	1.151	0.602 to 2.200	.670			
Diabetes	2.232	1.178 to 4.226	.014	1.229	0.485-3.110	0.664
BMI	1.003	0.922 to 1.092	.937			
SBP	1.004	0.991 to 1.018	.530			
DBP	1.011	0.990 to 1.032	.329			
CCI	1.300	1.084 to 1.559	.005	1.233	1.016-1.495	0.034
Hb	0.984	0.963 to 1.004	.116			
Scr	1.000	0.999 to 1.001	.442			
BUN	0.980	0.946 to 1.015	.255			
Alb	0.913	0.855 to 0.975	.006	0.931	0.869-0.998	0.045
Chol	1.053	0.860 to 1.289	.618			
TG	1.225	0.935 to 1.605	.140			
Ca	0.533	0.183 to 1.554	.249			
P	0.783	0.430 to 1.428	.425			
CRP	0.999	0.987 to 1.012	.915			

and 18.8% for serum albumin level above 30 g/L (P = .029) (Figure 1).

Prognosis of Patients with Different Peritoneal Transport Statuses

Kaplan–Meier survival analysis showed that the cumulative survival rate in the high transport group was significantly lower than that in the low transport, low average transport and high average transport groups (P < .001). There was no significant difference in technique failure rate among these four groups (P = .12) (Figure 2).

Analysis of Risk of All-cause Mortality and Technique Failure

In accordance with the univariate Cox regression analysis, age (HR = 1.046, 95% CI: 1.026 to 1.067), diabetes mellitus (HR = 2.708, 95% CI: 1.574 to 4.657), SBP (HR = 1.018, 95% CI: 1.006 to 1.031), CCI (HR = 1.532, 95% CI: 1.333 to 1.760), Chol

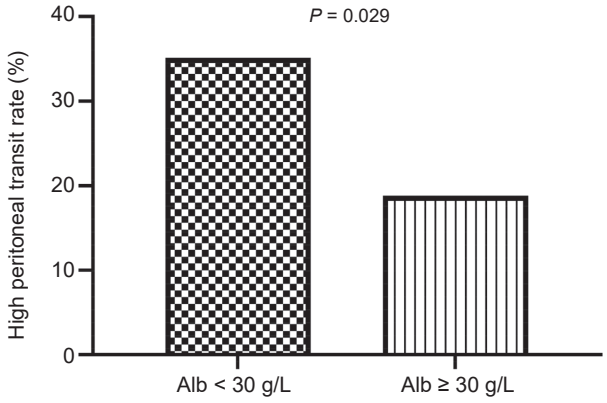

Figure 1. The incidence of developing high peritoneal transport for different albumin levels

(HR = 1.211, 95% CI: 1.043 to 1.405), TG (HR = 1.483, 95% CI: 1.165 to 1.889), CRP (HR = 1.013, 95% CI: 1.003 to 1.022), Kt/V (HR = 0.459, 95% CI: 0.267 to 0.789), and high transport (HR = 3.512, 95% CI: 1.858 to 6.640) were associated with all-cause death in patients undergoing PD. Male sex (HR = 1.827, 95% CI: 1.129 to 2.955), TG (HR = 1.218, 95% CI: 1.041 to 1.424), CRP (HR = 1.011, 95% CI: 1.005 to 1.017), and Kt/V (HR = 0.696, 95% CI 0.445 to 1.087) were related to technique failure in these patients. Subsequently, the above indicators with statistically significant differences were included in multivariate regression analysis. The results revealed that age (HR = 1.039, 95% CI: 1.017 to 1.062), CCI (HR = 1.623, 95% CI: 1.308 to 2.014), CRP (HR = 1.016, 95% CI: 1.005 to 1.027), and high transport (HR = 3.376, 95% CI: 1.595 to 7.145) at baseline were independent risk factors for all-cause death. In addition, male sex (HR = 1.672, 95% CI: 1.018 to 2.746), TG (HR = 1.239, 95% CI: 1.053 to 1.457), and CRP (OR = 1.010, 95% CI: 1.004 to 1.017) were independent risk factors for technique failure (Table 3).

DISCUSSION

PD is an important therapeutic approach for patients with ESKD. Its curative effect depends primarily on peritoneal solute clearance and fluid transport. The baseline peritoneal transport function has an important impact on the prognosis of patients undergoing PD, highlighting the need to determine factors affecting baseline peritoneal transport status. In our study, high CCI score, and low albumin level were decisive factors of high peritoneal transport at baseline, which was consistent with previous reports.[18,19]CCI was proposed by British scholars Charlson *et al.* in 1987. As diseases are not mutually exclusive, diseases of different causes may coexist in a person.[20] Currently, CCI is mainly used in clinical practice to assess the impact of comorbidities other than the underlying disease that is currently the main treatment for a patient's survival in the following 10 years.[21] Although the reason for the higher peritoneal transport status in high CCI score patients remains unclear, it may be related to the higher CCI scores with the worse nutritional status in this population. Moreover, several studies have acknowledged the relationship

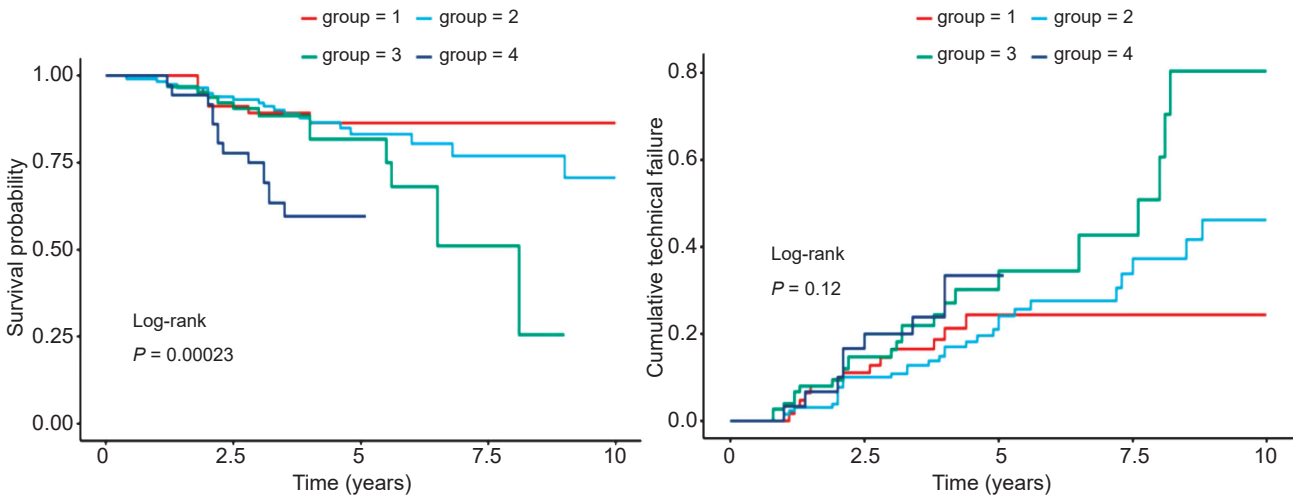

Figure 2. (A) Kaplan–Meier survival analysis of patients with different peritoneal transport characteristics, (B) Kaplan–Meier technique failure analysis of patients with different peritoneal transport characteristics

Table 3. Cox Regression Analysis of the Risk Factors for All-cause Mortality and Technique Failure

Variable	All-cause Mortality						Technique Failure					
	Univariate			Multivariate			Univariate			Multivariate		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Age	1.046	1.026 to 1.067	< .001	1.039	1.017 to 1.062	< .001	0.997	0.981 to 1.013	.715			
Male	1.358	0.781 to 2.361	.278				1.827	1.129 to 2.955	.014	1.672	1.018 to 2.746	.042
Diabetes	2.708	1.574 to 4.657	< .001	0.598	0.289 to 1.236	.165	1.475	0.915 to 2.377	.111			
BMI	0.987	0.915 to 1.066	.748				1.008	0.949 to 1.071	.788			
SBP	1.018	1.006 to 1.031	.003	1.020	1.007 to 1.033	.002	1.004	0.994 to 1.014	.405			
DBP	0.982	0.962 to 1.001	.069				1.003	0.988 to 1.019	.676			
CCI	1.532	1.333 to 1.760	< .001	1.623	1.308 to 2.014	< .001	1.148	0.996 to 1.324	.057			
Hb	1.009	0.993 to 1.026	.276				1.005	0.991 to 1.019	.472			
Scr	0.999	0.998 to 1.000	.079				1.000	1.000 to 1.001	.250			
BUN	0.987	0.958 to 1.016	.375				0.996	0.973 to 1.020	.765			
Alb	0.967	0.914 to 1.023	.246				0.963	0.920 to 1.009	.115			
Chol	1.211	1.043 to 1.405	.012	1.162	0.975 to 1.385	.094	1.177	0.992 to 1.395	.061			
TG	1.483	1.165 to 1.889	.001	1.247	0.897 to 1.732	.189	1.218	1.041 to 1.424	.014	1.239	1.053 to 1.457	.010
Ca	1.840	0.733 to 4.616	.194				1.059	0.499 to 2.247	.882			
P	0.931	0.581 to 1.490	.766				1.405	1.000 to 1.974	.050			
CRP	1.013	1.003 to 1.022	.008	1.016	1.005 to 1.027	.004	1.011	1.005 to 1.017	< .001	1.010	1.004 to 1.017	.001
Kt/V	0.459	0.267 to 0.789	.005	0.875	0.510 to 1.501	.628	0.585	0.375 to 0.913	.018	0.696	0.445 to 1.087	.111
CCr	0.993	0.982 to 1.004	.185				0.993	0.984 to 1.002	.127			
High transport	3.512	1.858 to 6.640	< .001	3.376	1.595 to 7.145	.001	1.516	0.719 to 3.197	.274			

between hypoalbuminaemia and high peritoneal transport status, and the increase in peritoneal protein loss to be the main reason. Previous studies have also reported a negative correlation between pre-dialysis albumin levels and the D/Pcr value, with a stronger correlation after dialysis.[22] In this study, we found that nonhigh peritoneal transport patients with serum albumin levels below 30 g/L were more likely to develop high transport; thus, we should enhance the nutritional status of patients and increase albumin levels, at least to above 30 g/L. However, the specific reasons require further study. Zhang YH *et al.* study found elevated serum albumin levels in patients with peritoneal hyperlipidaemia,[23] which supports the results of the current study.

In several previous studies, it was concluded that patients with high baseline peritoneal transport status have poor prognosis.[24,25] Similarly, in our study, the survival rate was lower in patients with high baseline peritoneal transport status, possibly due to (i) poor ultrafiltration function in patients with high transport status, (ii) excessive fluid load caused by water sodium retention, (iii) increased peritoneal protein loss, (iv) decreased appetite caused by excessive glucose uptake, and/or (v) malnutrition. Currently, it remains disputable whether baseline peritoneal high transport status is a risk factor for all-cause death and technique failure in patients undergoing PD.[26-28] The present study revealed that high peritoneal transport status at baseline is an independent risk factor for all-cause death in patients undergoing PD, yet no significant impact of high peritoneal transport status at baseline on technique failure in patients receiving PD has been observed. The reasons for the above differences may be related to many factors, including differences in PD mode, ethnicity, and distribution of primary diseases.

Our study has two unique strengths. To our knowledge, this study is the first to analyse associations between CCI scores and peritoneal transport status in PD patients. Another strength of this study is its analysis of nonhigh peritoneal transport patients with serum albumin levels below 30 g/L, who had a higher incidence of developing high peritoneal transport than those with serum albumin levels above 30 g/L.

A number of limitations should be considered when interpreting the findings. First, in retrospective studies, it is common to have missing follow-up records or data, resulting in a reduced sample size at the time of enrolment and statistical analysis. Second, owing to the limitations of a retrospective study, D/Pcr was not monitored continuously and regularly. Third, this was a single center retrospective study, and a prospective, multicenter study should be conducted.

CONCLUSION

In summary, high peritoneal transport status at baseline is an independent risk factor for patient survival, and its major determinants are high CCI scores and hypoproteinaemia. Adoption of measures to improve hypoproteinaemia before dialysis may be of great significance to improve the long-term prognosis of patients, i.e., haemodialysis should be implemented with high CCI score. Furthermore, serum albumin levels in PD patients with nonhigh peritoneal transport should be increased to at least 30 g/L.

ABBREVIATIONS

BMI, body mass index; CCI, Charlson's comorbidity index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hb, haemoglobin; Scr, serum creatinine; BUN, blood urea nitrogen; Alb, albumin; Chol, cholesterol; TG, triglyceride; CRP, C-reactive protein; CCr, creatinine clearance rate; and Kt/V, urea clearance index

ETHICAL APPROVAL

The study protocol was approved by the Ethics Committee of Affiliated Drum Tower Hospital, Medical School of Nanjing University (NO.2020-278-01).

CONFLICT OF INETREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data used in the article is obtained from the corresponding author upon reasonable request.

CONSENT FOR PUBLICATION

All authors and funding agency approved the final manuscript publication.

AUTHORS' CONTRIBUTIONS

Miao Zhang designed the research study,Ying Liu performed the research,Qingyan Zhang collected the data and analyzed the data,Yuan Feng supervised the research,Yangyang Xia and Chunming Jiang wrote and revised the manuscript,Yangyang Xia and Chunming Jiang made equal contributions as co first authors in this work.All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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