Research Article

Serum Sodium Modifies the Association of Systolic Blood Pressure with Mortality in Peritoneal Dialysis Patients

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Keywords

Serum sodium · Systolic blood pressure · Peritoneal dialysis · Mortality

Abstract

Introduction: High serum sodium is associated with increased blood pressure (BP) in dialysis patients, which is a risk factor for cardiovascular (CV) disease. However, the interaction between serum sodium and BP and their association with clinical outcomes in peritoneal dialysis (PD) patients is uncertain. **Methods:** We analyzed a retrospective cohort of 1,656 incident PD patients from January 2006 to December 2013, who were followed up until December 2018. Cox proportional hazards regression models were used to evaluate the association of serum sodium and BP with all-cause and CV mortality. A priori interaction between serum sodium and systolic BP (SBP) was explored, and a subgroup analysis was performed by stratifying SBP into the following 3 groups: <110, 110–130, and >130 mm Hg. **Results:** Mean baseline serum sodium was 140.2 ± 3.6 mmol/L, mean SBP was 137 ± 20 mm Hg, and diastolic BP was 85 ± 14 mm Hg. During a median (range) follow-up time of 46.5 (2.6–154.3) months, 507 patients died, 252 of whom died due to CV disease. SBP did not predict all-cause and CV mortality when BP was assessed as a continuous variable. However, SBP >130 or <110 mm Hg was associated with higher risk of all-cause and CV mortality compared with SBP of 110–130 mm Hg. There was a significant interaction between baseline serum sodium and SBP for all-cause mortality (p for interaction = 0.016). In subgroup analysis, among those with SBP >130 mm Hg, the risk of all-cause mortality was elevated in those with serum sodium ≥ 140 mmol/L (adjusted hazard ratio [aHR] 1.45 [95% confidence interval (CI): 1.07–1.98]), but not for those with serum sodium <140 mmol/L (aHR 1.27 [95% CI: 0.89–1.82]). Conversely, among those with SBP

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<110 mm Hg, those with serum sodium <140 mmol/L had an elevated risk of mortality (aHR 1.99 [95% CI: 1.31–3.02]), but not those with serum sodium $\geq$ 140 mmol/L (aHR 1.15 [95% CI: 0.74–1.79]) (p for interaction = 0.028). **Conclusion:** The association of BP with mortality was modified by serum sodium levels in PD patients. Further studies are needed to evaluate whether individualized BP control based on serum sodium levels contributes to improve patient outcomes.

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Introduction

Abnormal sodium levels may be associated with adverse outcomes in dialysis patients [1, 2]. A U-shaped relationship between serum sodium levels and mortality has been observed in non-dialysis CKD patients and hemodialysis (HD) patients, among whom both low and high levels of serum sodium are associated with an increased risk of mortality [3, 4]. Similarly, in peritoneal dialysis (PD) patients, our recent study and others have demonstrated that hyponatremia predicts a higher risk of infection-related and all-cause death [5, 6].

Blood pressure (BP) has been reported to be an independent predictor of mortality [7–10]. Associations between serum sodium concentration and BP have been observed both in the general population and dialysis patients. In a cohort study of 3,603 people from the general population, a higher serum sodium concentration was independently associated with an increased BP [11]. In addition, enhancing peritoneal sodium removal using low-sodium dialysate has advantages for hypertensive PD patients [12, 13]. Despite the close relationship between serum sodium and BP that has been identified, few studies have been performed to address the interaction effects between serum sodium concentration and BP on mortality in PD patients.

Therefore, in this retrospective cohort study, we evaluated the association of baseline BP with all-cause and cardiovascular (CV) mortality in PD patients. We then explored a priori interaction between BP, serum sodium, and mortality.

Materials and Methods

Participants

From January 1, 2006, to December 31, 2013, 1,884 participants were consecutively recruited from our center. Eligible participants were over 18 years of age and undergoing continuous ambulatory peritoneal dialysis (CAPD) treatment for >3 months. We excluded those with a history of kidney transplantation ($n = 16$), HD longer than 3 months ($n = 73$), malignant disease ($n = 30$), or missing serum sodium or BP data at baseline ($n = 2$). There were 1,656 participants included in the final analysis.

Demographic and Clinical Data

Participants' demographic, biochemical, and clinical data were collected at the time of study enrollment. Demographic and clinical characteristics were obtained from participant's medical record. Demographic data included age, gender, primary cause of ESRD, and comorbidities (CV diseases [CVDs] and diabetes). The presence of CVDs was defined as congestive heart failure, ischemic heart disease, cerebrovascular disease, and peripheral vascular disease [14]. Biochemical variables, including hemoglobin, serum sodium, albumin, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, calcium, phosphate, and intact parathyroid hormone, were measured at the clinical laboratory of the First Affiliated Hospital of Sun Yat-sen University within 3 months of PD initi-

ation. Residual renal function was determined by residual glomerular filtration rate (rGFR) derived from the average of 24-h urinary urea and Cr clearance normalized to a standard body surface area of 1.73 m². Total Cr clearance and total Kt/V_{urea} were calculated using PD Adequest software (Baxter Healthcare Corporation, Chicago, IL, USA). BP was measured twice at the baseline visit, and the mean of 2 measurements was used.

Outcomes

The primary outcome was all-cause mortality and the secondary outcome was CV mortality. CV mortality was defined as death due to myocardial infarction, congestive heart failure, arrhythmia, cerebrovascular accident, peripheral vascular disease, and sudden death. Sudden death was diagnosed as unexpected natural death that occurred within 1 h of symptom onset and without any previous condition that would appear fatal. We defined survival time for each participant as the time from enrollment to death or administrative censoring (i.e., transfer to HD, kidney transplantation, transfer to another dialysis center, loss to follow-up, or end of the study period on December 31, 2018).

Statistical Analysis

Results were presented as the mean ± standard deviation or median (25th, 75th percentile) for continuous variables, as appropriate, as well as number (percent) for categorical variables. Participants were stratified by baseline serum sodium with a threshold of 140 mmol/L, and baseline demographic and laboratory variables were compared between 2 groups using a 2-sample *t* test or Mann–Whitney U test for continuous variables and a χ^2 test for categorical variables, as appropriate.

Unadjusted and adjusted Cox proportional hazards regression models were used to evaluate the associations of SBP with all-cause and CV mortality. The following potential confounding covariates were included in the adjusted model: age, gender, history of CV disease (CVD), diabetic status, hemoglobin, serum albumin, 24-h urine volume, and anti-hypertensive medications. Curve fitting was further conducted with a fractional polynomial model to evaluate the possibility of a nonlinear association between continuous SBP levels and outcomes, which was predicted from Cox models after adjusting for the confounding factors described above. The interaction of serum sodium with the association between SBP and all-cause and CV mortality was also evaluated using the Cox regression model, with adjustments for potential confounders. Based on these results, we further investigated the relationship between SBP and outcomes by stratifying SBP into the following 3 groups: <110, 110–130, and >130 mm Hg. All analyses were performed using SPSS statistical software (version 19.0; IBM, Armonk, NY, USA) or Stata software (version 15.1; Stata Corp, College Station, TX, USA), as appropriate. A *p* value <0.05 was considered to be statistically significant.

Results

Participant Baseline Characteristics

Table 1 summarizes the baseline characteristics of participants stratified by serum sodium levels. The mean age of participants was 47.5 ± 15.3 years, and 59.8% were male. The leading cause of ESRD in the cohort was glomerulonephritis, with a prevalence of 61.1%. Thirty-seven percent of participants had a history of CVD and 25.5% had diabetes. The mean SBP was 137 ± 20 mm Hg and diastolic BP (DBP) was 85 ± 14 mm Hg. The mean serum sodium was 140.2 ± 3.6 mmol/L. Compared with participants with baseline serum sodium <140 mmol/L, those with baseline serum sodium ≥140 mmol/L were more likely to be male and had a higher BMI, SBP and DBP, hemoglobin, serum albumin, rGFR, 24-h urine volume, and

Table 1. Baseline characteristics by baseline serum sodium

Variables	Overall (n = 1,656)	Na <140 mmol/L (n = 636)	Na ≥140 mmol/L (n = 1,020)	p value
Serum sodium, mmol/L	140.2±3.6	136.7±2.6	142.3±2.1	NA
Age, years	47.5±15.3	47.7±15.6	47.3±15.1	0.595
Male, %	990 (59.8)	349 (54.9)	641 (62.8)	0.001
Cause of ESRD, n (%)				0.057
Glomerulonephritis	1,012 (61.1)	374 (58.8)	638 (62.5)	
Diabetic kidney disease	377 (22.8)	166 (26.1)	221 (20.7)	
Hypertension	119 (7.2)	39 (6.1)	80 (7.8)	
Others	148 (8.9)	57 (9.0)	91 (8.9)	
History of CVD, n (%)	612 (37.0)	225 (35.4)	387 (37.9)	0.318
Diabetes, n (%)	423 (25.5)	184 (28.9)	239 (23.4)	0.015
BMI, kg/m ²	21.6±3.2	21.2±3.0	21.9±3.2	<0.001
SBP, mm Hg	137±20	134±20	138±19	<0.001
DBP, mm Hg	85±14	83±15	86±14	<0.001
Hemoglobin, g/dL	105.5±21.8	102.6±22.7	107.3±21.1	<0.001
Serum albumin, g/L	37.3±5.2	36.1±5.4	38.0±4.9	<0.001
Total cholesterol, mmol/L	5.10±1.34	5.12±1.41	5.08±1.29	0.571
Triglycerides, mmol/L	1.42 (1.01–2.02)	1.39 (0.97–1.96)	1.44 (1.03–2.07)	0.220
HDL cholesterol, mmol/L	1.24±0.39	1.24±0.49	1.23±0.38	0.534
LDL cholesterol, mmol/L	2.94±1.01	2.93±1.06	2.94±0.98	0.883
Serum calcium, mmol/L	2.26±0.23	2.25±0.24	2.27±0.22	0.155
Serum phosphate, mmol/L	1.44±0.43	1.48±0.45	1.42±0.42	0.013
iPTH, pg/mL	227 (107–412)	221 (96–414)	229 (113–411)	0.476
rGFR, mL/min/1.73 m ²	3.26 (1.88–5.09)	2.83 (1.51–4.55)	3.53 (2.16–5.46)	<0.001
24-h urine volume, mL	800 (500–1,200)	700 (400–1,100)	800 (500–1,200)	<0.001
Total CCL, L/week per 1.73 m ²	86.78±29.06	83.66±27.65	88.67±29.73	0.002
Total Kt/Vurea	2.47±0.68	2.47±0.68	2.47±0.68	0.856
ACEi/ARB use	221 (49.3)	319 (50.2)	546 (53.5)	0.199

Data presented as mean ± SD, n (percentage), or median (25th, 75th). Bold values indicate *p* values less than 0.05. DBP, diastolic blood pressure; SBP, systolic blood pressure; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; iPTH, intact parathyroid hormone; rGFR, residual glomerular filtration rate; CCL, Cr clearance; Kt/Vurea, urea clearance (Kt) normalized to total body water (V); ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; SD, standard deviation.

total Cr clearance. However, fewer of these patients had a history of diabetes, and serum phosphorus levels were lower.

Factors Associated with SBP

Table 2 shows the regression coefficients of various factors that were associated with SBP levels using multivariate linear regression. After adjusting for sex, age, diabetes, history of CVD, serum albumin, hemoglobin, 24-h urine volume, and BMI, we found that serum sodium ($\beta = 0.626$, $p < 0.001$), 24-h urine volume ($\beta = 0.003$, $p = 0.001$), and BMI ($\beta = 0.478$, $p = 0.004$) were positively associated with SBP, while female sex ($\beta = -3.031$, $p = 0.004$), serum albumin ($\beta = -0.375$, $p = 0.001$), and hemoglobin ($\beta = -0.089$, $p < 0.001$) were negatively related to SBP.

Baseline SBP, Serum Sodium, and Mortality

Over a median follow-up of 46.5 (2.6–154.3) months, 507 participants (30.6%) died, of whom 252 (49.7%) died as a result of CVD. In our study, both all-cause and CV mortality rates among participants with a serum sodium <140 mmol/L were significantly higher than those with a serum sodium ≥140 mmol/L {82.5 vs. 65.3 events per 1,000 patient-years (HR 1.29, 95%

Table 2. Factors associated with SBP

Variables	Unstandardized coefficients		Standardized coefficients	T	p value
	B	standard error			
Sex (female)	−3.031	1.038	−0.075	−2.921	0.004
Age, year	−0.041	0.038	−0.031	−1.080	0.280
Diabetes (yes/no)	2.288	1.370	0.048	1.670	0.095
History of CVD (yes/no)	1.871	1.047	0.046	1.788	0.074
Serum albumin, g/L	−0.375	0.114	−0.096	−3.282	0.001
Serum sodium, mmol/L	0.626	0.142	0.112	4.407	<0.001
HGB, g/L	−0.089	0.025	−0.096	−3.605	<0.001
24-h Urine volume, mL/day	0.003	0.001	0.090	3.479	0.001
BMI, kg/m ²	0.478	0.167	0.076	2.867	0.004

$F = 11.50$, $p < 0.001$. $R^2 = 0.063$. Bold values indicate p values less than 0.05. Analysis of factors associated with SBP by multivariable linear regression. SBP, systolic blood pressure; HGB, hemoglobin; CVD, cardiovascular disease.

Table 3. Association of baseline BP with all-cause and CV mortality by baseline serum sodium levels

	All-cause mortality				CV mortality			
	unadjusted model		multivariate model		unadjusted model		multivariate model	
	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
<i>Interaction analysis for mortality in the overall cohort^b</i>								
SBP/DBP (5 mm Hg increase) × sodium group								
SBP × sodium group		$p_{\text{for interaction}} = \mathbf{0.007}$		$p_{\text{for interaction}} = \mathbf{0.016}$		$p_{\text{for interaction}} = 0.079$		$p_{\text{for interaction}} = 0.203$
DBP × sodium group		$p_{\text{for interaction}} = \mathbf{0.024}$		$p_{\text{for interaction}} = \mathbf{0.030}$		$p_{\text{for interaction}} = \mathbf{0.021}$		$p_{\text{for interaction}} = 0.058$
Overall cohort ($n = 1,656$) ^a								
SBP, 5 mm Hg increase	1.03 (1.01–1.05)	0.018	1.01 (0.99–1.03)	0.126	1.03 (1.00–1.06)	0.049	1.01 (0.98–1.04)	0.394
DBP, 5 mm Hg increase	0.87 (0.84–0.90)	<0.001	1.02 (0.98–1.05)	0.327	0.88 (0.84–0.92)	<0.001	1.03 (0.98–1.08)	0.236
MAP, 5 mm Hg increase	0.93 (0.90–0.96)	<0.001	1.02 (0.99–1.05)	0.266	0.94 (0.90–0.98)	0.006	1.03 (0.98–1.07)	0.258
Na <140 mmol/L ($n = 636$) ^b								
SBP, 5 mm Hg increase	1.00 (0.96–1.02)	0.761	0.97 (0.94–1.01)	0.129	1.00 (0.96–1.05)	0.919	0.98 (0.94–1.03)	0.433
DBP, 5 mm Hg increase	0.85 (0.81–0.89)	<0.001	0.99 (0.93–1.04)	0.650	0.84 (0.78–0.90)	<0.001	0.98 (0.91–1.06)	0.646
MAP, 5 mm Hg increase	0.90 (0.86–0.94)	<0.001	0.98 (0.93–1.03)	0.315	0.90 (0.84–0.96)	<0.001	0.98 (0.91–1.05)	0.512
Na ≥140 mmol/L ($n = 1,020$) ^b								
SBP, 5 mm Hg increase	1.06 (1.03–1.09)	<0.001	1.04 (1.01–1.07)	0.010	1.06 (1.02–1.11)	0.004	1.04 (1.00–1.08)	0.073
DBP, 5 mm Hg increase	0.89 (0.86–0.93)	<0.001	1.03 (0.99–1.08)	0.167	0.93 (0.87–0.99)	0.021	1.07 (1.00–1.14)	0.058
MAP, 5 mm Hg increase	0.97 (0.93–1.01)	0.118	1.05 (1.003–1.09)	0.034	0.99 (0.94–1.06)	0.850	1.06 (1.02–1.13)	0.043

DBP, diastolic BP; SBP, systolic blood pressure; CV, cardiovascular; CVD, cardiovascular disease; CI, confidence interval; HR, hazard ratio. Bold values indicate p values less than 0.05. ^a Multivariate models adjusted for age, gender, history of CVD, diabetic status, baseline serum sodium, hemoglobin, serum albumin, 24-h urine volume, and anti-hypertension drugs. ^b Multivariate models adjusted for age, gender, history of CVD, diabetic status, hemoglobin, serum albumin, 24-h urine volume, and anti-hypertension drugs.

CI 1.08–1.54), 42.6 vs. 24.4 events per 1,000 patient-years (HR 1.36, 95% CI 1.06–1.75), respectively}. These data suggest that serum sodium concentration at baseline may predict outcomes in PD patients. We further performed a stratified analysis of serum sodium levels to evaluate the relationship between baseline SBP and mortality. Overall, continuous SBP levels were not associated with all-cause and CV mortality after adjusting for potential confounders (Table 3).

There was a significant interaction between baseline SBP and serum sodium for all-cause mortality (p for interaction = 0.016 in the adjusted model), but not CV mortality (p for interaction = 0.203 in the adjusted model). Table 3 shows HRs for mortality in the subgroup stratified by baseline serum sodium levels. With a 5-mm Hg elevation in SBP, adjusted HRs of all-

Fig. 1. The restricted cubic splines for baseline SBP with all-cause and CV mortality. SBP, systolic blood pressure; CV, cardiovascular; HR, hazard ratio.

cause and CV mortality were 1.04 (95% CI 1.01–1.07, $p = 0.010$) and 1.04 (95% CI 1.00–1.08, $p = 0.073$), respectively, in participants with baseline serum sodium levels ≥ 140 mmol/L. However, there was no significant association of SBP with all-cause or CV mortality in those with serum sodium levels < 140 mmol/L.

Considering the nonlinear association between continuous SBP levels and outcomes, we conducted curve fitting with the HRs that were predicted from the Cox model. As shown in Figure 1, an approximate U-shaped association between SBP and risk of all-cause and CV mortality was observed. Patients with higher or lower SBP had higher risk of all-cause and CV mortality across serum sodium groups.

Based on these results, patients were split into 3 groups defined by SBP, with an SBP of 110–130 mm Hg as a reference. As shown in Table 4, in the entire cohort, all-cause mortality was greater in participants with SBP < 110 or > 130 mm Hg, with adjusted HRs of 1.51 (95% CI 1.12–2.03) and 1.40 (95% CI 1.11–1.76), respectively. Similar results were observed for CV mortality, with adjusted HRs of 1.66 (95% CI 1.09–2.53) and 1.50 (95% CI 1.09–2.09) for participants with SBP < 110 or > 130 mm Hg, respectively. In the subgroup analysis, among participants with serum sodium ≥ 140 mmol/L, SBP > 130 mm Hg was independently associated with increased all-cause mortality (HR: 1.45, 95% CI 1.07–1.98, p for interaction = 0.028 in the adjusted model), but not CV mortality (HR: 1.48, 95% CI 0.94–2.31, p for interaction = 0.257 in the adjusted model). In participants with serum sodium levels < 140 mmol/L, low SBP levels (< 110 mm Hg), but not high SBP levels (> 130 mm Hg) conferred an increased risk on both all-cause and CV mortality, with an adjusted HR of 1.99 (95% CI 1.31–3.02) and 2.17 (95% CI 1.17–3.96), respectively.

Table 4. Association of baseline SBP groups with all-cause and CV mortality by baseline serum sodium levels

	All-cause mortality		CV mortality	
	HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> value
Overall cohort (<i>n</i> = 1,656) ^a				
SBP groups				
110–130 mm Hg	Ref		Ref	
<110 mm Hg	1.51 (1.12–2.03)	0.007	1.66 (1.09–2.53)	0.019
>130 mm Hg	1.40 (1.11–1.76)	0.004	1.50 (1.09–2.09)	0.015
Na <140 mmol/L (<i>n</i> = 636) ^b				
SBP groups				
110–130 mm Hg	Ref		Ref	
<110 mm Hg	1.99 (1.31–3.02)	0.001	2.17 (1.19–3.96)	0.011
>130 mm Hg	1.27 (0.89–1.82)	0.184	1.55 (0.94–2.57)	0.087
Na ≥140 mmol/L (<i>n</i> = 1,020) ^b				
SBP groups				
110–130 mm Hg	Ref		Ref	
<110 mm Hg	1.15 (0.74–1.79)	0.546	1.32 (0.71–2.46)	0.383
>130 mm Hg	1.45 (1.07–1.98)	0.018	1.48 (0.94–2.31)	0.089

SBP, systolic blood pressure; CV, cardiovascular; CVD, cardiovascular disease; CI, confidence interval. Bold values indicate *p* values less than 0.05. ^a Multivariate models adjusted for age, gender, history of CVD, diabetic status, baseline serum sodium, hemoglobin, serum albumin, 24-h urine volume, and anti-hypertension drugs. ^b Multivariate models adjusted for age, gender, history of CVD, diabetic status, hemoglobin, serum albumin, 24-h urine volume, and anti-hypertension drugs.

Discussion

In the present study, we demonstrated that participants with SBP >130 or <110 mm Hg had a significantly higher mortality risk compared with those with an SBP between 110 and 130 mm Hg. There was a significant interaction between baseline SBP and serum sodium for all-cause, but not CV mortality. Participants with serum sodium <140 mmol/L were at greatest risk of all-cause and CV mortality when SBP was <110 mm Hg. Conversely, those with serum sodium ≥140 mmol/L were at greatest risk when SBP was >130 mm Hg. Our results suggest that serum sodium may alter the association of SBP with mortality. Put simply, both hypo- and hypertension are associated with worse outcomes in PD patients; but for those with lower serum sodium, the greatest risk is associated with hypotension, as opposed to those with higher serum sodium, for whom hypertension may carry the greater risk.

Previous large cohort studies have demonstrated that a higher serum sodium is associated with higher SBP in dialysis patients [15]. Although few reports have examined the associations between serum sodium and BP in PD patients, low-sodium dialysate lowers BP due to enhanced diffusive sodium removal [16, 17]. More recently, Rutkowski et al. [13] performed a post hoc analysis of a prospective, randomized, controlled double-blind clinical trial comparing a sodium-reduced PD solution with a standard-sodium PD solution. They showed that for a glomerular filtration rate of <6 mL/min/1.72 m² on low-sodium dialysis fluid, SBP was reduced from 152 mm Hg at baseline to 137 mm Hg at week 12, and DBP decreased from 90 to 83 mm Hg [13]. The beneficial effect is probably related to increased sodium clearance and reduced total body sodium. In the present study, our results showed that the serum sodium level was positively linearly associated with SBP levels among PD patients.

Many studies have attempted to investigate the impact of BP on clinical outcomes in both HD and PD patients [18–20]. For example, Zager et al. [18] found a U-shaped curve rela-

tionship between post-dialysis SBP and the risk of CV mortality in HD patients. Results from a cohort of 24,525 incident HD patients demonstrated that patients with an SBP of 110–129 or SBP ≥ 160 mm Hg had a higher mortality risk than those with an SBP of 130–159 mm Hg [20]. In the PD population, several studies have been reported that show a similar relationship between SBP and the risk of clinical outcomes, which indicates a greater risk for all-cause and CV mortality in patients with SBP < 110 mm Hg or even < 120 mm Hg [21, 22]. Similarly, our study also found a U-shaped relationship in PD patients, which showed that patients with baseline SBP > 130 or < 110 mm Hg had a significantly higher mortality risk than those with SBP between 110 and 130 mm Hg.

In subgroup analyses, we showed an interaction between baseline serum sodium concentration and BP for all-cause mortality. When the serum sodium level was ≥ 140 mmol/L, SBP > 130 mm Hg was associated with an increased risk of all-cause death. Conversely, when serum sodium levels were < 140 mmol/L, patients with lower SBP (< 110 mm Hg) had an increased risk of all-cause and CV mortality. There may be different interpretations of such phenomena in PD patients. Recent studies have shown that sodium accumulation in the peritoneal interstitium leads to structural and functional changes in the peritoneum, while sodium accumulation in the interstitial skin was linked to left ventricular hypertrophy [23]. A meta-analysis by Borrelli et al. [24] showed that dialytic sodium removal was closely correlated with ultrafiltration in CAPD patients. Therefore, fluid overload produced by sodium accumulation and SBP > 130 mm Hg may contribute to a multiplier interaction effect on the cardiac load and on the risk of CV mortality. Alternatively, hyponatremia is associated with a catabolic state and malnutrition in dialysis patients [25, 26]. We suggest that malnutrition may contribute to the increased risk of mortality in patients with both serum sodium levels < 140 mmol/L and SBP < 110 mm Hg. However, in the present study, the association of SBP with outcomes remained significant after adjusting for BMI and serum albumin level, indicating that perhaps other physiological effects of lower serum sodium in PD patients could be in play. Based on our study results, further studies could consider whether individualized BP targets should take serum sodium into consideration, with treatment of hypertension perhaps being more important in those with higher serum sodium.

The major strength of this study is the relatively large study population and long follow-up period. In addition, to the best of our knowledge, the interaction between serum sodium and SBP has not been studied in CAPD patients. However, there were several limitations to this retrospective cohort study. First, it was a single-center study in Chinese CAPD patients, meaning that its generalizability may be limited. Second, we could not control for the impact of fluid status on BP or serum sodium because detailed information regarding the patients' body composition or fluid status was lacking. Similarly, a large number of patients in our study did not have baseline peritoneal equilibration test data. Therefore, we could not adjust for the impact of effects of membrane transport sodium and BP control. Third, the analysis was based on single serum sodium values and on office BP data rather than ambulatory-monitored BP data. Thus, we could not determine the impact of changes in these parameters on outcomes.

Conclusion

Our study showed that higher or lower SBP was associated with all-cause and CV mortality in our entire cohort. Association of BP with mortality was modified by serum sodium levels. Further studies are needed to verify whether individualized BP control that is based on a serum sodium level would contribute to improving PD patient outcomes.

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Statement of Ethics

This study was approved by the Ethics Committee of The First Affiliated Hospital of Sun Yat-sen University. Written informed consent was obtained from all participants.

Conflict of Interest Statement

All authors declare that they have no conflict of interest to disclose.

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Author Contributions

All authors had access to the data and a role in writing this manuscript. H.P.M., Y.G.Q., and H.J.Y. contributed to the study conception and design. Y.G.Q. and H.J.Y. performed analyses of data, interpretation of data, and drafting manuscript. L.F., X.H.Z., and W.L. contributed to data collection and manuscript revision. H.P.M., X.F.H., W.C., and X.Y. provided overall supervision.

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