Kidney Medicine

Early Anuria in Incident Peritoneal Dialysis Patients: Incidence, Risk Factors, and Associated Clinical Outcomes

Shiyan Tu, Hongjian Ye,* Yangyang Xin, Yuan Peng, Ruihua Liu, Jing Guo, Chunyan Yi, Haiping Mao, and Xiao Yang*

Rationale & Objective: The development of anuria has been linked to worse clinical outcomes in patients undergoing peritoneal dialysis (PD). Our objective was to investigate the incidence, risk factors, and associated clinical outcomes of anuria within the first year after starting PD.

Study Design: Retrospective cohort study.

Setting & Participants: Patients who started continuous ambulatory peritoneal dialysis at our center between 2006 and 2020 were included and followed up until January 31, 2023.

Exposure: Age, sex, diabetes, temporary hemodialysis, angiotensin-converting enzyme inhibitors (ACEis) or angiotensin II receptor blockers (ARBs), diuretics, baseline urine volume, serum albumin, daily glucose exposure, peritonitis, and incremental PD.

Outcomes: The primary outcome was early anuria, defined as 24-hour urine volume ≤100 mL within the first year of PD initiation. Secondary outcomes included all-cause mortality, cardiovascular disease mortality, technique failure, and peritonitis.

Analytical Approach: Cox proportional hazards model.

Results: A total of 2,592 patients undergoing continuous ambulatory peritoneal dialysis aged 46.7 ± 14.9 years were recruited. Among them, 58.9% were male, and 24.0% had diabetes. Within the first year of PD therapy, 159 (6.13%) patients developed anuria, with a median duration of 7.53 (interquartile range, 3.93-10.0) months. Higher baseline urine volume (hazard ratio [HR], 0.93; 95% confidence interval [CI], 0.90-0.97), higher serum albumin (HR, 0.92; 95% CI, 0.88-0.95), having diabetes before PD (HR, 0.57; 95% CI, 0.35-0.92), and prescribed incremental PD (HR, 0.27; 95% CI, 0.14-0.51) were associated with a reduced risk for early anuria, whereas a higher level of daily glucose exposure (HR, 1.01; 95% CI, 1.00-1.01) was identified as a risk factor for early anuria. Subgroup analyses showed that using ACEis or ARBs was linked to a lower risk of early anuria (HR, 0.25; 95% CI, 0.09-0.69) in diabetic patients. Treating early anuria as a time-dependent covariate, early anuria was associated with a higher risk for all-cause mortality (HR, 1.69; 95% CI, 1.23-2.32) and technique failure (HR, 1.43; 95% CI, 1.00-2.04) after adjusting for confounding factors.

Limitations: Single-center and observational study.

Conclusions: Among PD patients at a single center in China, early anuria was relatively uncommon but associated with an increased risk of mortality and PD technique failure. Incremental PD, higher baseline urine output and serum albumin, and lower daily glucose exposure were associated with a lower risk of early anuria. Clinical trials are needed to evaluate the optimal PD techniques to preserve residual kidney function and maximaze outcomes.

Complete author and article information provided before references.

Correspondence to X. Yang (yxiao@mail.sysu.edu.cn)

**ST and HY contributed equally to this work.*

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The incidence of peritoneal dialysis (PD) has been increasing annually worldwide due to its ease of operation, convenience, and cost-effectiveness for individuals with chronic kidney failure.[1] In recent years, studies have found that compared with hemodialysis (HD), PD can better maintain patients' residual kidney function (RKF) and improve their clinical outcomes.[2,3] The associations between the reduction of RKF and increased mortality,[4,5] deteriorated overhydration,[6] decreased quality of life,[7,8] and increased rate of peritonitis[9] in patients who undergo PD have well been documented. The acceleration of RKF decline was associated with a higher risk for the increase in all-cause mortality among patients receiving PD.[5,10-12] Therefore, preserving RKF is of paramount importance for patients undergoing dialysis therapy.

The glomerular filtration rate (GFR) and residual urine volume were usually used to evaluate RKF in dialysis patients.[13] It has been reported that 55% of the variance in GFR can be attributed to daily urine volume.[13] A study has revealed that a 250-mL increase in urine volume per day was associated with a decreased risk of death in patients undergoing PD.[14] Additional research revealed that the assessment of prognosis in patients receiving dialysis can be better achieved by daily urine production, rather than relying on GFR determined by collecting urine for 24 hours and estimated GFR (eGFR) calculated using serum urea and creatinine concentrations.[15] Additionally, maintaining urine volume levels has been linked to a decreased likelihood of experiencing overhydration and the incidence of acute ischemic stroke.[16,17] According to the International Society for Peritoneal Dialysis practice

PLAIN-LANGUAGE SUMMARY

The development of anuria has been linked to worse clinical outcomes in patients undergoing peritoneal dialysis (PD). However, does the development of early anuria, which is defined as 24-hour urine volume ≤100 mL, within the first year after PD initiation influence the clinical outcomes of these patients? What are the predictors of early anuria? We conducted a single-center retrospective cohort study and found lower baseline urine volume, lower serum albumin, full-dose PD start, absence of diabetes mellitus, higher daily glucose exposure, and in patients with diabetes mellitus, non-use of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers were associated with early anuria. Early anuria was related to a higher risk for all-cause mortality and technique failure. The results provide information for optimizing patient care and improving the prognosis of patients undergoing PD.

guidelines, it is important for all patients undergoing PD to be conscious of their remaining urine volume and make efforts to maintain it for as long as possible.[18]

Previous studies have primarily focused on the clinical outcomes and predictive factors of patients undergoing PD with a total absence of urine output.[19-21] However, few studies have evaluated patients who develop anuria in the first year after PD therapy initiation. Optimizing patient care and improving prognosis requires a comprehensive understanding of the factors linked to early anuria in patients undergoing PD. The objective of our study was to examine the occurrence, associated factors, and clinical outcomes of early anuria among patients receiving PD.

METHODS

Study Population

This was a retrospective cohort study conducted at the First Affiliated Hospital of Sun Yat-sen University. The study protocol adhered to the ethical principles of the Helsinki Declaration and received approval from the Ethics Committee of The First Affiliated Hospital of Sun Yat-sen University (Grant no. [2016]215). The need for informed consent was waived due to the retrospective nature of the study and use of de-identified information. Patients starting continuous ambulatory PD from January 1, 2006, to December 31, 2020, were recruited. The exclusion criteria consisted of the following: (1) individuals aged <18 years when initiating PD treatment; (2) individuals who had undergone long-term HD or kidney transplantation before catheter insertion for PD; (3) individuals with a PD experience <3 months; (4) individuals with a baseline 24-hour urine volume ≤100 mL; and (5) individuals with incomplete urine volume data. Eligible patients were divided into 2 categories based on whether they developed anuria within 1 year of starting PD treatment and were followed up until January 31, 2023. Usually, the follow-up interval of our center is 1-3 months. Data from patients who transferred to HD, received kidney transplantation, or were lost to follow-up before January 31, 2023, were censored.

Data Collection

Baseline demographics including age, sex, primary kidney disease, history of type 2 diabetes mellitus (T2DM), and body mass index (18.5-23.9 kg/m^2 was considered as normal) during the first 1-3 months of PD therapy were collected. Clinical information was recorded, including baseline urine volume, ultrafiltration, daily glucose exposure, incremental PD, episodes of peritonitis, and medications, including the usage of diuretics, angiotensin-converting enzyme inhibitors (ACEis) or angiotensin II receptor blockers (ARBs), and β-blockers. Laboratory data, such as hemoglobin, serum albumin, serum sodium, serum potassium, blood glucose, serum calcium (uncorrected for albumin), serum phosphorus, serum urea, serum creatinine, serum uric acid, intact parathyroid hormone, total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were recorded. The eGFR (mL/min/1.73 m^2) was evaluated using the Chronic Kidney Disease Epidemiology Collaboration equation.[22] The Charlson comorbidity index was calculated to assess the comorbidity score of patients receiving PD.[23]

Definitions

Considering the previous literature and incorporating the features of follow-up methods used at our center, anuria was defined as 24-hour urine volume ≤100 mL for >2 consecutive follow-up periods.[5,10,11,17] The time of the first recording of urine volume ≤100 mL was regarded as the time to develop anuria. The follow-up data on urine volume were obtained from accurate 24-hour urine volume collection during hospitalization, every outpatient visit, or the patient's self-reported urine volume during telephone follow-up. Temporary HD was defined as accepting HD <3 months before PD initiation. Incremental PD was characterized as having ≤3 exchanges of 2 L/day, with a weekly Kt/V of ≥1.7 achieved within 6 months of starting PD.[24] The 24-hour glucose exposure was calculated under the daily prescription of dialysis.[25]

Outcomes

The primary outcome was early anuria, which was defined as experiencing anuria within the first year after the commencement of PD therapy. Secondary outcomes were clinical outcomes, including all-cause mortality, cardiovascular disease (CVD) mortality, technique failure, and peritonitis. CVD mortality was noted in patients who died of various CVDs.[26] Patients who transferred to HD permanently due to infection related to PD, inadequate

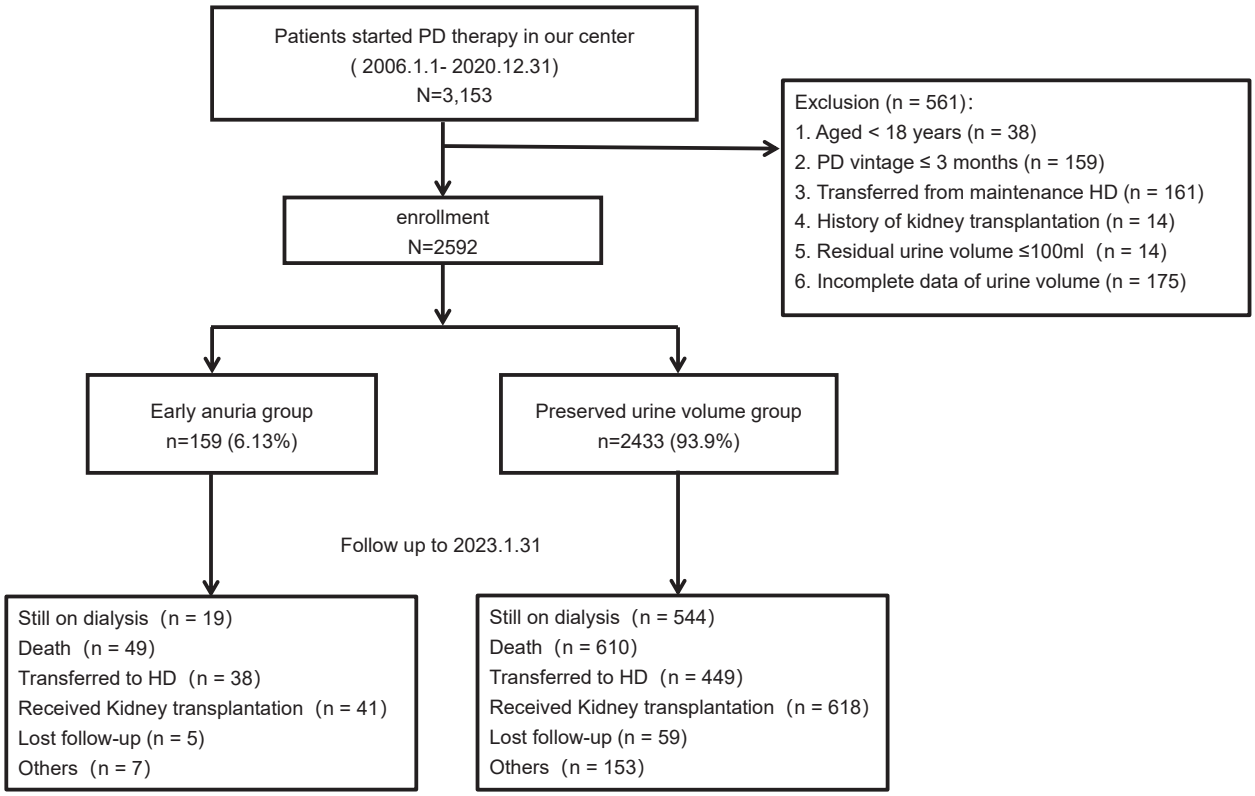

Figure 1. Flow chart of the study population. Abbreviations: HD, hemodialysis; PD, peritoneal dialysis.

dialysis, or other difficulties during PD periods, and who died of PD-related peritonitis were identified as technique failure.[27]

Statistical Analysis

Appropriate tests were used to measure the significant variances in baseline demographics, clinical data, and laboratory data between the early anuria group and the preserved urine volume group, depending on whether the variables were continuous or categorical. *t* tests were used to analyze continuously distributed variables, which are expressed as mean with standard deviation. Variables that did not follow a normal distribution were examined using Mann-Whitney *U* tests and are reported as the median with interquartile range (IQR). The χ^2 test was used to compare categorical variables, which are presented as frequency with the corresponding percentage.

To examine the factors associated with early anuria, both univariable and multivariable Cox proportional hazards regression analyses were performed. When exploring the associations between early anuria and the secondary outcomes, early anuria was parameterized as a time-dependent variable corresponding to the method suggested by a published report.[28] For patients who developed early anuria, the time from PD initiation to the time of early anuria onset and the time from early anuria onset to death, technique failure, and the first episode of peritonitis after early anuria were calculated. For those who developed peritonitis before early anuria, the time from PD start to the time of the first episode of peritonitis was also calculated. The associations between early anuria and all-cause mortality, CVD mortality, technique failure, and peritonitis were then assessed using Cox proportional hazards regression models.

Variables that were with a P-value < 0.2 or that were regarded as clinically meaningful were included in the regression model for multivariable analysis. The 2 steps above were repeated until all variables were eventually selected. The Cox regression model was used to test the interaction effects. Missing data were evaluated with the multiple imputation method. Statistical analyses were performed using SPSS (version 25.0) and Stata/SE (version 17.0). A 2-tailed $P < 0.05$ was considered statistically significant.

RESULTS

Patients' Characteristics

A total of 3,153 patients underwent continuous ambulatory PD therapy at our center between January 1, 2006 and December 31, 2020. After applying a specific criterion, 561 (17.8%) patients were excluded, leaving a final cohort of 2,592 patients (Fig 1). The median PD vintage of all patients enrolled was 3.45 (IQR, 1.76-5.94) years. The enrolled participants had an average age of 46.7 ± 14.9 years, with 1,528 (58.9%) being male. Among them, 623

(24.0%) had diabetes, and 851 (32.8%) had received temporary HD before PD initiation. Incremental PD was administered to 640 (24.7%) patients during the initial 6 months of PD therapy. Following glomerulonephritis (60.8%), diabetic nephropathy (19.7%) ranked as the second most prevalent kidney disease. The median urine volume was 1,200 mL/day (IQR, 800-1,800), and the median ultrafiltration was 450 mL/day (IQR, 200-700) at the beginning of PD.

Patients in the early anuria group were generally younger and more likely to receive temporary HD before PD and less likely to have diabetes and receive incremental PD than the preserved urine volume group. Moreover, the early anuria patients exhibited significantly lower urine volume ($P < 0.001$), eGFR ($P = 0.02$), hemoglobin ($P < 0.001$), serum albumin ($P < 0.001$), and serum calcium ($P < 0.001$) and higher levels of ultrafiltration ($P = 0.001$), daily glucose exposure ($P < 0.001$), serum creatinine ($P < 0.001$), serum urea ($P < 0.001$), serum phosphorus ($P < 0.001$), and serum potassium ($P = 0.002$) (Table 1).

Incidence and Risk Factors Associated With Early Anuria

By the end of the first year of PD therapy, 159 (6.13%) patients had experienced early anuria, with a median observation time of 7.53 (IQR, 3.93-10.0) months. To assess the factors associated with early anuria in patients receiving PD, both univariable and multivariable Cox regression analyses were conducted (Table 2). The results showed that higher baseline urine volume (hazard ratio [HR], 0.93; 95% confidence interval [CI], 0.90-0.97; $P < 0.001$), higher serum albumin (HR, 0.92; 95% CI, 0.88-0.95; $P < 0.001$), and prescribed incremental PD (HR, 0.27; 95% CI, 0.14-0.51; $P < 0.001$) were associated with a reduced risk for early anuria. Conversely, a higher level of daily glucose exposure (HR, 1.01; 95% CI, 1.00-1.01; $P = 0.04$) was identified as a risk factor for early anuria. During the first year after PD initiation, 74 (2.85%) patients died, 175 (6.75%) patients received kidney transplantation, and 52 (2.00%) patients transferred to HD. After further consideration of the competing risks of death, transplantation, and transference to HD, these results remained consistent. Interestingly, diabetes appeared to be an associated protective factor for early anuria in multivariable analysis (HR, 0.57; 95% CI, 0.35-0.92; $P = 0.02$). For further investigation into whether diabetes interacted with other factors, the interaction effects were tested.

The association between the use of ACEis/ARBs and early anuria differed according to the presence of T2DM after testing for interaction terms ($P = 0.003$). Based on that, multivariable Cox regression analyses were performed separately in T2DM and non-T2DM groups to explore the differences in predictive factors for early anuria between the 2 subgroups (Fig 2). The results revealed that the use of ACEis/ARBs was significantly associated with a lower risk for early anuria in T2DM patients (HR, 0.25; 95% CI, 0.09-0.69; $P = 0.007$). However, the effect was not observed in the non-T2DM subgroup. Irrespective of T2DM status, higher baseline urine volume (HR, 0.90; 95% CI, 0.82-0.99; $P = 0.02$ in the T2DM subgroup versus HR, 0.92; 95% CI, 0.89-0.96; $P = 0.001$ in the non-T2DM subgroup) and higher serum albumin (HR, 0.91; 95% CI, 0.84-1.00; $P = 0.04$ in the T2DM subgroup versus HR, 0.96; 95% CI, 0.92-1.00; $P = 0.03$ in the non-T2DM subgroup) were always associated protective factors for early anuria.

Early Anuria and Clinical Outcomes

During a median follow-up of 3.45 years, 659 (25.4%) patients died, 487 (18.8%) patients transferred to HD, 659 (25.4%) received kidney transplantation, and 64 (2.47%) were lost to follow-up. Of the deaths, 317 (12.2%) were ascribed to CVDs, 128 (4.94%) were ascribed to infection, 19 (0.73%) were ascribed to malignancy, 117 (4.51 %) were ascribed to other reasons, and 78 (3.01%) remained unidentified. In addition, 556 (21.5%) patients experienced technique failure, and 870 (33.6%) patients eventually developed peritonitis.

Treating early anuria as a time-dependent covariate, after adjusting for age, sex, diabetes, ACEis/ARBs, diuretics, β-blockers, daily glucose exposure, and serum albumin, early anuria was associated with a higher risk for all-cause mortality (HR, 1.69; 95% CI, 1.23-2.32; $P = 0.001$) and technique failure (HR, 1.43; 95% CI, 1.00-2.04; $P = 0.04$). However, the associations between early anuria and CVD mortality and peritonitis were not significant (Table 3).

DISCUSSION

In this retrospective cohort study comprising 2,592 patients who underwent PD, 159 (6.13%) patients developed early anuria during the first year of PD therapy, with a median duration of 7.53 months. Our findings revealed that higher baseline urine volume, higher serum albumin levels, a history of diabetes, and undergoing incremental PD were associated with decreased risk for early anuria among patients receiving PD, while a higher level of daily glucose exposure was observed to be an associated risk factor for early anuria. An episode of peritonitis was not found to be significantly associated with early anuria.

Subgroup analysis results showed that, in patients undergoing PD with a prior history of diabetes, the use of ACEis/ARBs was associated with a reduced risk for early anuria. Patients who experienced early anuria exhibited a higher risk for all-cause mortality and technique failure than patients with preserved urine volume.

Our study is the first to propose the concept of early anuria and reports a 6.13% rate of early anuria. The risk factor for early anuria in our research was mostly in line with the findings of prior studies. Szeto et al[4] discovered that higher glucose exposure was strongly linked to anuria progression.

Table 1. Baseline Characteristics of the Early Anuria Patients and Preserved Urine Volume Patients

Variables	Total N = 2,592	Missing Values, n (%)	Early Anuria Group N = 159	Preserved Urine Volume Group N = 2,433	*P*
Age, y (N = 2,592)	46.7 ± 14.9	0	43.6 ± 17.4	46.9 ± 14.7	0.007
Male, n (%) (N = 2,592)	1,528 (58.9%)	0	94 (59.1%)	1,434 (58.9%)	0.07
BMI, kg/m^2 (N = 2,455)	21.6 ± 3.09	137 (5.29%)	21.8 ± 3.30	21.9 ± 3.19	0.96
Urine volume, mL (N = 2,468)	1,200 (800-1,800)	124 (4.78%)	900 (500-1,400)	1,250 (800-1,800)	<0.001
eGFR, mL/min/1.73 m^2 (N = 2,557)	5.21 (4.01-6.86)	35 (1.35%)	4.64 (3.43-5.88)	5.23 (4.04-6.91)	0.02
CCI (N = 2,393)	2.69 ± 1.05	199 (7.68%)	3.32 ± 1.85	3.30 ± 1.64	0.49
Primary kidney disease, n (%) (N = 2,590)		2 (0.08%)			<0.001
Glomerulonephritis	1,576 (60.8%)		106 (66.6%)	1,470 (60.4%)	
Diabetic nephropathy	511 (19.7%)		23 (14.4%)	488 (20.1%)	
Hypertension disease	202 (7.79%)		11 (6.90%)	191 (7.85%)	
Others	301 (11.6%)		19 (11.9%)	282 (11.6%)	
Diabetes, n (%) (N = 2,516)	623 (24.0%)	76 (2.93%)	28 (17.6%)	595 (24.5%)	0.02
Temporary HD, n (%) (N = 2,535)	851 (32.8%)	57 (2.20%)	75 (47.2%)	776 (31.9%)	<0.001
Medications, n (%)					
ACEi/ARBs (N = 2,390)	1,398 (53.9%)	202 (7.79%)	91 (57.2%)	1,307 (53.7%)	0.07
Diuretics (N = 2,372)	257 (9.92%)	220 (8.49%)	15 (9.43%)	242 (9.95%)	0.08
β-Blockers (N = 2,364)	1,259 (48.6%)	228 (8.80%)	75 (47.2%)	1,184 (48.7%)	0.72
Dialysis prescription					
UF, m, (N = 2,468)	450 (200-700)	124 (4.78%)	550 (300-800)	440 (200-700)	0.001
Daily glucose exposure, g (N = 2,443)	126 ± 24.9	149 (5.75%)	137 ± 31.1	128 ± 25.6	<0.001
Incremental PD, n (%) (N = 2,455)	640 (24.7%)	137 (5.29%)	12 (7.55%)	628 (25.8%)	<0.001
Laboratory variables					
Hemoglobin, g/L (N = 2,533)	87.6 ± 22.0	59 (2.28%)	79.5 ± 20.1	88.6 ± 21.8	<0.001
Albumin, g/L (N = 2,520)	35.3 ± 5.20	72 (2.78%)	32.6 ± 5.35	34.9 ± 5.26	<0.001
iPTH, pg/mL (N = 2,476)	273 (139-452)	116 (4.48%)	290 (125-488)	273 (140-448)	0.97
Creatinine, mg/dL (N = 2,522)	11.2 ± 4.16	70 (2.70%)	12.4 ± 4.65	10.4 ± 4.04	<0.001
Urea, mmol/L (N = 2,533)	22.1 (16.1-30.5)	59 (2.28%)	25.7 (19.2-35.1)	21.9 (16.0-30.1)	<0.001
UA, mg/dL (N = 2,437)	8.17 ± 2.40	155 (5.98%)	8.11 ± 2.36	8.00 ± 2.37	0.18
Calcium, mmol/L (N = 2,526)	2.08 ± 0.28	66 (2.56%)	1.99 ± 0.31	2.09 ± 0.27	<0.001
Phosphorus, mmol/L (N=2,459)	1.78 ± 0.56	133 (5.13%)	2.05 ± 0.66	1.76 ± 0.55	<0.001
Sodium, mmol/L (N = 2,528)	139 ± 6.11	64 (2.47%)	137 ± 4.84	140 ± 27.4	0.35
Potassium, mmol/L (N = 2,526)	4.25 ± 0.79	66 (2.55%)	4.42 ± 0.93	4.23 ± 0.80	0.002
Glucose, mmol/L (N = 2,525)	5.18 ± 1.90	67 (2.58%)	5.69 ± 2.39	5.75 ± 2.75	0.80
TC, mmol/L (N = 2,442)	4.72 ± 1.33	150 (5.79%)	4.88 ± 1.36	4.78 ± 1.42	0.37
TG, mmol/L (N = 2,438)	1.54 ± 0.93	154 (5.94%)	1.58 ± 0.99	1.61 ± 1.00	0.73
HDL-C, mmol/L (N = 2,436)	1.14 ± 0.37	156 (6.02%)	1.08 ± 0.33	1.13 ± 0.39	0.09
LDL-C, mmol/L (N = 2,435)	2.86 ± 0.96	157 (6.06%)	3.03 ± 1.05	2.89 ± 1.00	0.09

Note: Continuous variables are presented as mean ± standard deviation or median (interquartile range) and categorical variables are presented as frequency (percentage).
Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HD, hemodialysis; HDL-C, high-density lipoprotein cholesterol; iPTH, intact parathyroid hormone; LDL-C, low-density lipoprotein cholesterol; PD, peritoneal dialysis; TC, total cholesterol; TG, total triglyceride; UA, uric acid; UF, ultrafiltration.

Table 2. Cox Regression Models for Evaluating Predictors for Early Anuria in PD Patients

Variables	Univariable Analysis			Multivariable Analysis											
				Common Model			Death-Competing Risk Model			Transplantation-Competing Risk Model			HD-Competing Risk Model		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Age (per y)	0.98	0.97-0.99	<0.001	0.99	0.97-1.00	0.07	0.99	0.97-1.00	0.07	0.99	0.97-1.00	0.07	0.99	0.97-1.00	0.07
Sex (male/female)	0.97	0.71-1.33	0.85	1.02	0.71-1.46	0.92	1.02	0.71-1.45	0.93	1.01	0.71-1.45	0.95	1.02	0.71-1.46	0.93
Diabetes (yes/no)	0.71	0.47-1.07	0.10	0.57	0.35-0.92	0.02	0.56	0.35-0.90	0.02	0.56	0.35-0.89	0.02	0.56	0.35-0.90	0.02
Temporary HD (yes/no)	1.93	1.40-2.65	<0.001	1.39	0.97-2.00	0.07	1.40	0.99-1.99	0.06	1.40	0.99-1.99	0.06	1.40	0.98-1.98	0.06
ACEi/ARBs (yes/no)	1.14	0.83-1.57	0.40	1.12	0.78-1.59	0.55	1.11	0.78-1.60	0.56	1.11	0.77-1.59	0.58	1.11	0.77-1.60	0.57
Diuretics (yes/no)	0.95	0.56-1.63	0.87	0.82	0.47-1.44	0.50	0.82	0.47-1.44	0.50	0.82	0.47-1.43	0.49	0.82	0.47-1.44	0.49
Urine volume (per 100mL)	0.92	0.89-0.94	<0.001	0.93	0.90-0.97	<0.001	0.93	0.90-0.97	<0.001	0.93	0.90-0.97	<0.001	0.93	0.90-0.97	<0.001
Albumin (per 1 g/L)	0.92	0.89-0.95	<0.001	0.92	0.88-0.95	<0.001	0.92	0.88-0.95	<0.001	0.92	0.88-0.95	<0.001	0.92	0.88-0.95	<0.001
Daily glucose exposure (per 1 g)	1.01	1.00-1.01	<0.001	1.01	1.00-1.01	0.04	1.01	1.00-1.01	0.03	1.01	1.00-1.01	0.04	1.01	1.00-1.01	0.04
Peritonitis (yes/no)	1.11	0.71-1.74	0.66	0.91	0.56-1.50	0.72	0.91	0.55-1.50	0.71	0.91	0.55-1.50	0.71	0.91	0.55-1.49	0.70
Incremental PD (yes/no)	0.23	0.13-0.41	<0.001	0.27	0.14-0.51	<0.001	0.27	0.15-0.50	<0.001	0.28	0.15-0.50	<0.001	0.27	0.15-0.50	<0.001

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CI, confidence interval; HD, hemodialysis; HR, hazard ratio; PD, peritoneal dialysis.

This might be related to the fact that an increase of glucose load enhances the peritoneal transport rate, which could potentially lead to an elevation in ultrafiltration and expedite the decline of RKF. Unexpectedly, our study did not discover a notable correlation between the occurrence of peritonitis and early anuria. In previous research, the presence of peritonitis in PD patients was reported to be linked to the development of anuria.[4,29] The association may be due to the prolonged observation period in those studies. Our study specifically focused on the initial year following the commencement of PD, during which a lower incidence and higher treatment effects of peritonitis may have less influence on early anuria. In line with the findings reported by Singhal et al,[29] we observed that there was no significant correlation between temporary HD before PD and the GFR slope. This may be attributed to the preservation effect of PD therapy on kidney function and the short duration of temporary HD. Strangely, diabetes, which was not significant in univariable analysis, emerged as a protective factor for early anuria in multivariable analysis. This finding contradicts those of most previous studies.[4,5,10,11] This may be due to a higher eGFR in diabetic patients (6.69 ± 3.04 mL/min/1.73 m^2) at the start of PD than those without diabetes (5.41 ± 3.50 mL/min/1.73 m^2), and the observation time of our study was shorter than previous studies. The existence of other potential causes for this discovery remains uncertain.

To further explore the potential influences, we conducted interaction tests and revealed an interaction between diabetes and the use of ACEis/ARBs in relation to early anuria. Subgroup analyses were conducted based on the presence or absence of diabetes subsequently. Previous studies on the effect of using ACEis/ARBs on preserving residual urine volume have been controversial. Shen et al[30] reported no association between the use of ACEis/ARBs and a decrease in RKF in all PD patients. However, other studies discovered that using ACEis/ARBs, especially long-term, diminished the deterioration of RKF in patients undergoing PD and prolonged the progression to anuria.[4,31-34] Our study revealed a protective effect of ACEis/ARBs on urine volume in diabetic patients receiving PD in the early stage of PD. Two possible explanations can be proposed. The first explanation suggests that the preservation of RKF is threatened by proteinuria,[4] even though ACEis/ARBs are widely recognized as beneficial for reducing proteinuria and further delaying the progression to anuria.[35,36] As a second explanation, ACEis/ARBs reduce the risk of microvascular complications in diabetic patients and improve blood pressure control.[37] This indicates that doctors should consider prescribing ACEis/ARBs to diabetic patients undergoing PD for better preservation of urine volume during the initial phase of PD. Further prospective research and randomized controlled trials are necessary to examine whether the use of ACEis/ARBs has a favorable or unfavorable impact on urine volume in patients receiving PD, particularly in individuals with pre-existing diabetes.

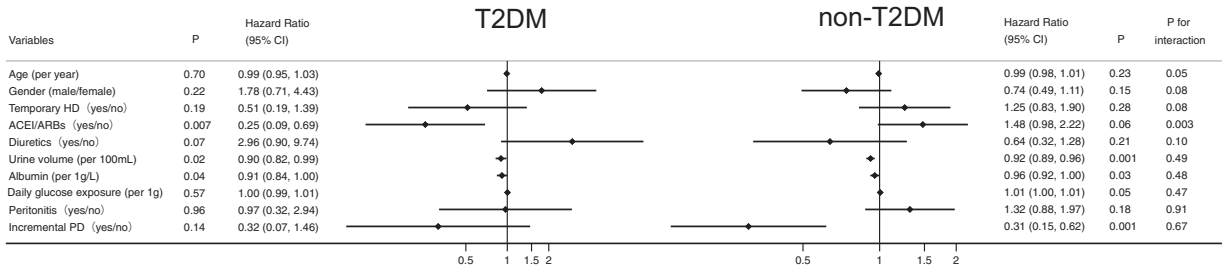

Figure 2. Forest graph showing the differences in risk factors for early anuria between T2DM and non-T2DM PD patients. Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CI, confidence interval; DM, diabetes mellitus; HD, hemodialysis; PD, peritoneal dialysis.

The results of our study indicate that the presence of early anuria increases the risk of all-cause mortality and technique failure, which aligns with previous research suggesting that maintaining RKF and urine volume improves survival and reduces technical failure.[4,5,14,15,21] A more rapid decrease in RKF has been observed to be associated with higher mortality.[5,10–12] Furthermore, patients who have progressed to anuria usually had a higher risk for mortality, technical failure, and inflammatory, nutritional, and metabolic characteristics compared with PD patients with residual urine volume.[19,21] Interestingly, our study showed that the associations between early anuria and CVD mortality and peritonitis were not significant. However, previous studies have reported that reduced RKF was associated with a higher risk for the development of peritonitis[9] and adverse cardiovascular effects.[21] The differences might be because our study mainly focused on the initial year of PD therapy, during which there was a lower incidence of early anuria, which may have influenced the statistical outcomes. Both patients and health care professionals must accord heightened importance to maintaining residual urine volume to improve clinical outcomes for PD patients, particularly in the initial phases of PD.

Several highlights of this study are worth mentioning. We enrolled a large cohort of patients undergoing PD and followed them up for >10 years. Follow-up data were collected and reported in detail. However, there are several limitations in our study. We carried out the study at a single center, making it less applicable to other centers. The results may not be generalizable to patients who have previously received kidney transplants, were previously on chronic HD, or who were aged <18 years because those patients were excluded from this study. Furthermore, causal relationships could not be determined because of the observational study. In addition, there are some biases present in this study, including ascertainment bias derived from 561 (17.8%) patients who were excluded from analysis, detection bias depending on the frequency of

Table 3. Cox Regression Models to Investigate the Association Between Early Anuria and Clinical Outcomes in PD Patients

	All-Cause Mortality			CVD Mortality			Technique Failure			Peritonitis		
Variables	**HR**	**95% CI**	**P value**	**HR**	**95% CI**	**P value**	**HR**	**95% CI**	**P value**	**HR**	**95% CI**	**P value**
Early anuria (yes/no)[a]	1.69	1.23-2.32	0.001	1.50	0.93-2.42	0.10	1.43	1.00-2.04	0.04	1.13	0.84-1.53	0.42
Age (per year)	1.03	1.02-1.03	<0.001	1.02	1.02-1.03	<0.001	1.00	0.99-1.00	0.34	1.01	1.00-1.01	<0.001
Sex (male/female)	1.20	1.02-1.42	0.03	1.05	0.83-1.33	0.70	1.09	0.90-1.32	0.37	1.21	1.05-1.39	0.007
Diabetes (yes/no)	3.04	2.54-3.64	<0.001	3.40	2.64-4.39	<0.001	1.20	0.95-1.51	0.13	0.97	0.82-1.15	0.73
ACEi/ARBs (yes/no)	1.05	0.89-1.23	0.59	1.09	0.86-1.39	0.46	1.08	0.90-1.31	0.42	1.02	0.89-1.18	0.76
Diuretics (yes/no)	0.80	0.59-1.07	0.13	0.77	0.51-1.17	0.22	0.93	0.67-1.29	0.66	0.92	0.73-1.16	0.46
β-Blockers (yes/no)	0.82	0.69-0.96	0.02	0.82	0.65-1.03	0.09	1.23	1.02-1.48	0.03	1.02	0.89-1.17	0.76
Daily glucose exposure (per 1g)	1.01	1.00-1.01	<0.001	1.01	1.00-1.01	<0.001	1.00	1.00-1.01	0.27	1.00	1.00-1.01	0.10
Albumin (per 1g/L)	0.98	0.97-1.00	0.08	1.00	0.97-1.02	0.91	0.98	0.96-1.00	0.02	0.98	0.97-0.99	0.005

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB angiotensin II receptor blocker; CI, confidence interval; CVD, cardiovascular disease.
[a]Early anuria was treated as a time-dependent covariate.

measurement of urine volume, attrition bias due to some participants who were not followed for the full 12-month period of the primary outcome, recall bias due to the retrospective design of the study, era bias due to the long period of the study, misclassification bias if anuria was assessed by patient self-report, and bias by residual confounding due to other possible confounders. Furthermore, the peritoneal dialysates used in our center were not neutral pH, low glucose degradation product solutions, making the findings of this study not generalizable to patients receiving neutral pH, low glucose degradation product solutions. To validate our conclusion, it is necessary to conduct additional studies that are multicenter and prospective, using neutral pH and low glucose degradation product dialysate solutions.

In conclusion, early anuria was associated with lower baseline urine volume, lower serum albumin, full-dose PD start, absence of T2DM, higher daily glucose exposure, and in patients with T2DM, non-use of ACEis/ARBs. For urine preservation in diabetic patients undergoing PD, using ACEis/ARBs could be beneficial. The occurrence of early anuria is associated with an increased risk for all-cause mortality and technical failure in patients undergoing PD. Strictly monitoring urine volume preservation is crucial in following the International Society for Peritoneal Dialysis guidelines. The appropriate use of ACEis/ARBs, proper selection of incremental PD, and careful and dynamic adjustment of dialysis prescription may have a significant impact.

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Shiyan Tu, MS,* Hongjian Ye, MD, PhD,* Yangyang Xin, MS, Yuan Peng, MD, Ruihua Liu, MD, Jing Guo, MS, Chunyan Yi, BN, Haiping Mao, MD, PhD, and Xiao Yang, MD, PhD

Authors' Affiliations: Department of Nephrology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China (ST, HY, YX, RL, JG, CY, HM, XY); Key Laboratory of Nephrology, Ministry of Health and Guangdong Province, Guangzhou, China (ST, HY, YX, RL, JG, CY, HM, XY); and Department of Nephrology, People's Hospital of Ganzhou, Ganzhou, Jiangxi, China (YP).

Address for Correspondence: Xiao Yang, MD, PhD, Department of Nephrology, The First Affiliated Hospital, Sun Yat-sen University, 58th, Zhongshan Road II, Guangzhou 510080, China. Email: yxiao@mail.sysu.edu.cn

Authors' Contributions: Research area and study design: ST, XY. Data acquisition: YX, YP, RL, JG, CY, HM. Data analysis and interpretation: ST, HY. Statistical analysis: ST, HY. Supervision and mentorship: XY. Each author contributed important intellectual content during article drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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REFERENCES

1. Bello AK, Okpechi IG, Osman MA, et al. Epidemiology of peritoneal dialysis outcomes. *Nat Rev Nephrol*. 2022;18(12):779-793.
2. Teitelbaum I. Peritoneal dialysis. *N Engl J Med*. 2021;385(19):1786-1795.
3. He L, Liu X, Li Z, et al. Rate of decline of residual kidney function before and after the start of peritoneal dialysis. *Perit Dial Int*. 2016;36(3):334-339.
4. 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(2):180-188.
5. Hu SL, Joshi P, Kaplan M, et al. Rapid change in residual renal function decline is associated with lower survival and worse residual renal function preservation in peritoneal dialysis patients. *Perit Dial Int*. 2017;37(4):477-481.
6. Guo Q, Yi C, Li J, Wu X, Yang X, Yu X. Prevalence and risk factors of fluid overload in Southern Chinese continuous ambulatory peritoneal dialysis patients. *PLOS ONE*. 2013;8(1):e53294.
7. Termorshuizen F, Korevaar JC, Dekker FW, et al. The relative importance of residual renal function compared with peritoneal clearance for patient survival and quality of life: an analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)-2. *Am J Kidney Dis*. 2003;41(6):1293-1302.
8. Zhou W, Hu W, Han G, Wang H, Zhang J, Mei C. The impact of residual renal function on quality of life in patients with peritoneal dialysis. *Clin Nephrol*. 2018;90(2):106-111.
9. Han SH, Lee SC, Ahn SV, et al. Reduced residual renal function is a risk of peritonitis in continuous ambulatory peritoneal dialysis patients. *Nephrol Dial Transplant*. 2007;22(9):2653-2658.
10. Lu YH, Hwang JC, Jiang MY, Wang CT. Comparison of the impact of "fast decline" in residual renal function and "initial anuria" on long-term outcomes in CAPD patients. *Perit Dial Int*. 2015;35(2):172-179.
11. Ethier I, Cho Y, Hawley C, et al. Rate of decline in residual kidney function pre and post peritoneal dialysis initiation: a post hoc analysis of the IDEAL study. *PLOS ONE*. 2020;15(11):e0242254.
12. Wang J, Xie X, Yan X, et al. A fast decline of residual renal function in the first year is a predictor for early withdrawal from peritoneal dialysis in non-diabetic patients. *Kidney Blood Press Res*. 2019;44(1):12-21.
13. 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(3):276-283.
14. Bargman JM, Thorpe KE, 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(10):2158-2162.
15. Lee MJ, Park JT, Park KS, et al. Prognostic value of residual urine volume, GFR by 24-hour urine collection, and eGFR in

patients receiving dialysis. *Clin J Am Soc Nephrol*. 2017;12(3):426-434.
16. Chen Y, Liu H, Zou J, et al. 24-h residual urine volume at hemodialysis initiation: a possible predictor for acute ischemic stroke incurrence in hemodialysis patients. *Clin Neurol Neurosurg*. 2013;115(5):557-561.
17. Jung ES, Sung JY, Han SY, et al. Residual urinary volume is a predictor of overhydration in patients on peritoneal dialysis. *Tohoku J Exp Med*. 2014;233(4):295-300.
18. Brown EA, Blake PG, Boudville N, et al. International Society for Peritoneal Dialysis practice recommendations: prescribing high-quality goal-directed peritoneal dialysis. *Perit Dial Int*. 2020;40(3):244-253.
19. Park JY, Cho JH, Jang HM, et al. Survival predictors in anuric patients on peritoneal dialysis: A prospective, multicenter, propensity score-matched cohort study. *PLOS ONE*. 2018;13(4):e0196294.
20. Jansen MAM, Termorshuizen F, Korevaar JC, et al. Predictors of survival in anuric peritoneal dialysis patients. *Kidney Int*. 2005;68(3):1199-1205.
21. Wang AY, Woo J, Wang M, et al. Important differentiation of factors that predict outcome in peritoneal dialysis patients with different degrees of residual renal function. *Nephrol Dial Transplant*. 2005;20(2):396-403.
22. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. *Am J Kidney Dis*. 2010;55(4):622-627.
23. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
24. Liu R, Ye H, Peng Y, et al. Incremental peritoneal dialysis and survival outcomes: a propensity-matched cohort study. *J Nephrol*. 2023;36(7):1907-1919.
25. Uiterwijk H, Franssen CFM, Kuipers J, Westerhuis R, Nauta FL. Glucose exposure in peritoneal dialysis is a significant factor predicting peritonitis. *Am J Nephrol*. 2020;51(3):237-243.
26. Xia X, He F, Wu X, Peng F, Huang F, Yu X. Relationship between serum uric acid and all-cause and cardiovascular mortality in patients treated with peritoneal dialysis. *Am J Kidney Dis*. 2014;64(2):257-264.
27. Wu H, Huang R, Yi C, et al. Risk factors for early-onset peritonitis in Southern Chinese peritoneal dialysis patients. *Perit Dial Int*. 2016;36(6):640-646.
28. Liu J, Weinhandl ED, Gilbertson DT, Collins AJ, St Peter WL. Issues regarding 'immortal time' in the analysis of the treatment effects in observational studies. *Kidney Int*. 2012;81(4):341-350.
29. Singhal MK, Bhaskaran S, Vidgen E, Bargman JM, Vas SI, Oreopoulos DG. Rate of decline of residual renal function in patients on continuous peritoneal dialysis and factors affecting it. *Perit Dial Int*. 2000;20(4):429-438.
30. Shen JI, Saxena AB, Vangala S, Dhaliwal SK, Winkelmayer WC. Renin-angiotensin system blockers and residual kidney function loss in patients initiating peritoneal dialysis: an observational cohort study. *BMC Nephrol*. 2017;18(1):196.
31. Zhang L, Zeng X, Fu P, Wu HM. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for preserving residual kidney function in peritoneal dialysis patients. *Cochrane Database Syst Rev*. 2014;2014(6):CD009120.
32. Liu Y, Ma X, Zheng J, Jia J, Yan T. Effects of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers on cardiovascular events and residual renal function in dialysis patients: a meta-analysis of randomised controlled trials. *BMC Nephrol*. 2017;18(1):206.
33. Ding L, Yang J, Li L, Yang Y. Effects of ACEIs and ARBs on the residual renal function in peritoneal dialysis patients: a meta-analysis of randomized controlled trials. *Biomed Res Int*. 2020;2020:6762029.
34. Herget-Rosenthal S, von Ostrowski M, Kribben A. Definition and risk factors of rapidly declining residual renal function in peritoneal dialysis: an observational study. *Kidney Blood Press Res*. 2012;35(4):233-241.
35. Thallas-Bonke V, Coughlan MT, Bach LA, Cooper ME, Forbes JM. Preservation of kidney function with combined inhibition of NADPH oxidase and angiotensin-converting enzyme in diabetic nephropathy. *Am J Nephrol*. 2010;32(1):73-82.
36. Ren F, Tang L, Cai Y, et al. Meta-analysis: the efficacy and safety of combined treatment with ARB and ACEI on diabetic nephropathy. *Ren Fail*. 2015;37(4):548-561.
37. Vejakama P, Thakkinstian A, Lertrattananon D, Ingsathit A, Ngarmukos C, Attia J. Reno-protective effects of renin-angiotensin system blockade in type 2 diabetic patients: a systematic review and network meta-analysis. *Diabetologia*. 2012;55(3):566-578.