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Interdialytic blood pressure variability and the risk of stroke in maintenance hemodialysis patients

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Abstract

Studies on nondialysis populations have linked visit-to-visit blood pressure (BP) variability (BPV) to cerebrovascular events and mortality. In view of the high prevalence of hypertension in hemodialysis patients, the predictive values of numerous factors for stroke, especially visit-to-visit BPV, were evaluated in this prospective cohort study.

A total of 151 patients were enrolled in this study. The demographic features and various laboratory parameters were analyzed. At each routine hemodialysis visit, the predialysis, intradialysis, and post-dialysis BP measurements were systematically performed. We defined BPV using 4 metrics: standard deviation of the BP, coefficient of variation, average real variability (ARV), and variability independent of mean (VIM). Differences in the predialysis BPs from one treatment to the next (ie, interdialytic variability) and differences in the BPs from predialysis to post-dialysis (ie, intradialytic variability) were both studied in this work.

Twenty-one patients developed stroke and 25 patients died. The multivariate Cox proportional hazards regression model revealed a significant relationship between stroke and the interdialytic BPV (both predialysis systolic BP variability and predialysis diastolic BP variability) and low-density lipoprotein-cholesterol (LDL-C).

Our results indicate that a high interdialytic BPV is associated with an increased risk for stroke that is independent of several factors, including age, sex, antihypertensive medication use, and mean BP over time. There is potential that the optimal treatment goal for hemodialysis patients may be to reduce the interdialytic BPV rather than either the mean BP or the intradialytic BPV.

Abbreviations: ADBP = average diastolic blood pressure, ARV = average real variability, ASBP = average systolic blood pressure, BMI = body mass index, BP = blood pressure, BPV = blood pressure variability, CGN = chronic glomerulonephritis, CIs = confidence intervals, CKD = chronic kidney disease, CV = coefficient of variation, DBP = diastolic blood pressure, DKD = diabetic kidney disease, DN = diabetic nephropathy, ESRD = end-stage renal disease, HR = hazard ratio, iPTH = parathyroid hormone, KDIGO = Kidney Disease: Improving Global Outcomes, LDL-C = low-density lipoprotein-cholesterol, SBP = systolic blood pressure, SD = standard deviation, TC = total cholesterol, TG = triglyceride, VIM = variability independent of mean.

Keywords: blood pressure variability, diastolic blood pressure, hemodialysis, stroke, systolic blood pressure

1. Introduction

Hypertension is highly prevalent in hemodialysis patients, and it is often poorly controlled.[1,2] Several studies have indicated that hypertension is associated with an increased risk for stroke.[3,4] In a recent series of articles, Rothwell et all reported that blood pressure (BP) variability (BPV) is a risk factor for stroke, independent of the mean BP, among high-risk patients, suggesting that the visit-to-visit variability in BP may have an important additional role in increasing the risk for vascular events, particularly for stroke.[5,6] To our knowledge, the influence of BP vBPV on the risk for stroke in the end-stage renal disease (ESRD) population has not been widely studied, especially in hemodialysis patients. Moreover, previous studies in hemodialysis patients focused more on the impact of short-term BPV on prognosis[7–11]; the effects of long-term BPV are less well-investigated.[12–14] Therefore, we planned to examine the association between long-term BPV and the occurrence of stroke in patients with maintenance hemodialysis.

The optimum method for evaluating BPV for hemodialysis patients is unclear. Previous studies have suggested that visit-to-visit pre-dialysis BPV is associated with mortality among hemodialysis patients.[12,15,16] However, these studies are limited by short duration of follow-up[12,16] and use of measures of BPV that are associated with mean BP levels.[16] Therefore, more comprehensive and objective metrics were used to define BPV in this study. Moreover, differences in the predialysis BPs from one

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treatment to the next (ie, interdialytic variability) and differences in the BPs from predialysis to post-dialysis (ie, intradialytic variability) were both studied in this work because factors such as rapid fluid removal through ultrafiltration, abrupt changes in serum osmolarity, acid-base composition, and electrolyte composition may lead to BP fluctuation.

2. Patients and methods

2.1. Patients

Patients aged 18 to 75 years with ESRD who were undergoing maintenance hemodialysis for at least 3 months in the Department of Nephrology in the General Hospital of Western Theater Command were included in the study. The exclusion criteria included a previous stroke before undergoing maintenance hemodialysis. Furthermore, patients with systemic vasculitis, polycystic kidney disease, malignancy, and other autoimmune diseases were excluded to avoid the possible effects of these comorbid conditions on the vascular condition of these patients. Between July 2012 and November 2012, a total of 151 patients were enrolled in this study. A prospective study was performed on this group of hemodialysis patients. Baseline demographic indexes were recorded at the time of entry into the study. The type of vascular access, whether complicated with atrial fibrillation, and the use of anti-hypertensive drugs, antiplatelet drugs, and statins were recorded. The patients were followed for 48 months or until stroke or death occurred.

All of the patients received 4 hours of conventional hemodialysis with a bicarbonate bath 3 times weekly (GAMBRO, polyflux 17R, Germany). The blood flow rates ranged from 200 to 300 mL/min, with a fixed dialysate flow rate of 500 mL/min. The dialysate composition was as follows: Na+ 135 to 145 mmol/L, K + 2.0 mmol/L, and Ca++ 1.5 mmol/L. Low-molecular-weight heparin was used routinely during the dialysis. Antihypertensive drugs (angiotensin-converting enzyme inhibitors, calcium channel blockers, β blockers, and so on) were prescribed if hypertension persisted despite the patient's volume status being well controlled. Dialysis-related variables including dialysis vintage, ultrafiltration rate, equilibrated Kt/V, and average dose of low molecular heparin were collected.

The study protocol was approved by the local Ethics Committee, and all of the patients provided written informed consent.

2.2. Laboratory methods

Blood samples were drawn every 3 months after enrolment. The blood was taken at the interval day of dialysis. The numbers of white blood cells, platelet count, and serum levels of hemoglobins, albumin, creatinine, phosphate, calcium, potassium, sodium, low-density lipoprotein-cholesterol (LDL-C), LDL-C triglyceride, total cholesterol, and intact parathyroid hormone (iPTH) were measured using automated and standardized methods at a centralized laboratory. All of the clinical data referenced above are expressed as the means with standard deviation (SD).

2.3. BP measurements and definitions of BPV

At each routine hemodialysis visit, BP measurements were performed by trained nurses in the right or left arm of the patient, who was in a supine body position, using a mercury sphygmomanometer with an appropriate cuff. Predialysis, intradialytic (after 2 hours of dialysis), and post-dialysis measurements were systematically performed. The visit-to-visit BPV was quantified by 4 metrics: the SD of the BP, the coefficient of variation (CV = SD/mean × 100%),[17] the average real variability (ARV),[18] which takes an average of the absolute differences in BP over consecutive visits, and variability independent of mean (VIM).[5,13,19,20] VIM is the proportional to SD/mean^x, with x derived from curve fitting.

To distinguish between the BPV during the dialysis period and the BPV in the dialysis interphase, the SD, CV, ARV, and VIM of the predialysis BP was used to represent the BPV in the dialysis interphase, whereas the residual visit-to-visit variability of BP (residual visit-to-visit variability of BP = total variance of all BP – between-individual variance in mean BP – between-individual variance in within-individual visit-to-visit BP) was used to represent the BPV during the dialysis period.[21]

2.4. Stroke events

Newly developed cerebrovascular disease was diagnosed by both clinical symptoms and brain imaging examination (computed tomography or magnetic resonance imaging scan).

2.5. Statistical analysis

The data are expressed either as the means with SD or as number of patients (percentage), and 95% confidence intervals (CIs) are provided where appropriate. Differences in continuous values between 2 groups were assessed with the independent-samples *t* test. Associations between the outcome of stroke and the categorical factors were determined by the Kaplan–Meier method. The survival curves were estimated using the Kaplan–Meier method, and differences in the survival rate distributions were evaluated by the log-rank test. A multivariate analysis of survival was performed using a Cox proportional hazards regression model. The age, sex, and the factors that met the significance criterion (univariate analysis, $P < .05$) were considered for inclusion in an initial model (Model 1). Model 2 included covariates in Model 1 plus the mean BP. All of the tests were 2-sided, and differences were considered significant at $P < .05$. All of the statistical analyses were performed using SPSS software, version 16.

3. Results

3.1. Patient characteristics and laboratory data

A total of 151 patients were enrolled in this study. Twenty-one patients developed stroke (ischemic stroke occurred in 11 patients, hemorrhagic stroke occurred in 5 patients, subarachnoid hemorrhage occurred in 2 patients, and another 3 patients developed hemorrhagic infarction) and 25 patients died (10 patients died due to cardiovascular events, 8 patients died due to stroke, 2 patients died due to upper gastrointestinal bleeding, 4 patients died due to serious infection, and 1 patient died due to acute severe pancreatitis).

The baseline characteristics and laboratory indexes of the study population are summarized in Table 1. The average age of the patients was 51.95 ± 15.26 years, and the patients' average dialysis vintage was 5.60 ± 3.69 years. The description of BPV is

Table 1

Demographics and clinical characteristics of the study population (n = 151).

		N (%)	Mean ± SD
Sex	Female	69 (45.70)	
	Male	82 (54.30)	
Age, y			51.95 ± 15.26
Age group, y	<60	107 (70.86)	
	≥60	44 (29.14)	
Hemoglobin, g/L			107.81 ± 10.45
Hemoglobin group, g/L	<90	9 (5.96)	
	≥90	38 (25.17)	
	≥105	91 (60.26)	
	≥120	13 (8.61)	
Platelets ($\times 10^9$ cells/L)			139.32 ± 44.64
Platelets group($\times 10^9$ cells/L)	<139.32*	78 (51.66)	
	≥139.32	73 (48.34)	
Albumin, g/L			39.46 ± 2.98
Albumin group, g/L	<35†	86 (56.95)	
	≥35	65 (43.05)	
LDL-C, mmol/L			2.02 ± 0.59
LDL-C group, mmol/L	<2.02*	78 (51.66)	
	≥2.02	73 (48.34)	
Total cholesterol, mmol/L			3.76 ± 0.74
Total cholesterol group, mmol/L	<3.76*	82 (54.30)	
	≥3.76	69 (45.70)	
Calcium, mmol/L			2.27 ± 0.18
Calcium group, mmol/L	<2.0	11 (7.28)	
	≥2.0	129 (85.43)	
	≥2.5	11 (7.28)	
Phosphorus, mmol/L			1.81 ± 0.44
Phosphorus group, mmol/L	<1.78†	75 (49.67)	
	≥1.78	76 (50.33)	
Intact parathyroid hormone, pg/mL			367.33 ± 405.06
Intact parathyroid hormone group, pg/mL	<150	44 (29.14)	
	≥150	53 (35.10)	
	≥300	30 (19.87)	
	≥660	24 (15.89)	
Diabetes mellitus	No	129 (85.43)	
	Yes	22 (14.57)	
Smoke	Never	76 (50.33)	
	Ever	75 (49.67)	
Dialysis vintage, y			5.60 ± 3.69
Dialysis vintage group, y	<5.60*	89 (58.94)	
	≥5.60	62 (41.06)	
Average dose of low molecular heparin, U			3596.00 ± 730.00
Average dose of low molecular heparin group, U	<2000	13 (8.61)	
	≥2000	38 (25.17)	
	≥3000	100 (66.23)	
Antihypertensive drug types	≤1	26 (17.22)	
	2	73 (48.34)	
	3	52 (34.44)	
BMI, kg/m^2			22.07 ± 3.82
BMI group, kg/m^2	<18.5	28 (18.54)	
	≥18.5	79 (52.32)	
	≥24.0	44 (29.14)	
Kt/V			1.41 ± 0.14
Kt/V group	<1.41*	89 (58.94)	
	≥1.41	62 (41.06)	
Ultrafiltration ratio (%)			3.84 ± 1.14
Ultrafiltration ratio group	<3	32 (21.19)	
	≥3	98 (64.90)	
	≥5	21 (13.91)	
Vascular access	Arteriovenous fistula	144 (95.36)	
	Cuff catheter	7 (4.64)	
Atrial fibrillation	No	140 (92.72)	
	Yes	11 (7.28)	
Antiplatelet drugs	No	140 (92.72)	
	Yes	11 (7.28)	
Statins	No	146 (96.69)	
	Yes	5 (3.31)	
hsCRP, g/L			7.52 ± 11.22
hsCRP group, g/L	<3	82 (54.30)	
	≥3	69 (45.70)	
Homocysteine, μmol/L			20.43 ± 10.43
Homocysteine group, μmol/L	<20	101 (66.89)	
	≥20	50 (33.11)	
Predialysis ASBP, mmHg			139.28 ± 9.31
Predialysis ASBP group, mmHg	<130	18 (11.92)	
	≥130	67 (44.37)	
	≥140	48 (31.79)	
	≥150	18 (11.92)	
Predialysis ADBP, mmHg			85.49 ± 5.87
Predialysis ADBP group, mmHg	<90	115 (76.16)	
	≥90	36 (23.84)	

* Grouping by means.

† Grouping by normal reference value.

ADBP = average diastolic blood pressure, ASBP = average systolic blood pressure, BMI = body mass index, hsCRP = high sensitive C-reactive protein, LDL-C = low density lipoprotein-cholesterol.

summarized in Table 2. The SD, CV, ARV, and VIM of both the predialysis systolic BP (SBP) and predialysis diastolic BP (DBP) were displayed. The BPV during the dialysis period was also displayed.

3.2. Univariate analysis

The Kaplan–Meier analysis showed that age, albumin level, dialysis vintage, LDL-C level, atrial fibrillation, anti-platelet therapy, and statins were correlated with increased/decreased incidence of stroke (Table 3, Log-rank test: $P < .05$). A higher predialysis SBP variability (calculated using SD, CV, ARV, and VIM) was significantly associated with higher rates of stroke (Table 3, Log-rank test: $P < .05$). A higher predialysis DBP variability (calculated using SD, CV, and VIM) was also related to stroke (Table 3, Log-rank test: $P < .05$). The results showed that the serum levels of high-sensitive C-reactive protein, homocystine, cholesterol, calcium, phosphorus, and iPTH were not related to stroke (data shown in Supplemental Digital Content [Table 1 Appendix, http://links.lww.com/MD/E525]). Additionally, the hemoglobin and platelet count values were also not related to stroke (data shown in Supplemental Digital Content [Table 1 Appendix, http://links.lww.com/MD/E525]). The average systolic BP and average diastolic BP measured at predialysis were also not related to stroke (data shown in Supplemental Digital Content [Table 1 Appendix, http://links.lww.com/MD/E525]).

Table 2

Description of BPV.

	Mean ± SD	Median (P_{25}, P_{75})	Min, Max
Pre-dialysis SBP variability			
SD	10.94 ± 3.05	10.89 (8.75, 12.99)	3.05, 18.27
CV (%)	7.80 ± 1.91	7.73 (6.42, 9.24)	2.33, 12.22
ARV	47.87 ± 15.92	50 (40, 60)	20, 100
VIM ($\times 10^6$)	2.59 ± 0.64	2.5 (2.18, 2.95)	0.89, 5.38
Predialysis DBP variability			
SD	7.03 ± 1.59	6.97 (5.99, 7.76)	3.75, 15.91
CV (%)	8.23 ± 1.86	7.88 (7.04, 9.07)	4.22, 19.12
ARV	30.95 ± 11.13	30 (20, 38)	10, 120
VIM ($\times 10^6$)	1.23 ± 0.28	1.18 (1.06, 1.35)	0.64, 2.86
SBP residual visit-to-visit variability	41.31 ± 26.49	36.5 (22.35, 50.15)	7.42, 174.28
DBP residual visit-to-visit variability	29.56 ± 17.57	27.35 (15.27, 40.51)	1.90, 83.85

ARV = average real variability, CV = coefficient of variation, DBP = diastolic blood pressure, SBP = systolic blood pressure, SD = standard deviation, VIM = variability independent of mean.

3.3. Multivariate analysis

Multivariate Cox proportional hazards model was performed to assess the independent association of each parameter with the rates of stroke. An initial model (Model 1) provided hazard ratio (HR) for stroke with BPV, adjusting for sex, age, albumin level, dialysis vintage, LDL-C level, atrial fibrillation, antiplatelet therapy, and statins (Table 4). Model 2 included covariates in Model 1 plus the average BP (Table 4). Cox proportional hazards multivariate analysis revealed a significant relationship between the stroke outcome and the predialysis SBP variability calculated using SD (HR 3.110, $P = .032$, Model 1), ARV (HR 2.600, $P = .040$, Model 1), and VIM (HR 5.184, $P = .005$, Model 1). Similar results were observed in Model 2, when variability of SBP was calculated using SD, ARV, and VIM. Moreover, after

Table 3

Univariate analysis of factors influencing stroke.

		Stroke				
		No/censored, n = 130	Yes, n = 21	Mean of the survival time, mo (mean ± SE)	χ^{2*}	*P*
Age group, y	<60	96 (89.72)	11 (10.28)	45.10 ± 0.92	5.176	.023
	≥60	34 (77.27)	10 (22.73)	42.02 ± 1.82		
Albumin group, g/L	<35	70 (81.40)	16 (18.60)	43.21 ± 1.21	3.879	.049
	≥35	60 (92.31)	5 (7.69)	45.61 ± 1.11		
LDL-C group, mmol/L	<2.02	72 (92.31)	6 (7.69)	46.17 ± 0.80	5.034	.025
	≥2.02	58 (79.45)	15 (20.55)	42.26 ± 1.48		
Dialysis vintage group, y	<5.60	72 (80.90)	17 (19.10)	42.70 ± 1.31	4.857	.028
	≥5.60	58 (93.55)	4 (6.45)	46.52 ± 0.76		
Atrial fibrillation	No	123 (87.86)	17 (12.14)	44.74 ± 0.83	6.503	.011
	Yes	7 (63.64)	4 (36.36)	37.83 ± 4.31		
Antiplatelet drugs	No	123 (87.86)	17 (12.14)	44.74 ± 0.83	6.503	.011
	Yes	7 (63.64)	4 (36.36)	37.83 ± 4.31		
Statins	No	127 (86.99)	19 (13.01)	44.54 ± 0.83	4.547	.033
	Yes	3 (60.00)	2 (40.00)	35.53 ± 7.27		
Predialysis SBP-SD group	<Median	71 (93.42)	5 (6.58)	45.94 ± 0.96	6.494	.011
	≥Median	59 (78.67)	16 (21.33)	42.60 ± 1.36		
Predialysis SBP-CV group (%)	<Median	70 (92.11)	6 (7.89)	45.49 ± 1.05	4.518	.034
	≥Median	60 (80.00)	15 (20.00)	43.02 ± 1.31		
Predialysis SBP-ARV group	<Median	96 (90.57)	10 (9.43)	45.58 ± 0.82	6.655	.010
	≥Median	34 (75.56)	11 (24.44)	41.16 ± 2.00		
Predialysis SBP-VIM group ($\times 10^6$)	<Median	72 (94.74)	4 (5.26)	46.37 ± 0.83	9.751	.002
	≥Median	58 (77.33)	17 (22.67)	42.09 ± 1.44		
Predialysis DBP-SD group	<Median	71 (93.42)	5 (6.58)	46.07 ± 0.87	7.000	.008
	≥Median	59 (78.67)	16 (21.33)	42.41 ± 1.42		
Predialysis DBP-CV group (%)	<Median	69 (92.00)	6 (8.00)	45.54 ± 1.00	4.462	.035
	≥Median	61 (80.26)	15 (19.74)	42.98 ± 1.34		
Predialysis DBP-VIM group ($\times 10^6$)	<Median	70 (92.11)	6 (7.89)	45.57 ± 0.99	4.766	.029
	≥Median	60 (80.00)	15 (20.00)	42.91 ± 1.35		

* Kaplan–Meier method, Log-rank test statistics.

ARV = average real variability, CV = coefficient of variation, DBP = diastolic blood pressure, LDL-C = low density lipoprotein-cholesterol, SBP = systolic blood pressure, SD = standard deviation, VIM = variability independent of mean.

Table 4

Multivariate analysis based on Cox proportional hazards model.

	Model 1			Model 2		
	HR	HR 95% CI	P	HR	HR 95% CI	P
Predialysis SBP variability						
SD (≥median VS <median)	3.110	1.102, 8.776	.032	4.875	1.619, 14.675	.005
CV (≥median VS <median)	2.392	0.889, 6.434	.084	3.358	1.173, 9.611	.024
ARV (≥median VS <median)	2.600	1.045, 6.407	.040	3.893	1.381, 10.973	.010
VIM (≥median VS <median)	5.184	1.647, 16.321	.005	5.225	1.656, 16.484	.005
Predialysis DBP variability						
SD (≥median VS <median)	4.589	1.609, 13.088	.004	5.328	1.852, 15.331	.002
CV (≥median VS <median)	3.226	1.213, 8.583	.019	3.148	1.173, 8.449	.023
VIM (≥median VS <median)	3.537	1.342, 9.323	.011	3.521	1.329, 9.326	.011

Model 1: adjusted by sex, age, albumin level, dialysis vintage, LDL-C level, atrial fibrillation, anti-platelet therapy, and statins.

Model 2: adjusted by sex, age, albumin level, dialysis vintage, LDL-C level, atrial fibrillation, anti-platelet therapy, statins, and the pre-dialysis average BP.

ARV = average real variability, CI = confidence interval, CV = coefficient of variation, DBP = diastolic blood pressure, HR = hazard ratio, SBP = systolic blood pressure, SD = standard deviation, VIM = variability independent of mean.

adjustment for the average predialysis SBP, CV was significantly associated with the incidence of stroke (HR 3.358, $P = .024$, Model 2). The associations between variability of predialysis DBP and the risk of stroke were also calculated. In Model 1, stroke was detected to be significantly associated with SD of DBP (HR 4.589, $P = .004$, Model 1), CV of DBP (HR 3.226, $P = .019$, Model 1), and VIM of DBP (HR 3.537, $P = .011$, Model 1). Similar results were also observed when adjusted by the average predialysis DBP. In addition, dialysis vintage was observed to be significantly associated with the rates of stroke. The patients with relatively short dialysis vintage (<5.6 years) were more prone to stroke. Results also showed that high levels of LDL-C were associated with stroke (data shown in Supplemental Digital Content [Table 2 Appendix, http://links.lww.com/MD/E526]).

4. Discussion

Numerous studies on nondialysis populations have linked visit-to-visit BPV to cerebrovascular events and mortality.[5,6,22,23] A recent study demonstrated an association between the visit-to-visit BPV and mortality in a chronic kidney disease (CKD) population, supporting the notion that BP fluctuation may be particularly detrimental to patients with decreased kidney function.[24] As we know, ESRD is associated with an increased risk for stroke.[25] BPV is potentially of an even greater significance among hemodialysis patients than among other populations. In this study, the link between the visit-to-visit BPV and stroke in hemodialysis patients was observed. Evidence from recent studies suggests that the visit-to-visit variability over longer periods of follow-up may have a greater prognostic value than the mean BP or the short-term variability.[12] Therefore, the patients in this study were followed for 48 months or until stroke or death occurred.

As for the influence of factors such as the rapid fluid removal through ultrafiltration, which leads to abrupt changes in the serum osmolarity, acid-base composition, and electrolyte composition, the activation of neurohormonal axes, and the dialytic removal of vasoactive medications, the intradialytic and interdialytic BP were distinguishable in our study.[17] The intradialytic BPV expresses the fluctuation of the BP from predialysis to post-dialysis, and the inter-dialytic BPV expresses the difference in the predialysis BP from one treatment to the next. To better describe and quantify the BPV, we considered 4 metrics of the BPV including SD, CV, ARV, and VIM, which is a transformation of the SD that is uncorrelated with mean BP.

During hemodialysis, patients are routinely exposed to rapid fluid and osmolarity shifts that result in BP fluctuation. Nevertheless, an association between the intradialytic BPV and stroke was not observed in this study. There is potential that the fine interdialytic weight control (the mean dehydration ratio was $3.84\% \pm 1.14\%$) helped lower the BP fluctuation in these patients, which possibly weakened the relationship between the intradialytic BPV and stroke.

Our analysis shows that a high predialysis SBP variability is associated with a higher risk for stroke. The findings from our study are consistent with a few previous studies conducted in hemodialysis patients showing that higher predialysis SBP variability is independently associated with a higher risk for adverse outcomes. For example, an observational study of 1088 prevalent patients on hemodialysis in Italy showed that higher predialysis SBP variability was associated with a significantly higher risk of cardiovascular mortality.[26] Similarly, another randomized trial comparing fosinopril to placebo in patients on hemodialysis with left ventricular hypertrophy[20] demonstrated an increased risk of the composite outcome of cardiovascular events or cardiovascular death associated with higher predialysis SBP CV. Most previous studies on the BPV and outcomes focused on the SBP variability,[5,23,27,28] and relatively little is known about the relationship between the DBP variability and stroke. Our results indicate that a high predialysis DBP variability is associated with an increased risk for stroke that is independent of several factors, including age, sex, antihypertensive medication use, and mean BP over time. These findings have implications for clinical practice. The interdialytic BPV (not only predialysis SBP variability but also predialysis DBP variability) might be more closely correlated with the stroke outcome than either the mean BP or the intradialytic BPV, although the reasons for this are unknown. The optimal treatment goal for hemodialysis patients may be to reduce the interdialytic BPV rather than the mean BP values. The putative factors that explain the link between the interdialytic BPV and stroke are unclear. Atherosclerosis, angiostenosis, increased wall stress, baroreceptor dysfunction, and endothelial dysfunction are possible mechanisms.[29–31]

Furthermore, our results indicated that the level of LDL-C was associated with stroke, which has been identified in several previous studies on different populations.[32,33] The Kidney Disease: Improving Global Outcomes clinical practice guidelines have suggested that statins or a statin/ezetimibe combination should not be initiated in adults with dialysis-dependent CKD.[34]

Table 5

Comparison of 2 groups of patients with long or short dialysis vintage, mean ± SD.

	Dialysis vintage, y			
	<5.60, n = 89	≥5.60, n = 62	*t*	*P**
Predialysis ASBP, mmHg	140.62 ± 9.08	137.36 ± 9.37	2.135	.034
Predialysis SBP-SD	11.15 ± 2.94	10.65 ± 3.21	1.001	.318
Predialysis SBP-CV (%)	7.87 ± 1.78	7.70 ± 2.10	0.532	.595
Predialysis SBP-ARV	49.43 ± 15.80	45.65 ± 15.96	1.441	.152
Predialysis SBP-VIM ($\times 10^6$)	2.56 ± 0.54	2.64 ± 0.77	0.792	.430
SBP residual visit-to-visit variability	42.03 ± 27.47	40.29 ± 25.21	0.395	.693
Predialysis ADBP, mmHg	86.17 ± 5.87	84.53 ± 5.78	1.696	.092
Pre-dialysis DBP-SD	7.05 ± 1.60	7.00 ± 1.57	0.170	.865
Predialysis DBP-CV (%)	8.19 ± 1.89	8.30 ± 1.82	0.333	.740
Predialysis DBP-ARV	31.20 ± 12.70	30.60 ± 8.45	0.328	.743
Predialysis DBP-VIM ($\times 10^6$)	1.23 ± 0.28	1.24 ± 0.27	0.289	.773
DBP residual visit-to-visit variability	30.94 ± 16.76	27.58 ± 18.63	1.157	.249

* The independent-samples *t* test.

ADBP = average diastolic blood pressure, ARV = average real variability, ASBP = average systolic blood pressure, CV = coefficient of variation, DBP = diastolic blood pressure, SBP = systolic blood pressure, SD = standard deviation, VIM = variability independent of mean.

Whether there are any other methods that could be adopted to decrease the stroke risk in hemodialysis patients with a high LDL-C level needs to be studied further.

Interestingly, we found that patients with shorter dialysis vintage (<5.6 years) were more likely to have stroke in this study. Detailed analysis showed that the mean BP of patients with shorter dialysis vintage (<5.6 years) was higher than that in patients with longer dialysis vintage (≥5.6 years) (Table 5). This was probably the reason for the increased risk of stroke in patients with shorter dialysis vintage. There might be survivor bias in individual cases. For example, the only patients who would survive that long on hemodialysis were exceptionally healthy, with better cardiovascular health. However, other possible reasons need further study.

There are some limitations of the present study that need to be addressed. The study was performed in a single hospital, and thus, the sample size was not large enough, and there was a lack of baseline radiographic data from the patients. Considering the small sample size of this study, when analyzing the relationship between the BPV and the outcome of stroke, we did not differentiate between ischemic stroke and hemorrhagic stroke. Further studies using a larger patient cohort and involving several centers are needed to provide insight into the mechanistic link between the inter-dialytic BPV and different types of stroke.

Author contributions

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