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ORIGINAL ARTICLE

Association of blood pressure variability with target organ damage in older patients with essential hypertension

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Abstract

Background: Although multiple measures of blood pressure variability (BPV) have been proposed, whether they are better than mean blood pressure in predicting target organs is unclear. We aimed to determine the relationship between short term BPV and target organ injury.

Methods: This study was a retrospective study, and 635 inpatients in the Department of Cardiology from 2015 to 2020 were selected. We divided participants into four groups on the basis of the quartiles of BPV. One-way analysis of variance was used to compare the differences between the groups, and linear regression was used to analyze the relationship between BPV and target organ damage.

Results: The average age of 635 patients was 74.36 ± 6.50 years old. Among them, 354 of 627 patients had diminished renal function (56.5%), 221of 604 patients had associated left ventricular hypertrophy (36.6%), and 227 of 231 patients had carotid plaque formation (98.3%). The baseline data indicated significant differences in fasting glucose, total cholesterol, low-density lipoprotein, creatinine, glomerular filtration rate, sex, calcium channel blocker use, and the rate of diminished renal function. Multiple linear regression analysis showed that BPV was negatively correlated with renal injury (creatinine: $r = 0.306$, $p < 0.01$; estimated glomerular filtration rate: $r = 0.058$, $p < 0.01$), and BPV is positively correlated with cardiac injury ($r = 0.083$, $p < 0.01$). Elevated BPV was not found to be associated with vascular injury.

Conclusion: Renal function decreases with increasing BPV and left ventricular mass increases with increasing BPV.

KEYWORDS

ambulatory blood pressure monitoring, blood pressure variability, hypertension, target organ damage

Highlights

- Increased blood pressure variability was associated with left ventricular hypertrophy and decreased renal function, not with vascular injury (carotid plaque).

Zhiquan Jing and Gang Wang contributed equally to this study.

- Which indicators of blood pressure variability (BPV) are more closely related to the damage of target organs? Therefore, this study covers almost all indicators of BPV. We analyzed renal function in terms of both creatinine and glomerular filtration rate.

1 | INTRODUCTION

Both the incidence and mortality of cardiovascular diseases rank first among chronic noncommunicable diseases,[1] and improvement in blood pressure (BP) significantly decreases cardiovascular disease and death.[2] Ambulatory blood pressure monitoring can assess a person's blood pressure in everyday life and exclude the white coat effect; it can measure blood pressure levels throughout the day and detect hidden hypertension; and it can predict cardiovascular events and deaths more accurately than office blood pressure.[3] Occasional blood pressure measurements are often used as a reference during the treatment of hypertension. However, one or two measurements of blood pressure do not objectively reflect the patient's blood pressure changes and average levels throughout the day.[4,5]

For the treatment of hypertension, not only the average blood pressure but also blood pressure variability (BPV) is considered. Blood pressure fluctuation refers to the degree of change in blood pressure within a certain time; this fluctuation is also called BPV.[6] However, the effect of BPV on target organ damage (TOD) is not fully understood, and no recommendations are available for determining its normal range, let alone for knowing which indicators of BPV have a stronger correlation with TOD. Therefore almost all indicators of BPV were included in this study. Moreover, because ambulatory blood pressure is more difficult to obtain than home blood pressure, few studies have examined the relationship between BPV and TOD according to ambulatory blood pressure calculations, particularly in older adults.

The presence of TOD, that is, left ventricular hypertrophy, carotid artery plaque, and renal abnormalities has important prognostic and therapeutic implications in the management of patients with arterial hypertension, as acknowledged by international guidelines.[7] Recent studies have shown that BPV may be a better indicator of cardiovascular activity than blood pressure levels and is more closely associated with TOD in hypertension.[8–10] Consequently, controlling blood pressure and decreasing blood pressure fluctuation is very important in decreasing TOD.

Therefore, in this study, we aimed to investigate the effects of elevated BPV on TOD in older patients with hypertension.

2 | METHODS

We retrospectively included 635 patients with essential hypertension who were hospitalized in the Department of Cardiology of Beijing Friendship Hospital from 2015 to 2020. After the patients were admitted, 3.5 ml venous blood was collected from 5 a.m. to 6 a.m. after fasting for 12 h, and ambulatory blood pressure monitoring was carried out by professionals. The included patients were grouped according to quartiles of the 24h-SBP-CV (24-h-systolic blood pressure-coefficient of variation). All participants used an automatic noninvasive cuff sphygmomanometer (fixed model) to monitor their blood pressure. The cuff is fixed on each participant's left upper arm and could be worn in daily work and activities but not in strenuous exercise. Blood pressure was monitored every 30 min during the day (8:00–22:00) and every hour from 22:01 to 7:59 the next day. The effective blood pressure reading is indicated by SBP 70–260 mmHg (1 mmHg = 0.133 kPa), diastolic blood pressure (DBP) 40–150 mmHg, and pulse pressure 20–120 mmHg. Hypertension was defined according to the diagnostic criteria of the Chinese Guidelines for Prevention and Treatment of Hypertension (2018 revision).[11] Hypertension was diagnosed in patients with SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg who were not taking antihypertensive drugs, or in patients with a history of hypertension who were currently taking antihypertensive drugs and had a blood pressure < 140/90 mmHg. The inclusion criteria were as follows: 1. age ≥ 65 years according to Chinese Older Hypertension Management Guidelines 2019[12]; 2. diagnosis of essential hypertension; and 3. 24-h ambulatory blood pressure monitoring performed during hospitalization. The exclusion criteria were as follows: 1. secondary hypertension; 2. acute stage of stroke, myocardial infarction, or heart failure (<3 months); 3. hypertension without systematic treatment, stage 4–5 chronic kidney disease (glomerular filtration rate < 30%), postural hypotension (SBP decreased by more than 20 mmHg or DBP decreased by more than 10 mmHg after standing compared with supine position); and 4. pregnancy, cognitive impairment, or severe hearing and vision impairment preventing patients from communicating. This study was a retrospective cohort study in which informed consent was waived, and all baseline information was obtained from the medical record system. This study was approved by the ethics committee of Beijing Friendship Hospital, Capital Medical University (No. 2021-P2-430-01).

2.1 | Target organ measurement standard

Echocardiography for detection of LVH: two-dimensional M-mode or B-mode images were obtained using an ultrasound examination device. The left ventricular mass (LVM) was calculated with the formula: $LVM = 0.8 \times (1.04 \times ((LVEDD + PWTD + IVSTD)^3 - (LVEDD)^3)) + 0.6$,[13] in which IVSTD (mm) is the interventricular septum thickness in diastole, LVEDD (mm) is the LV end-diastolic diameter, and PWTD (mm) is the posterior wall thickness in diastole. The left ventricular mass index (LVMI) was calculated as LVM/body surface area. LVH was considered when LVMI ≥ 115 g/m^2 for men or ≥95 g/m^2 for women.[11]

Carotid Doppler ultrasound was performed for measurement of the carotid intima-media thickness. According to the relevant diagnostic criteria in China hypertension management guidelines in 2018, carotid intima-media thickness > 0.9 mm is defined as a thickening and carotid plaque formation. Renal damage: According to the relevant diagnostic criteria in China Hypertension Management Guidelines in 2018, decreased renel function was defined as as a slight increase in serum creatinine (115–133 μmol/L [1.3–1.5 mg/dL] for males and 107–124 μmol/L [1.2–1.4 mg/dL] for females). The estimated glomerular filtration rate was decreased [eGFR 30–59 mL/min/1.73 m^2]. $eGFR = 186 \times creatinine^{-1.154} \times year^{-0.203}$ (female × 0.790).

2.2 | Statistical analysis

We used SPSS 25.0 software (International Business Machines Corporation) for statistical analysis. Normally distributed measurement data are expressed as mean ± SD. One-way analysis of variance (ANOVA) was used for the comparison of means among multiple groups. Measurement data with a nonnormal distribution are expressed as median M (P25–P75). χ^2 tests were used for comparisons between dichotomous variables. Adjusted by age, male sex, body mass index, abdominal circumference, smoking, drinking, hyperlipidemia, diabetes, average SBP, and average DBP, and Stepwise multiple linear regression and multiple logistic regression were used to evaluate the effect of BPV on TOD. r represents the correlation coefficient and b represents the regression coefficient. A p value < 0.05 was considered statistically significant.

3 | RESULT

3.1 | Baseline characteristics

We included 655 patients in the study. Of these, 20 participants had a glomerular filtration rate of less than 30% and were excluded. Thus, 635 patients were finally included in the analysis.

Tables 1 and 2 reported the clinical characteristics and ABPM parameters for each group, according to high or low BPV. Overall, significant differences were observed between groups for glucose, total cholesterol, low-density lipoprotein (LDL), creatinine, and glomerular filtration rate.

According to the results of the χ^2 test, the ratio of females is positively correlated with higher BPV. Calcium channel blockers are considered the most effective drugs to decrease BPV,[14] and their use was higher in the low-level BPV group in this study. We also found a low rate of diuretic use in the population (17.3%). Many patients with hypertension have water and sodium retention, particularly overweight/obese patients, thus making correction of water and sodium retention and elevated BPV difficult.

3.2 | Assessment of TOD

3.2.1 | Relationship between BPV and LVMI

In simple linear regression, an elevated LVMI was associated with an elevated nocturnal systolic smoothing index ($r = 0.012$, $b = 0.264$, $p < 0.010$) and nocturnal diastolic CV ($r = 0.009$, $b = -57.806$, $p < 0.05$); however, this correlation was not found in the other blood pressure variables. As shown in Figure 1, in multiple linear regression analysis, after adjustment for age, sex, body mass index, abdominal circumference, smoking, alcohol consumption, hyperlipidemia, diabetes mellitus, mean SBP, and mean DBP, an increase in the nocturnal systolic smoothing index ($r = 0.083$, $b = 0.423$, $p < 0.01$) was associated with an increase in the LVMI.

3.2.2 | Relationship between BPV and renal function

In simple linear regression, impairment of renal function was associated with increases in 24-h diastolic standard deviation, daytime diastolic standard deviation, nighttime diastolic standard deviation, 24-h systolic CV, 24-h diastolic CV independently of the mean, nighttime diastolic CV independently of the mean, SBP-ASV and DBP-ASV. The results are shown in Table 3. As shown in Figure 2, in multiple linear regression analyses, an increase in the 24-h systolic CV ($r = 0.306$, $b = 51.183$, $p < 0.001$) was associated with renal impairment after adjustment for age, sex, body mass index, abdominal circumference, smoking, alcohol consumption, hyperlipidemia, diabetes mellitus, mean SBP, and mean DBP. An increase in the 24-h systolic CV was also associated with diminished renal function ($r = 0.083$, $b = -35.172$, $p < 0.01$). The results are shown in Table 4.

TABLE 1 Characteristics of the study population.

Parameters	Q1 (n = 159)	Q2 (n = 159)	Q3 (n = 158)	Q4 (n = 159)	p Values
Gender (F/M)	86/73	90/69	112/46	104/55	0.010
Age (years)	74.3 ± 6.3	74.2 ± 6.5	73.9 ± 6.5	75.1 ± 6.8	0.410
Current smokers	41 (25.8)	40 (25.2)	29 (18.4)	37 (23.3)	0.388
Current drinkers	31 (19.5)	28 (17.6)	22 (13.9)	33 (20.8)	0.414
BMI (kg/m^2)	25.8 ± 3.4	25.4 ± 3.5	26.1 ± 3.5	25.7 ± 3.2	0.087
Abdominal circumference (cm)	91.4 ± 9.8	92.8 ± 11.0	92.6 ± 10.9	92.4 ± 10.4	0.780
Diabetes	65 (40.9)	64 (40.3)	50 (31.6)	47 (29.6)	0.071
History of coronary angiography	31 (19.5)	36 (22.6)	25 (15.8)	32 (20.1)	0.494
SBP (mmHg)	124.8 ± 14.5	121.8 ± 12.9	121.0 ± 13.8	121.8 ± 12.9	0.308
DBP (mmHg)	66.0 ± 9.4	65.9 ± 8.2	66.1 ± 9.3	67.7 ± 8.7	0.169
Heart rate (beats per minute)	66.3 ± 8.4	65. 5± 9.4	67.9 ± 9.3	65.5 ± 8.8	0.068
FPG (mg/dL)	5.9 ± 1.8	5.7 ± 1.6	5.9 ± 1.8	5.4 ± 1.5	0.050
Urea nitrogen (mmol/L)	6.1 ± 2.0	5.8 ± 1.9	5.9 ± 1.7	6.3 ± 2.3	0.099
SCr (mg/dL)	70.6 ± 19.0	73.4 ± 17.3	72.2 ± 19.2	81.4 ± 20.5	0.010
Total cholesterol (mg/dL)	4.1 ± 1.1	4.1 ± 1.0	4.3 ± 1.1	4.5 ± 1.0	0.010
Triglyceride (mg/dL)	1.4 ± 0.8	1.4 ± 0.9	1.6 ± 1.6	1.4 ± 0.7	0.149
HDL (mg/dL)	1.1 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	1.2 ± 0.3	0.576
LDL (mg/dL)	2.3 ± 0.7	2.2 ± 0.6	2.4 ± 0.7	2.5 ± 0.7	0.118
Trace albumin	8.7 ± 41.9	2.4 ± 7.2	7.6 ± 40.5	4.1 ± 11.7	0.224
α1-microglobulin	1.1 ± 1.2	1.0 ± 1.0	1.1 ± 1.3	1.0 ± 1.0	0.888
transferrin	0.5 ± 2.2	0.2 ± 0.2	0.5 ± 2.5	0.6 ± 3.8	0.568
Immunoglobulin IgG	1.2 ± 4.9	0.6 ± 0.8	0.9 ± 2.6	0.8 ± 1.9	0.265
Uric acid (mmol/L)	337.5 ± 85.1	331.5 ± 86.3	349.3 ± 91.7	336.2 ± 87.9	0.339
Ejection fraction (%)	67.5 ± 4.9	66.2 ± 6.5	67.3 ± 5.6	67.7 ± 5.3	0.115
LVMI (g/m^2)	98.0 ± 27.0	95.0 ± 19.5	95.1 ± 19.9	100.3 ± 20.7	0.108
eGFR (mL/min/1.73 m^2)	64.5 ± 24.4	59.5 ± 15.0	59.6 ± 15.9	54.2 ± 14.3	0.010
E/A	0.8 ± 0.2	0.8 ± 0.3	0.8 ± 0.3	0.8 ± 0.2	0.086
Class of BP lowering drugs, n (%)					
ACEI/ARB	84 (52.8)	91 (57.2)	95 (60.1)	94 (59.1)	0.566
B blockers	43 (27)	42 (26.4)	46 (29.1)	48 (30.2)	0.866
CCB	103 (64.8)	83 (52.2)	80 (50.6)	85 (53.5)	0.010
Diuretics	23 (14.5)	23 (14.5)	33 (20.9)	31 (19.5)	0.291
Left ventricular hypertrophy[a]	49 (31.8)	47 (32)	59 (39.3)	66 (43.1)	0.103
Decreased renal function[a]	66 (41.8)	84 (53.8)	86 (55.1)	118 (75.2)	0.010
Carotid plaque[a]	57 (100)	66 (97.1)	56 (98.2)	48 (98)	0.656

Note: Data are presented as mean ± SD or n (%).

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; BMI, body mass index; CCB, calcium channel blockers; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; LVMI, left ventricular mass index; Q1, first quartile group; Q2, second quartile group; Q3, third quartile group; Q4, fourth quartile; SBP, systolic blood pressure; Scr, serum creatinine; SD, standard deviation.

[a]Among the total population of 635 patients, 31 did not have echocardiography data, 8 did not have creatinine data, and 404 did not have carotid artery ultrasound data.

TABLE 2 Ambulatory blood pressure parameters of the study patients.

Parameter	All patients (n = 635)
24h-PP	55.3 ± 11.2
24h-SBP-SD	13.6 ± 4.6
24h-DBP-SD	9.4 ± 3.2
D-SBP-SD	13.2 ± 4.0
D-DBP-SD	9.0 ± 2.8
N-SBP-SD	10.5 ± 4.5
N-DBP-SD	8.2 ± 3.1
24h-SBP-SI	9.9 ± 3.5
24h-DBP-SI	7.8 ± 2.7
D-SBP-SI	10.1 ± 3.0
D-DBP-SI	8.2 ± 3.3
N-SBP-SI	13.8 ± 9.2
N-DBP-SI	9.3 ± 5.6
24h-SBP-CV	0.15 ± 0.07
24h-DBP-CV	0.14 ± 0.05
D-SBP-CV	0.11 ± 0.03
D-DBP-CV	0.14 ± 0.04
N-SBP-CV	0.09 ± 0.04
N-DBP-CV	0.13 ± 0.05
24h-BPVR	1.52 ± 0.5
D-BPVR	1.51 ± 0.4
N-BPVR	1.42 ± 0.8
24h-SBP-VIM	8.9 ± 3.0
24h-DBP-VIM	8.8 ± 3.0
D-SBP-VIM	7.9 ± 2.4
D-DBP-VIM	4.7 ± 1.4
N-SBP-VIM	7.7 ± 3.3
N-DBP-VIM	6.6 ± 2.6
SBP-ASV	14.9 ± 6.0
DBP-ASV	10.3 ± 4.5

Note: Data are presented as mean ± SD.

Abbreviations: ASV, average successive variability; BPVR, blood pressure variety ratio; CV, coefficient of variation; D, daytime; DBP, diastolic blood pressure; N, nighttime; SBP, systolic blood pressure; SD, standard deviation; SI, smoothing index; VIM, variation independent of mean.

3.2.3 | Relationship between BPV and carotid plaques

Carotid ultrasound indicated the presence or absence of plaque formation and the plaque size, and it was, therefore, a dichotomous variable. In univariate logistic regression, vascular injury was associated with the CV for nocturnal SBP [95% confidence interval (0–0.009), p = 0.016]. However, no such association was found in other indicators of BPV. In multivariate logistic regression analyses, after adjustment for age, sex, body mass index, abdominal circumference, smoking, alcohol consumption, hyperlipidemia, diabetes mellitus, mean SBP, and mean DBP, an increase in the CV in nocturnal SBP (p = 0.654) was not associated with vascular injury.

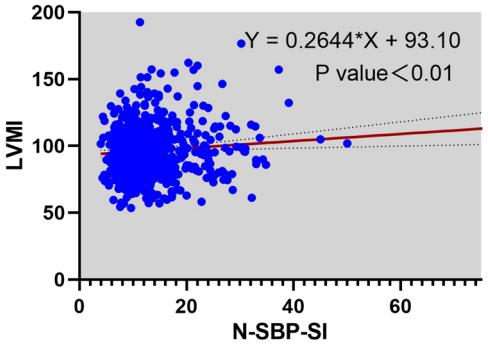

FIGURE 1 Effect of blood pressure variability on left ventricular mass index (LVMI). N, nighttime; SBP, systolic blood pressure; SI, smoothing index.

4 | DISCUSSION

Our findings indicated that elevated BPV is associated with heart and kidney injury, independently of blood pressure levels. However, no correlation was found between vascular injury and BPV, possibly because the population studied herein was older and had a higher incidence of vascular injury.

The clinical characteristics of older patients with hypertension include large arterial stiffening, decrease in compliance, elevated SBP, and significantly elevated arterial blood pressure fluctuation. Hypertension is often accompanied by disorders of glucose and lipid metabolism.[15] The BPV indicates the degree of blood pressure fluctuation within a certain period of time.[16] Under physiological and environmental changes, blood pressure fluctuates to maintain adequate blood flow to organs.[17]

Studies have shown that different durations of BPV have different predictive values for TOD and cardiovascular events. Long-term BPV has shown superior clinical predictive value in studies.[18] However, the link between BPV and TOD remains incompletely understood. Recent cohort studies have shown that elevated BPV is associated with TOD in relatively low-risk populations but does not predict the development of future TOD.[19,20] These findings may suggest that elevated BPV is associated with TOD but may not be causal. A recent study on adverse cardiovascular events, which had endpoints differing from those in our study but also

TABLE 3 Simple linear regression of blood pressure variability indices and target organ damage markers.

	Creatinine			eGFR			LVMI		
Parameter	***r***	***b***	***P***	***r***	**b**	***P***	***r***	**b**	***P***
24h-PP	0	0.010	0.892	0.006	0.133	0.058	0.002	0.098	0.254
24h-SBP-SD	0.006	0.329	0.052	0.001	−0.151	0.340	0.001	−0.181	0.358
24h-DBP-SD	0.007	0.507	< 0.05	0.002	−0.245	0.274	0	−0.050	0.856
D-SBP-SD	0.006	0.369	0.058	0.003	−0.261	0.154	0.002	0.264	0.242
D-DBP-SD	0.010	0.666	<0.05	0.002	−0.294	0.251	0	0.110	0.732
N-SBP-SD	0	−0.003	0.986	0.004	0.248	0.140	0.004	−0.313	0.132
N-DBP-SD	0.008	0.560	<0.05	0.001	−0.154	0.517	0	0.132	0.648
24h-SBP-SI	0	0.072	0.764	0	−0.002	0.992	0.005	0.443	0.081
24h-DBP-SI	0	−0.052	0.859	0	−0.120	0.660	0	0.139	0.680
D-SBP-SI	0.001	−0.165	0.523	0.003	0.329	0.173	0	−0.040	0.893
D-DBP-SI	0.001	−0.216	0.364	0	−0.026	0.908	0	0.108	0.690
N-SBP-SI	0.001	−0.165	0.523	0.004	−0.129	0.113	0.012	0.264	<0.01
N-DBP-SI	0.001	−0.216	0.364	0.001	−0.119	0.373	0	0.066	0.686
24h-SBP-CV	0.037	51.883	<0.01	0.032	−45.016	<0.01	0	5.769	0.639
24h-DBP-CV	0	4.155	0.804	0	−5.727	0.715	0.002	−18.882	0.328
D-SBP-CV	0	9.385	0.703	0.003	−30.410	0.187	0	9.277	0.744
D-DBP-CV	0	8.839	0.651	0	−2.717	0.882	0	−11.799	0.605
N-SBP-CV	0.003	−29.716	0.169	0.002	23.261	0.252	0.009	−57.806	0.020
N-DBP-CV	0	1.291	0.922	0	2.108	0.864	0	0.876	0.953
24h-BPVR	0	−0.302	0.846	0.001	−0.968	0.508	0.003	−2.571	0.151
D-BPVR	0	−0.991	0.614	0	−0.636	0.730	0.001	1.253	0.577
N-BPVR	0.004	−1.529	0.114	0.002	0.878	0.334	0.004	−1.605	0.145
24h-SBP-VIM	0.005	0.478	0.066	0.001	−0.232	0.342	0.002	−0.301	0.321
24h-DBP-VIM	0.007	0.539	<0.05	0.002	−0.259	0.281	0	−0.058	0.846
D-SBP-VIM	0.005	0.575	0.081	0.003	−0.441	0.154	0.002	0.415	0.277
D-DBP-VIM	0.008	1.183	< 0.05	0.002	−0.507	0.317	0	0.137	0.829
N-SBP-VIM	0	−0.041	0.863	0.004	0.346	0.121	0.005	−0.462	0.097
N-DBP-VIM	0.007	0.610	< 0.05	0	−0.138	0.634	0	0.101	0.774
SBP-ASV	0.008	0.280	<0.05	0	0.085	0.600	0.001	−0.135	0.373
DBP-ASV	0.007	0.351	<0.05	0	−0.048	0.689	0.001	0.167	0.404

Abbreviations: ASV, average successive variability; *b*, regression coefficient; BPVR, blood pressure variety ratio; CV, coefficient of variation; D, daytime; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LVMI, left ventricular mass index; N, nighttime; *r*, correlation coefficient; SBP, systolic blood pressure; SD, standard deviation; SI, smoothing index; VIM, variation independent of mean.

focused on BPV, has noted that among adults with optimal SBP levels, regardless of whether they had hypertension, visit-to-visit SBP variability is significantly associated with the risk of MACE.[21] Therefore, visit-to-visit SBP variability may warrant further attention, even at the guideline-recommended optimal blood pressure levels. This aspect may provide a new direction for the development of new drugs in the future, to decrease both blood pressure and blood pressure fluctuations. The recent advent of sacubitril valsartan promises to achieve this goal. Several studies have indicated a greater decrease in 24-h ambulatory blood pressure with this treatment than with other antihypertensive drugs.[22] However, compared with 24-h ambulatory blood pressure monitoring, office blood pressure monitoring is less accurate in assessing BPV.

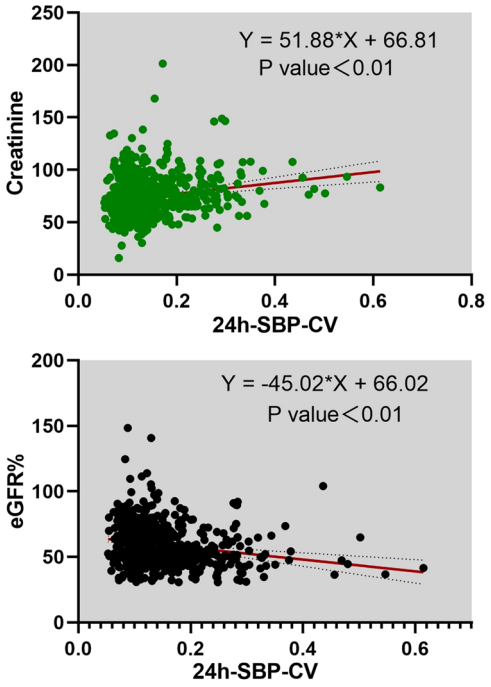

FIGURE 2 Effect of blood pressure variability on renal function. eGFR, estimated glomerular filtration rate; SBP-CV, systolic blood pressure-coefficient of variation.

TABLE 4 Multiple linear regression of blood pressure variability indices and target organ damage markers.

Items	*r*	*b*	*p*
Creatinine			
24h-SBP-CV	0.306	51.183	<0.01
eGFR			
24h-SBP-CV	0.058	−35.172	<0.01
LVMI			
N-SBP-SI	0.083	0.423	<0.01

Abbreviations: *b*, regression coefficient; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; LVMI, left ventricular mass index; N, nighttime; *r*, correlation coefficient; SBP, systolic blood pressure; SI, smoothing index.

LVH can impair both diastolic and systolic function of the left ventricle, thus decreasing cardiac output and leading to heart failure. The mechanism through which increased BPV leads to LV hypertrophy may be associated with the following mechanisms: when BPV is elevated, expression of monocyte chelator protein-1 and transforming growth factor-β is upregulated in the heart, thus inducing cardiovascular cell proliferation and apoptosis under the regulation of the renin-angiotensin system, and leading to the development of LVH in patients with hypertension.[23] Therefore, the correlation between BPV and LVMI was analyzed in this study. An increase in the nocturnal systolic smoothing index was found to be a risk factor independent of mean arterial blood pressure. In a previous study, correlation analysis showed no significant correlation between blood pressure variability (BPVR) and LVMI, E/A (early mitral valve inflow velocity/late mitral valve inflow velocity) (LVMI: $p = 0.58$; E/A ratio: $p = 0.82$).[24] Similarly, in our study, there was no correlation between the BPV index and E/A, and we did not find a correlation between standard deviation and LV hypertrophy, but we did find a previously unreported correlation between smoothness index and left ventricular hypertrophy. Most previous studies have shown that LV hypertrophy is associated with SD, CV, ARV, and other indices[23,25]; However, we did not find a correlation between the above indicators, which may be related to the fact that we selected a population of elderly people, who generally have reduced diastolic function. Another important reason may be related to the different types of antihypertensive drugs used by the patients. Consequently, the smoothing index, an indicator of BPV, might also be of interest to the older population. A recent study with a 3-year follow-up period has indicated that the regression of hypertension-mediated organ damage is associated with improved BPV after 3 years of successful treatment in patients with hypertension. LVMI improvement is associated with both sBPV ($p < 0.01$) and dBPV reduction ($r = 0.2$, $p < 0.05$ and $r = 0.2$, $p < 0.05$, respectively).[26] A similar study in a Chinese population had similar findings, wherein multivariate 24-h SBPV was associated with intima-media thickness, LVMI, and proteinuria.[27] Our findings were similar between left ventricular hypertrophy and renal injury; our results reinforce the relationship between BPV and TOD in the Chinese population. In this study, compared with prior studies, we had a larger sample size and also selected older individuals. Therefore, elevated BPV is a risk factor for left ventricular hypertrophy and suggests a diagnosis of left ventricular hypertrophy.

The kidney is a major target organ for hypertensive damage. The mechanisms of renal and vascular damage due to BPV can be summarized in two points: (1) Elevated BPV in patients with hypertension stimulates the self-defense system, promotes the expression of inflammatory factors, and aggravates the inflammatory response, which in turn accelerates vascular sclerosis, thus resulting in carotid artery injury. (2) When BPV is elevated, microvascular resistance increases, thus resulting in glomerular basement membrane thickening, renal arteriole media hyaline degeneration, monocyte exudation, and other pathological changes culminating in renal injury.[23] Our study is similar to the results of other studies. Previous studies have also shown that an increase in BPV is negatively associated with eGFR, independently of mean blood pressure, BPV, and pulse wave velocity.[24] The reason for these different results may be associated with an older population being

included in this study, whereas the mean age in the above study was younger than 50 years. Another study has reported the same results associating BPV with diminished kidney function.[27] The reason for the different results might be associated with the small sample size of the aforementioned study and the inclusion of patients >80 years of age. CV may be a more appropriate indicator for the older population. This study did not assess renal function by using eGFR alone but also assessed creatinine levels. CV had the same effect on creatinine, thus further confirming the correlation between CV as an indicator and renal function. Numerous studies have shown that elevated BPV is associated with kidney damage, including long-term BPV and short-term BPV. Similar findings have been found in relation to declining renal function: results from a 2022 study have suggested that year-by-year BPV is associated with the presence of hypertensive TOD, but in the general population, increases in BPV do not necessarily predict the development of future hypertensive TOD.[19] This study reports the first assessment of the value of elevated BPV in the general population in predicting diminished renal function. Unlike left ventricular hypertrophy and diminished renal function, the present study did not find any indicators of BPV associated with vascular injury, a finding potentially associated with the population that we included.

One study limitation is that the elderly population included herein did not represent the whole population. Moreover, the sample size included in this study was small. Although ambulatory blood pressure monitoring is currently one of the best methods available for measuring blood pressure, this method is not always available or acceptable to patients and cannot be repeated frequently, thus making it unsuitable for routine assessment of long-term BPV in clinical practice. Most importantly this study is cross-sectional and does not predict future TOD in patients. Therefore, more large cohort studies are needed to verify its relevance.

In conclusion, renal function is negatively correlated with BPV, while left ventricular hypertrophy is positively correlated with BPV. Increased BPV is a risk factor for decreased renal function and left ventricular hypertrophy.

AUTHOR CONTRIBUTIONS

Zhiquan Jing completed the research design, data entry, data analysis, and the writing of the paper. Gang Wang participated in the research design, data analysis, and paper writing. Zeya Li participated in the research design and paper modification. Shanshan Wu participated in the data analysis and research design. Xiang Qiu participated in the data entry and research design. Rongchong Huang participated in the research design, data analysis and paper modification.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Professor Rongchong Huang is a member of Chronic Diseases and Translational Medicine editorial board and is not involved in the peer review process of this article.

DATA AVAILABILITY STATEMENT

The data are available from the corresponding author uponreasonable request.

ETHICS STATEMENT

This study has been approved by the Ethics Committee of Beijing Friendship Hospital Affiliated to the Capital Medical University (No. 2021-P2-430-01).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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