Correlation Analysis of Blood Pressure Variability, Crystalloid Osmotic Pressure, and Cardiovascular Events in Maintenance Hemodialysis Patients

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Introduction. This study aimed to analyze the correlation between blood pressure variability (BPV), crystalloid osmotic pressure, and cardiovascular events (CEs) in patients undergoing maintenance hemodialysis (MHD).
Methods. This retrospective analysis was conducted on 71 patients with end-stage kidney disease who underwent hemodialysis at Beilun District People's Hospital from September 2021 to September 2022. The patients were divided into two groups based on the occurrence of CEs: a cardiovascular event group and a non-cardiovascular event group.
Results. The 71 patients were divided into two groups based on the occurrence of CEs: the CEs group (25 patients who experienced CEs) and the non-CEs group (46 patients who did not experience CEs). The CEs group had significantly higher levels of crystalloid osmotic pressure, standard deviation of systolic BP (SBP-SD), coefficient of variation of SBP (SBP-CV), SD of diastolic BP (DBP-SD), and DBP-CV ($P < .05$). Multivariate logistic regression analysis identified crystalloid osmotic pressure, SBP-CV, and DBP-CV as independent risk factors for CEs. The ROC curve analysis indicated that the combined predictive value of crystalloid osmotic pressure, SBP-CV, and DBP-CV was significant, with an area under the curve (AUC) of 0.963.
Conclusion. Elevated crystalloid osmotic pressure, SBP-CV, and DBP-CV are critical risk factors with strong predictive value for predicting CEs in MHD patients.

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INTRODUCTION

MHD is the primary treatment method for patients with end-stage kidney disease. Its principle involves replacing the lost functions of kidney failure through diffusion, osmosis, convection, and ultrafiltration to maintain the body's internal equilibrium, such as water and electrolyte balance, which are typically regulated by the kidneys. Adverse CEs are the principal complications and leading causes of death in MHD patients, accounting for 42% of total mortality.[1] Previous studies have demonstrated that changes in crystalloid osmotic pressure before and after dialysis significantly affect BP.[2] Crystalloid osmotic pressure refers to the pressure exerted by crystalloid solutes (such as sodium and chloride) in a solution, which influences the movement of water across cell membranes,[3] Moreover, it affects the fluid balance in the body during dialysis.

Investigations into the effects of crystalloid

osmotic pressure levels during dialysis on BP remain limited. Hypertension serves as an independent predictor of cardiovascular incidents and is notably prevalent among patients undergoing MHD.[4] BPV is defined as fluctuations in BP across a specified timeframe. The standard deviation (SD) and CV of dynamic BP measurements are utilized clinically to quantify BPV.[4] Recent findings suggest a significant association between BPV and the frequency of CEs.[6-8] However, research into the correlation between BPV, changes in crystalloid osmotic pressure during MHD, and adverse CEs is limited. This study aims to analyze whether an association exists between crystalloid osmotic pressure, BPV during MHD, and adverse CEs. We hypothesize that higher levels of crystalloid osmotic pressure, systolic BPV (SBP-CV), and diastolic BPV (DBP-CV) during dialysis are linked to an increased risk of CEs in MHD patients. Identifying these associations could aid in developing targeted interventions to monitor and manage crystalloid osmotic pressure and BPV during hemodialysis, potentially reducing the incidence of CEs and enhancing the prognosis and quality of life for MHD patients.

MATERIALS AND METHODS

Research object

This study encompassed 71 patients with end-stage kidney disease (ESKD) treated at Beilun District People's Hospital from September 1, 2021, to September 30, 2022. The cohort consisted of 43 males and 28 females, aged between 34 and 89 years, with an average age of 64.5 years. A systematic selection approach was adopted from the hospital's case series. The Ethics Committee of Beilun District People's Hospital, Ningbo City, approved the research protocol (Approval Number: YS202105), adhering to the ethical guidelines set forth in the 1964 Helsinki Declaration and its later amendments. All participants provided written informed consent before joining the study.

Inclusion criteria were as follows: (1) Clinical and laboratory confirmation of ESKD; (2) Receiving regular hemodialysis thrice weekly, each lasting 4-6 hours; (3) Achieving a urea clearance index (Kt/v) of at least 1.2 and maintaining a urine output of less than 200 mL/day; (4) Consent to participate in the study was documented in writing. (5) Agreement to have dynamic BP monitored during dialysis treatments. Exclusion criteria comprised: (1) Severe heart failure (NYHA Class III or IV) or a recent myocardial infarction (within 6 months); (2) Presence of acute infections or chronic debilitating diseases that could interfere with study outcomes; (3) Concurrent malignancy that requires active treatment; (4) Pregnant or lactating women; (5) Inability to provide informed consent due to cognitive impairment or lack of legal capacity. (6) Patients receiving treatments that could significantly alter BPV, such as recent initiation or dosage adjustment (within the last month) of antihypertensive medications known to affect BPV (e.g., vasodilators, calcium channel blockers, centrally acting antihypertensives, angiotensin II receptor blockers); (7) Patients receiving other forms of renal replacement therapy besides MHD, such as peritoneal dialysis or those who have undergone kidney transplantation.

Data Collection

Comprehensive clinical information from all patients, including sex, age, duration of dialysis, and presence of mellitus, hypertension, and hyperlipidemia were collected. During hemodialysis, five mL of fasting venous blood was collected from the enrolled patients for hematological tests, including liver function (albumin, alanine transaminase, aspartate transaminase), renal function (creatinine, blood urea nitrogen), lipid profile (total cholesterol, low-density lipoprotein, high-density lipoprotein), and electrolytes (sodium, potassium, calcium, phosphorus). Plasma colloid osmotic pressure is calculated as 2 × (plasma sodium concentration + plasma potassium concentration) + blood glucose concentration + blood urea nitrogen concentration] (units: mmol/L).[9] Kt/v, the ratio of urea clearance by the dialyzer to the volume of urea distribution, incorporates K (effective urea clearance), t (effective dialysis time), and v (urea volume distribution).

Ambulatory Blood Pressure Monitoring (ABPM)

The ABPM cuff to the non-fistula arm, two finger-widths above the elbow crease, during hemodialysis was applied. BP monitoring was conducted at 15-minute intervals, with a valid measurement constituting at least 90% of readings. Variability of SBP and DBP is calculated using the SD and CV, where CV is the SD divided by the mean BP, as described by Rothwell *et al.*[10]

MHD Protocol

Patients with MHD received routine heparin anticoagulation and used the same model of dialysis machine and bicarbonate dialysis solution. The dialysate temperature was set at 36.5°C with 500 mL/min. Vascular access was an autogenous forearm arteriovenous fistula, with a blood flow rate between 200-250 mL/min.

Tracking Major Adverse Cardiovascular Events (MACE)

Patients were monitored for major adverse CEs, including recurrent angina, acute myocardial infarction, severe arrhythmias, heart failure, coronary heart disease-related death, and stroke.

Statistical analysis

Data analysis was conducted using SPSS (version 26.0). Descriptive statistics summarized the demographic and clinical characteristics of the participants. The study employed independent samples t-tests and Mann-Whitney U tests for analyzing normally distributed and skewed data, respectively, between groups with and without CEs. The Chi-square test evaluated differences in categorical data. Multivariable logistic regression was utilized to ascertain independent risk factors for cardiovascular incidents, adjusting for potential confounders. The predictive capacities of crystalloid osmotic pressure and SBP-CV, DBP-CV were assessed via Receiver Operating Characteristic (ROC) curve analysis, with the AUC providing diagnostic accuracy. $P < .05$ was deemed statistically significant, ensuring a thorough and rigorous analysis of the collected data.

RESULTS

Comparison of data between the two groups

Patients were categorized based on the occurrence of cardiovascular adverse events into the non-CEs group (46 patients) and the CEs group (25 patients). There were no statistically significant differences in patient sex, age, or dialysis duration between the two groups ($P > .05$), confirming that the groups were comparable in these baseline characteristics. Statistically significant differences were noted in the levels of triglycerides and blood urea nitrogen (BUN) between the groups ($P < .05$), indicating that elevated BP fluctuations and higher crystalloid osmotic pressure may contribute to an increased risk of CEs (Table 1). This highlights the critical need for precise monitoring and control of these parameters during dialysis sessions.

Comparison of crystal osmotic pressure and BPV between non-CEs and CEs groups

The group experiencing CEs demonstrated elevated levels of crystal osmotic pressure, SBP-SD, SBP-CV, DBP-SD, and DBP-CV, in comparison to those without CEs. These significant differences ($P < .05$) suggest a correlation between enhanced variability of these metrics and an elevated risk of cardiovascular incidents in MHD patients (Table 2). Effective monitoring of these indicators may help in early identification and intervention for patients at elevated risk.

Multivariable logistic regression analysis of risk factors for CEs

In the multivariable logistic regression analysis, variables such as triglycerides, BUN, crystal osmotic pressure, and variability coefficients for both systolic and DBP, identified as significant in the univariate phase, were included. This analysis pinpointed crystal osmotic pressure and the variability coefficients of systolic and DBP as independent predictors of CEs (Table 3). This indicates that these factors independently contribute to the likelihood of CEs, highlighting the importance of comprehensive management of BP and osmotic pressure during dialysis.

The predictive value of crystal osmotic pressure, SBP-CV, and DBP-CV for cardiovascular adverse events

ROC curve analysis revealed that crystal osmotic pressure had an AUC of 0.851, with an optimal threshold set at 314.20 mmol/L, achieving a sensitivity of 0.840 and a specificity of 0.717. The AUC for systolic BPV was 0.860, with a threshold of 8.540 mmHg, and sensitivity and specificity values of 0.840 and 0.826, respectively. Diastolic BPV had an AUC of 0.875, with a threshold of 7.705 mmHg, and sensitivity and specificity of 0.800 and 0.826, respectively. When these parameters were analyzed together, the combined AUC reached 0.963, with sensitivity and specificity of 0.800 and 0.913, respectively, indicating robust predictive capability. The combined AUC was significantly larger than that for crystal osmotic

Table 1. Comparison of data between the non-CEs group and the CEs group

Data and parameters	Non-CEs group (n=46)	CEs group (n=25)	t/χ^2/z	*P*
Sex [male (%)]	30 (65.22)	13 (52.00)	1.185	0.276
Age (years)	61.43 ± 13.02	65.68 ± 6.62	-1.82	0.073
Dialysis history/month	33.00 (14.50,73.00)	27.00 (10.50,71.00)	-0.114	0.909
Dialysis frequency	3.00 (3.00,3.00)	3.00 (3.00,3.00)	0.110	0.913
Pre-dialysis hypertension [Number (%)]	11 (23.91)	7 (28.00)	0.143	0.705
Pre-dialysis mellitus [Number (%)]	8 (17.39)	2 (8.00)	1.181	0.277
Fasting blood glucose (mmol·L-1)	7.95 ± 3.70	8.56 ± 3.68	-0.663	0.509
Total cholesterol (mmol·L-1)	3.36 ± 0.91	3.54 ± 1.11	-0.73	0.468
Triglyceride (mmol·L-1)	1.89 ± 0.99	1.41 ± 0.43	2.805	0.007
High density lipoprotein cholesterol (mmol·L-1)	0.85 ± 0.26	0.95 ± 0.27	-1.395	0.168
Low-Density Lipoprotein Cholesterol (mmol·L-1)	1.76 ± 0.75	1.98 ± 0.89	-1.105	0.273
BUN (mmol·L-1)	16.13 ± 4.85	24.74 ± 3.00	-9.224	<0.001
Serum creatinin (μmol·L-1)	757.98 ± 287.58	639.16 ± 204.25	1.828	0.072
Blood uric acid (μmol·L-1)	385.20 ± 85.52	383.20 ± 76.04	0.098	0.923
Hemoglobin (g·L-1)	108.43 ± 14.95	108.96 ± 10.11	-0.176	0.861
Blood potassium (mmol·L-1)	4.47 ± 0.83	4.46 ± 0.62	0.085	0.932
Blood sodium (mmol·L-1)	138.96 ± 3.15	138.24 ± 7.70	0.562	0.576
Blood chlorine (mmol·L-1)	99.98 ± 6.27	99.38 ± 3.86	0.436	0.664
Blood calcium (mmol·L-1)	2.18 ± 0.22	2.22 ± 0.20	-0.783	0.436
Blood magnesium (mmol·L-1)	1.12 ± 0.14	1.11 ± 0.11	0.464	0.644
Blood phosphorus (mmol·L-1)	1.48 ± 0.46	1.57 ± 0.60	-0.727	0.470
Albumin (g·L-1)	39.07 ± 3.79	38.32 ± 4.00	0.786	0.435
Alanine aminotransferase (U·L-1)	16.00 (7.75,24.25)	11.00 (8.00,15.50)	-1.771	0.076
Aspartate aminotransferase (U·L-1)	16.13 ± 5.78	15.28 ± 7.72	0.525	0.601
Alkaline phosphatase (U·L-1)	89.76 ± 33.28	100.08 ± 31.01	-1.277	0.206
Gamma-glutamyltransferase (U·L-1)	21.50 (14.75,41.75)	20.00 (16.00,32.50)	0.060	0.952

Table 2. Comparison of crystal osmotic pressure and BPV between non-CEs and CEs groups

Parameters	Non-CEs group (n=46)	CEs group (n=25)	t	*P*
Crystal osmotic pressure	310.95 ± 5.87	321.88 ± 9.46	-5.25	<0.001
SBP-SD	9.08 ± 2.27	12.75 ± 3.09	-5.735	<0.001
SBP-CV	6.61 ± 1.80	9.14 ± 1.67	-5.799	<0.001
DBP-SD	5.66 ± 2.09	7.98 ± 1.45	-4.941	<0.001
DBP-CV	6.08 ± 1.84	9.03 ± 1.74	-6.578	<0.001

Table 3. Multivariable logistic regression analysis of risk factors for CEs

Parameters	B	Standard error	Wald	*P*	OR	95%CI
Crystal osmotic pressure	0.320	0.118	7.349	0.007	1.377	(1.093,1.735)
SBP-CV	0.881	0.359	6.023	0.014	2.413	(1.194,4.878)
DBP-CV	1.010	0.427	5.606	0.018	2.747	(1.190,6.339)

pressure, SBP-CV, and DBP-CV alone (P = .008, P = .020, P = .019) (Figure 1), indicating that monitoring and controlling these parameters can reduce cardiovascular risk and provide a robust tool for identifying high-risk patients and guiding personalized treatment strategies.

DISCUSSION

Current literature suggests that cardiovascular incidents remain a principal cause of mortality among individuals receiving renal replacement therapy through MHD. Investigations have linked variability in BP, both pre- and post-dialysis, with poor outcomes, underscoring its importance as a prognostic indicator.[11] Additionally, changes in neuroendocrine regulation in MHD patients can lead to metabolic disorders in the internal environment, poor energy control, and excessive salt intake, all contributing to changes in crystal osmotic pressure.[12,13]

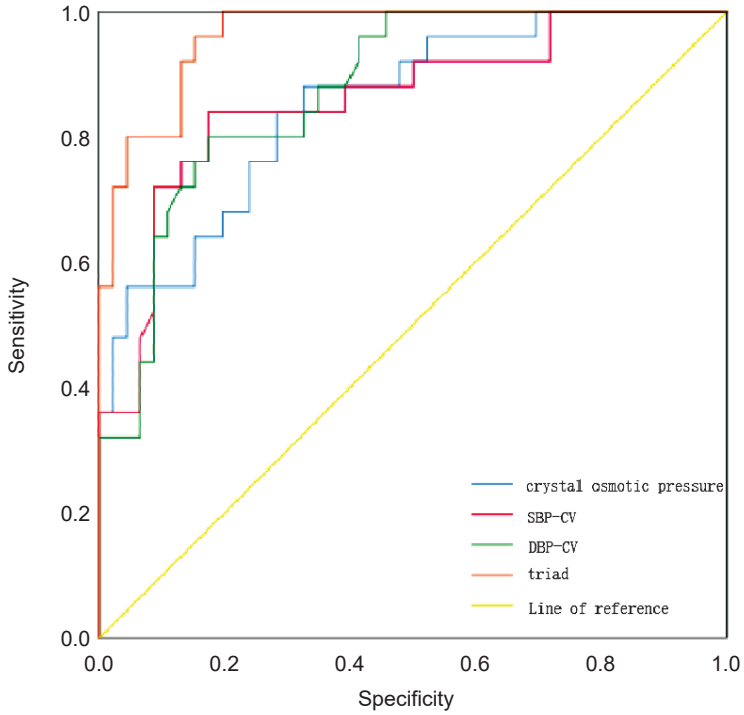

Figure 1. ROC curve for prediction of BPV and crystalloid osmotic pressure.

This study observed BPV and crystal osmotic pressure levels during hemodialysis among MHD patients. Of the 71 MHD study participants, 25 experienced CEs, resulting in an incidence rate of approximately 35.21%, which is relatively high. Further research has confirmed that BPV, independent of BP standard deviation, may exhibit an increasing trend, suggesting some patients experience unstable BPV during dialysis.[14-16] This instability may be related to vascular sclerosis, microvascular disease, tissue metabolic damage, and autonomic nervous system disorders,[12,13] indicating a significant correlation between BPV and CEs.

Further multivariable logistic regression analysis identified crystal osmotic pressure, SBP-SD, and DBP-SD as independent risk factors for cardiovascular incidents. The essence and central link of kidney failure is the decrease in glomerular filtration rate (GFR), leading to dysfunction in the reabsorption or excretion of substances that constitute crystal osmotic pressure. Although MHD partially replaces the filtration function of the glomerulus, significant differences remain compared to the body's own filtration. These differences can result in fluctuations in crystal osmotic pressure. The role of blood crystal osmotic pressure is crucial in maintaining proper fluid exchange and electrolyte balance across cellular membranes, as well as preserving the integrity and functionality of blood cells. A disruption in this balance markedly raises the risk of cardiovascular complications.[17]

In patients without renal disease, an increase in BPV correlates with a heightened risk of cardiovascular incidents and mortality. Notably, patients receiving MHD demonstrate elevated BPV when compared to non-MHD recipients.[18,19] SBP-CV and DBP-CV are key parameters that reflect BPV. Therefore, effective management of BP should simultaneously consider three pivotal factors to reduce cardiovascular complications associated with BPV fluctuations. In this context, crystal osmotic pressure, together with SBP-CV and DBP-CV, emerges as an independent predictor of adverse cardiovascular outcomes in MHD patients.

Finally, ROC curve analysis was used to evaluate the predictive value of crystal osmotic pressure, SBP-CV, and DBP-CV for adverse CEs. When the crystal osmotic pressure reached 314.20 mmol/L, the sensitivity was 0.840 and the specificity was 0.717. The SBP-CV was 8.540 mmHg, with a sensitivity of 0.840 and a specificity of 0.826. The DBP-CV was 7.705 mmHg, with a sensitivity of 0.800 and

a specificity of 0.826. The combined AUC area for the three factors was 0.963, with a sensitivity of 0.800 and a specificity of 0.913. This demonstrates that each factor significantly predicts adverse CEs in MHD patients.

Study Limitations

This study has several limitations, including its retrospective design, which limits causal inferences; the single-center setting, which may affect generalizability; a relatively small sample size, potentially limiting statistical power; variability in BP measurement techniques; and potential residual confounding by unmeasured variables such as medication adherence, diet, and other comorbidities. Future research should focus on multicenter, prospective studies with larger sample sizes to confirm the associations identified in this study and establish causality. Additionally, investigating the underlying mechanisms linking crystalloid osmotic pressure and BPV to CEs could provide deeper insights into potential therapeutic targets. Research should also explore the development and testing of interventions aimed at stabilizing BP and osmotic pressure during dialysis to reduce cardiovascular risk. Finally, studies investigating the impact of individualized treatment plans based on these predictive parameters on patient outcomes would be valuable.

Future Directions

The findings of this study can be directly applied to clinical practice to enhance the care for patients undergoing MHD. Routine monitoring of crystalloid osmotic pressure and BPV during dialysis sessions can help identify patients at higher risk of CEs. Clinicians can then implement targeted interventions such as adjusting dialysis protocols, optimizing fluid management, and using medications to stabilize BP. Personalized treatment plans based on these predictive parameters can lead to more effective management of cardiovascular risk, ultimately improving patient outcomes. Educating patients regarding the importance of maintaining stable BP and electrolyte balance can also empower better adherence to treatment recommendations and lifestyle modifications.

CONCLUSION

In conclusion, pronounced levels of SBP-SD, DBP-SD, along with elevated crystal osmotic pressure during hemodialysis, are identified as significant risk factors for CEs in MHD patients. These indicators also possess prognostic value. Consequently, the intensity of hemodialysis should be customized based on the individual's BPV and crystal osmotic pressure measurements. It is advisable to implement early screening for cardiovascular conditions and to actively engage in secondary prevention strategies aimed at curtailing the incidence of adverse cardiovascular outcomes during MHD sessions.

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ETHICAL COMPLIANCE

This study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. The research protocol was reviewed and approved by the Ethics Committee of Beilun District People's Hospital (Approval Number: YS202105). Written informed consent was obtained from all patients prior to their participation in the study.

CONFLICT OF INTEREST

The authors declare no potential conflicts of interest with respect to this article.

AUTHOR CONTRIBUTIONS

TC and LZ designed the study and performed the experiments, SC collected the data, LS analyzed the data, TC and LZ prepared the manuscript. All authors read and approved the final manuscript.

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