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SHORT COMMUNICATION

Effects of long-term blood pressure variability on renal function in community population

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High blood pressure is a significant contributor to premature mortality, resulting in nearly 10 million deaths and over 200 million disabilities worldwide.[1] In recent years, hypertension treatment has shifted focus not only to average blood pressure but also to blood pressure variability (BPV), categorized into very short-term, short-term, and long-term BPV based on the time period of occurrence.[2,3] Long-term BPV has emerged as clinically significant, with studies demonstrating its superiority in predicting long-term cardiovascular events, stroke, and mortality compared to short-term variability. Given its association with pre-renal function decline, reducing blood pressure fluctuations is imperative.

Chronic kidney disease (CKD) poses a global public health challenge, with its incidence rising alongside aging populations and increasing rates of conditions like diabetes and hypertension. Hypertension and kidney disease are closely intertwined, with hypertension exacerbating renal damage. At present, the management of hypertension mainly focuses on average blood pressure, but the average blood level does not accurately reflect the long-term control status of blood pressure. Notably, some patients with ostensibly controlled average blood pressure still experience renal function deterioration within 5–10 years, potentially due to blood pressure fluctuations. Emerging evidence suggests a link between cardiovascular events, renal injury, and BPV, independent of average blood pressure.[4,5] However, the precise relationship between BPV and renal function remains elusive. This study aimed to explore the association between fluctuating blood pressure and rapid renal function decline in a prospective community health checkup-based cohort.

A total of 7153 patients aged ≥18 years who received at least twice regular physical examinations at the Community Health Service Centre in Beijing, between 2015 and 2021, were recruited consecutively in this study. Exclusion criteria included CKD stage 4–5, acute stroke, myocardial infarction, and heart failure (<3 months). Finally, 7130 patients were enrolled in the analysis (Figure S1).

Sociodemographic information, comorbidities, and lifestyle habits were obtained through questionnaires.

Zhao Feng and Zhiquan Jing contributed equally to this work.

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Blood pressure was measured twice during each visit, and BPV indices were calculated based on measurements across all visits. Additionally, blood samples were collected after an 8-h fast for biochemical analyses. We calculated several indicators as measures of BPV based on data from all visits, including standard deviation (SD), coefficient of variation (CV), variation independent of the mean (VIM), and average successive variability (ASV). The measures have been used in previous studies.[6,7]

Baseline data for this study were derived from the results of the initial annual health checkup, while endpoint data were obtained from the final annual health checkup. The primary endpoint of the study was the decline in the estimated glomerular filtration rate (eGFR), defined as an eGFR slope ≥3 mL/min/1.73 m^2. The secondary study endpoint was the new onset of CKD, defined as an eGFR mL/min/1.73 m^2. The eGFR slope was calculated as the regression coefficient between eGFR and time, expressed in mL/min/1.73 m^2/year.

The continuous variable of clinical features was expressed as mean (SD), and the categorical variable was expressed as numbers (%). Logistic regression analyses were conducted to explore the correlation between GFR decline and BPV. Cox proportional hazards model analysis was used to investigate the impact of baseline BPV on the new onset of CKD. Multivariate analysis was performed with adjustment for confounding factors including age, gender, mean blood pressure, body mass index (BMI), waist circumference, smoking, and alcohol consumption. Hazard ratios (HRs) and 95% confidence intervals (CI) were calculated. In all cases, a two-sided $p < 0.05$ was considered significant. All statistical analyses were performed using SPSS 25.0.

Of the 7130 study participants (mean age, 60.7 ± 6.8 years), 5108 (71.6%) were women and 2022 (28.4%) were men. Among the participants, 35.5% had hypertension, and 21% had diabetes. The average BMI was 26.1 ± 3.7 kg/m^2 and the average eGFR was 96.0 ± 19.3. The demographic and clinical characteristics of the study participants are detailed in Table S1. During the 5-year follow-up period, 1394 participants received three times physical examinations, 1476 participants received four times physical examinations, 1729 participants received five times physical examinations, and 2531 participants received three times physical examinations.

A total of 1802 participants reached the primary composite endpoint during the 5-year follow-up period. After adjusting for confounders, including age, gender, mean blood pressure, BMI, waist circumference, smoking, and alcohol consumption, the multivariate logistic regression showed significant associations between SBP-ASV and eGFR decline (odds ratio [OR]: 1.01, 95% confidence interval [CI]: 1.00–1.02, $p = 0.005$). Similarly, DBP-ASV was also associated with eGFR decline (OR: 1.02, 95% CI: 1.01–1.03, $p = 0.001$) (Table 1).

TABLE 1 Association between blood pressure variability indices and eGFR decline.

	Univariate			Multiple		
Index	**OR**	**95% CI**	***p* Value**	**OR**	**95% CI**	***p* Value**
SBP-SD	1.00	1.00–1.01	0.395	1.00	0.99–1.01	0.729
SBP-CV	1.28	0.35–4.64	0.707	1.34	0.37–4.92	0.657
SBP-VIM	1.01	0.99–1.02	0.408	1.00	0.99–1.01	0.727
SBP-ASV	1.01	1.01–1.02	0.001	1.01	1.00–1.02	0.005
DBP-SD	1.03	1.01–1.04	0.001	1.01	1.00–1.03	0.166
DBP-CV	6.62	2.16–20.28	0.001	3.24	0.93–11.3	0.065
DBP-VIM	1.03	1.01–1.04	0.001	1.01	1.00–1.03	0.163
DBP-ASV	1.03	1.02–1.04	<0.001	1.02	1.01–1.03	0.001

Note: Multivariate analysis was performed with adjustment for confounding factors including age, gender, mean blood pressure, BMI, waist circumference, smoking, and alcohol consumption.

Abbreviations: ASV, average successive variability; CI, confidence interval; CV, coefficient of variation; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; OR odds ratio (per 1 unit); SBP, systolic blood pressure; SD, standard deviation; VIM, variation independent of mean.

Among the 6991 patients with normal renal function baseline, a total of 199 participants reached the secondary endpoint during the 5-year follow-up period, and the median follow-up time was 48 months. After adjusting for confounders, the Cox proportional hazards model analysis showed significant associations between SBP variability indices (SBP-SD, SBP-VIM, and SBP-ASV) and the new-onset of CKD. Similarly, DBP variability indices (DBP-SD, DBP-CV, DBP-VIM, and DBP-ASV) were also associated with the new onset of CKD (Table 2).

Our study showed the predictive value of BPV in forecasting future eGFR decline and the onset of CKD, both for SBP and DBP. Therefore, it is imperative to prioritize the monitoring of elevated BPV.

In 2010, Rothwell et al. demonstrated that follow-up systolic blood pressure variability (SBPV) independently predicted stroke risk, highlighting the importance of BPV alongside mean blood pressure for hypertensive patient prognosis.[8] Subsequent studies have further solidified the link between increased BPV and cardiovascular and cerebrovascular diseases, regardless of mean blood pressure levels. Notably, long-term BPV has emerged as a particularly valuable predictor of target organ damage and cardiovascular events.[9,10] Furthermore, a large cohort study conducted in the United States revealed a notable rise in the incidence of all-cause mortality, coronary heart disease, stroke, and end-stage renal disease with escalating SBPV levels within the population.[5] The mechanism by which BPV affects renal function may involve micro-vascular resistance, leading to pathological changes such as thickening of

TABLE 2 Association between blood pressure variability indices and new-onset of CKD.

	Univariate			Multiple		
Index	**HR**	**95% CI**	***p* Value**	**HR**	**95% CI**	***p* Value**
SBP-SD	1.04	1.02–1.07	<0.001	1.03	1.00–1.05	0.030
SBP-CV	117.19	3.72–3688.34	0.007	24.3	0.84–702.07	0.063
SBP-VIM	1.05	1.02–1.08	<0.001	1.03	1.00–1.06	0.031
SBP-ASV	1.04	1.03–1.06	<0.001	1.03	1.02–1.05	<0.001
DBP-SD	1.07	1.03–1.11	<0.001	1.05	1.01–1.08	0.010
DBP-CV	239.99	15.51–3713.19	<0.001	41.62	2.78–622.28	0.007
DBP-VIM	1.07	1.03–1.12	<0.001	1.05	1.01–1.09	0.010
DBP-ASV	1.07	1.05–1.1	<0.001	1.05	1.02–1.07	<0.001

Note: Multivariate analysis was performed with adjustment for confounding factors including age, gender, mean blood pressure, BMI, waist circumference, smoking, and alcohol consumption.

Abbreviations: ASV, average successive variability; CI, confidence interval; CKD, chronic kidney disease; CV, coefficient of variation; DBP, diastolic blood pressure; HR, hazard ratio (per 1 unit); SBP, systolic blood pressure; SD, standard deviation; VIM, variation independent of mean.

the glomerular basement membrane, hyaline degeneration of renal arterioles, and exudation of monocytes, ultimately resulting in renal injury.[8,11]

The kidneys are among the primary target organs vulnerable to damage from hypertension. Our study uncovered a strong link between increased BPV and eGFR decline, consistent with findings from a Japanese study.[9] However, previous studies did not account for eGFR trends over time. In our study, we introduced a new definition of renal function damage based on eGFR decline (eGFR slope ≥3 mL/min/1.73 m^2) to address this issue, which is crucial for individuals with eGFR levels nearing the CKD threshold.

The impact of BPV on renal function was inconsistent across studies.[9,12,13] Post hoc analyses of the ASPREE trial, ONTARGET, and TRANSCEND trials yielded negative results partly due to the composition of the study populations. The ASPREE trial included individuals with an average age over 70 years, suggesting that advanced age may mitigate the effect of BPV. Moreover, the ONTARGET and TRANSCEND trials excluded patients with blood pressure levels ≥160/100 mmHg, resulting in relatively low BPV. Our study, based on a real-world population representing both middle-aged and elderly participants, offers valuable insights into the impact of variability in visit-to-visit SBP on renal function management, even among patients with normal blood pressure.[14]

There were several limitations to this study that warrant consideration. First, due to limitations in the available check-up information, the analysis of antihypertensive medication usage was not included. Additionally, the composition of the population attending the health service center skewed toward females, potentially influencing the overall BPV observed in the study. Finally, the follow-up period lasted for 31.8 months, and further longitudinal follow-up could yield additional information regarding the long-term impact of BPV on renal damage.

In conclusion, long-term BPV is associated with future renal damage, and further attention should be paid to the variability in visit-to-visit SBP.

AUTHOR CONTRIBUTIONS

Rongchong Huang, Feng Zhao, and Zhiquan Jing contributed to the conception of the study. Rongchong Huang, Feng Zhao, Zhiquan Jing, Zeya Li, Gang Wang, Shanshan Wu, Dan Li, Jing Hao, Chunlei Yang, Jiashu Song, and Xianzhong Gu contributed to the data acquisition. Rongchong Huang, Feng Zhao, Zhiquan Jing, Zeya Li, and Shanshan Wu contributed to the data analysis. Rongchong Huang, Feng Zhao, Zhiquan Jing, and Zeya Li contributed to the manuscript preparation, editing, and review.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The study protocol was approved by the Ethics Committee of Beijing Friendship Hospital associated with Capital Medical University (Beijing, China) (approval no. 2021-P2-163-02) and conducted in

accordance with the ethical principles for medical research involving human subjects described in the Declaration of Helsinki.

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REFERENCES

1. Chenniappan M. Blood pressure variability: assessment, prognostic significance and management. *J Assoc Physicians India*. 2015;63(5):47-53.
2. Grassi G, Bombelli M, Brambilla G, Trevano FQ, Dell'oro R, Mancia G. Total cardiovascular risk, blood pressure variability and adrenergic overdrive in hypertension: evidence, mechanisms and clinical implications. *Curr Hypertens Rep*. 2012;14(4):333-338. doi:10.1007/s11906-012-0273-8
3. Parati G, Ochoa JE, Lombardi C, Bilo G. Assessment and management of blood-pressure variability. *Nat Rev Cardiol*. 2013;10(3):143-155. doi:10.1038/nrcardio.2013.1
4. Kawai T, Ohishi M, Kamide K, et al. The impact of visit-to-visit variability in blood pressure on renal function. *Hypertension Res*. 2012;35(2):239-243. doi:10.1038/hr.2011.170
5. Muntner P, Whittle J, Lynch AI, et al. Visit-to-visit variability of blood pressure and coronary heart disease, stroke, heart failure, and mortality: a cohort study. *Ann Intern Med*. 2015;163(5):329-338. doi:10.7326/m14-2803
6. Zhang Y, Bie L, Li M, et al. Visit-to-visit blood pressure variability is associated with arterial stiffness in Chinese adults: a prospective analysis. *J Clin Hypertension*. 2021;23(4):802-812. doi:10.1111/jch.14166
7. Wang Y, Zhao P, Chu C, et al. Associations of long-term visit-to-visit blood pressure variability with subclinical kidney damage and albuminuria in adulthood: a 30-year prospective cohort study. *Hypertension*. 2022;79(6):1247-1256. doi:10.1161/HYPERTENSIONAHA.121.18658
8. Rothwell PM. Limitations of the usual blood-pressure hypothesis and importance of variability, instability, and episodic hypertension. *Lancet*. 2010;375(9718):938-948. doi:10.1016/s0140-6736(10)60309-1
9. Sugiura T, Takase H, Machii M, et al. Blood pressure variability and the development of hypertensive organ damage in the general population. *J Clin Hypertension*. 2022;24:1405-1414. doi:10.1111/jch.14526
10. Tedla YG, Yano Y, Carnethon M, Greenland P. Association between long-term blood pressure variability and 10-year progression in arterial stiffness: the multiethnic study of atherosclerosis. *Hypertension*. 2017;69(1):118-127. doi:10.1161/hypertensionaha.116.08427
11. Rothwell PM. Does blood pressure variability modulate cardiovascular risk? *Curr Hypertens Rep*. 2011;13(3):177-186. doi:10.1007/s11906-011-0201-3
12. Ernst ME, Fravel MA, Webb KL, et al. Long-term blood pressure variability and kidney function in participants of the ASPREE trial. *Am J Hypertens*. 2022;35(2):173-181. doi:10.1093/ajh/hpab143
13. Mancia G, Schumacher H, Böhm M, et al. Visit-to-visit blood pressure variability and renal outcomes: results from ONTARGET and TRANSCEND trials. *J Hypertens*. 2020;38(10):2050-2058. doi:10.1097/hjh.0000000000002567
14. Liu M, Chen X, Zhang S, et al. Assessment of visit-to-visit blood pressure variability in adults with optimal blood pressure: a new player in the evaluation of residual cardiovascular risk? *J Am Heart Assoc*. 2022;11(9):e022716. doi:10.1161/jaha.121.022716

SUPPORTING INFORMATION

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

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