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Correlation between home systolic blood pressure variability and cognitive impairment in maintenance hemodialysis patients

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Abstract

Introduction: To investigate the correlation between home blood pressure variability and cognitive function in maintenance hemodialysis (MHD) patients.

Methods: Patients who received MHD were included. Their home blood pressure on nondialysis days within 1 week was collected. All patients were assessed with the Montreal Cognitive Assessment scale, according to which the patients were divided into cognitive impairment (CI) group and non-CI group, and the differences between two groups were compared.

Results: A total of 224 patients were included in the study, of which 168 had CI (75%). Compared with non-CI group, patients in CI group had larger variability of systolic blood pressure (SBPV) (8.4 [6.7, 10.6]% vs. 6.9 [4.9, 8.8]%, $P < 0.001$). The smooth fitting curve (OR = 1.2, 95% CI [1.1–1.4], $P < 0.001$) and trend test (P for trend = 0.004) showed that the risk of CI raised with the increase of SBPV. The patients were further divided into tertiles according to the SBPV. We also found a gradual increase in the proportion of incident CI in the three tertiles. Multiple logistic regression analysis showed that age, shorter years of education, less frequency of hemodialysis, and greater SBPV were the dependent risk of CI.

Conclusion: In conclusion, greater SBPV indicates higher risk of cognitive impairment in MHD patients.

1 | INTRODUCTION

Cognition is a process in which human brain receives external information and then processes and transformed it into internal psychological activities, so as to obtain or apply knowledge. Cognition includes memory, language, visual space, execution, calculation, understanding, and judgment. CI refers to the impairment of one or more of the above cognitive functions, which affects individual's daily or social ability.[1] CI in maintenance hemodialysis (MHD) patients may disturb their daily life, work, and mood, reduce their compliance with medication and treatment, increase the rate of hospitalization, lead to deterioration and termination of dialysis, and even death and poor prognosis.[2] The prevalence rate of CI is 3.2% to 42% in general population,[3,4] while is much lower than 60% to 80% in MHD patients.[5–7]

Due to the influence of hemodialysis-related factors and the primary kidney disease that leads to uremia, there may be more influencing factors of CI. Therefore, understanding the risk factors of

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CI in MHD patients is of great significance to improve their cognitive function. At present, studies have confirmed that advanced age, hypertension, diabetes, and years of education are the influencing factors of CI.[8] In recent years, more and more research have shown that blood pressure variability (BPV) is related to CI, and it has been proved to be an independent risk factor.[9–11] BPV refers to the degree of blood pressure fluctuation over a period of time.[12,13] Previous studies have also found that the prevalence of hypertension in MHD patients is as high as 80%.[14] Affected by hemodialysis, their blood pressure is more likely to fluctuate than the general population However, whether the effect of BPV on CI is different between MHD and non-hemodialysis patients is rarely reported. Compared with the consulting room blood pressure, home blood pressure is more repeatable, free of white coat effect and has greater prognostic significance.[15] Therefore, the purpose of this study was to investigate the correlation between home BPV and cognitive function in patients with MHD.

2 | MATERIALS AND METHODS

2.1 | Population

Patients who received maintenance hemodialysis in the Blood Purifacation Department of Wuhan Fourth Hospital from December 1, 2019, to August 31, 2020, were selected. The following were the inclusion criteria: (1) age ≥18 years, (2) dialysis vintage ≥3 months, (3) upper limb blood pressure could be measured at home, and (4) patients who voluntarily cooperated with cognitive function evaluation. The following were the exclusion criteria: (1) patients who could not cooperate with home blood pressure measurement; (2) patients with sequelae of craniocerebral trauma and cerebral stroke, vasculitis, alcoholism, malignant tumor, acute myocardial infarction, acute heart failure and severe infection; and (3) patients were blind and deaf-mute.

2.2 | Methods

Before the study, each patient learned the right way of blood pressure measurement. All patients used validated, electronic sphygmomanometer to measure brachial artery blood pressure, and their blood pressure was recorded continuously for four times (before breakfast [7:00–8:30], before lunch [10:30–12:00], before dinner [17:00–19:00], and before sleep) on nondialysis days in a week. If the patient took antihypertensive drugs, he or she would be asked to measure blood pressure before taking the medicine. The calculation method for BPV CV (coefficient of variance) is as follows: CV = (standard deviation/mean) * 100%, which can better reflect the degree of dispersion in the unit mean. At the same time, baseline clinical data were collected, including gender, age, years of education, smoking history, dialysis vintage, dialysis prescription, vascular access, primary renal disease, complications, hemoglobin, serum albumin, creatinine, urea nitrogen, triglyceride, total cholesterol, parathyroid hormone, calcium, phosphorus, sodium, and serum uric acid. Blood specimens for biochemical tests were collected from the vascular access before midweek hemodialysis sessions. They were collected 7:00–8:00 h before morning sessions and 11:00–12:00 h before midday sessions. The cognitive function was scored by two professionally trained personnel according to the MoCA scoring criteria and rules (the creditability of grader was more than 0.90). Each patient completed MoCA test during the first hour of hemodialysis,[16,17] and the score less than 26 (less than 25 if years of education was less than 12) was defined as CI.

2.3 | Statistics

Categorical and continuous normal distribution variables were expressed as percentage and mean ± SD, respectively. Continuous variables of nonnormal distribution were expressed as median concentration and quartile distance. The analysis of linear trends was used to assess the associations between increasing the variability in SBPV levels and risk of CI after the sample was divided into tertiles based on the distribution of controls. Multivariate logistic regression analysis was used to identify the independent predictors of CI. And the nomogram model was used for calculating the patient-specific probabilities of the occurrence of CI. The receiver operating characteristic (ROC) methodology was used to assess the accuracy of the nomogram. All statistical tests were two-tailed, and a P value less than 0.05 was considered statistically significant. Analyses were performed with R version 3.6.0. GraphPad Prism8 and Photoshop version 6.0 software were used in graphic production.

3 | RESULTS

According to the inclusion and exclusion criteria, 224 patients were included in this study. There were 138 males (62%) and 86 females (38%). The youngest patient was 25 years old; the oldest was 88 years old (mean age 58 ± 14 years), and the median age was 60 years. There were 206 cases of hypertension (92%), 77 of diabetes (34%), 115 (51%) of less than 12 years of education, 109 (49%) of 12 years of education and 44 with smoking history (20%). The shortest and longest dialysis vintage was 3 months and 182 months, respectively. The average dialysis vintage was 47 ± 36 months, and the median dialysis vintage was 37 months; 154 patients (69%) had arteriovenous fistula as vascular access for hemodialysis, and 70 patients (31%) had tunneled cuffed catheters; 101 (45%) had the primary renal diseases as primary glomerulonephritis, and 72 (32%) had the diabetic nephropathy.

We divided patients into cognitive impairment group and non-cognitive impairment group in order to determine whether there was a difference in baseline clinical data between the two groups. There were 168 cases (75%) in CI group and 56 (25%) in non-cognitive impairment group. Compared with noncognitive impairment group, patients in CI group were older (61 ± 12 vs. 49 ± 13, $P = 0.000$) and

TABLE 1 Demographic and clinical characteristics of the patients at baseline

Characteristics	CI group $N = 168$	Non-CI group $N = 56$	*P* value
Gender, *N* (%)			0.874
Female	65 (38.7)	21 (37.5)	
Male	103 (61.3)	35 (62.5)	
Age (years), mean ± SD	61 ± 12	49 ± 13	<0.001
Educational level (years), *N* (%)			<0.001
<12	100 (59.5)	15 (26.8)	
≥12	68 (40.5)	41 (73.2)	
History of smoking, *N* (%)	32 (19.0)	12 (21.4)	0.698
Dialysis vintage (months), median (IQR)	35 (18, 65)	45 (24, 74)	0.148
Dialysis prescription, *N* (%)			0.016
Twice a week	50 (29.8)	6 (10.7)	
Five times every 2 weeks	23 (13.7)	11 (19.6)	
Three times a week	95 (56.5)	39 (69.6)	
Dry weight (kg), mean ± SD	58.8 ± 11.0	62.1 ± 11.3	0.054
Interdialytic weight gain (kg), mean ± SD	2.9 ± 1.0	2.8 ± 1.0	0.717
Vascular access, *N* (%)			0.067
Tunneled cuffed catheter	58 (34.5)	12 (21.4)	
AvF	110 (65.5)	44 (78.6)	
Primary renal disease, *N* (%)			0.027
Renal allograft dysfunction	2 (1.2)	3 (5.4)	
Glomerulonephritis	67 (39.9)	34 (60.7)	
Hypertensive kidney lesion	26 (15.5)	5 (8.9)	
Diabetic nephropathy	62 (36.9)	10 (17.9)	
Obstructive nephropathy	5 (3.0)	1 (1.8)	
Polycystic kidney	5 (3.0)	2 (3.6)	
Lupus nephritis	1 (0.6)	1 (1.8)	
Comorbidities, *N* (%)			
Hypertension	158 (94.0)	48 (85.7)	0.083
Diabetes	65 (38.7)	12 (21.4)	0.019
Anti-hypertensive drugs, *N* (%)			
ACEI	72 (42.9)	23 (41.1)	0.815
ARB	89 (53.0)	27 (48.2)	0.537
β-blockers	140 (83.3)	42 (75.0)	0.166
CCB	147 (87.5)	44 (78.6)	0.103
α-blockers	46 (27.4)	16 (28.6)	0.863
Hemoglobin (g/L), median (IQR)	102 (90, 112)	110 (93, 117)	0.031
Albumin (g/L), mean ± SD	37.4 ± 4.1	38.1 ± 3.9	0.25
Creatinine (μmol/L), mean ± SD	858.1 ± 314.9	942.4 ± 274.1	0.075
Urea nitrogen (mmol/L), median (IQR)	22.28 (17.60, 27.75)	22.46 (17.07, 27.00)	0.855
Triglyceride (mmol/L), median (IQR)	1.33 (0.88, 1.84)	1.43 (0.94, 2.47)	0.285
TC (mmol/L), median (IQR)	3.82 (3.06, 4.56)	3.84 (3.29, 4.41)	0.972
PTH (pg/ml), median (IQR)	401.1 (215.5, 668.0)	417.1 (209.9, 674.2)	0.936
Calcium (mmol/L), mean ± SD	2.14 ± 0.27	2.09 ± 0.23	0.23
Phosphorus (mmol/L), median (IQR)	1.69 (1.39, 1.95)	1.57 (1.33, 2.09)	0.503
Sodium (mmol/L), mean ± SD	138.6 ± 3.5	138.6 ± 3.0	0.937
Uric acid (μmol/L), median (IQR)	435 (371, 496)	444 (361, 503)	0.736

(Continues)

TABLE 1 (Continued)

Characteristics	CI group $N = 168$	Non-CI group $N = 56$	*P* value
SBPV (%), median (IQR)	8.4 (6.7, 10.6)	6.9 (4.9, 8.8)	<0.001
DBPV (%), median (IQR)	7.9 (6.1, 9.5)	6.8 (4.9, 9.3)	0.077

Abbreviations: ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blocker; AvF, arteriovenous fistula; CCB, calcium channel blocker; CI, cognitive impairment; DBPV, diastolic blood pressure variability; IQR, interquartile range; *N*, number; PTH, parathyroid hormone; TC, total cholesterol; SBPV, systolic blood pressure variability.

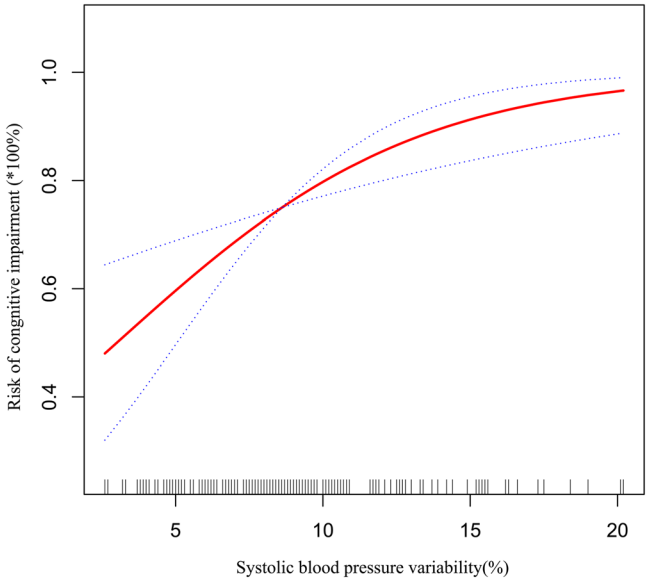

FIGURE 1 Relationship between SBPV and risk of cognitive impairment. Longitudinal coordinates the risk of cognitive impairment, the abscissa indicates SBPV

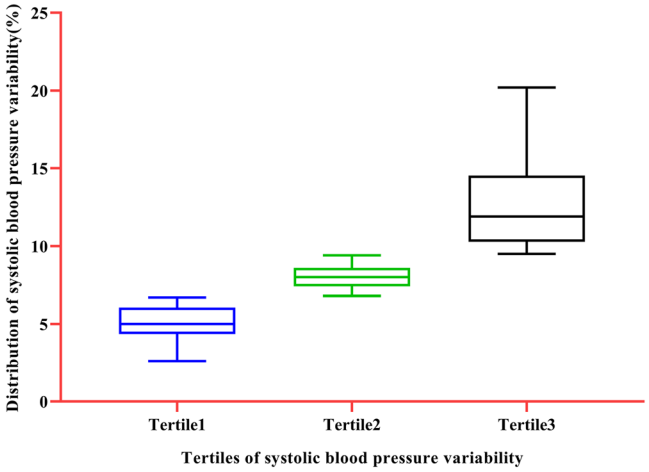

FIGURE 2 SBPV levels in MHD patients who were grouped in tertiles

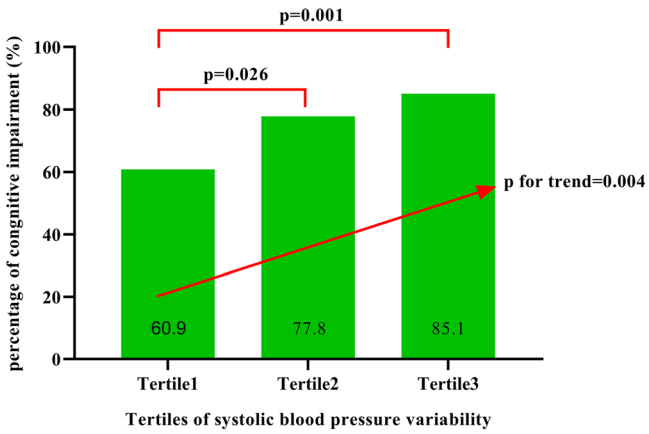

FIGURE 3 SBPV and rates of CI. Tertile1, Tertile2 and Tertile3 are tertile groupings based on SBPV levels

had significantly more individuals with education less than 12 years (100 vs.15, $P < 0.001$), lower proportion in receiving hemodialysis three times a week (56.5% vs. 69.6%, $P = 0.016$), higher proportion of patients with diabetes (38.7% vs. 21.4%, $P = 0.019$), lower level of hemoglobin (102 [90, 112] vs. 110 [93, 117], $P = 0.031$) and larger SBPV (8.4 [6.7, 10.6] % vs. 6.9 [4.9, 8.8]%, $P < 0.001$). However, there were no significant differences in gender, history of smoking, dialysis vintage, vascular access, prevalence of hypertension, use of antihypertensive drugs, serum albumin, creatinine, urea nitrogen, triglyceride, total cholesterol, parathyroid hormone, calcium, phosphorus, sodium, uric acid, or diastolic BPV between two groups ($P > 0.05$; Table 1).

In order to clarify the relationship between SBPV and CI in patients with MHD, we drew a smooth fitting curve for analysis. The results showed that, with the increase of SBPV, patients had a higher risk of CI (OR = 1.2, 95% CI [1.1–1.4], $P < 0.001$; Figure 1). The patients were further divided into tertiles according to the SBPV, compared with Tertile 1, patients in Tertile 2 (5.0 [4.4, 6.1]% vs. 8.0 [7.4, 8.6]%, $P < 0.001$) and Tertile 3 (5.0 [4.4, 6.1]% vs. 11.9 [10.3, 14.5]%, $P < 0.001$) had significantly higher SBPV, compared with Tertile 2, the SBPV of Tertile 3 was higher (8.0 [7.4, 8.6] % vs. 11.9 [10.3, 14.5] %, $P < 0.001$). The distribution of SBPV in the three groups is shown in Figure 2. We also compared the clinical baseline data among the tertiles. Compared with Tertile 1, patients in Tertile 2 and Tertile 3 were older ($P = 0.005$) and had a higher proportion of diabetes ($P = 0.027$). Patients in Tertile 3 showed lower levels of serum albumin, creatinine and uric acid ($P < 0.05$). Compared with Tertile 2 and Tertile 3, serum total cholesterol levels in Tertile 1 were lower ($P = 0.018$). We also found a gradual

TABLE 2 Characteristics of 224 patients with MHD by SBPV tertiles

Range of SBPV	Tertile 1 2.6–6.8 *N* = 69	Tertile 2 6.8–9.4 *N* = 81	Tertile 3 9.4–20.2 *N* = 74	*P* value
Gender, *N* (%)				0.365
Female	22 (31.9)	32 (39.5)	32 (43.2)	
Male	47 (68.1)	49 (60.5)	42 (56.8)	
Age (years), mean ± SD	55 ± 14	58 ± 13	63 ± 13	0.005
Educational level (years), *N* (%)				0.053
<12	28 (40.6)	42 (51.9)	45 (60.8)	
≥12	41 (59.4)	39 (48.1)	29 (39.2)	
History of smoking, *N* (%)	16 (23.2)	14 (17.3)	14 (18.9)	0.651
Dialysis vintage (months), median (IQR)	32 (16, 63)	36 (20, 71)	44 (24, 67)	0.194
Dialysis prescription, *N* (%)				0.293
Twice a week	21 (30.4)	17 (21.0)	18 (24.3)	
Five times every 2 weeks	12 (17.4)	15 (18.5)	7 (9.5)	
Three times a week	36 (52.2)	49 (60.5)	49 (66.2)	
Dry weight (kg), mean ± SD	60.2 ± 11.0	60.2 ± 10.8	58.4 ± 11.5	0.445
Interdialytic weight gain (kg), mean ± SD	2.7 ± 0.9	3.0 ± 1.0	2.9 ± 1.0	0.311
Vascular access, *N* (%)				0.223
Tunneled cuffed catheter	18 (26.1)	31 (38.3)	21 (28.4)	
AvF	51 (73.9)	50 (61.7)	53 (71.6)	
Primary renal disease, *N* (%)				0.002
Renal allograft dysfunction	1 (1.4)	3 (3.7)	1 (1.4)	
Glomerulonephritis	46 (66.7)	35 (43.2)	20 (27.0)	
Hypertensive kidney lesion	4 (5.8)	13 (16.0)	14 (18.9)	
Diabetic nephropathy	13 (18.8)	26 (32.1)	33 (44.6)	
Obstructive nephropathy	3 (4.3)	2 (2.5)	1 (1.4)	
Polycystic kidney	2 (2.9)	2 (2.5)	3 (4.1)	
Lupus nephritis	0 (0.0)	0 (0.0)	2 (2.7)	
Comorbidities, *N* (%)				
Hypertension	61 (88.4)	77 (95.1)	68 (91.9)	0.327
Diabetes	16 (23.2)	28 (34.6)	33 (44.6)	0.027
Antihypertensive drugs, *N* (%)				
ACEI	27 (39.1)	36 (44.4)	32 (43.2)	0.794
ARB	35 (50.7)	42 (51.9)	39 (52.7)	0.972
β-blockers	57 (82.6)	64 (79.0)	61 (82.4)	0.811
CCB	57 (82.6)	70 (86.4)	64 (86.5)	0.755
α-blockers	18 (26.1)	21 (25.9)	23 (31.1)	0.726
Hemoglobin (g/L), median (IQR)	104 (94, 116)	105 (91, 112)	103 (89, 113)	0.785
Albumin (g/L), mean ± SD	38.2 ± 4.1	38.1 ± 3.3	36.5 ± 4.6	0.03
Creatinine (μmol/L), median (IQR)	884.7 (672.8, 1108.9)	937.3 (713.8, 1111.1)	792.9 (653.4, 999.4)	0.038
Urea nitrogen (mmol/L), median (IQR)	21.81 (17.93, 27.96)	22.61 (18.44, 27.34)	22.57 (15.97, 26.03)	0.752
Triglyceride (mmol/L), median (IQR)	1.22 (0.79, 1.78)	1.52 (1.00, 2.16)	1.30 (0.95, 1.83)	0.206
TC (mmol/L), median (IQR)	3.49 (3.01, 3.96)	3.93 (3.41, 4.61)	3.87 (3.09, 4.60)	0.018
PTH (pg/ml), median (IQR)	381.5 (179.8, 546.5)	416.5 (227.0, 827.3)	420.7 (215.4, 742.9)	0.275
Calcium (mmol/L), median (IQR)	2.12 (1.97, 2.27)	2.16 (2.02, 2.30)	2.14 (1.95, 2.27)	0.482
Phosphorus (mmol/L), mean ± SD	1.70 ± 0.49	1.71 ± 0.53	1.71 ± 0.48	0.948
Sodium (mmol/L), median (IQR)	139.0 (137.1, 141.0)	138.0 (136.4, 140.5)	138.0 (136.0, 140.0)	0.196

(Continues)

TABLE 2 (Continued)

Range of SBPV	Tertile 1 2.6–6.8 $N = 69$	Tertile 2 6.8–9.4 $N = 81$	Tertile 3 9.4–20.2 $N = 74$	*P* value
Uric acid (μmol/L), median (IQR)	433 (366, 489)	459 (407, 518)	410 (329, 485)	0.004
DBPV(%), median (IQR)	5.5 (4.6, 7.2)	7.4 (6.1, 8.9)	9.5 (7.9, 11.2)	0.001
Cognitive function, *N* (%)				0.003
CI	42 (60.9)	63 (77.8)	63 (85.1)	
Non-CI	27 (39.1)	18 (22.2)	11 (14.9)	

Abbreviations: ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blocker; AvF, arteriovenous fistula; CCB, calcium channel blocker; IQR, interquartile range; *N*, number; PTH, parathyroid hormone; SBPV, systolic blood pressure variability; TC, total cholesterol.

TABLE 3 Logistic regression of cognitive function

	Univariate			Multivariate		
Variable	OR	95% CI	*P* value	OR	95% CI	*P* value
Age	1.079	1.050–1.108	<0.001	1.062	1.030–1.095	<0.001
Educational level						
<12 years	Reference			Reference		
≥12 years	0.249	0.128–0.485	<0.001	0.411	0.193–0.876	0.021
Dialysis prescription						
Twice a week	Reference			Reference		
Five times every 2 weeks	0.251	0.083–0.762	0.015	0.295	0.085–1.019	0.054
Three times a week	0.292	0.116–0.737	0.009	0.314	0.110–0.896	0.03
Diabetes	2.314	1.138–4.706	0.021	1.277	0.555–2.938	0.565
Hemoglobin	0.981	0.964–0.999	0.036	0.981	0.960–1.002	0.075
SBPV	1.216	1.088–1.361	0.001	1.141	1.008–1.291	0.037

Abbreviations: CI, confidence interval; OR, odds ratio; SBPV, systolic blood pressure variability.

increase in the proportion of incident CI in the three groups, which was 60.9%, 77.8% and 85.1%, respectively ($P = 0.003$). We further conducted a trend test. When setting patients in Tertile 1 as reference, the risk of CI in Tertile 2 and Tertile 3 increased gradually, with *P* values of 0.026 and 0.001, respectively, and *P* for trend = 0.004 (Figure 3). There was no significant difference among the three groups in terms of gender, years of education, history of smoking, dialysis age, dialysis scheme, vascular access option, and so forth ($P > 0.05$, Table 2).

According to the results of Table 1, we included age, year of education, dialysis prescription, diabetes, hemoglobin, and SBPV in multiple logistic regression analysis, which showed that older (OR = 1.062, 95% CI [1.030–1.095], $P = 0.000$), shorter years of education (OR = 0.411, 95% CI [0.193–0.876], $P = 0.021$), less frequency of hemodialysis (OR = 0.314, 95% CI [0.110–0.896], $P = 0.030$), and greater SBPV (OR = 1.141, 95% CI [1.008–1.291], $P = 0.037$) all indicated higher risk of cognitive impairment (Table 3). Nomogram model can be used to individually evaluate the risk of CI in patients, according to the results of multivariate logistic regression analysis, we put the independent risk factors of CI into the Nomogram model, including age, years of education, dialysis prescription and SBPV. Each of the above four independent influencing factors was given a corresponding score, and then a total score of the four factors was accumulated to estimate the risk of CI (Figure 4). In order to evaluate the accuracy of nomogram model in the diagnosis of CI in patients with MHD, we drew a ROC curve. The results showed that nomogram model had a higher accuracy in the diagnosis of CI, the area under the ROC curve was 0.8040 (95% CI: 0.7410–0.8671), the specificity was 67.86%, and the sensitivity was 80.95% (Figure 5).

4 | DISCUSSION

This paper discussed the incidence and related risk factors of CI in patients with MHD. The results showed that the prevalence of CI in patients with MHD was significantly higher, and greater SBPV indicated higher risk of CI. Meanwhile, we also found that aging, shorter years of education, and less frequency of dialysis per week all increased the risk of CI.

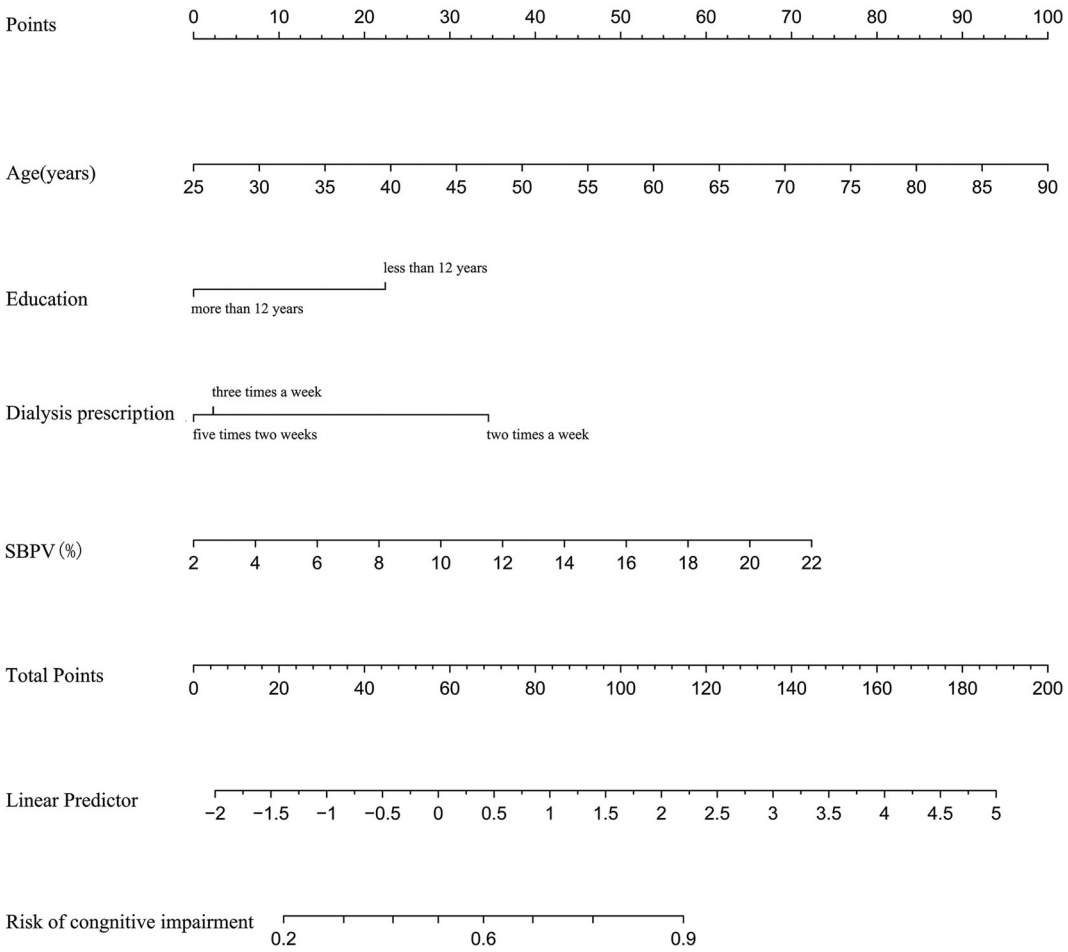

FIGURE 4 Nomogram predicts risk of cognitive impairment in MHD patients

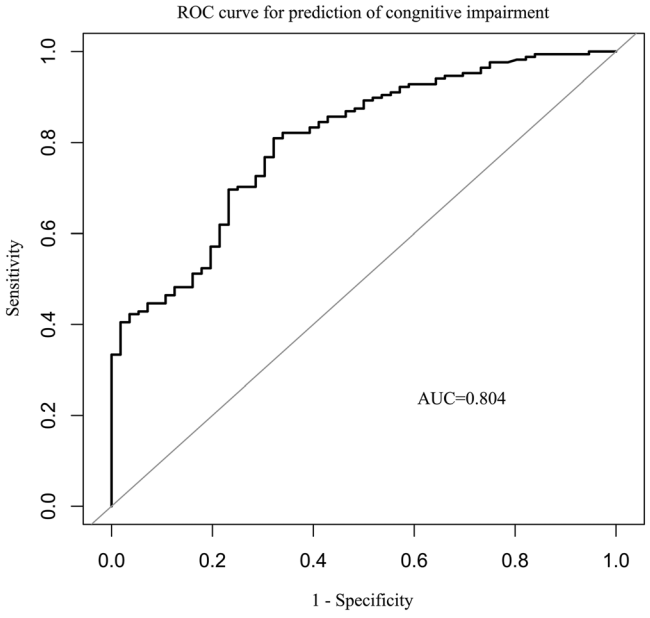

FIGURE 5 Receiver operating characteristic curve (ROC) for the prediction of cognitive impairment

At present, many indicators can quantify BPV. Standard deviation (SD) is a traditional classical indicator of BPV quantification but many studies have shown that SD is related to mean blood pressure and fails to fully reflect the characteristics of BPV. In recent years, some new BPV indicators, such as coefficient of variation (CV), variation independent of mean blood pressure (VIM), and average real variability (ARV), have eliminated the effect of mean blood pressure on BPV, and their predictive ability may be stronger than that of SD.[18–21] Some studies have also shown that CV is a powerful predictor of cardiovascular and cerebrovascular diseases[22] and is easier to calculate in clinical practice, so this paper used CV to calculate BPV. This study found that greater SBPV indicated higher risk of CI, which was basically consistent with previous studies.[11,23,24] However, diastolic BPV in our study had no significant effect on cognitive function. Qin et al. also found no association between diastolic BPV and cognitive function decline in 65-year-old adults.[11] However, some studies have found that there is a significant correlation between diastolic BPV and the decline of cognitive function,[24] which also needs to be further confirmed by more studies. BPV may affect cognitive function by the following mechanisms. First of all, increasing BPV reflects unstable

systematic hemodynamics, which may lead to microvascular damage and changes in brain structure and function.[25] Second, large fluctuations in blood pressure can induce frequent hypotension attack, insufficient cerebral perfusion, nerve damage, and cell death, which in turn lead to cerebral microvascular disease and hippocampal atrophy, accelerating CI.[11,26] Third, Sabayan et al.[24] believe that cerebral microhemorrhage and cortical infarction may also be the potential pathogenesis of the relationship between BPV and CI. Finally, other studies have found that hypertension variability is also associated with white matter lesions, which may affect cognitive function.[27,28] It should be noted that, in several observations studies, antihypertensive medication use is associated with less cognitive decline.[29] There are no similar findings in our study; this may be that most patients in our study had hypertension and used a variety of antihypertensive drugs. More studies are needed to confirm it in the future.

In the current study, the incidence of CI in patients with MHD was as high as 75%, which was basically consistent with previous studies.[5–7] As is known to all, there are many factors that affect cognitive dysfunction. Many studies have shown that older non-hemodialysis patients have an increasing risk of CI. Our study also showed that age was a risk factor for CI, and the older the age, the higher the risk of cognitive impairment. Drew et al. also had a similar finding.[30,31] The possible reason is that the elderly is often accompanied with cerebral arteriosclerosis, resulting in vascular stenosis, insufficient cerebral perfusion, and CI.

Some studies have shown that longer years of education indicates lower risk of cognitive impairment, which is basically consistent with our study.[32] The possible reason may be that education is associated with healthier lifestyles and better socioeconomic status.[33] Another possible explanation is that highly educated patients engage in more mental activity, which can promote brain metabolic activity and blood circulation and complicate brain structure; besides, brain neurons may have more abundant reserves, which alleviates the process of CI to some extent.

We also found that increasing hemodialysis frequency per week was able to decrease the risk of cognitive impairment. The possible mechanism is that more frequent and adequate dialysis helps reduce toxins accumulation. There are many indicators to evaluate the adequacy of dialysis; the common one is Kt/V.[34] Unfortunately, we did not monitor Kt/V. And based on dialysis prescription, we could only speculate that more adequate dialysis indicates lower risk of CI. Whether higher dialysis adequacy is more beneficial to cognitive function is still controversial.[35] Lu et al. found that low spKt/V is an independent risk factor for CI in MHD patients.[32] However, Kurella et al. believed that frequent hemodialysis did not improve overall cognitive function,[36] which also needs to be confirmed by more in-depth researches.

In addition, we should also acknowledge that alcohol, cerebrovascular disease, and lipid status can also affect cognitive function. Chronic alcohol abuse increases the risk of cognitive impairment. This is partly due to the deficiency of thiamine, which is related to oxidative stress, excitotoxicity, inflammatory response, and blood–brain barrier dysfunction. Moreover, ethanol may have direct neurotoxicity.[37] Cerebrovascular disease can cause ischemic or hemorrhagic changes in the brain, resulting in various forms of neurological impairment including ischemic or hemorrhagic stroke and cognitive impairment.[38] Patients with sequelae of craniocerebral trauma and cerebral stroke, vasculitis, and alcoholism were excluded in our study. Many studies have explored the relationship between plasma lipids and cognitive function, but no clear conclusion has been reached. The mechanism may include blood–brain barrier injury, effect on small blood vessels in brain, amyloid deposition, and neuroprotection.[39] In our study, we did not find dyslipidemia was associated with cognitive impairment.

Our study has some limitations: (1) there may be selective bias. In the process of cognitive function assessment, some patients were aware of their CI, and they might refuse to conduct cognitive assessment; (2) this study was a cross-sectional study, so we were unable to evaluate the relationship between BPV and cognitive function over time; (3) other covariates that might affect cognitive function had not been included in the study, such as inflammatory factors (procalcitonin, C-reactive protein), spKt/V, homocysteine, and vitamin D, which might affect our results.

In conclusion, the prevalence of cognitive impairment in MHD patients is significantly higher. Greater systolic BPV is associated with a higher risk of cognitive impairment. In addition, the risk of CI is higher for MHD patients with older age, less years of education, and less frequency of dialysis per week.

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CONFLICT OF INTEREST

The authors declared that they have no conflicts of interest to disclose.

ETHICS STATEMENT

This study was approved by the Ethics Committee of Wuhan Fourth Hospital.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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