Plasma fibrinogen as a predictor of residual renal function in patients undergoing peritoneal dialysis

Ling Qi
The First Affiliated Hospital of Wenzhou Medical University
Peipei Huang
The First Affiliated Hospital of Wenzhou Medical University
Xiaoping Wang
The First Affiliated Hospital of Wenzhou Medical University
Shan Zhu
The First Affiliated Hospital of Wenzhou Medical University
Xiaomei Wang
The First Affiliated Hospital of Wenzhou Medical University
Zhen Su (sz_dor@126.com)
The First Affiliated Hospital of Wenzhou Medical University

Research Article

Keywords: Plasma fibrinogen, Inflammation, Peritoneal dialysis, Residual renal function, Anuria

Posted Date: September 27th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-927250/v1

Abstract

Background Inflammatory markers are powerful predictors of prognosis in patients undergoing peritoneal dialysis (PD). Plasma fibrinogen (FIB), an inflammatory marker, is considered an independent predictor of cardiovascular events and mortality in PD patients. However, little is known about the association between FIB and residual renal function (RRF) in PD patients.

Material/Methods: We reviewed the clinical data of patients who started PD between January 2012 and December 2020 at the First Affiliated Hospital of Wenzhou Medical University. This study covered 472 patients in total. Residual renal function (RRF) was determined by a 24-hour urine collection and calculated from the average of creatinine and urea clearance. Clinical and biochemical data at the initiation of peritoneal dialysis was collected as baseline data.

Results: The median follow-up duration was 31.55 (20.43-49.00) months. The RRF reduction rate was significantly greater in patients in the high-fibrinogen group (fibrinogen >4.0 g/L) compared with those in the control group (fibrinogen ≤4.0 g/L; 0.13 ± 0.15 mL/min/month/1.73m2 vs. 0.088 ± 0.10 mL/min/month/1.73m2; p<0.001). Using multiple linear regression analysis and adjusting for other risk factors, high FIB was an independent predictor of rapid RRF decline (P=0.033). The Cox proportional hazard model and the competing risk model revealed that an elevated plasma FIB level (HR=1.219, 95%CI 1.058-1.404; SHR=1.154, 95%CI 1.012-1.317) was independent factors for the progression to anuria.

Conclusions: We demonstrated that a higher plasma fibrinogen level was significantly associated with a higher rate of RRF decline, and hyperfibrinogenemia was an independent risk factor for anuria in PD patients.

Introduction

Peritoneal dialysis is one of the survival treatments for patients with end-stage renal disease (ESRD). Numerous studies have shown that people treated with peritoneal dialysis have a lower risk of RRF loss than those on hemodialysis[1–3]. In uremia patients, RRF is clinically important as it influences the quality of life and mortality [4–6]. Thus, early identification of risk factors for RRF decline is particularly important. Previous research has shown rapid loss of RRF in PD patients is associated with diabetes, peritonitis, high baseline RRF and a high level of proteinuria [2, 7, 8].

Inflammation is a causative factor leading to adverse outcomes in chronic kidney disease (CKD) patients, and also an important indicator for predicting cardiovascular events and mortality in those people[9]. Plasma fibrinogen, as an important indicator of the inflammation-coagulation axis, plays a potent role in the regulation of inflammatory reactions and is accepted as a risk factor for the development of pro-inflammatory states and vascular inflammatory diseases[10]. Hyperfibrinogenemia is common in PD patients. Prior studies have shown that high FIB is associated with cardiovascular events and all-cause mortality in patients among PD[11, 12]. However, the relationship between FIB and renal outcomes in PD

patients is not clear. The aim of this study is to investigate the association between high plasma fibrinogen and RRF loss by reviewing the clinical data of PD patients in the First Affiliated Hospital of Wenzhou Medical University.

Methods

Participants

We enrolled 472 patients who initiated PD therapy at a single PD center of the First Affiliated Hospital of Wenzhou Medical University between January 2012 and June 2020 and were given a peritoneal equilibration test (PET) and dialysis adequacy assessment within 3 months of PD. Eligible patients included those older than 18 years and those who received PD for more than 6 months. We excluded patients who had anuria (24-hour urine volume < 100mL) at baseline, those who had received a kidney transplant or undergone long-term hemodialysis, those with malignant tumors (Fig. 1). The study is approved by the Ethics Committee in Clinical Research of the First Affiliated Hospital of Wenzhou Medical University, and all study procedures are in adherence to the Declaration of Helsinki.

Data Collection

We collected demographic data, including age, body mass index (BMI), underlying cause of ESRD, comorbid conditions, episodes of peritonitis. Laboratory data collected included TC, TG, HDL-C, LDL-C, erythrocytes, leukocytes, hemoglobin, serum albumin, hypersensitive C-reactive protein, plasma fibrinogen, and uric acid, were recorded. We recorded medications such as angiotensin converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), calcium channel blocker (CCB) and diuretics at baseline. The first 24-hour urine was collected within 3 months of initiation of peritoneal dialysis and then every 6 months. Residual renal function (RRF) was calculated as the average of creatinine and urea clearance, and corrected for standard body surface area. Anuria was defined as urine volume less than 100mL twice in a row. All patients were followed until anuria, transfer to hemodialysis (HD), kidney transplantation, death, follow-up loss, or the end of the study on March 1, 2021.

Statistical analysis

Statistical analyses were performed using the SPSS version 26.0. Continuous variables were expressed as mean ± standard deviations or medians (interquartile ranges), and categorical variables were expressed as percentages. The rate of RRF decline was computed by the least squares linear regression formula. According to the normal reference value of plasma fibrinogen (2.0-4.0g/L) in our laboratory, the study population was divided into two groups: the control group (FIB ≤ 4.0g/L) and the high-fibrinogen group (FIB > 4.0g/L). To evaluate the differences between the two groups, the Student t test, Mann-Whitney-U test and Chi-square test were used. A multiple linear regression model was performed to investigate the correlation between the rate of decline in RRF and other variables. A Kaplan-Meier survival

curve was generated for the descriptive analysis of the difference in the cumulative incidence of anuria between the control group and the high-fibrinogen group. A Cox proportional risk model was constructed to determine significant predictors of anuria. Additionally, considering that the occurrence of death, loss of follow-up, transferring to hemodialysis, kidney transplantation and anuria constitute a competitive relationship, we further used Stata statistical analysis software to build a competitive risk model to screen the risk factors for the occurrence of anuria. $P < 0.05$ was considered statistically significant.

Result

Baseline characteristics of the study population

A total of 472 subjects who started PD between January 2012 and June 2020 were examined retrospectively. The mean age of patients was 48.19±12.61 years, and 260 (55.08%) were males. The major cause of ESRD was chronic glomerulonephritis (260,55.1%), hypertensive nephropathy (80,16.9%), diabetic nephropathy (46,9.7%), and polycystic kidney (14,3.0%).

Comparison of the control and high-fibrinogen group at baseline

The study population was divided into two groups according to baseline plasma FIB: Control Group (FIB≤4.0 g/L) and High-fibrinogen Group (FIB>4.0 g/L). The results of comparison between two groups were summarized in Table 1. The patients with higher fibrinogen levels had a higher proportion of males (P<0.001), higher BMI (P□0.001), a higher proportion of patients with diabetes (P<0.001) and CCVd (P=0.003), a higher percentage of patients receiving ACEI/ARB (p=0.032) and diuretics (p=0.013). In laboratory data, serum albumin (P<0.001), serum uric acid (P=0.028), hs-CRP (P<0.001), leukocytes (P<0.001), 24-hour urine protein (P<0.001), TG (P=0.029), TC (P=0.008), HDL-c (P=0.016), LDL-c (P=0.005) were significantly different between two groups. There was no significant difference in the age, proportion of patients with hypertension, rate of peritonitis, diastolic blood pressure (DBP), hemoglobin, erythrocytes, baseline RRF and use of CCB between the control and high-fibrinogen group.

Table 1□Comparison of baseline clinical data between the two groups

Variables	The rate of decline of residual renal function			P values
	Total (n=472)	Control Group (n=204)	Hyperfibrinogenemia Group (n=268)	
Age (years)	48.19±12.61	46.94±12.62	49.14±12.55	0.060
Gender (male)	260(55.1%)	91(44.6%)	169(63.1%)	**0.001**
Body mass index (Kg/m^2)	21.11±3.01	20.15±2.55	21.83±3.12	**0.001**
Major causes of ESRD				
Glomerulonephritis	260(55.1%)	113(55.4%)	147(54.9%)	
Diabetic nephropathy	46(9.7%)	6(2.9%)	40(14.9%)	
Hypertensive nephropathy	80(16.9%)	33(16.2%)	47(17.5%)	
Polycystic kidney disease	14(3.0%)	8(3.9%)	6(2.2%)	
Others	72(15.3%)	44(21.6%)	28(10.4%)	
Major comorbid conditions				
Diabetes	87(18.4%)	16(7.8%)	71(26.5%)	**0.001**
Hypertension	429(90.9%)	180(88.2%)	249(92.9%)	0.080
CCVd	33(7.0%)	6(2.9%)	27(10.1%)	**0.003**
Peritonitis rate (/year)	0.46±0.27	0.46±0.24	0.46±0.29	0.488
SBP (mmHg)	147.22±18.84	144.63±18.64	149.20±18.79	**0.009**
DBP (mmHg)	85.87±12.39	86.08±12.32	85.71±12.46	0.743
Laboratory data				
Hemoglobin (g/L)	83.36±18.02	84.25±18.73	82.67±17.47	0.345
Cholesterol (mmol/L)	4.54±1.16	4.40±1.02	4.64±1.24	**0.029**
Triglycerides (mmol/L)	1.49(1.10-1.96)	1.37(1.02-1.81)	1.54(1.16-2.03)	**0.008**
HDL-C (mmol/L)	1.03±0.32	1.07±0.32	1.00±0.33	**0.016**
LDL-C (mmol/L)	2.52±0.82	2.41±0.69	2.61±0.89	**0.005**
Serum albumin (g/L)	36.76±6.55	38.07±6.20	35.77±6.65	**0.001**
Serum uric acid (umol/L)	495.24±129.11	495.43±127.36	495.09±130.67	**0.028**
Hs-CRP (mg/L)	3.23(1.95-6.15)	3.02(1.57-3.92)	4.24(3.02-8.25)	**0.001**

Leukocytes (X10^9/L)	6.48±2.10	5.91±1.65	6.90±2.29	**0.001**
Erythrocytes (X10^12/L)	2.85±0.65	2.86±0.67	2.84±0.63	0.748
24h urine protein (g/24h)	2.13(1.29-3.57)	1.71(1.07-2.72)	2.64(1.56-4.10)	**0.001**
Baseline RRF (mL/min/1.73m²)	4.05±2.53	4.00±2.51	4.09±2.55	0.704
Medications				
ACEI/ARB	214(45.3%)	81(39.7%)	133(49.6%)	**0.032**
CCB	402(85.2%)	174((85.3%)	228(85.1%)	0.947
Diuretics	216(45.8%)	80(39.2%)	136(50.7%)	**0.013**

Values are presented as mean ±SD, number (%), or median (25th, 75th percentile); ESRD, end stage of renal disease; CCVD, cardiovascular and cerebrovascular disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; Hs-CRP, high sensitive C-creative protein; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker;

Independent prognostic factors of the rate of RRF decline

As shown in Table 2, in simple regression analysis, the proportion of males, BMI, the proportion of patients with diabetes and hypertension, the percentage of patients receiving CCB, hemoglobin, TC, baseline RRF, proteinuria, FIB, hs-CRP, leukocytes, erythrocytes were positively correlated with the rate of RRF decline. While there was no significant correlation between the rate of RRF decline and other variables, including age, the proportion of patients with CCVd, systolic blood pressure, diastolic blood pressure, incidence of peritonitis, TG, HDL-c, LDL-c, serum albumin, uric acid, the use of ACEI/ARB and diuretics. Furthermore, multiple linear regression analysis revealed that high baseline RRF ($P<0.001$), high proteinuria ($P<0.001$) and high FIB levels ($P=0.033$) were independent risk factors for the rate of RRF decline. Fit evaluation indicated that the overall model was significant ($P < 0.001$, adjusted $R^2 = 0.369$).

Table 2 Independent associated factors of the Rate of decline of residual renal function in a multiple linear regression model

Variables	Univariate analyses		Multivariate analyses	
	β（SE）	P value	β（SE）	P value
Gender (male)	0.074（0.012）	**<0.001**		
Body mass index (Kg/㎡)	0.013（0.002）	**<0.001**		
Diabetes	0.066（0.015）	**<0.001**		
Hypertension	0.062(0.021)	**0.003**		
Hemoglobin (g/L)	0.001（0.001）	**<0.001**		
Triglycerides (mmol/L)	0.019 (0.007)	**0.006**		
Hs-CRP (mg/L)	0.006（0.001）	**<0.001**		
FIB (g/L)	0.028（0.005）	**<0.001**	0.011（0.005）	**0.033**
Leukocytes (X10^9/L)	0.009（0.003）	**0.001**		
Erythrocytes (X10^12/L)	0.041（0.009）	**<0.001**		
24-Hour urine protein (g/24h)	0.018（0.002）	**<0.001**	0.012（0.002）	**<0.001**
Baseline RRF (mL/min/1.73m²)	0.027（0.002）	**<0.001**	0.023（0.002）	**<0.001**
CCB	0.043（0.017）	**0.010**		

SE, standard error; Hs-CRP, high sensitive C-creative protein; FIB, fibrinogen; RRF, residual renal function; CCB, calcium channel blocker;

Progression to anuria

At the median of 31.55 (20.43-49.00) months of follow-up, 205 patients (43.4%) progressed to anuria. Another 2 patients (0.4%) died before the development of anuria. During the same period, 34 patients (7.2%) were converted to long-term hemodialysis, 45 patients (9.5%) underwent kidney transplantation, and 25 patients (5.3%) were lost to follow-up after a median follow-up of 25.60 (15.40-39.10) months. Kaplan-Meier survival curve analysis demonstrated that the cumulative occurrence of anuria in the high-fibrinogen group is significantly higher than in the control group (P<0.001) (Figure 2).

Independent risk factors of progression to anuria

Univariate Cox analysis for the risk of progressing to anuria was summarized in Table 3. Male gender, BMI, diabetes, hypertension, cardiovascular and cerebrovascular disease, peritonitis, systolic blood pressure (SBP), hemoglobin, serum albumin, hs-CRP, FIB, leukocytes, erythrocytes, 24-hour urine protein, baseline RRF and the use of ACEI/ARB, CCB were associated with the risk of developing anuria. In contrast, age, TG, TC, HDL-c, LDL-c, serum uric acid, and the use of diuretics did not show an association with the development of anuria.

A Cox proportional hazard model was also constructed to determine the independent predictors of progression to anuria. In this model, male gender, high FIB, high proteinuria, and the presence of hypertension were independent predictors of anuria, while a higher baseline RRF was protective (Table 3).

Then, we treated the occurrence of transferring to hemodialysis, kidney transplantation, death, loss of follow-up as the competing event of the development of anuria, and established a competitive risk model to reveal the risk factors for the occurrence of anuria. The results indicated that the independent risk predictors for anuria were higher FIB, higher proteinuria, and the presence of hypertension, while a higher baseline RRF was protective (Table 4).

Table 3 Independent risk factors of anuria in PD patients (Cox regression analysis)

Variables	Univariate analyses			Multivariate analyses		
	Adjusted HR	95% CI	P values	Adjusted HR	95% CI	P values
Gender (male)	1.336	1.013-1.763	**0.040**	1.464	1.071-2.001	**0.017**
Body mass index (Kg/□)	1.064	1.017-1.113	**0.007**			
Diabetic	1.563	1.123-2.174	**0.008**			
Hypertension	2.850	1.549-5.244	**0.001**	2.260	1.113-4.589	**0.024**
CCVd	1.700	1.015-2.847	**0.044**			
Peritonitis rate (/year)	1.932	1.165-3.204	**0.011**			
SBP (mmHg)	1.010	1.003-1.018	**0.006**			
Hemoglobin (g/L)	0.992	0.984-1.000	**0.044**			
Serum albumin (g/L)	0.947	0.925-0.969	**□0.001**			
hs-CRP (mg/L)	1.036	1.009-1.063	**0.008**			
FIB (g/L)	1.361	1.231-1.505	**□0.001**	1.219	1.058-1.404	**0.006**
Leukocytes (X10^9/L)	1.073	1.010-1.139	**0.022**			
Erythrocytes (X10^12/L)	0.800	0.643-0.994	**0.044**			
24-Hour urine protein (g/24h)	1.177	1.121-1.237	**□0.001**	1.102	1.032-1.178	**0.004**
Baseline RRF (mL/min/1.73m²)	0.916	0.861-0.975	**0.006**	0.851	0.790-0.917	**<0.001**
ACEI/ARB	1.340	1.016-1.767	**0.038**			
CCB	1.908	1.234-2.951	**0.004**			

CCVd, cardiovascular and cerebrovascular disease; SBP, systolic blood pressure; Hs-CRP, high sensitive C-creative protein; FIB, fibrinogen; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker;

Table 4　Independent risk factors of anuria in PD patients (Competitive risk model)

Variables	Univariate analyses			Multivariate analyses		
	SHR	95% CI	P values	SHR	95% CI	P values
Diabetic	1.400	1.021-1.918	**0.037**			
Hypertension	2.213	1.287-3.806	**0.004**	1.966	1.041-3.713	**0.037**
Peritonitis rate (/year)	1.798	1.095-2.954	**0.021**			
Serum albumin (g/L)	0.963	0.941-0.987	**0.002**			
hs-CRP (mg/L)	1.030	1.002-1.059	**0.035**			
FIB (g/L)	1.243	1.114-1.386	**0.001**	1.154	1.012-1.317	**0.032**
Erythrocytes (X10^12/L)	0.781	0.629-0.971	**0.026**			
24-Hour urine protein (g/24h)	1.121	1.055-1.192	**0.001**	1.102	1.028-1.182	**0.006**
Baseline RRF (mL/min/1.73m²)	0.920	0.861-0.983	**0.013**	0.898	0.834-0.967	**0.004**
CCB	1.530	1.026-2.283	**0.037**			

Hs-CRP, high sensitive C-creative protein; FIB, fibrinogen; RRF, residual renal function; CCB, calcium channel blocker;

Discussion

Protecting residual renal function has always been an important goal in the management of dialysis patients. A large body of evidence underlines that the reserving of RRF is closely related to the prognosis of dialysis patients, which can not only maintain fluid, electrolyte, and acid-base balance, remove small molecule, medium molecule and protein-binding toxoid, but also play an important role in nutrition maintenance and blood pressure control[4]. In a CANUSA study on PD, an increase of 5L/wk/1.73m^2 in

GFR was associated with a 12% decrease in the risk ratio of death. And for each increase of 250mL of urine per day, there was a 36% reduction in the risk ratio of death[13]. Therefore, early identification of risk factors for the decline of RRF and intervention may be of great help to the post-dialysis management of PD patients.

In our study, we analyzed the risk factors for RRF loss in PD patients. The results showed that high proteinuria and high baseline RRF were the risk factors for the rapid decrease of RRF. Meanwhile, proteinuria and hypertension were independent risk factors for the development of anuria, while high baseline RRF was protective, which was consistent with the results of Szeto et al[7]. In addition, 268 cases (56.8%) of this study population developed hyperfibrinogenemia at baseline. Our further study showed that an elevated plasma fibrinogen level was an independent risk factor for the rate of RRF decline and the progression to anuria. There has previously been no report on the relationship between FIB and renal outcome in PD patients; this study is the first to do so.

Inflammation and oxidative stress are the potent pathophysiological changes in the occurrence and the development of kidney disease. Prior studies have shown that cytokines and other inflammatory mediators can activate the clotting system [14, 15]. Elevated plasma FIB levels in CKD patients suggest an inflammatory state[10]. In this study, hs-CRP and leukocytes in the high-fibrinogen group were significantly higher than those in the control group, and the serum albumin was significantly lower. All of these indicated that there was a microinflammatory state in PD patients when plasma FIB was elevated.

Fibrinogen is a soluble glycoprotein synthesized and secreted in the liver that has been identified as a key regulator of atherosclerosis, inflammation, and thrombosis[16, 17]. It is considered to be a typical marker of acute phase inflammation. During acute inflammatory injury, the synthesis of acute-phase proteins in the liver increased significantly, leading to an increase in plasma fibrinogen levels[18, 19]. However, plasma FIB levels have also been elevated slightly in chronic inflammatory diseases such as Alzheimer's disease, cancer, and renal fibrosis[20, 21]. Goldwasser P et al. have confirmed that the plasma FIB levels tend to be higher in PD patients than in hemodialysis patients, with a difference of about 100mg/dL[22].

As a surrogate of systemic inflammation, fibrinogen promotes the synthesis of pro-inflammatory cytokines such as interleukin-1, interleukin-6 and tumor factor-α, thereby promoting the occurrence and development of inflammation. It can bind to multiple integrin receptors expressed in inflammatory cells, such as CD11b/CD18, and activate inflammatory regulatory signaling pathways such as mitogen-activated protein kinase (MAPK) and nuclear factor-κB (NF-κB), to promote the increase of inflammatory cytokines in local tissues such as TNF-α and IL-1β [23–26]. The fibrinogen-derived peptides released by the hydrolysis of fibrinogen, such as fibrinogen-derived peptide B, act as chemokines for leukocytes, to regulate the inflammatory reaction independently [27]. These inflammatory pathways have been proven to be key mediators of renal microinflammation and renal fibrosis.

In addition, Sörensen et al. suggested that FIB deficiency provided significant protection from tubule-interstitial damage. FIB deposited in the renal interstitial region, promotes renal fibroblast proliferation,

tubular atrophy, and renal interstitial cell expansion by binding to Toll-like receptors 2, 4 (TLR2, TLR4) and intercellular adhesion molecule 1 (CAM-1), resulting in renal fibrosis[28]. At the same time, STAT3 activated by IL-6 can bind to the FIB chain promoters, and the upregulation of FIB triggers the expression and proliferation of TGF-β1. TGF-β1 induces renal fibrosis by activating both classical (SMAD-based) and non-classical (non-Smad-based) signaling pathways, resulting in activation of myofibroblasts, overaccumulation of ECM, and inhibition of ECM degradation.[29] Drew et al. found that glomeruli in the control group developed severe disease including fibrin deposits, inflammatory cell accumulation, and crescent formation, and fibrinogen-deficient mice developed significantly milder disease when anti-glomerular basement membrane nephritis was induced in fibrinogen-deficient and control mice[30].

Several clinical studies have demonstrated that an elevated plasma FIB level is associated with adverse renal outcomes in pre-dialysis patients [31–34], and FIB is a risk factor for cardiovascular events and all-cause mortality in patients with CKD 3–4 stage and ESRD[11, 35, 36]. The Chronic Renal Insufficiency Cohort (CRIC) Study, which investigated a variety of inflammatory factors, such as interleukin-1 (IL-1), IL-1 receptor antagonist, IL-6, tumor necrosis factor-α, transforming growth factor-β, high-sensitivity C-reactive protein, and fibrinogen, showed that elevated plasma fibrinogen levels are associated with a rapid loss of renal function[37]. Similarly, we also found that RRF loss more rapidly in PD patients with high baseline plasma fibrinogen (Pearson correlation coefficient of 0.27, $P < 0.001$).

In this study, we propose a new indicator for predicting RRF loss in patients undergoing peritoneal dialysis. We find that plasma fibrinogen is still a risk factor affecting the rate of RRF decline and accelerating the occurrence of anuria, even in dialysis patients with very low residual renal function. This is closely related to the role of fibrinogen in renal inflammation, fibrosis and other aspects.

This study has certain limitations. First, it was a single-center retrospective observation study and may have inherent biases. Second, all parameters in the study were collected at baseline. Third, some confounding factors may not have been completely eliminated.

In conclusion, an elevated plasma fibrinogen level is associated with poor renal outcomes in patients on peritoneal dialysis. Patients with hyperfibrinogenemia may benefit from aggressive treatment to postpone RRF decreases.

Declarations

Acknowledgements

The authors would like to thank their colleagues in the Department of Nephrology at The First Affiliated Hospital of Wenzhou Medical University for their invaluable support and selfless help during this study.

Author contributions

Z.S., Q.L. and H.P.P was involved in the study's formulation, design, data acquisition and analysis, and the drafting of the manuscript. W.X.P, Z.S. and W.X.M. help with data analysis. Z.S. funded and oversaw the study. The final manuscript was read and approved by all authors.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Ethical approval

Ethical approval for this study was obtained from Ethics Committee in Clinical Research of the First Affiliated Hospital of Wenzhou Medical University.

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: Health Science and technology plan of Zhejiang Province（2021KY203）; the National Natural Science Foundation of China (81671403、30871179).

Informed consent

Written informed consent was obtained from all subjects before the study.

References

1. Horinek A and Misra M. Does residual renal function decline more rapidly in hemodialysis than in peritoneal dialysis? How good is the evidence? *Adv Perit Dial* 2004; 20: 137-140. 2004/09/24.

2. Jansen MA, Hart AA, Korevaar JC, et al. Predictors of the rate of decline of residual renal function in incident dialysis patients. *Kidney Int* 2002; 62: 1046-1053. 2002/08/08. DOI: 10.1046/j.1523-1755.2002.00505.x.

3. Moist LM, Port FK, Orzol SM, et al. Predictors of loss of residual renal function among new dialysis patients. *J Am Soc Nephrol* 2000; 11: 556-564. 2000/03/07. DOI: 10.1681/asn.V113556.

4. Wang AY and Lai KN. The importance of residual renal function in dialysis patients. *Kidney Int* 2006; 69: 1726-1732. 2006/04/14. DOI: 10.1038/sj.ki.5000382.

5. Shemin D, Bostom AG, Lambert C, et al. Residual renal function in a large cohort of peritoneal dialysis patients: change over time, impact on mortality and nutrition. *Perit Dial Int* 2000; 20: 439-444. 2000/09/28.

6. Brener ZZ, Kotanko P, Thijssen S, et al. Clinical benefit of preserving residual renal function in dialysis patients: an update for clinicians. *Am J Med Sci* 2010; 339: 453-456. 2010/04/09. DOI: 10.1097/MAJ.0b013e3181cf7d5b.

7. Szeto CC, Kwan BC, Chow KM, et al. Predictors of residual renal function decline in patients undergoing continuous ambulatory peritoneal dialysis. *Perit Dial Int* 2015; 35: 180-188. 2014/02/06. DOI: 10.3747/pdi.2013.00075.

8. Johnson DW, Mudge DW, Sturtevant JM, et al. Predictors of decline of residual renal function in new peritoneal dialysis patients. *Perit Dial Int* 2003; 23: 276-283. 2003/08/27.

9. Silverstein DM. Inflammation in chronic kidney disease: role in the progression of renal and cardiovascular disease. *Pediatr Nephrol* 2009; 24: 1445-1452. 2008/12/17. DOI: 10.1007/s00467-008-1046-0.

10. Davalos D and Akassoglou K. Fibrinogen as a key regulator of inflammation in disease. *Semin Immunopathol* 2012; 34: 43-62. 2011/11/01. DOI: 10.1007/s00281-011-0290-8.

11. Yu J, Lin T, Huang N, et al. Plasma fibrinogen and mortality in patients undergoing peritoneal dialysis: a prospective cohort study. *BMC Nephrol* 2020; 21: 349. 2020/08/19. DOI: 10.1186/s12882-020-01984-6.

12. Irish A. Cardiovascular disease, fibrinogen and the acute phase response: associations with lipids and blood pressure in patients with chronic renal disease. *Atherosclerosis* 1998; 137: 133-139. 1998/05/06. DOI: 10.1016/s0021-9150(97)00273-6.

13. Bargman JM, Thorpe KE and Churchill DN. Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. *J Am Soc Nephrol* 2001; 12: 2158-2162. 2001/09/20. DOI: 10.1681/asn.V12102158.

14. Skeppholm M, Wallén NH, Mobarrez F, et al. Inflammation and thrombin generation cause increased thrombin activatable fibrinolysis inhibitor levels in experimental human endotoxemia. *Blood Coagul Fibrinolysis* 2009; 20: 611-613. 2010/06/04. DOI: 10.1097/MBC.0b013e32833161c5.

15. Levi M and van der Poll T. Inflammation and coagulation. *Crit Care Med* 2010; 38: S26-34. 2010/01/30. DOI: 10.1097/CCM.0b013e3181c98d21.

16. Kaptoge S, White IR, Thompson SG, et al. Associations of plasma fibrinogen levels with established cardiovascular disease risk factors, inflammatory markers, and other characteristics: individual participant meta-analysis of 154,211 adults in 31 prospective studies: the fibrinogen studies collaboration. *Am J Epidemiol* 2007; 166: 867-879. 2007/09/06. DOI: 10.1093/aje/kwm191.

17. Weisel JW. Fibrinogen and fibrin. *Adv Protein Chem* 2005; 70: 247-299. 2005/04/20. DOI: 10.1016/s0065-3233(05)70008-5.

18. Castell JV, Gómez-Lechón MJ, David M, et al. Acute-phase response of human hepatocytes: regulation of acute-phase protein synthesis by interleukin-6. *Hepatology* 1990; 12: 1179-1186. 1990/11/01. DOI: 10.1002/hep.1840120517.

19. Castell JV, Gómez-Lechón MJ, David M, et al. Interleukin-6 is the major regulator of acute phase protein synthesis in adult human hepatocytes. *FEBS Lett* 1989; 242: 237-239. 1989/01/02. DOI: 10.1016/0014-5793(89)80476-4.

20. van Oijen M, Witteman JC, Hofman A, et al. Fibrinogen is associated with an increased risk of Alzheimer disease and vascular dementia. *Stroke* 2005; 36: 2637-2641. 2005/11/05. DOI: 10.1161/01.Str.0000189721.31432.26.

21. Kołodziejczyk J and Ponczek MB. The role of fibrinogen, fibrin and fibrin(ogen) degradation products (FDPs) in tumor progression. *Contemp Oncol (Pozn)* 2013; 17: 113-119. 2013/06/22. DOI: 10.5114/wo.2013.34611.

22. Goldwasser P, Feldman JG, Emiru M, et al. Effect of dialysis modality on plasma fibrinogen concentration: a meta-analysis. *Am J Kidney Dis* 2004; 44: 941-949. 2004/11/24. DOI: 10.1053/j.ajkd.2004.08.019.

23. Solovjov DA, Pluskota E and Plow EF. Distinct roles for the alpha and beta subunits in the functions of integrin alphaMbeta2. *J Biol Chem* 2005; 280: 1336-1345. 2004/10/16. DOI: 10.1074/jbc.M406968200.

24. Fan ST and Edgington TS. Integrin regulation of leukocyte inflammatory functions. CD11b/CD18 enhancement of the tumor necrosis factor-alpha responses of monocytes. *J Immunol* 1993; 150: 2972-2980. 1993/04/01.

25. Perez RL and Roman J. Fibrin enhances the expression of IL-1 beta by human peripheral blood mononuclear cells. Implications in pulmonary inflammation. *J Immunol* 1995; 154: 1879-1887. 1995/02/15.

26. Perez RL, Ritzenthaler JD and Roman J. Transcriptional regulation of the interleukin-1beta promoter via fibrinogen engagement of the CD18 integrin receptor. *Am J Respir Cell Mol Biol* 1999; 20: 1059-1066. 1999/05/05. DOI: 10.1165/ajrcmb.20.5.3281.

27. Skogen WF, Senior RM, Griffin GL, et al. Fibrinogen-derived peptide B beta 1-42 is a multidomained neutrophil chemoattractant. *Blood* 1988; 71: 1475-1479. 1988/05/01.

28. Sörensen I, Susnik N, Inhester T, et al. Fibrinogen, acting as a mitogen for tubulointerstitial fibroblasts, promotes renal fibrosis. *Kidney Int* 2011; 80: 1035-1044. 2011/07/08. DOI: 10.1038/ki.2011.214.

29. Craciun FL, Ajay AK, Hoffmann D, et al. Pharmacological and genetic depletion of fibrinogen protects from kidney fibrosis. *Am J Physiol Renal Physiol* 2014; 307: F471-484. 2014/07/11. DOI: 10.1152/ajprenal.00189.2014.

30. Drew AF, Tucker HL, Liu H, et al. Crescentic glomerulonephritis is diminished in fibrinogen-deficient mice. *Am J Physiol Renal Physiol* 2001; 281: F1157-1163. 2001/11/13. DOI: 10.1152/ajprenal.2001.281.6.F1157.

31. Muslimovic A, Rasic S, Tulumovic D, et al. Inflammatory Markers and Procoagulants in Chronic Renal Disease Stages 1-4. *Med Arch* 2015; 69: 307-310. 2015/12/02. DOI: 10.5455/medarh.2015.69.307-310.

32. Shlipak MG, Fried LF, Crump C, et al. Elevations of inflammatory and procoagulant biomarkers in elderly persons with renal insufficiency. *Circulation* 2003; 107: 87-92. 2003/01/08. DOI: 10.1161/01.cir.0000042700.48769.59.

33. Hiramoto JS, Katz R, Peralta CA, et al. Inflammation and coagulation markers and kidney function decline: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Kidney Dis* 2012; 60: 225-232. 2012/05/09. DOI: 10.1053/j.ajkd.2012.02.335.

34. Gupta J, Mitra N, Kanetsky PA, et al. Association between albuminuria, kidney function, and inflammatory biomarker profile in CKD in CRIC. *Clin J Am Soc Nephrol* 2012; 7: 1938-1946. 2012/10/02. DOI: 10.2215/cjn.03500412.

35. Goicoechea M, de Vinuesa SG, Gómez-Campderá F, et al. Serum fibrinogen levels are an independent predictor of mortality in patients with chronic kidney disease (CKD) stages 3 and 4. *Kidney Int Suppl* 2008: S67-70. 2008/11/27. DOI: 10.1038/ki.2008.519.

36. Zoccali C, Mallamaci F, Tripepi G, et al. Fibrinogen, mortality and incident cardiovascular complications in end-stage renal failure. *J Intern Med* 2003; 254: 132-139. 2003/07/16. DOI: 10.1046/j.1365-2796.2003.01180.x.

37. Amdur RL, Feldman HI, Gupta J, et al. Inflammation and Progression of CKD: The CRIC Study. *Clin J Am Soc Nephrol* 2016; 11: 1546-1556. 2016/06/25. DOI: 10.2215/cjn.13121215.

Figures

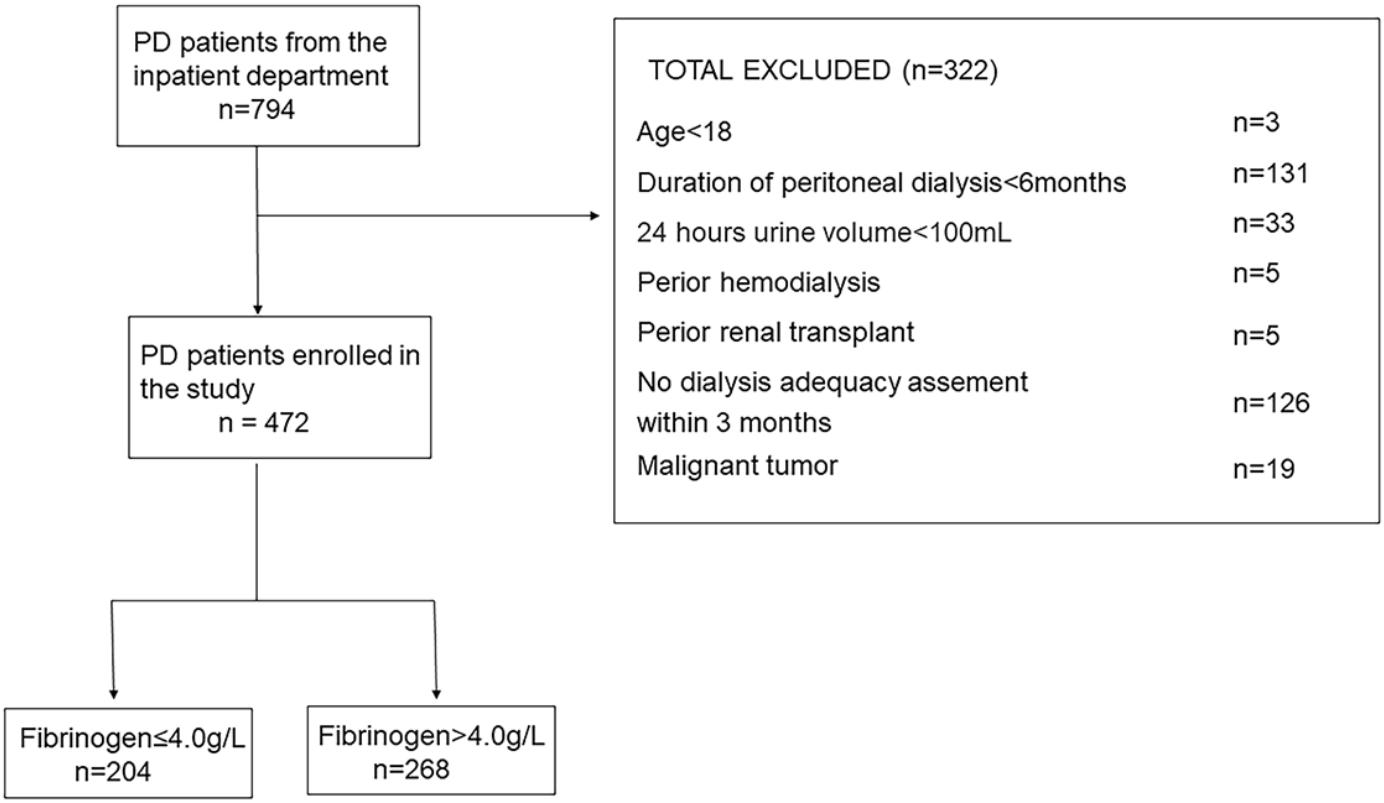

Figure 1

Flow chart for the inclusion of patients in the present study.

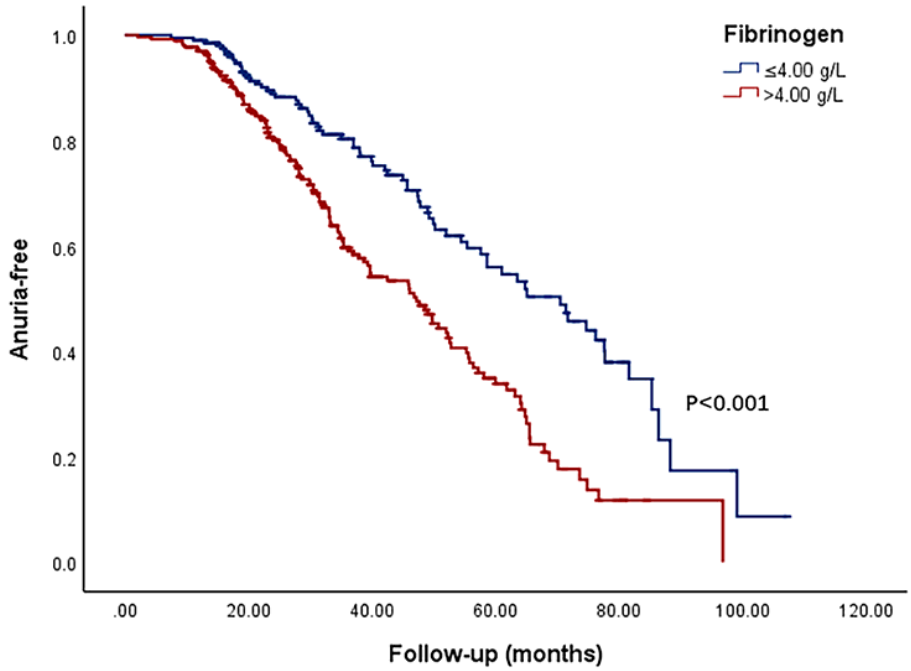

Figure 2

Kaplan Meier plot of the risk of developing anuria.