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Hypertriglyceridemic waist phenotype is associated with left ventricular hypertrophy in Chinese hypertension patients

Qiligeer Bao MM[1,2] | Yun Li MM[1,3] | Shouyuan Ma MM[4] | Jiaojiao Qiu MM[2] | Jin Sun MM[1,2] | Yongkang Su MM[1,2] | Anhang Zhang MM[1,2] | Shuang Cai MM[1,2] | Bokai Cheng MM[1,2] | Man Li MD[2] | Yan Zhang MM[5] | Shuxia Wang MD[2] | Ping Zhu MM[2]

[1]Medical School of Chinese PLA, Beijing, China

[2]Department of Geriatrics, The Second Medical Center & National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, Beijing, China

[3]The 305 Hospital of PLA, Beijing, China

[4]Department of Geriatric Cardiology, The Second Medical Center, Chinese PLA General Hospital, Beijing, China

[5]Department of Outpatient, The First Medical Center, Chinese PLA General Hospital, Beijing, China

Correspondence
Shuxia Wang MD, Department of Geriatrics, The Second Medical Center & National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, No. 28, FuXing Road, Haidian District, Beijing 100853, China.
Email: wangsx301@163.com

Ping Zhu MM, Department of Geriatrics, The Second Medical Center & National Clinical Research Center for Geriatric Diseases, Chinese PLA General Hospital, No. 28, FuXing Road, Haidian District, Beijing 100853, China.
Email: zhuping301hospital@163.com

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Abstract

Left ventricular hypertrophy (LVH), the most common target organ damage in patients with hypertension, is closely related to excessive visceral adipose tissue (VAT) accumulation in the body. The hypertriglyceridemic waist (HTHW) phenotype can act as a surrogate marker of excessive VAT. However, the relationship between the HTHW phenotype and LVH in patients with hypertension remains unknown. The present study aimed to investigate whether the HTHW phenotype is associated with LVH, using echocardiography in a cross-sectional study involving 4470 middle-aged and older Chinese patients with hypertension. Logistic regression analysis revealed that patients with the HTHW phenotype were 1.52-fold more likely to experience LVH than those with normal triglyceride levels and normal waist circumference. This association was independent of age, sex, and other potentially confounding factors. In the stratified analysis, a stronger correlation was found among women, people of at least 70 years of age, and people with hyperuricemia. These results suggest that distinguishing the HTHW phenotype in patients with hypertension could serve as a simple and effective screening strategy for identifying people with a higher risk of developing LVH.

KEYWORDS
echocardiography, hypertension, hypertriglyceridemic waist, left ventricular hypertrophy

1 | INTRODUCTION

The prevalence of hypertension has increased substantially in China owing to the overconsumption of high-calorie fast foods coupled with an increasingly sedentary lifestyle.[1] Hypertension, which is characterized by chronic hemodynamic overload, is closely associated with an increased risk of cardiovascular disease (CVD).[2] Left ventricular hypertrophy (LVH) is the most common target organ damage resulting from

Qiligeer Bao, Yun Li, and Shouyuan Ma contributed equally to this work.

hypertension, and it is a major risk factor for cardiovascular morbidity and mortality.[3]

Obesity is a known risk factor for developing LVH.[4] Specifically, excessive visceral adipose tissue (VAT) appears to be a stronger and more independent risk factor than other types of adipose tissue.[5–8] Epidemiological studies have shown that VAT is associated with numerous adverse health outcomes, and it is an independent risk marker for morbidity and mortality in cardiovascular and metabolic diseases.[9] Moreover, VAT is metabolically active and has a higher energy demand than subcutaneous adipose tissue, further increasing the cardiac workload in hypertensive patients and contributing to the development of LVH.[10] A study involving 1941 participants in Korea showed that when the visceral fat area (VFA) was examined in tertiles, as assessed on computed tomography (CT), the mean left ventricular mass index (LVMI) increased with increasing tertiles of VFA.[11] Moreover, they found that VFA was independently associated with LVMI and impaired LV diastolic parameters. However, precise appraisal of VAT requires expensive imaging modalities or methods that involve radiation and may have contraindications (eg, magnetic resonance imaging (MRI) and computed tomography (CT)), thus limiting the feasibility of screening for VFA in the general population. The hypertriglyceridemic waist (HTHW) phenotype, defined as an increased waist circumference (WC) with elevated fasting triglyceride levels, has been proposed as a surrogate marker of excess VAT accumulation and is an effective and inexpensive tool used in daily clinical practice.[12] Since it was first proposed in 2000 by Lemieux in the Quebec Cardiovascular Study, several studies have shown that it is positively associated with the risk of prediabetes and diabetes,[13] atherosclerosis,[14] and cardiovascular events.[15] Recently, a cross-sectional study in China involving 9015 adults suggested that the HTHW phenotype was a strong risk factor for the development of hypertension.[16] However, the association between the HTHW phenotype and LVH in the hypertensive population remains unclear. Considering that VAT is positively related to LVH and the highly sensitive role of the HTHW phenotype in identifying VAT, we hypothesized that the HTHW phenotype could serve as a screening strategy for LVH in hypertensive populations. Therefore, the present study aimed to investigate whether the HTHW phenotype is associated with LVH using echocardiography in a sample of middle-aged and older Chinese people with hypertension.

2 | MATERIALS AND METHODS

2.1 | Participants

The study protocol was approved by the Ethics committees of Fuwai Hospital and local hospitals. All participants provided informed consent before their recruitment.

A community-based cross-sectional study was conducted in Xinyang County, Henan Province, China, between 2004 and 2005. Multistage cluster sampling was employed to select a sample of residents between 40 and 75 years of age from local rural communities. A total of 13 444 participants comprising 5270 men and 8174 women from 63 districts in seven communities in Xinyang County completed the survey. The response rate was 84.9%. Of the participants, 5421 were identified as being hypertensive using the following diagnostic criteria: diastolic blood pressure (DBP) ≥ 90 mm Hg, systolic blood pressure (SBP) ≥ 140 mm Hg, physician diagnosis, or current medication for hypertension (as defined by WHO 1999). Of the 5421 hypertensive participants, 4805 had left ventricular mass (LVM) measured through echocardiography and 4470 had completed biochemical measurement data. Finally, 4470 participants (1485 men and 2985 women) with integrated clinical and echocardiography data were included in the final analysis.

2.2 | Exposure definition

WC was measured with a non-elastic measuring tape positioned midway between the lowest rib and iliac crest while patients were standing. Triglycerides (TG) were measured using an automatic analyzer (Hitachi 7060, Hitachi, Tokyo, Japan). Participants were classified into one of four triglyceride waist phenotypes according to their WC and TG levels: (1) normal triglyceride levels and normal WC (NTNW; TG < 1.7 mmol/L; WC < 90 cm for men and WC < 80 cm for women); (2) high triglyceride levels and normal WC (HTNW; TG ≥ 1.7 mmol/L; WC < 90 cm for men and WC < 80 cm for women); (3) normal triglyceride levels but enlarged WC (NTHW; TG < 1.7 mmol/L; WC ≥ 90 cm for men and WC ≥ 80 cm for women); and (4) high triglyceride levels and enlarged WC (HTHW; TG ≥ 1.7 mmol/L; WC ≥ 90 cm for men and WC ≥ 80 cm for women).[16]

2.3 | Echocardiographic methods

Transthoracic echocardiography was performed according to the standard protocol, using the HP 5500 (Phillips Health Care System, Boston, MA, USA) or HDI 3000 (ATL, Bothell, WA, USA) systems with the participant in the left lateral position. Transthoracic echocardiography included M-mode, two-dimensional (2D), and color Doppler records from the parasternal long-axis and short-axis windows, and 2D and color Doppler evaluations from the apical window to yield 2-, 3-, and 4-chamber images. The transducer frequency range was 2.5–3.5 MHz. Optigo echocardiographic recorders (Agilent, Boston, MA, USA) were used to screen participants who were unable to travel to the local study center. All echocardiographic examinations were performed by two technicians trained in echocardiographic protocol at the Cardiovascular Institute of the Chinese Academy of Medical Sciences, under the supervision of two ultrasound physicians with at least 2 years of experience.

According to the recommendations of the American Society of Echocardiography, the left atrial diameter, diastolic interventricular septal thickness (IVSd), left ventricular internal end-diastolic diameter (LVIDd), and diastolic left ventricular posterior wall thickness (PWTd) were measured at the end of the systolic and diastolic periods of up to three cardiac cycles.

2.4 | Definitions and calculation of derived variables

The LVM, LVMI, relative wall thickness (RWT), waist–hip ratio (WHR) and body surface area (BSA) were calculated using the following equation:

$$LVM(g) = 0.8 + 1.04 * ((IVSd + LVIDD + PWTd)^3 - LVIDD^3) + 0.6$$

$$LVM1 = \frac{LVM}{height^{2.7}}$$

$$RWT = 2 \times \left(\frac{PWTd}{LVIDD}\right)$$

$$WHR = \frac{weight\ circumference}{hip\ circumference}$$

$$\text{BSA (m2)} = 0.0061 \times \text{height (cm)} + 0.0128 \times \text{weight (kg)} - 0.1529$$

Coronary artery disease (CAD) was diagnosed either on coronary arteriography or on account of prior myocardial infarction, surgery, or coronary revascularization. Stroke was defined as an event requiring hospitalization or symptoms of neurological deficit confirmed from local hospital records, and 81% of cases were confirmed via CT and MRI. Diabetes mellitus was diagnosed considering a fasting plasma glucose level ≥7.0 mmol/L and/or if patients were receiving antidiabetic medications. Hyperuricemia was diagnosed as uricemia > 420 μmol/L for men and > 360 μmol/L for women. A partition value of .43 was used for RWT.

The diagnostic criteria for LVH were as follows: LVMI ≥ 49.2 g/m$^{2.7}$ for men and ≥46.7 g/m$^{2.7}$ for women.[17]

2.5 | Statistical analyses

Data management and statistical analysis were performed using IBM SPSS Statistics software, Version 22.0 (IBM Corp, Armonk, NY, USA). Data are expressed as mean ± standard deviation for normal distributions and median (interquartile range) for skewed distributions. Categorical data are expressed as numbers (percentages). The characteristics of different phenotype groups were compared using analysis of variance or the Kruskal–Wallis test for continuous data and the χ^2 test for categorical variables. Binary logistic regression analyses were performed to determine associations between different triglyceride waist phenotypes and LVH in hypertensive patients. Odds ratios (OR) and 95% confidence intervals (CI) were calculated with NTNW as the reference group. Model 1 was adjusted for sex and age and Model 2 for age, sex, SBP, DBP, WHR, serum glucose, TG, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), uric acid, blood urea nitrogen (BUN), creatinine, history of stroke, CAD, diabetes mellitus, and antihypertensive drugs. Subgroup analyses by sex (male vs. female), age (< 70 years vs. ≥ 70 years), and uricemia level (absence vs. presence of hyperuricemia) were performed to test the robustness of the results. Statistical significance was set at $P < .05$ (two-sided).

3 | RESULTS

3.1 | Participant baseline characteristics divided by phenotype according to the different triglyceride waist phenotypes

Table 1 reports clinical characteristics and echocardiographic data of the participants according to their triglyceride waist phenotypes. The mean age of the selected 4470 participants was 58 years. There were 1307 participants (29.2%) in the NTNW phenotype group, 311 (7%) in the HTNW group, 1616 (36.2%) in the NTHW group, and 1236 (27.7%) the HTHW group. Except for SBP, DBP, RWT, and history of stroke, the other variables were significantly different among the four phenotype groups. Compared with those in the NTNW phenotype group, participants in the HTHW phenotype group were more likely to be female with a longer history of hypertension; higher use rate of antihypertensive drugs; higher WC, hip circumference, WHR, heart rate, glucose, TG, total cholesterol, LDL-C, uric acid, IVSd, LVIDd, PWTd, LVM, LVMI; and lower HDL-C, BUN, and creatinine levels. In addition, participants in the HTHW phenotype group were more likely to have had stroke, CAD, and diabetes mellitus, but less likely to be current drinkers or smokers.

3.2 | Prevalence of LVH in the four subgroups

The prevalence of LVH among the hypertensive participants was 43.7% (1955/4470) (Table 1). Participants in the HTHW group had the highest prevalence of LVH (595/1236; 48.1%; $P < .001$), while participants in the NTHW group had a higher prevalence of LVH (766/1616; 47.4%) than those in the NWNT (482/1307; 36.9%) and HTNW (112/311; 36.0%) groups ($P < .001$). The results from this study showed that a higher proportion of women were in the NTHW and HTHW groups than in other groups.

3.3 | Association of the different triglyceride waist phenotypes with LVH

Table 2 shows the association between different triglyceride waist phenotypes and LVH in the unadjusted and adjusted models. Compared with the NTNW group, the HTHW group was significantly associated with an increased LVH risk in the unadjusted model (OR 1.59; 95% CI, 1.36–1.86; $P < .001$) and in Model 1 after adjusting for sex and age (OR 1.74, 95% CI, 1.47–2.05; $P < .001$). The relationship remained significant after further adjustment for SBP, DBP, WHR, serum glucose, TG, cholesterol, HDL-C, LDL-C, uric acid, BUN, creatinine, history of stroke, CAD, diabetes mellitus, and antihypertensive drugs in Model 2 (OR 1.52, 95% CI, 1.20–1.92; $P < .001$). Similar results were observed for participants in the NTHW group, who had a significantly higher LVH risk in the unadjusted model (OR 1.54, 95% CI, 1.33–1.79; $P < .001$), Model 1 (OR 1.69, 95% CI, 1.44–1.98; $P < .001$), and Model 2 (OR 1.67, 95% CI, 1.39–2.01; $P < .001$) than those in the NTNW group.

TABLE 1 Baseline characteristics according to the different triglyceride waist phenotypes

	NTNW	HTNW	NTHW	HTHW	*P*-value
N	1307	311	1616	1236	
Mean age (years)	59.38 ± 8.62	58.26 ± 8.64	57.41 ± 8.35	57.46 ± 7.71	<.001
Men	697 (53.3%)	156 (50.2%)	347 (21.5%)	285 (23.1%)	<.001
Postmenopausal women	510 (39.0%)	133 (42.8%)	1036 (64.1%)	829 (67.1%)	<.001
Waist circumference (cm)	76.32 ± 6.39	78.79 ± 7.07	90.52 ± 6.95	92.36 ± 7.53	<.001
Hip circumference (cm)	91.73 ± 5.70	94.19 ± 5.66	102.39 ± 6.38	103.58 ± 6.81	<.001
WHR	.84 ± .20	.84 ± .06	.88 ± .05	.89 ± .05	<.001
SBP (mm Hg)	162.71 ± 25.18	163.58 ± 24.08	163.79 ± 24.29	163.96 ± 24.37	.565
DBP (mm Hg)	96.41 ± 13.16	97.73 ± 13.40	97.31 ± 13.05	97.72 ± 12.42	.056
Heart rate	71.90 ± 12.22	74.41 ± 13.89	72.34 ± 11.52	73.87 ± 12.25	<.001
Glucose (mmol/L)	5.34 ± 1.40	5.73 ± 1.79	5.45 ± 1.48	5.93 ± 2.09	<.001
Triglyceride (mmol/L)	1.00 (.79–1.28)	2.17 (1.87–2.73)	1.19 (.97–1.42)	2.32 (1.98–3.02)	<.001
Cholesterol (mmol/L)	5.23 ± .95	5.97 ± 1.20	5.38 ± 1.03	5.96 ± 1.13	<.001
HDL-C (mmol/L)	1.69 ± .36	1.47 ± .34	1.57 ± .32	1.40 ± .28	<.001
LDL-C (mmol/L)	2.89 ± .75	3.28 ± .91	3.16 ± .83	3.39 ± .90	<.001
Uric Acid (μmol/L)	280.56 ± 81.83	310.91 ± 95.26	282.50 ± 83.30	315.26 ± 89.25	<.001
BUN (mmol/L)	5.76 ± 1.90	5.52 ± 2.38	5.38 ± 1.61	5.25 ± 1.75	<.001
Creatinine (μmol/L)	66.30 (55.50–78.70)	65.50 (55.90–79.60)	60.05 (51.40–70.80)	61.50 (52.30–73.00)	<.001
Duration of hypertension	4.27 (1.67–9.40)	4.69 (1.22–9.24)	5.04 (2.06–9.76)	4.88 (2.17–9.81)	<.05
Current drinkers	95 (7.3%)	17 (5.5%)	53 (3.3%)	41 (3.3%)	<.001
Current smokers	111 (8.5%)	26 (8.4%)	57 (3.5%)	50 (4.0%)	<.001
Antihypertensive drug	555 (42.5%)	144 (46.3%)	785 (48.6%)	644 (52.1%)	<.001
History of stroke	141 (10.8%)	39 (12.5%)	142 (8.8%)	135 (10.9%)	.087
History of CAD	79 (6.1%)	21 (6.8%)	148 (9.2%)	161 (13.1%)	<.001
Diabetes mellitus	28 (2.1%)	14 (4.5%)	73 (4.5%)	101 (8.2%)	<.001
IVSd (mm)	9.79 ± 1.63	9.78 ± 1.62	9.99 ± 1.56	10.16 ± 1.56	<.001
LVIDd (mm)	44.95 ± 5.24	44.73 ± 5.13	45.82 ± 4.96	45.80 ± 5.06	<.001
PWTd (mm)	9.60 ± 1.40	9.54 ± 1.37	9.76 ± 1.36	9.79 ± 1.30	<.001
LVM (g)	152.84 ± 45.12	151.02 ± 44.51	161.01 ± 42.92	163.11 ± 43.54	<.001
RWT	.43 ± .08	.43 ± .08	.43 ± .07	.43 ± .07	.896
LVMI	44.44 ± 12.24	43.50 ± 12.13	47.39 ± 12.29	47.84 ± 12.70	<.001
LVH	482 (36.9%)	112 (36.0%)	766 (47.4%)	595 (48.1%)	<.001

Abbreviations: BUN, blood urea nitrogen; CAD, coronary artery disease; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HTHW, high triglyceride levels and enlarged waist circumference; HTNW, high triglyceride levels but normal waist circumference; IVSd, end-diastolic interventricular septal thickness; LDL-C, low-density lipoprotein cholesterol; LVH, left ventricular hypertrophy; LVIDd, left ventricular internal end-diastolic diameter; LVM, left ventricular mass; LVMI, left ventricular mass index divided by height in meters powered by 2.7; NTHW, normal triglyceride levels but enlarged waist circumference; NTNW, normal triglyceride levels and normal waist circumference; PWTd, end-diastolic posterior wall thickness; RWT, relative wall thickness calculated by 2× PWTd/LVIDD; SBP, systolic blood pressure; WHR, waist–hip ratio.

However, compared with that in the NTNW group, the risk of LVH was not significantly higher in the HTNW group in any of the models.

3.4 | Stratified analysis

A stratification analysis using multivariable logistic regression was used to examine the association of different triglyceride waist phenotypes with LVH in different subgroups of sex, age, and hyperuricemia (Table 3). The associations between different triglyceride waist phenotypes and the risk of LVH remained consistent across most subgroups, except in the group of men. A stronger positive association of the HTHW phenotype with LVH was found in the subgroup of women (OR 1.70, 95% CI, 1.26–2.30; $P = .001$), those aged at least 70 years (OR 3.22, 95% CI, 1.43–7.30; $P = .005$), and those with hyperuricemia (OR 2.43, 95% CI, 1.15–5.14; $P<.05$), but not in the subgroup of men

TABLE 2 Odds ratio for left ventricular hypertrophy by different triglyceride waist phenotypes

	NTNW	HTNW		NTHW		HTHW	
	OR (95% CI)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Crude model	Reference	.96 (.74–1.25)	.776	1.54 (1.33–1.79)	<.001	1.59 (1.36–1.86)	<.001
Model 1	Reference	1.00 (.77–1.29)	.972	1.69 (1.44–1.98)	<.001	1.74 (1.47–2.05)	<.001
Model 2	Reference	.88 (.66–1.18)	.401	1.67 (1.39–2.01)	<.001	1.52 (1.20–1.92)	<.001

Model 1: adjusted for age, sex.
Model 2: adjusted for age, sex, systolic blood pressure, diastolic blood pressure, waist–hip ratio, serum glucose, triglyceride, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, uric acid, blood urea nitrogen, creatinine, history of stroke, coronary artery disease, diabetes mellitus, and antihypertensive drugs.
Abbreviations: 95% CI, 95% confidence interval; HTHW, high triglyceride levels and enlarged waist circumference; HTNW, high triglyceride levels but normal waist circumference; NTHW, normal triglyceride levels but enlarged waist circumference; NTNW, normal triglyceride levels and normal waist circumference.; OR, odds ratio.

(OR 1.21, 95% CI, .81–1.82; $P = .357$), those aged less than 70 years (OR 1.38, 95% CI, 1.09–1.75; $P = .009$), and those without hyperuricemia (OR 1.44, 95% CI, 1.12–1.85; $P = .005$). Similar results were observed for patients in the NTHW group. Finally, no significant associations were found between the HTNW group and the risk of LVH in all stratified groups.

4 | DISCUSSION

As a common cause of end-stage CVD, LVH is also strongly associated with excessive VAT, which is accurately assessed on CT or MRI. A cross-sectional study using data from 997 community-based participants with a mean age of 60 years showed that VAT was directly associated with LV mass.[5] Similar results have been reported among Indonesian women.[6] Another cross-sectional study involving 124 patients with aortic stenosis (AS) showed that VAT was significantly associated with LVH, independent of AS severity and hypertension.[7] Recently, a study using a bioelectrical impedance analyzer to quantify VFAs in 568 patients with type 2 diabetes in China reported that visceral fat area was the strongest independent risk factor for LVMI and was closely associated with cardiovascular risk factors in patients with type 2 diabetes mellitus.[8] These results provide robust evidence for an independent and strong association between excessive VAT and LVH. However, accurate measurement of VAT requires CT and MRI, which are expensive procedures, involve radiation, and are not suitable for screening the general population. The HTHW phenotype was proposed as a surrogate marker of increased VAT levels.[12] A previous study conducted in China showed that the HTHW phenotype had a high specificity (90.91%) and satisfactory sensitivity (81.08%) for abdominal visceral fat area, as quantified on MRI.[18] Considering the strong correlation between LVH and excessive VAT and the strong predicter role of the HTHW phenotype of excess VAT accumulation, we hypothesized that there is an association between the HTHW phenotype and LVH, especially in hypertensive populations. The present study proved our hypothesis correct. Patients with the HTHW phenotype were 1.52-fold more likely to develop LVH than those with the NTNW phenotype, and this association was independent of age, sex, and other potentially confounding factors. Moreover, participants in the HTHW group had the highest prevalence of LVH among the four phenotypes, which was even higher than the prevalence of all hypertensive patients. The highest prevalence of LVH and LVMI findings in patients with the HTHW phenotype suggests a critical role for the HTHW phenotype in the development of LVH in hypertensive patients. The participants in our study were middle-aged and older people with hypertension in rural China with a high prevalence of obesity and middle-aged women accounted for more because of a large number of male rural residents leaving home to work in cities. The previous study demonstrated that LVMI indexed by height 2.7 was more sensitive than LVMI indexed by BSA in identifying LVH in women and obesity with hypertension and the results also suggest that LVH defined by LVMI indexed by height 2.7 is a strong and independent correlate of extracardiac organ damage.[19] Another study also indicated that LVMI indexed by height 2.7 was an independent predictor of incident ischemic stroke even after taking into account traditional clinical risk factors after a median follow-up of 8.8 years.[20] Moreover, in our study, 1696 out of 4470 patients (37.9%) were found to have LVH when LVM was indexed to BSA, and 1955 (43.7%) when indexed to height 2.7, the diagnostic criteria for LVH defined by LVMI indexed by BSA were as follows: LVMI>115 g/m^2 for men and>95 g/m^2 for women (as defined by ESH/ESC 2013). LVMI indexed by height 2.7 can identify individuals at higher risk for LVH more sensitive than LVMI indexed by BSA in these hypertensive patients, this may therefore help in a more precise risk evaluation of hypertensive patients and in determining therapy. So LVMI was calculated as LVM/height$^{2.7}$ in our study.

The underlying mechanisms could be partially explained by the strong correlation between the HTHW phenotype and excessive VAT accumulation. The simultaneous presence of larger WC and elevated fasting hypertriglyceridemia represents the patient's relative inability to store excess energy in the subcutaneous adipose tissue, which further led to accumulation in the VAT or other ectopic depots (eg, pancreas, liver, and heart). This further induced a cluster of metabolic abnormalities and the related failure of pancreatic beta-cells, causing insulin resistance. A meta-analysis of 48 studies involving 242 879 participants showed that the HTHW phenotype significantly correlated with insulin resistance and abnormal glucose metabolism.[21] In line with

TABLE 3 Odds ratio for left ventricular hypertrophy by different triglyceride waist phenotypes in stratification analysis

	NTNW	HTNW		NTHW		HTHW	
		Crude OR (95%CI); *P*-value	Adjusted OR (95%CI); *P*-value	Crude OR (95%CI); *P*-value	Adjusted OR (95%CI); *P*-value	Crude OR (95%CI); *P*-value	Adjusted OR (95%CI); *P*-value
Sex							
Male	Reference	.78 (.55–1.12); .184	.78 (.50–1.20); .256	1.48 (1.14–1.92); .003	1.47 (1.06–2.03); .022	1.21 (.91–1.59); .188	1.21 (.81–1.82); .357
Female	Reference	1.23 (.85–1.78); .273	1.02 (.68–1.53); .933	1.84 (1.50–2.25); <.001	1.89 (1.48–2.41); <.001	2.02 (1.63–2.50); <.001	1.70 (1.26–2.30); .001
Years							
<70	Reference	.97 (.74–1.28); .823	.86 (.63–1.18); .348	1.47 (1.25–1.72); <.001	1.50 (1.24–1.81); <.001	1.54 (1.30–1.82); <.001	1.38 (1.09–1.75); .009
≥70	Reference	.92 (.44–1.93); .829	1.05 (.45–2.47); .903	2.45 (1.58–3.79); <.001	3.61 (2.03–6.41); <.001	2.14 (1.34–3.42); .001	3.22 (1.43–7.30); .005
Hyperuricemia							
No	Reference	.91 (.69–1.21); .508	.82 (.59–1.12); .213	1.55 (1.32–1.81); <.001	1.62 (1.34–1.97); <.001	1.60 (1.35–1.90); <.001	1.44 (1.12–1.85); .005
Yes	Reference	1.17 (.59–2.33); .652	1.68 (.74–3.79); .215	1.46 (.87–2.44); .154	2.31 (1.18–4.53); <.05	1.43 (.88–2.32); .151	2.43 (1.15–5.14); <.05

Adjusted: adjusted for age, sex, systolic blood pressure, diastolic blood pressure, waist–hip ratio, serum glucose, triglyceride, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, uric acid, blood urea nitrogen, creatinine, history of stroke, coronary artery disease, diabetes mellitus and antihypertensive drug.

Abbreviations: 95% CI, 95% confidence interval; HTHW, high triglyceride levels and enlarged waist circumference; HTNW, high triglyceride levels but normal waist circumference; NTHW, normal triglyceride levels but enlarged waist circumference; NTNW, normal triglyceride levels and normal waist circumference.; OR, odds ratio.

this finding, our study showed that the prevalence of diabetes in the HTHW group was approximately four times higher than that in the NTNW group (2.1% vs. 8.2%), and that the HTHW group had the highest glucose concentration of the four groups. Insulin resistance affects cardiomyocyte size by influencing insulin signaling pathways, including AKt, TGF-β, and PPAR signaling,[22] and also stimulates angiotensin II signaling, leading to cardiomyocyte hypertrophy.[23] The HTHW phenotype is closely related to low-grade inflammation, with increased levels of high-sensitivity C-reactive protein, tumor necrosis factor-α, and interleukin-6.[24] The secretion of these factors is also correlated with VAT, which is a dynamic endocrine organ that produces and secretes numerous bioactive adipocytokines, including inflammatory factors. These inflammatory factors play critical roles in the pathophysiological process of LVH through the inflammatory cascade and affect fibroblasts and the myocardium, resulting in collagen accumulation and cardiomyocyte hypertrophy.[25,26] The results of the present study showed that participants with the HTHW phenotype had a higher risk of LVH among patients with hypertension, which might further support these mechanisms.

Our study showed that participants with the HTHW phenotype had the highest WC, WHR, and triglyceride levels and were most likely to have had stroke, CAD, and diabetes mellitus. In addition, the HTHW phenotype also seemed to be associated with increased left ventricle structural parameters and more metabolic problems, including dyslipidemia and abnormal uric acid metabolism. These findings are consistent with those of previous studies showing that the HTHW phenotype is characterized by a clustering of metabolic abnormalities, which further lead to increased cardiovascular risk.[27] Hence, the HTHW phenotype can be a simple alternative to NCEP-ATP III and IDF for detecting people with worsening cardiometabolic risk markers.[28] It has been reported that patients with the HTHW phenotype were 2.13-fold more likely to develop CVD than those with the NTNW phenotype 7.5 years after the initial evaluation.[29] In the stratified analysis, the association between the HTHW phenotype and LVH in the hypertensive population remained significant for all subgroups, except for the male group. In addition, a stronger correlation was found among women, participants of at least 70 years of age, and participants in the hyperuricemia group. Increased visceral fat accumulation in postmenopausal women could account for the stronger correlation observed in the female group. We observed that the majority of the HTHW phenotype group were postmenopausal women (67.1%), and participants in the HTHW group had the highest percentage of postmenopausal women among the four phenotype groups. Estrogen exerts an inhibitory effect on visceral fat accumulation by participating in the regulation of energy metabolism through various pathways; thus, reduced estrogen levels in postmenopausal women are associated with increased visceral fat accumulation.[30] Moreover, it has been reported that estrogen plays a protective role in the heart; hence, postmenopausal women are at a higher risk of LVH owing to the reduction in estrogen.[31] Data from the Strong Heart Study with participants who had a mean age of 45–74 years showed that LVMI, calculated by LVM/height$^{2.7}$, was significantly higher in obese women than in

obese men. The authors speculated that this difference was owing to biological sex differences in visceral fat.[32]

Multiple lines of evidence suggest that age is positively correlated with increased VAT deposition[30] and LVH. A 16-year longitudinal study of 4217 participants from the Framingham offspring study reported that age is strongly correlated with LVH.[33] Moreover, a study of northern Manhattan participants showed that the average LVMI increased from 45.0 to 50.3 g/m$^{2.7}$ over 8.5 years.[34] Consistent with previous studies, we found that participants aged ≥70 years in the HTHW phenotype group were more likely to develop LVH than those aged < 70 years (OR 3.22 vs. 1.38). The present study also showed that participants with hyperuricemia in the HTHW phenotype group had a higher risk of developing LVH than those with normal uric acid levels. The level of uric acid, the final product of purine metabolism, correlated with increased myocardial oxidative stress, and activation of the renin–angiotensin–aldosterone system may further contribute to cardiomyocyte growth and interstitial fibrosis.[35,36] A cross-sectional study demonstrated that participants in the HTHW phenotype group had 4.54 times higher risk of developing hyperuricemia than those in the NTNW group.[37] The author speculated that visceral adiposity might be partly responsible for this correlation. These results emphasize the importance of considering in daily clinical practice the presence of the HTHW phenotype in women aged ≥ 70 years and in people with hyperuricemia, to accurately assess the LVH profile of hypertensive patients.

A recent survey of 3.3 million people from all 31 provinces in China, demonstrated that the prevalence of hypertension was up to 47.6% in people aged 35–75 years.[38] Such a large number of hypertensive patients and a high incidence of LVH caused by hypertension will pose a considerable social and economic burden in China. Thus, a study is required to address LVH risk factors in hypertensive populations possessing a high CVD risk. In the present study, we found that the HTHW phenotype could help further identify people at a higher risk of developing LVH among patients with hypertension. To the best of our knowledge, this is the first study to investigate the association between the HTHW phenotype and LVH in hypertensive adults by quantifying the LVM on echocardiography, which can dynamically display intracardiac structures and is more sensitive and specific than ECG. Additionally, we used a multistage cluster sampling method to select a representative sample of middle-aged and older Chinese hypertensive populations in rural communities, which improved the representativeness of the sample.

This study has certain limitations. First, this was a cross-sectional study; thus, the causal relationship between the HTHW phenotype and LVH in hypertensive patients cannot be inferred. Second, the study sample included a hypertensive population in rural China, which may not represent the general population. Third, we speculated that the correlation between the HTHW phenotype and LVH could be due to excessive VAT accumulation; however, we did not have CT or MRI data to support this conjecture. Finally, no significant association between the HTHW phenotype and LVH in men was observed. This could be attributed to the small sample size and low proportion of men with the HTHW phenotype. Additional large-scale prospective studies are required to confirm these results and further explore the underlying mechanisms and observed sex differences.

5 | CONCLUSIONS

We found that the HTHW phenotype was strongly associated with an increased LVH risk in the Chinese hypertensive population and that this correlation remained significant when further adjusted for sex, age, and traditional CVD risk factors. The major finding of the present study was that the HTHW phenotype, a simple and inexpensive marker of excess VAT accumulation, is a strong marker of LVH in this community-based Chinese hypertensive population. Future large-scale prospective studies are required to focus on hypertensive patients with the HTHW phenotype to further confirm our conclusions and study the potential underlying mechanisms of the correlation between the HTHW phenotype and LVH in hypertensive patients.

AUTHOR CONTRIBUTIONS

In this study, Qiligeer Bao was responsible for study design, data analysis, manuscript writing, and manuscript revisions. Yun Li and Shouyuan Ma contributed to manuscript preparation and data analysis. Jiaojiao Qiu, Jin Sun, and Yongkang Su contributed to data interpretation and manuscript revisions. Anhang Zhang, Shuang Cai, and Bokai Cheng assisted with data analysis and manuscript preparation. Man Li and Yan Zhang contributed to data collection. Shuxia Wang and Ping Zhu contributed to study design, review of the manuscript, and manuscript revision.

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CONFLICT OF INTEREST

All the authors declared that they have no conflict of interest.

ORCID

Ping Zhu MM https://orcid.org/0000-0002-3231-0631

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