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Research Article

The Association between Visit-to-Visit Variability of Blood Pressure and the Risk of Metabolic Syndrome: The Moderating Effect of Weight

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Aims. Metabolic syndrome (MetS) affects approximately one-third of the global population. Visit-to-visit variability of blood pressure (VVV-BP) constitutes a substantial risk factor for numerous chronic conditions. Thus, this study aimed to assess the relationship between VVV-BP and MetS and identify potential moderating factors between these. *Methods*. Data were obtained from the China Health and Retirement Longitudinal Study, a nationally representative study. Multiple logistic regression analyses were utilized to explore the association between VVV-BP and MetS while incorporating moderation analyses. MetS was defined according to the criteria outlined in the Joint Interim Statement. VVV-BP was expressed by the standard deviation, coefficient of variation, average real variability, and root mean square error. *Results*. Individuals with the highest levels of VVV of systolic blood pressure (SBP) exhibited a 70% increased risk of MetS compared to those with the lowest levels (OR = 1.70, 95% CI = 1.31–2.21). In addition, they had a 41% increased risk of VVV of diastolic blood pressure (DBP) (OR = 1.41, 95% CI = 1.09–1.81). Notably, weight change status significantly influenced the relationship between VVV-BP and MetS ($P_{\text{interaction}} = 0.01$). *Conclusions*. VVV-BP is a significant contributor to the risk of developing MetS. Importantly, individuals who experienced weight loss during the follow-up period did not face a significantly higher risk of developing MetS.

1. Introduction

Metabolic syndrome (MetS) primarily manifests through obesity, particularly central obesity, hyperglycemia, dyslipidemia, and hypertension [1]. It is concerning that nearly one-third of the global population is afflicted by MetS, signifying a worldwide public health concern [2–5]. Individuals with MetS face an elevated risk of developing diabetes, cardiovascular events, stroke, all-cause mortality, and various cancers [6–9]. Notably, research indicates that individuals with MetS experience three times higher mean annual costs than those without MetS, with costs escalating as the number of MetS components increases [10]. Thus, identifying risk factors associated with MetS holds significant implications for the prevention of noncommunicable chronic diseases and the alleviation of financial burdens.

Hypertension represents a significant global public health concern. The Global Burden of Disease Study (2019) has highlighted that high systolic blood pressure is the principal risk factor contributing to mortality, accounting for 19.2% (or 10.8 million) of total deaths [11]. Epidemiological investigations have demonstrated that blood pressure exhibits fluctuations over short- and long-term periods, rather than remaining constant. The visit-to-visit variability in blood pressure (VVV-BP), a form of long-term blood pressure variability (BPV), has been documented as a potent risk

factor for stroke, cardiovascular events, and overall mortality [12–14]. Nevertheless, limited evidence exists concerning the relationship between VVV-BP and the risk of MetS. In a study conducted by Faramawi et al., data from the Third National Health and Nutrition Examination Survey in the US between 1988 and 1994 were utilized to investigate the impact of MetS and its components on VVV-BP [15]. The findings revealed a clear dose-response relationship between the number of MetS components and visit-to-visit variability of systolic blood pressure (VVV-SBP). Yet, the association between VVV-BP and the potential risk of MetS onset remains largely unexplored, with no studies investigating the underlying factors driving this relationship.

We hypothesize that individuals with elevated VVV-BP are at a heightened risk of developing MetS. Consequently, this study probed into the association between VVV-BP and the risk of MetS, as well as the exploration of potential contributing factors.

2. Methods

2.1. Study Design and Participants. This study is a retrospective analysis conducted at a national level, utilizing data from the China Health and Retirement Longitudinal Study (CHARLS). CHARLS is an ongoing longitudinal study that recruited representative samples from 450 villages and urban communities in 28 provinces of China, focusing on individuals aged 45 years and above [16]. The baseline survey was conducted from 2011 to 2012 and included 17,708 respondents who were subsequently followed up every two years via face-to-face computer-assisted personal interviews conducted by trained staff members. The datasets, which have been published and are accessible on the official CHARLS website (https://charls.pku.edu.cn/), were obtained for analysis. Ethical approval for the CHARLS project was obtained from the Peking University Ethics Committee, and every respondent provided informed consent (IRB00001052-11015) [16, 17]. The present study was reported in light of the STROBE guideline (Supplementary Table 1).

In total, 5,751 participants were enrolled in the study at baseline in 2011 and were subsequently followed up in 2013 and 2015. Participants younger than 45 years old were excluded ($n = 302$) due to the possibility of their status as family members of the participants. Individuals with missing data on waist circumference (WC), blood pressure (BP), high-density lipoprotein cholesterol (HDL-C), triglycerides (TGs), or fasting plasma glucose (FPG) at baseline or in 2015 ($n = 445$), missing data on BP in 2013 ($n = 115$), those diagnosed with MetS at baseline ($n = 2{,}229$), and those with outliers data on VVV-BP ($n = 66$) were also excluded. Eventually, 2,594 participants were included for analysis (Figure 1).

2.2. Demographic, Anthropometric, and Biochemical Variables. Demographic information, such as age, sex, smoking history, drinking history, disease history, and medication history, was collected through structured questionnaires. Anthropometric indices (including body weight, height, WC, and BP) and biochemical parameters were measured following standardized procedures outlined in the CHARLS handbook [17]. BP was measured using an automatic monitor (Omron™ HEM-7200) three times at 45-second intervals while participants were in a sitting posture, and the average value was used to calculate VVV-BP. Biochemical parameters were assessed by analyzing venous blood samples obtained after an overnight fast. The study headquarters conducted assays for several parameters, including FPG, HbA1c, TC, TG, HDL-C, low-density lipoprotein cholesterol (LDL-C), uric acid (UA), creatinine, white blood cell count (WBC), C-reactive protein (CRP), and blood urea nitrogen (BUN). To determine the triglyceride-and-glucose (TyG) index, a reliable surrogate marker for insulin resistance [18], the following formula was employed: ln (fasting TG (mg/dL) × fasting glucose (mg/dL)). The body mass index (BMI), visceral adiposity index (VAI), and lipid accumulation product (LAP) were computed utilizing the subsequent equations:

$$
\begin{aligned}
\mathrm{BMI} &= \frac{(\text{body weight [kg]})}{\text{height (m)}^2};\\
\mathrm{VAI\,(male)} &= \left(\frac{\mathrm{WC\,[cm]}}{39.68} + 1.88 \times \mathrm{BMI}\left[\frac{\mathrm{kg}}{\mathrm{m}^2}\right]\right) \times \left(\mathrm{TG}\left[\frac{\mathrm{mg}}{\mathrm{dl}}\right] \times \frac{0.01129}{1.03}\right) \times \left(\frac{1.31}{0.02586/\mathrm{HDL}} - \mathrm{C}\left[\frac{\mathrm{mg}}{\mathrm{dl}}\right]\right);\\
\mathrm{VAI\,(female)} &= \left(\frac{\mathrm{WC[cm]}}{36.58} + 1.89 \times \mathrm{BMI}\left[\frac{\mathrm{kg}}{\mathrm{m}^2}\right]\right) \times \left(\mathrm{TG}\left[\frac{\mathrm{mg}}{\mathrm{dl}}\right] \times \frac{0.01129}{0.81}\right) \times \left(\frac{1.52}{0.02586/\mathrm{HDL}} - \mathrm{C}\left[\frac{\mathrm{mg}}{\mathrm{dl}}\right]\right);\\
\mathrm{LAP\,(male)} &= (\mathrm{WC\,(cm)} - 65) \times \mathrm{TG}\left(\frac{\mathrm{mg}}{\mathrm{dl}}\right) \times 0.01129;\\
\mathrm{LAP\,(female)} &= (\mathrm{WC\,(cm)} - 58) \times \mathrm{TG}\left(\frac{\mathrm{mg}}{\mathrm{dl}}\right) \times 0.01129.
\end{aligned}
\tag{1}
$$

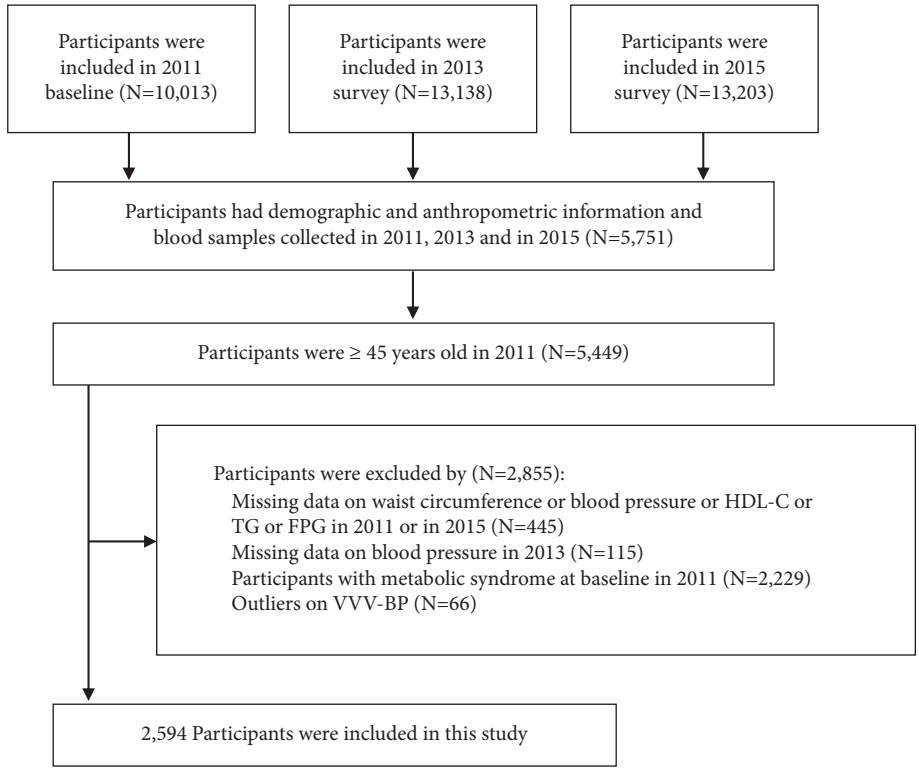

Figure 1: Flowchart.

2.3. Definitions. The diagnosis of MetS was based on the Joint Interim Statement (JIS) by multiple organizations in 2009. According to this statement, any three out of five risk factors qualifies as a diagnosis of MetS. These risk factors include (1) elevated WC (in China, ≥85 cm for men, ≥80 cm for women), (2) elevated TG or use of drug treatment (≥150 mg/dL or 1.7 mmol/L), (3) reduced HDL-C or use of drug treatment (<40 mg/dL or 1.0 mmol/L in males; <50 mg/dL or 1.3 mmol/L in females), (4) elevated BP or use of antihypertensive drug treatment (systolic ≥130 mmHg and/or diastolic ≥85 mmHg), and (5) elevated FPG or use of drug treatment (≥100 mg/dL) [1].

VVV-BP was determined by averaging the blood pressure values obtained in 2011, 2013, and 2015. Several indices were computed using methods recommended by previous studies [19]. These indices included the standard deviation (SD), coefficient of variation (CV: calculated by dividing the SD by the mean), average successive variability (ASV: calculated as the average absolute difference between successive blood pressure measurements), and root mean square error (RMSE: representing the deviation around the fitted linear regression line of blood pressure). Both VVV-SBP and VVV-DBP were analyzed separately.

Changes in obesity indicators were calculated by determining the difference in weight, WC, BMI, VAI, or LAP from baseline. Similarly, changes in glycemic control (FPG, HbA1c, and TyG), lipid profiles (TC, TG, HDL-C, and LDL-C), and inflammatory markers (CRP and WBC) were calculated utilizing the same approach. We determined the changes in the status of these indicators by considering positive values (indicating an increase) and negative values (indicating a decrease) in their respective changes.

2.4. Statistical Analysis. Normally distributed data were reported as means ± standard deviation (SD) or as *n* (%) and were analyzed utilizing the *t*-tests or chi-square tests for continuous and categorical variables, respectively. Non-normally distributed data were presented as the median (25% quartile and 75% quartile) and were tested utilizing the Wilcoxon rank-sum test. Multiple logistic regression analyses were conducted to examine the association between VVV-SBP and VVV-DBP with the risk of MetS. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated. VVV-BP was categorized into tertiles (lowest tertile, middle tertile, and highest tertile) and was included in three models for analysis. Model 1 was unadjusted, Model 2 was adjusted for age, gender, baseline SBP, and DBP, and Model 3 was adjusted for the variables in Model 2 as well as smoking status, drinking habits, baseline WC, BUN, FPG, HbA1c, TC, TG, HDL-C, LDL-C, creatinine, UA, CRP, and the use of antihypertensive, lipid-lowering, and antidiabetic medications. Pearson correlation analysis was conducted to assess the relationships between different VVV-BP indices. Sensitivity analyses were performed to assess the robustness of our findings based on Model 3. These analyses involved excluding participants with stroke, arthritis or rheumatism, kidney diseases, digestive system diseases, or asthma individually. Subgroup analyses were performed based on age (≥60 years vs. <60 years), gender (female vs. male), BMI (≥24 kg/m^2 vs. <24 kg/m^2), smoking status (yes vs. no), and drinking habits (yes vs. no) at baseline. Furthermore, subgroup analyses were conducted based on the changes in the status of obesity indicators, glycemic control, lipid profiles, and inflammatory markers. For subgroup analysis, the

interaction between the subgroup factors and VVV-BP was examined to identify potential moderators. The statistical analyses were completed with the help of STATA (Version 14.0, StataCorp LP, College Station, Texas), and a significance level of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Baseline Characteristics. During the 4-year follow-up, 591 (22.78%) participants developed MetS. Their baseline characteristics are detailed in Table 1. The average age of these participants was 58.8 ± 8.88 years. In comparison to participants who did not develop MetS, those who did were predominantly female, had a lower prevalence of smoking and drinking, had higher weight, WC, BMI, SBP, DBP, HbA1c, TyG, TC, TG, LDL-C, CRP, WBC, and UA, and had lower levels of HDL-C. In addition, they exhibited a higher percentage of medication use (all $P < 0.05$). Participants with MetS had significantly greater values for all indices of VVV-SBP than those without MetS. Regarding VVV-DBP, only the value for DBP-SD was significantly higher in participants with MetS.

3.2. VVV-BP and the Risk of Metabolic Syndrome. After adjusting for covariate parameters, the multiple logistic regression analysis revealed that participants belonging to the highest tertile of VVV in SBP-SD had a 70% increased risk of developing MetS (OR: 1.70, 95% CI: 1.31–2.21), in comparison to those in the lowest tertile. Similarly, the odds of VVV in DBP-SD were linked with a 40% increased risk of MetS (OR: 1.41, 95% CI: 1.09–1.81) (Table 2). The other indices of VVV-SBP, namely, SBP-CV, SBP-RMSE, and SBP-ASV, demonstrated similar results to SD, showing an increased risk of MetS ranging from 31% to 63%. However, the indices of VVV-DBP, including DBP-CV, DBP-RMSE, and DBP-ASV, did not increase the risk of MetS in participants in the highest tertile (Supplementary Table 2). Sensitivity analyses, which excluded participants with stroke, arthritis or rheumatism, kidney diseases, digestive system disease, or asthma, did not significantly affect the primary outcomes. These results suggested that the impact of VVV on MetS was relatively stable, as indicated by the analysis of SD (Supplementary Table 3). Pearson correlation analysis demonstrated a strong positive correlation (all $P < 0.001$) between the various indices of VVV-BP (Supplementary Table 4).

3.3. Subgroup Analysis and Interaction of VVV-BP and MetS. The subgroup analysis revealed a significant association between VVV in SBP-SD and the risk of MetS among females, nondrinkers, and individuals with elevated weight, WC, BMI, VAI, LAP, FPG, TyG, and TG. Similarly, the risk of VVV in DBP-SD and MetS was significant among females, smokers, nondrinkers, and individuals with increased weight, WC, BMI, VAI, LAP, HbA1c, TG, and CRP.

The interaction analyses revealed that changes in weight and the white blood cell count significantly influenced the relationship between VVV in SBP-SD and the risk of MetS ($P_{\text{interaction}} = 0.006$, $P_{\text{interaction}} = 0.016$, respectively). Similarly, the association between VVV in DBP-SD and the risk of MetS was significantly affected by changes in weight and WC ($P_{\text{interaction}} = 0.007$, $P_{\text{interaction}} = 0.014$, respectively) (Table 3). The change in weight status served as a significant mediator of VVV-BP and MetS.

4. Discussion

This study examined the association between VVV-BP and the risk of MetS using data from a prospective cohort study. The findings indicated that VVV-SBP significantly increased the risk of MetS by 70% for participants in the highest tertile of SBP-SD compared to those in the lowest tertile. Similarly, participants in the highest tertile of DBP-SD had a 41% increased risk of MetS compared to those in the lowest tertile. The observed associations remained statistically significant even after excluding individuals with conditions that could potentially influence the development of MetS, such as stroke, arthritis, or rheumatism. Furthermore, changes in body weight and WC were identified as significant mediators in the relationship between VVV-BP and MetS.

This study demonstrated that VVV-BP, regardless of systolic or diastolic measurements, significantly increased the risk of MetS among individuals without the condition. Previous research has consistently shown that individuals with MetS exhibit higher BPV than those without the syndrome [20, 21]. However, most of these studies were cross-sectional and treated BPV as the dependent variable. In contrast, our longitudinal cohort study specifically examined the association between VVV-BP and the development of MetS. The results revealed a significant relationship between VVV-BP and the risk of MetS, particularly for systolic BPV. Various indicators of VVV-SBP were found to induce MetS, while the impact of VVV-DBP was only significant for the standard deviation indicator. These findings were consistent with those of a study by Faramawi et al. who reported a significant dose-response relationship between VVV-SBP, but not VVV-DBP, and the number of MetS components [15]. A sensitivity analysis was performed to ensure the validity of our research findings. After excluding participants with underlying conditions such as stroke, arthritis or rheumatism, kidney diseases, digestive system disease, or asthma, the multivariate analysis confirmed that VVV-BP significantly increased the risk of MetS. However, the underlying mechanism behind this association remains unclear.

Numerous studies have established a strong association between MetS and its components, specifically obesity, hyperglycemia, and hypertension, with increased arterial stiffness. This connection is primarily fueled by metabolic changes such as insulin resistance [22, 23]. In addition, a significant body of evidence demonstrates a clear relationship between BPV and arterial stiffness, with arterial stiffness amplifying the impact of BPV on cardiac events [24, 25]. Arterial stiffening has been proposed as a potential driver of increased BPV [26, 27]. In light of these findings, we postulated that the significant relationship observed between VVV-BP and MetS in our study may potentially be explained by underlying arterial stiffness. However, due to the absence of data on

Table 1: Baseline characteristics of study participants.

Characteristics	Total cohort ($N = 2,594$)	Without incident MetS ($N = 2,003$)	With incident MetS ($N = 591$)	P
Age (years)	58.76 ± 8.83	58.98 ± 8.79	58.76 ± 9.01	0.2951
Male (n, %)	1413 (54.47%)	1161 (57.96%)	252 (42.64%)	<0.0001
Smoking (n, %)	1171 (45.14%)	961 (47.99%)	210 (35.53%)	<0.0001
Drinking (n, %)	968 (37.32%)	779 (38.89%)	189 (31.98%)	0.002
Weight (kg)	55.43 ± 9.75	54.60 ± 9.40	58.27 ± 10.37	<0.0001
WC (cm)	79.83 ± 10.75	78.84 ± 10.15	83.18 ± 12.00	<0.001
BMI (kg/m^2)[a]	22.08 ± 3.44	21.68 ± 3.15	23.43 ± 3.44	<0.0001
SBP (mmHg)	123.55 ± 18.71	122.62 ± 18.24	126.73 ± 19.92	<0.001
DBP (mmHg)	72.34 ± 11.00	71.68 ± 10.81	74.34 ± 11.42	<0.001
FPG (mg/dl)	101.65 ± 23.43	101.40 ± 22.80	102.48 ± 25.46	0.1633
HbA1c (%)[a]	5.14 ± 0.57	5.12 ± 0.57	5.19 ± 0.58	0.0057
TyG index	8.35 ± 0.44	8.31 ± 0.44	8.49 ± 0.43	<0.0001
TC (mg/dl)	189.50 ± 35.31	187.15 ± 34.54	197.48 ± 36.71	<0.0001
TG (mg/dl)	92.31 ± 39.37	88.86 ± 38.32	104.01 ± 40.64	<0.0001
HDL-C (mg/dl)	57.59 ± 14.84	58.72 ± 15.12	53.75 ± 13.14	<0.0001
LDL-C (mg/dl)	115.18 ± 30.90	112.43 ± 29.94	124.52 ± 32.28	<0.0001
CRP (mg/L)[b]	0.79 (0.47, 1.66)	0.77 (0.45, 1.62)	0.86 (0.53, 1.75)	0.0028
WBC (10^9/L)[a]	6.09 ± 1.85	6.04 ± 5.96	6.27 ± 6.10	0.0049
UA (mg/dl)	2.29 ± 1.18	4.28 ± 1.16	4.32 ± 1.24	0.2331
Creatinine (mg/dl)	0.78 ± 0.18	0.78 ± 0.17	0.77 ± 0.19	0.4088
Medication use				
Antihypertensive drugs (n, %)	422 (16.27%)	256 (12.78%)	166 (28.09%)	<0.0001
Antidiabetic drugs (n, %)	57 (2.20%)	31 (1.55%)	26 (4.40%)	<0.0001
Lipid-lowering drugs (n, %)	52 (2%)	3 (0.15%)	49 (8.29%)	<0.0001
VVV-BP				
SBP-SD	10.18 ± 6.70	9.81 ± 6.51	11.43 ± 7.16	<0.0001
SBP-CV*100[c]	8.02 ± 4.90	7.83 ± 4.84	8.67 ± 5.04	0.0001
SBP-ASV	12.88 ± 9.43	12.45 ± 9.13	14.37 ± 10.27	<0.0001
SBP-RMSE	9.04 ± 8.13	8.73 ± 7.85	10.06 ± 8.94	0.0002
DBP-SD	6.34 ± 3.73	6.25 ± 6.09	6.67 ± 6.36	0.0079
DBP-CV*100[c]	8.70 ± 5.00	8.68 ± 5.07	8.79 ± 4.76	0.3228
DBP-ASV	8.07 ± 5.37	7.99 ± 5.37	8.31 ± 5.17	0.1015
DBP-RMSE	5.68 ± 4.73	5.62 ± 4.75	5.88 ± 4.69	0.1173

MetS, metabolic syndrome; WC, waist circumference; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; TyG, triglyceride-and-glucose, TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CRP, C-reactive protein; WBC, white blood cell; UA, uric acid; BUN, blood urea nitrogen. [a]There were 7, 13, and 50 participants having missed measurement of BMI, HbA1c, and WBC, respectively. [b]Data were presented as the median, 25% quartile, and 75% quartile; the statistical method was the Wilcoxon rank-sum test. [c]The value was expanded by a factor of 100 because the original value was too small.

arterial stiffness, we were unable to confirm this hypothesis. In light of the association between arterial stiffness and metabolic changes, we aimed to investigate the influence of these metabolic changes on the relationship between VVV-BP and MetS. Subgroup analysis results revealed that individuals who experienced weight loss during the follow-up period did not exhibit a significantly higher risk of MetS, despite having higher VVV-BP. Moreover, interaction results suggested that changes in weight status (weight gain/weight loss) acted as a mediator between VVV-BP and MetS. In addition, a reduction in WC, indicating a decrease in central obesity, was found to mitigate the risk effect of BPV on MetS. These findings highlight the potential role of weight loss in modulating the relationship between VVV-BP and MetS.

The clinical management guidelines for MetS prioritize weight loss-based lifestyle interventions as the primary approach for managing the different components of the condition [28]. A secondary analysis of the Finnish Diabetes Prevention Study (FDPS) demonstrated that intensive lifestyle interventions leading to moderate weight loss resulted in a reduction of MetS prevalence from 74.0% to 62.6% after an average follow-up of 3.9 years. In comparison, the control group experienced a decrease in prevalence from 74.0% to 71.2% [29]. Moderate weight loss, a reduction of 5–10% in body weight, can benefit pancreatic β-cell function and insulin sensitivity in organs [30]. Both the guidelines from the American College of Cardiology/American Heart Association and the European Society of Cardiology/European Society of Hypertension emphasize the importance of weight loss as part of nonpharmacological interventions in managing hypertension [31]. However, there is currently no consensus on effective interventions for VVV-BP. Thus, selecting a reasonable and effective comprehensive lifestyle intervention for weight management may be a viable approach to counteract the development of MetS caused by VVV-BP. In nursing, it is crucial to prioritize health education and intervention programs focusing on weight loss to mitigate public health problems caused by MetS.

Table 2: Visit-to-visit variability of blood pressure and the risk of metabolic syndrome.

Visit-to-visit variability of blood pressure	No. of cases/total	Model 1[a] OR (95% CIs)	Model 2[b] OR (95% CIs)	Model 3[c] OR (95% CIs)
SBP-SD				
Low (1st tertile, ≤6.55 mmHg)	160/865	1 (ref.)	1 (ref.)	1 (ref.)
Middle (2nd tertile, 6.55–11.47 mmHg)	188/865	1.22 (0.97–1.55)	1.25 (0.99–1.59)	1.30 (1.01–1.69)
High (3rd tertile, ≥11.47 mmHg)	243/864	1.72 (1.37–2.16)	1.65 (1.30–2.09)	1.70 (1.31–2.21)
DBP-SD				
Low (1st tertile, ≤4.33 mmHg)	176/865	1 (ref.)	1 (ref.)	1 (ref.)
Middle (2nd tertile, 4.33–7.31 mmHg)	201/865	1.19 (0.94–1.48)	1.15 (0.91–1.45)	1.17 (0.91–1.52)
High (3rd tertile, ≥7.31 mmHg)	214/864	1.29 (1.03–1.62)	1.27 (1.01–1.60)	1.41 (1.09–1.81)

OR, odds ratio; CIs, confidence intervals; VVV, visit-to-visit variability; SBP, systolic blood pressure; RMSE, root mean square error; SD, standard division; DBP, diastolic blood pressure; [a]Model 1: unadjusted. [b]Model 2: adjusted for age, gender, and baseline systolic blood pressure and diastolic blood pressure. [c]Model 3: Model 2 plus smoking, drinking, baseline value of waist circumference, blood urea nitrogen, fasting plasma glucose, HbA1c, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, creatinine, uric acid, C-reactive protein, and use of antihypertensive, lipid-lowering, and antidiabetic drugs.

Table 3: Subgroup analysis and interaction of visit-to-visit variability of blood pressure and metabolic syndrome.

Subgroups		SBP-SD		DBP-SD	
		OR (95% CIs)[a]	P^b	OR (95% CIs)[a]	P^b
Age	≥60 years	1.02 (1.01–1.05)	0.140	1.02 (1.00–1.05)	0.207
	<60 years	1.05 (1.02–1.07)		1.05 (1.02–1.07)	
Gender	Female	1.04 (1.02–1.07)	0.111	1.04 (1.01–1.08)	0.784
	Male	1.02 (0.99–1.04)		1.03 (0.99–1.07)	
Smoking	Yes	1.04 (1.01–1.06)	0.655	1.04 (1.01–1.09)	0.670
	No	1.03 (1.01–1.05)		1.03 (0.99–1.07)	
Drinking	Yes	1.01 (0.99–1.04)	0.168	1.02 (0.97–1.07)	0.614
	No	1.04 (1.02–1.06)		1.04 (1.01–1.08)	
Weight change status	Increase	1.05 (1.03–1.07)	0.006	1.07 (1.03–1.11)	0.007
	Decrease	1.01 (0.98–1.03)		0.99 (0.95–1.04)	
WC change status	Increase	1.04 (1.02–1.06)	0.300	1.04 (1.02–1.06)	0.014
	Decrease	1.02 (0.99–1.05)		1.02 (0.99–1.05)	
BMI change status	Increase	1.04 (1.02–1.06)	0.064	1.05 (1.01–1.09	0.173
	Decrease	1.01 (0.98–1.04)		1.02 (0.97–1.06)	
VAI change status	Increase	1.04 (1.02–1.06)	0.145	1.04 (1.01–1.08)	0.523
	Decrease	1.00 (0.97–1.04)		1.01 (0.96–1.07)	
LAP change status	Increase	1.04 (1.02–1.06)	0.407	1.04 (1.00–1.07)	0.996
	Decrease	1.01 (0.97–1.05)		1.05 (0.98–1.11)	
FPG change status	Increase	1.04 (1.01–1.06)	0.225	1.03 (0.98–1.07)	0.775
	Decrease	1.02 (0.99–1.04)		1.04 (1.00–1.08)	
HbA1c change status	Increase	1.03 (1.01–1.05)	0.631	1.04 (1.01–1.07)	0.543
	Decrease	1.07 (1.01–1.13)		1.04 (0.94–1.16)	
TyG change status	Increase	1.04 (1.02–1.06)	0.974	1.03 (0.99–1.07)	0.332
	Decrease	1.03 (0.99–1.06)		1.06 (1.01–1.12)	
TC change status	Increase	1.04 (1.02–1.07)	0.237	1.03 (0.98–1.07)	0.551
	Decrease	1.02 (1.00–1.04)		1.04 (1.01–1.08)	
TG change status	Increase	1.04 (1.02–1.06)	0.301	1.04 (1.01–1.08)	0.805
	Decrease	1.01 (0.98–1.04)		1.03 (0.97–1.08)	
HDL-C change status	Increase	1.04 (1.01–1.07)	0.791	1.04 (0.98–1.09)	0.814
	Decrease	1.03 (1.01–1.05)		1.03 (1.00–1.07)	
LDL-C change status	Increase	1.03 (1.01–1.05)	0.282	1.03 (0.98–1.09)	0.975
	Decrease	1.04 (1.01–1.07)		1.04 (1.01–1.07)	
CRP change status	Increase	1.03 (1.01–1.05)	0.380	1.04 (1.01–1.08)	0.648
	Decrease	1.03 (1.00–1.07)		1.03 (0.98–1.09)	
WBC change status	Increase	1.04 (1.02–1.06)	0.160	1.03 (0.99–1.07)	0.804
	Decrease	1.03 (1.00–1.05)		1.04 (1.00–1.08)	

SBP, systolic blood pressure; DBP, diastolic blood pressure; SD, standard division; OR, odds ratio; CIs, confidence intervals; WC, waist circumference; BMI, body mass index; VAI, visceral adiposity index; LAP, lipid accumulation product; FPG, fasting plasma glucose; TyG, triglyceride-and-glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CRP, C-reactive protein; WBC, white blood cell. [a]Adjusted for variables involved in Model 3. [b]The interaction effect.

4.1. Limitations. This study possesses several limitations. First, it was impossible to completely eliminate the residual confounding effects of certain unknown factors despite controlling for numerous potential confounding factors to assess the risk relationship between VVV-BP and MetS. Second, the insulin resistance index and the visceral fat index employed in this study were not considered the gold standard for assessment, leading to some insignificant findings, even though TyG demonstrated a close association with insulin resistance and LAP with visceral fat. Third, the discussion on potential influencing factors of VVV-BP and MetS did not include deeper-level indicators, such as cellular factors, and further verification is needed to establish potential mechanisms. Finally, the study had a relatively short follow-up period and solely focused on the Chinese population aged 45 years and older, therefore necessitating further validation of the results in a larger and more diverse sample population.

In conclusion, our study uncovered a significant association between VVV-BP and an increased risk of MetS. The sensitivity analysis confirmed the robustness of this relationship. In addition, through the analysis of interaction effects, we found that changes in weight status served as a significant mediator linking VVV-BP and MetS.

Data Availability

The data supporting the results of this study can be found at the website https://charls.pku.edu.cn/.

Conflicts of Interest

The authors declare that they no conflicts of interest.

Authors' Contributions

Ruxue Li designed the study, dealt with and analyzed the data, and wrote the manuscript. Wuai Zhou contributed to the methods and manuscript revision. Xue Cai helped design the study and contributed to the methods. Dan Luo contributed to the introduction and edited the manuscript. Huijing Zhang contributed to the methods. MingZi Li designed the study, contributed to the introduction, reviewed the manuscript, and edited the manuscript. All the authors have read and approved the final manuscript.

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Supplementary Materials

Supplementary Table 1: STROBE checklist. Supplementary Table 2: other indices of visit-to-visit variability of blood pressure and the risk of metabolic syndrome. Supplementary Table 3: sensitivity analyses. Supplementary Table 4: Pearson analysis between different VVV-BP indices. (*Supplementary Materials*)

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