



Research Article

Hypertriglyceridemic Waist Phenotype was associated with Hypertension-Mediated Organ Damage in Chinese Middle Aged-Old Hypertensives: A Cross-Sectional Study in Shanghai

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Abstract

Background: This cross-sectional study aimed to evaluate the relationship between the hypertriglyceridemia waist (HTGW) phenotype and hypertension-mediated organ damage (HMOD) in a sample of 4455 adults with primary hypertension from Shanghai, China.

Methods: The HTGW phenotype was defined as elevated waist circumference (WC) and elevated triglyceride (TG) concentration. HMOD was defined as the presence of follow: left ventricular hypertrophy (LVH); renal abnormalities as assessed by urine albumin/creatinine ratio above normal values and/or estimated glomerular filtration rate (eGFR). Logistic regression analysis was used to evaluate the association between the HTGW phenotype and HMOD and its permeants.

Results: The prevalence of HMOD was significantly higher in individuals with the HTGW phenotype, than in those with the normal waist normal triglyceride (NWNT) phenotype (67.7% vs. 61.2%). After adjusting for age, sex, BMI and other potential confounders, the HTGW phenotype was associated with HMOD (Odds Ratio (OR)1.95; 95% CI 1.03–3.71) regardless of sex. HTGW phenotype was a risk factor in presence of renal abnormalities (OR1.65, 95% CI 1.26-2.16) in both genders, whereas the association was attenuated toward null in female with presence of LVH (OR1.16, 95% CI 0.53-2.54).

Conclusion: This study indicated that the HTGW phenotype was strongly associated with the presence of HMOD. We suggested a combined use of hypertriglyceridemia waist phenotype in identifying participants who are at high risk of HMOD.

Keywords: Hypertriglyceridemia waist phenotype; Hypertension-Mediated Organ Damage; Chinese hypertensive population

Introduction

Hypertension and its complications pose a major threat to public health in China with rapid lifestyle transitions such as westernization of diets and sedentary behaviour [1]. Hypertension prevalence was up to 23.2% prevalence in Chinese people aged 18 and older, or an estimated 244.5 million individuals [2]. The rapid epidemic of hypertension has led to a substantial burden of hypertension-mediated organ damage (HMOD). In previous Chinese regional studies, the prevalence of HMOD was between 20.2 and 42.8% among the community-based hypertensive population [3,4]. The heart and kidney represent two main target organs of primary hypertension. Left ventricular hypertrophy (LVH) is confirmed to be an independent risk factor for cardiovascular (CV) morbidity and mortality [5]. As well as chronic kidney disease (CKD), the leading cause of end-stage renal disease (ESRD) to haemodialysis, is an independent predictor of cardiovascular events in patients with hypertension [6,7]. The association of metabolic risk factors and hypertension has long been a topical issue. Previous studies have validated that lipid levels and obesity indices, especially visceral obesity, were associated with hypertension [8-10]. Triglycerides and waist circumference were the classical obesity indices and related to cardiovascular events [11], atherosclerosis [12] and renal impairment [13]. The hypertriglyceridemic waist (HTGW) phenotype, composed of elevated waist circumference and high levels of triglycerides (TGs) [14], is useful to identify individuals with higher risk of metabolic abnormalities compared to elevated TG or enlarged WC used alone [15]. Our previous study has showed the strong positive association with HTGW phenotype and presence of hypertension in the Chinese middle-old population [16]. Furthermore, the HTGW phenotype has been proven to be associated with cardiovascular diseases (CVD) [17]. We also found the association of HTGW phenotype and chronic kidney disease in Chinese diabetes patients [18]. However, those previous studies few focused on investigating whether HTGW phenotype was associated with hypertension-mediated organ damage especially heart and kidney function in Chinese hypertensive [19]. Taking into account the rising prevalence of hypertension and HMOD, efforts to prevent the progression of HMOD by identifying novel metabolic risk factors that could be modifiable are imperative. Besides, the growing concerns that patients with hypertension and obesity are more likely to have severe evolution and mortality during the COVID-19 pandemic, especially those with hypertension-mediated organ damage [20,21]. Thus, it is urgent to control some novel metabolic risk factors contributing to HMOD in hypertension patients. Furthermore, previous studies on the HTGW phenotype rarely considered other simultaneous

triglyceride waist phenotypes, which were always combined as a subgroup for analysis. Therefore, we aimed to explore the association of four triglyceride waist phenotypes with HMOD based on our previous research to early detection, intervention and reversal of HMOD.

Materials and Methods

Study population

During March to August 2020, about 10,824 participants (aged ≥ 40 years) did health check in the health centre of Ruijin Hospital, Luwan branch, Huangpu district, Shanghai. First, from March to August 2020, individuals aged 40 years or older who were natives of Shanghai municipality or those who had lived in Shanghai for at least 5 years who underwent health checks in this health centre were enrolled. Second, we invited participants to participate in the study by telephone. The details were described in previous study [16,22]. The exclusion criteria were as follows: no diagnosis of hypertension and normal blood pressure; secondary hypertension; kidney diseases (such as glomerulonephritis, nephrotic syndrome, IgA nephropathy, and other kidney diseases); established cardiovascular diseases (such as documented coronary artery disease, cardiac failure, valvar heart disease, peripheral arterial disease, and cerebrovascular disease), Patients who had a poor-quality ultrasound recording and/or incomplete medical history and/or laboratory tests were excluded from the analysis. Finally, 4455 subjects were included in the analysis (Figure 1). The study protocol (No. LWEC2020024) was approved by the Ethics Committee of the Shanghai Ruijin Hospital, Luwan branch, Shanghai Jiao Tong University School of Medicine. Informed consent was obtained from all participants included in our study.

Clinical, anthropometric and laboratory measurements

A questionnaire about sociodemographic characteristics, medical history, family history, and lifestyle factors was adopted during the interview. It was conducted the interviews and clinical examinations, including measurements of weight, height, and blood pressure, according to a standard protocol. The same group of trained experienced personnel involved in the previous study [16] took the questionnaire. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in meters squared). BMI < 24 kg/m² was defined as normal weight, while BMI ≥ 24 kg/m² was defined as overweight/obese, as determined by the Cooperative Meta-Analysis Group of the Working Group on Obesity in China criteria [23]. A trained physician measured blood pressure (BP) with an electronic sphygmomanometer (Omron HEM-7200 Monitor, Batteries, and Stopwatch). The participants in this study were required to rest in a seated position for at least 5 minutes before the BP measurement, and BP was measured 3 times at 5-minute intervals. The mean of the 3 readings was calculated. A current smoker was defined as having

smoked at least 100 cigarettes over a lifetime and still currently smoking [24]. A current drinker was defined as consuming alcohol regularly in the past 6 months [25]. Educational level was categorized as below high school or not. The physical activity intensity was defined as durations of 20–30 min, frequencies of ≥ 3 days/week, intensities that are moderate to vigorous activity. Physical activity included occupational and leisure-time physical activity, which were merged and regrouped into the self-reported high level of both occupational and leisure-time physical activity or below [26]. Blood samples were obtained in the morning after fasting for at least 8 hours, and they were refrigerated immediately after phlebotomy and centrifuged within 2 hours of collection. Serum samples were aliquot and frozen at a central laboratory. Glycated haemoglobin (HbA1c) was measured by a high-performance liquid chromatography (MQ-2000PT) (HPLC) automatic HbA1c analyser (MEDCONN, Huizhong Medical Science and Technology Co., Ltd, Shanghai, China; Shanghai Hunched Biological Reagent Co., Ltd, Shanghai, China). Fasting plasma glucose (FPG), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL-C) and low-density lipoprotein cholesterol (LDL-C), uric acid (UA) and serum creatinine were also measured (AU680 Chemistry Analyser, Beckman Coulter, Brea, CA, USA). TG was measured with assay kits from Beckman Coulter (catalogue number: AUZ5612, assay sensitivity: 0.01 mmol/L, intra-assay variability: 6.25%), as was FPG (catalogue number: AUZ4686, assay sensitivity: 0.04 mmol/L, intra-assay variability: 2.5%). Morning urine samples were collected in the refrigerator immediately to measure the levels of urine albumin and creatinine with a Beckman Coulter AU 680 (Brea, USA); then, the urine albumin to creatinine ratio (uACR) was calculated. The estimated glomerular filtration rate (eGFR) was calculated by the Chronic Kidney Disease Epidemiology Collaboration equation for Chinese individuals²⁷.

Definition of variables

Hypertension was defined as a systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, according to the European guidelines did almost all countries/regions in Asia⁷, or self-reported use of antihypertensive medications in the past 2 weeks irrespective of BP.

Left Ventricular Hypertrophy

The presence of LVH was assessed on the parasternal long axis view of a transthoracic cardiac ultrasound (Philips Health Care, Andover, MA, USA) in M-mode by two experienced ultrasonographers in the health center. A cut-off value of ≥ 11 mm for septal thickness was used to define the presence of LVH²⁸.

HMOD Indices

HMOD was defined as the presence of follow:(1) left

ventricular hypertrophy (LVH);(2) renal abnormalities as assessed by urine albumin/creatinine ratio (uACR) between 30 and 300 mg/g) and/or chronic kidney disease (CKD). CKD was defined as estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m²) and/or albuminuria (uACR ≥ 300 mg/g) according to KDIGO guidelines²⁹.

Definitions of HTGW and the Rest of the Phenotypes

Central obesity was defined as a waist circumference ≥ 90 cm in men and ≥ 80 cm in women as widely used in Chinese population studies [18,22,30,31]. Participants were grouped into four phenotype groups according the measurements of TG and WC: (1) NWNT: normal waist circumference and normal triglycerides (TG < 1.7 mmol/L, WC < 90 cm for men and WC < 80 cm for women); (2) NWET: normal waist circumference and elevated triglycerides (TG ≥ 1.7 mmol/L, WC < 90 cm for men and WC < 80 cm for women); (3) EWNT: elevated waist circumference and normal triglycerides (TG < 1.7 mmol/L, WC ≥ 90 cm for men and ≥ 80 cm for women); and (4) HTGW: hypertriglyceridemic waist (TG ≥ 1.7 mmol/L, WC ≥ 90 cm for men and ≥ 80 cm for women) [32]. WT Index (WTI) was waist circumference-triglyceride index and calculated by WC combined TG³³.

Statistical analyses

Data analyses were performed using IBM SPSS version 25 statistical software (IBM Corp., Armonk, NY, USA). $P < 0.05$ indicated statistical significance (two-sided). Continuous variables are presented as mean \pm standard deviation (SD), and categorical variables are presented as percentages (%), as appropriate. Group differences were compared with ANOVA tests for continuous variables and or chi-square test for categorical variables. Logistic regression was performed to evaluate the association between the four phenotype groups and HMOD. Model 1 was adjusted for age, sex, BMI, current smoker and current drinker. Model 2 was adjusted for Model 1 plus TC, LDL, HbA1c, eGFR, physical activity, education status, systolic blood pressure, diastolic blood pressure, current smoker, current drinker, diabetes, antihypertensive drugs, statin. Moreover, stratified analyses by sex, BMI and presence of diabetes, current smoker and current drinker were performed. To further investigate the relationship between HTGW phenotype and HMOD, we used WTI to predict HMOD using receiver operating characteristic (ROC) curve analysis. We calculated the optimal cut-point according to the Youden index (=sensitivity - [1 - specificity])

Results

Baseline clinical characteristics

Of the 4455 patients with primary hypertension, 2812(58.6%) were female, and the mean age was 61.6(SD, 7.13) years. The baseline anthropometric parameters and biochemical indices

according to four triglyceride waist phenotypes are shown in Table 1. Overall, participants in HTGW phenotype subgroup were older, had a higher proportion of female, worse life habits, were more likely to have a history of diabetes, overweight or obesity, CVD and poorer metabolic profiles including higher BMI, WC, blood pressure, lipids, FPG, HbA1c, UA and uACR and lower levels of HDL-C and eGFR ($P < 0.05$, Table 1). In participants with HTGW phenotype, antihypertensive medications and statin were more prevalent ($P < 0.001$). In Table 1, the prevalence of HMOD was 63.4% (2825/4455). Participants in the HTGW group had the highest prevalence of LVH(417/1152(36.2%)) and renal abnormalities (427/1152(37.1%)) among the four subgroups ($P < 0.001$). Participants in the NWET and EWNT groups had a higher prevalence of HMOD (429/696(61.7%) and 745/1184 (62.9%), respectively) than those in the NWNT Group (871/1423 (61.2%)) ($P < 0.001$).

Association of the different triglyceride waist phenotypes with HMOD

In logistic regression models, HTGW phenotype was positively associated with the risk of HMOD (in Table 2). After adjusting for age, sex, BMI, current smoking status and current drinking status, subjects with HTGW phenotype had 2.15 times (95% confidence interval (CI):1.14–4.05) more likely to have HMOD than those with NWNT phenotype. After adjusted for all confounders, the OR (95% CI) of HMOD was 1.95 (CI:1.03–3.71) for participants with HTGW phenotype. After stratification by sex ($P < 0.001$ for interaction with sex), the HTGW phenotype was significantly associated with HMOD after full adjustments in men (1.61, 95% CI: 1.39-2.95, $P < 0.05$) and women (3.27, 95% CI: 1.17-9.13, $P < 0.05$).

Subgroup analyses

Then we did the subgroup analyses in all subjects. After different subgroups of age, BMI, diabetes, current smoker and current drinker, the results of HTGW phenotype relative to HMOD did not consistence in all population subgroups examined in Table 3. The positive association of HTGW phenotype with HMOD was found in the subgroup of age older than 60 years (OR 1.95, 95% CI:1.01–3.77, $P=0.049$), the presence of diabetes (OR 2.02, 95% CI:1.06–3.86, $P=0.033$) and current smoker (OR 6.12,

95% CI:1.20–12.31, $P < 0.001$). No significant interaction effect was observed between the triglyceride waist phenotypes and all subgroup variables in HMOD risk.

Association of the different triglyceride waist phenotypes with HMOD indices

Furthermore, we assessed the association between four triglyceride waist phenotypes and HMOD indices. The results were not always similar in all groups. HTGW phenotype was positively associated with LVH (OR 1.71, 95% CI:1.27–2.88, $P=0.013$) after adjusted for age, sex, BMI, current smoker and current drinker, TC, LDL, HbA1c, eGFR, physical activity, education status, blood pressure, diabetes, antihypertension drug, statin (Table 4). But stratified by gender, the association of HTGW phenotype and LVH persisted among men (OR 1.56, 95% CI:1.13–2.14, $P=0.027$) not in women (OR 1.16, 95% CI:0.53–2.54, $P=0.703$). For renal impairment, the association remained unchanged (OR 1.65, 95% CI:1.26–2.16, $P < 0.001$) after adjusted for all potential confounders even stratified by gender. Additionally, we assessed the associations of HTGW phenotype with decreased eGFR and high uACR, respectively. HTGW phenotype was a strong risk factor of both decreased eGFR (OR 1.59, 95% CI:1.15–2.97, $P=0.039$) and high uACR (OR1.71, 95% CI:1.31–2.23, $P < 0.001$) regardless of sex (Supplement Table 1).

The AUCs (and 95% CIs) of WTI for HMOD

In addition, we drew a ROC curve according to the WTI and prevalence of HMOD, as well as LVH and CKD, respectively, as shown in Figure 2. In the ROC curve of the WTI as a predictor of HMOD, the area under the curve was the largest (0.731, 95% CI: 0.708-0.754, $P < 0.001$) with a WTI of 90.1 in Figure 2(A), with a corresponding sensitivity and specificity of 90.6 and 59.5%, respectively; In the ROC curve of the WTI as a predictor of LVH, the area under the curve was the largest (0.616, 95% CI: 0.565-0.668, $P < 0.001$) with a WTI of 90.2 in Figure 2(B), with a corresponding sensitivity and specificity of 89.9 and 60.5%, respectively; In the ROC curve of the WTI as a predictor of CKD, the area under the curve was the largest (0.604, 95% CI: 0.556-0.653, $P < 0.001$) with a WTI of 90.1 in Figure 2(C), with a corresponding sensitivity and specificity of 90.2 and 60.4%, respectively.

	NWNT	NWET	EWNT	HTGW	P for trend
No. of participants (%)	1423(31.9)	696(15.6)	1184(26.6)	1152(25.8)	
Age at baseline (year)	61.19±7.93	61.02±7.92	62.41±7.15	62.58±7.13	<0.001
Male (%)	716(50.3)	386(55.4)	354(29.9)	387(33.6)	0.092
BMI (kg/m ²)	23.07±2.35	23.78±2.26	26.83±3.01	27.19±2.67	<0.001
WC (cm)	81.64±8.49	84.95±8.45	87.15±8.34	88.72±8.23	<0.001
SBP (mmHg)	135.50±15.74	142.71±15.37	145.88±16.28	145.97±17.49	<0.001
DBP (mmHg)	85.90±10.78	91.25±9.53	90.56±9.47	90.89±10.07	0.168
FBG (mmol/L)	5.23±1.43	5.60±1.88	5.54±1.62	5.86±1.97	<0.001
HbA1c (%)	5.67±0.86	5.90±1.08	5.90±0.99	6.07±1.09	<0.001
TG (mmol/L)	1.09±0.29	2.68±1.59	1.19±0.27	2.72±1.51	<0.001
TC (mmol/L)	4.93±0.82	5.28±0.87	5.31±0.84	5.37±0.91	<0.001
HDL-C (mmol/L)	1.50±0.34	1.21±0.29	1.45±0.32	1.18±0.27	<0.001
LDL-C (mmol/L)	3.17±0.73	3.33±0.80	3.29±0.75	3.43±0.86	<0.001
eGFR (mL/m/1.73 m ²)	89.79(17.60)	88.51(16.40)	89.23(16.74)	87.85(17.35)	0.002
uACR (mg/g)	48.30(177.07)	54.57(242.91)	45.95(164.44)	65.34(224.57)	<0.001
UA (mmol/l)	300.98±78.12	319.38±79.10	331.38±82.41	348.28±87.51	<0.001
HMOD (%)	871(61.2)	429(61.7)	745(62.9)	780(67.7)	<0.001
Renal abnormalities (%)	208(14.6)	147(21.1)	324(27.3)	427(37.1)	<0.001
LVH (%)	225(15.8)	157(22.5)	337(28.4)	417(36.2)	<0.001
Diabetes (%)	120(8.4)	81(11.6)	208(17.6)	248(21.6)	<0.001
CVD (%)	132(9.2)	149(21.4)	371(31.3)	417(36.2)	<0.001
Overweight/obesity (%)	342(32.7)	313(45.1)	773(65.3)	1037(90.1)	<0.001
Current smoker (%)	196(13.8)	107(15.4)	234(19.8)	306(26.6)	<0.001
Current drinker (%)	33(2.3)	15(2.1)	31(2.6)	32(2.8)	<0.001
Education (≥high school) (%)	90(6.3)	31(4.5)	98(8.3)	61(5.3)	<0.001
High physical activity (%)	119(8.4)	50(7.2)	57(4.8)	37(3.2)	<0.001
Hypertension treatment (%)	428(30.1)	264(38)	512(43.3)	576(50)	<0.001
CCB (%)	376(26.4)	171(24.6)	328(27.7)	558(48.4)	<0.001
ACEI/ARB (%)	129(9.1)	116(16.7)	265(22.3)	369(32)	<0.001
β-block(%)	155(10.9)	130(18.6)	131(11.1)	189(16.4)	<0.001
Statin used (%)	85(5.9)	36(5.2)	234(19.7)	243(21.1)	0.233

Data are expressed as the mean ±SD, median value [interquartile range] or as n (%), as appropriate. BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting blood glucose; TC, total cholesterol; TG, HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol, eGFR, estimated glomerular filtration rate; uACR, urinary albumin creatinine ratio; UA, uric acid; LVH: left ventricular hypertrophy; CCB: calcium channel blockers; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker;

Table 1: Characteristics of the participants in each phenotype group (n = 4455).

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	HMOD			
	Model 1	P value	Model 2	P value
NWNT	ref	ref	ref	ref
NWET	2.01(1.11,3.63)	0.021	1.85(0.65,3.37)	0.054
EWNT	1.33(0.69,2.56)	0.398	1.30(0.67,2.50)	<0.001
HTGW	2.15(1.14,4.05)	0.018	1.95(1.03,3.71)	0.041
Men				
NWNT	ref	ref	ref	ref
NWET	1.26(1.01,2.64)	0.004	1.69 (0.79,3.62)	0.786
EWNT	1.45(0.15,1.38)	0.441	1.36(0.57,3.22)	0.484
HTGW	1.29(1.11,3.73)	0.009	1.61(1.39,2.95)	0.028
Women				
NWNT	ref	ref	ref	ref
NWET	3.21(1.13,9.15)	0.029	2.62 (0.90,7.62)	0.979
EWNT	1.60(0.55,4.69)	0.389	1.60 (0.55,4.73)	0.391
HTGW	3.74(1.36,10.28)	<0.001	3.27 (1.17,9.13)	0.024

Model 1 was adjusted for age, sex, BMI, current smoker and current drinker.

Model 2 was adjusted for model 1 plus TC, LDL, HbA1c, eGFR, physical activity, education status, systolic blood pressure, diastolic blood pressure, diabetes, antihypertension drug, statin.

Table 2: Odds ratios for HMOD at different levels of triglyceride waist phenotypes.

Subpopulation	Cases/ Participants	NWNT	NWET	EWNT	HTGW	P-trend	P-interaction
Age, years a							0.342
<60	855 /4455	1.00 (ref)	1.95(0.21,1.82)	1.71(0.23,2.36)	2.28(0.16,2.69)	0.558	
≥60	3600/4455	1.00 (ref)	1.80(0.96,3.37)	1.40(0.71,2.75)	1.95(1.01,3.77)	0.049	
BMI, kg/m ² b							0.519
< 24	1592/4455	1.00 (ref)	1.97(0.85,4.58)	1.59(0.50,5.09)	2.20(0.67,7.29)	0.336	
≥ 24	2863/4455	1.00 (ref)	1.54(0.65,3.68)	0.81(0.37,1.76)	1.18(0.56,2.47)	0.4	
Presence of T2DM ^c							0.316
No	3798/4455	1.00 (ref)	1.35(0.26,7.16)	1.67(0.34,8.19)	2.93(0.66,12.9)	0.42	
yes	657/4455	1.00 (ref)	1.19(0.57,2.48)	1.19(0.57,2.48)	2.02(1.06,3.86)	0.033	
Current smoker d							0.223
No	3680/4455	1.00 (ref)	1.41(0.72,2.79)	0.94(0.45,1.95)	1.71(0.86,3.44)	0.176	
Yes	775/4455	1.00 (ref)	3.06(0.46,7.96)	5.45(0.91,9.45)	6.12(1.20,12.31)	<0.001	
Current drinker ^e							0.576
No	4344/4455	1.00 (ref)	1.44 (0.41,1.89)	1.94 (0.61,2.33)	1.49(0.65,2.98)	0.354	
yes	111/4455	1.00 (ref)	1.18 (0.50,2.82)	0.72 (0.31,1.66)	1.16 (0.38,3.03)	0.289	

^a for age subgroup: adjusted for sex, BMI, LDL-C, HDL-C, TC, HbA1c, eGFR, physical activity, education status, current smoker and current drinker, blood pressure, diabetes, antihypertension drug, statin; ^b for BMI subgroup: adjusted for age, sex, LDL-C, HDL-C, TC, HbA1c, eGFR, physical activity, education status, current smoking and current drink , blood pressure, diabetes, antihypertension drug, statin; ^c for T2DM subgroup: adjusted for age, sex, BMI, LDL-C, HDL-C, TC, eGFR, physical activity, education status, current smoker and current drinker, blood pressure, antihypertension drug, statin; ^d for smoke status subgroup: adjusted for age, sex, BMI, HbA1c, LDL-C, HDL-C, TC, eGFR, physical activity, education status, current drinker, blood pressure, diabetes, antihypertension drug, statin; ^e for drink status subgroup: adjusted for age, sex, BMI, LDL-C, HDL-C, TC, HbA1c, eGFR, physical activity, education status, current smoker; blood pressure, diabetes, antihypertension drug, statin;

Table 3: Odds ratios for HMOD according to triglyceride waist phenotypes by various subgroups.

HMOD indices	Total		Men		Women	
	OR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
LVH						
NWNT	ref	ref	ref	ref	ref	ref
NWET	1.95(0.67,1.35)	0.784	1.89(0.61,1.31)	0.021	1.05(0.46,2.40)	0.918
EWNT	1.88(0.61,1.29)	0.885	1.77(0.49,2.21)	0.26	1.31(0.63,2.72)	0.464
HTGW	1.71(1.27,2.88)	0.013	1.56(1.13,2.14)	0.027	1.16(0.53,2.54)	0.703
Renal abnormalities						
NWNT	ref	ref	ref	ref	ref	ref
NWET	1.19(0.91,1.54)	0.205	1.34(0.96,1.87)	0.089	1.17(0.83,1.67)	0.371
EWNT	1.39(0.94,2.07)	0.097	1.48(0.90,2.42)	0.121	1.01(0.71,1.43)	0.949
HTGW	1.65(1.26,2.16)	<0.001	1.63(1.13,2.33)	0.008	1.14(1.04,2.17)	0.033

Model was adjusted for was adjusted for age, sex, BMI, current smoker and current drinker, TC, LDL, HbA1c, eGFR, physical activity, education status, blood pressure, diabetes, antihypertension drug, statin.

Table 4: Odds ratios for HMOD indices at different levels of triglyceride waist phenotypes.

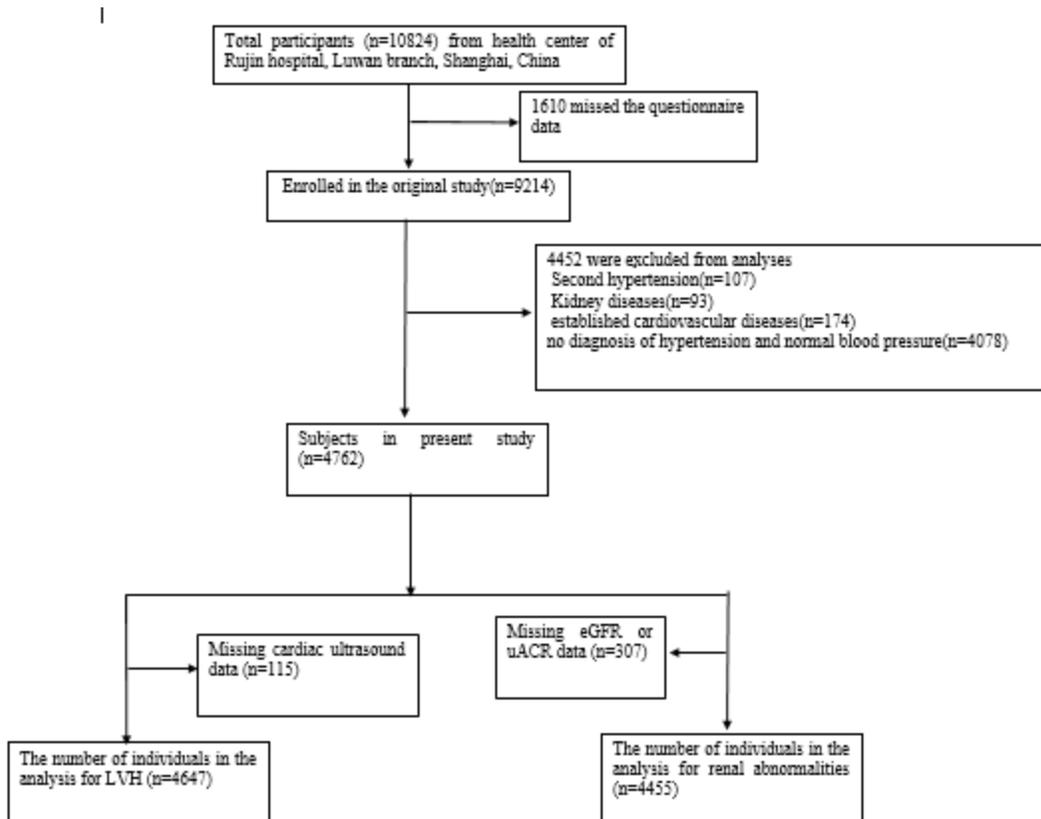


Figure 1: Flow chart describing the enrolment of the subjects in this study.

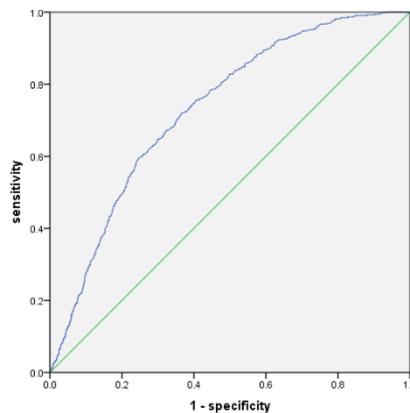


Figure 2(A): ROC analysis for the WT Index and HMOD. ROC receiver operator characteristic, WT Index waist circumference-triglyceride index.

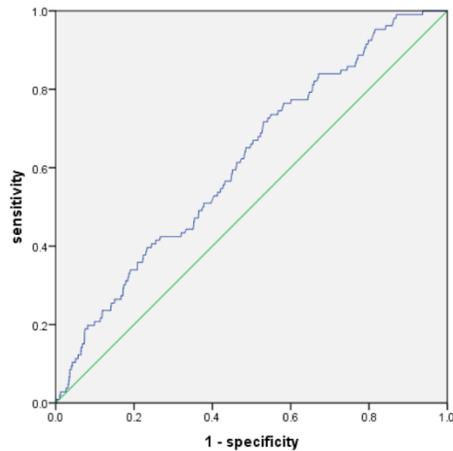


Figure 2(B): ROC analysis for the WT Index and LVH. ROC receiver operator characteristic, WT Index waist circumference-triglyceride index.

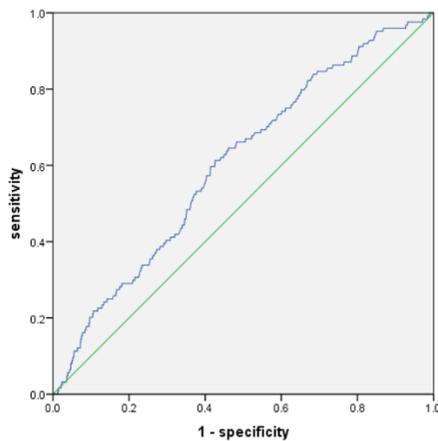


Figure 2(C): ROC analysis for the WT Index and CKD. ROC receiver operator characteristic, WT Index waist circumference-triglyceride index.

Discussion

In this large sample of Chinese patients with hypertension, HTGW phenotype was independently associated with prevalence of HMOD compared with the other three phenotype groups. Subjects with the HTGW phenotype were 2.15-fold more likely to have HMOD than those with the NWNT phenotype. This positive relationship was independent of age, sex, BMI, history of diabetes, lipids, eGFR, smoking, drinking, physical activity, education status, use of antihypertension medicine and statin. Moreover, when assessed by HMOD indices, the associations of HTGW phenotype with presence of LVH was significant in men. The relationship of HTGW phenotype with renal abnormalities was

consistence across both sexes. These results indicate that HTGW phenotype was indicated as a crucial risk factor of HMOD for both sexes in this middle-aged to elderly Chinese hypertension patients. Hypertension and HMOD were responsible for enormous health care burdens worldwide. Our study indicates that the prevalence of HMOD in a middle to older patients with hypertension was 63.2%, 51.1% in men and 48.9% in women, respectively. The data was similar to the previous study³⁴. The HMOD prevalence of the NWNT, NWET, EWNT, and HTGW phenotype groups was 61.2%, 61.7%, 62.9% and 67.7%, respectively. When assessed by HMOD indices, the presence of LVH (36.2%) and kidney impairment (37.1%) were significant higher in HTGW phenotype than patients in NTNW group (15.8%, 14.6%, 63.3%, respectively). The present study provides evidence that the participants with HTGW were 1.71-fold as likely to have LVH as those with normal waist circumference and TG concentration (NWNT). Our results are consistent with the limited data available on high-level TG and waist circumference and LVH measures in hypertension patients. In a cross-sectional study of Chinese hypertension patients with LVH, LVH was related to plasma TGs after controlling for age, gender, smoking, blood pressure and plasma fasting glucose. They identified male subjects that presented LVH and tested if plasma TGs were independently associated with LVH in this subgroup. On the contrary, plasma TGs were not associated with LVH in females [35]. In a study conducted in France, they showed that plasma triglyceride levels were associated with left ventricular wall thickness independently of hemodynamic and neurohormonal factors in hypertensive subjects [36]. On the other hand, there was a positive relation between waist circumference and high LVH in the patients originated from the Second Manifestations of Arterial Diseases (SMART) cohort [37]. However, these studies involved relatively small numbers of patients at late stages of LVH. The results linking HTGW and LVH are still controversial [38,39], the critical role of current acknowledged hypotheses is atherogenic dyslipidaemia and visceral obesity caused by fatty acids dysfunction and insulin resistance (IR). Most of the fatty acids inserting myocardium are used for energy production, whereas only a small amount is stored in the intracellular myocardial lipid pool. When there is an imbalance between lipid storage and lipolysis in cardio myocytes, cardiac steatosis and myocardial hypertrophy are observed [40]. Besides, insulin acts as a growth factor in many tissues, including cardiovascular tissues. In present study, we found that the prevalence of type 2 diabetes was higher in the HTGW phenotype group than in the NTNW group (21.6% vs. 8.4%). The participants with the HTGW phenotype simultaneously had elevated glucose (FBG, 5.86 mmol/l vs. 5.23 mmol/l) and poor glucose control (HBA1c, 6.07% vs. 5.67%) compared with those in the NTNW group. This situation showed the more severe IR status in HTGW group. Insulin modulates intracellular cation regulation by reducing the activity of sodium/potassium ATPase (Na⁺/K⁺ ATPase) enzymes and increasing the Na⁺/K⁺ pump

of vascular smooth muscle cells, increasing their sensitivity to catecholamine's and angiotensin II. In addition, IR factors, including fatty acids, cytokines, and adiponectin, are released from excess adipose tissue [41]. IR enhances lipid accumulation, fatty acid oxidation and stimulation of the angiotensin II signalling, all leading to pathologic LVH [39].

The intriguing finding of the disassociation of HTGW phenotype with LVH between men and women, also merits attention. A possible explanation for this phenomenon may be attributed to the difference in tissue metabolic profile and myocardial energy use between the two genders. Recently, an experimental study showed that females, compared to males, may be protected from cardiomyopathy through mechanisms related to genetically-determined normal cardiac glucose uptake and preserved cytochrome c-oxidase activity, a mitochondrial enzyme regulating tissue metabolism and energy production [42]. The current study extends the existing knowledge by demonstrating an association between HTGW and LVH in a large sample of hypertensive patients, which suggests that high TGs and waist circumference may both cause cardiovascular structure damage in hypertension population. For renal abnormalities, there was a much higher prevalence of renal impairment (37.1% vs 14.6%) in HTGW compared with NTNW. Compared to NTNW, eGFR was significantly decreased (87.85mL/m/1.73 m² vs 89.79mL/m/1.73 m²) and uACR was significantly increased (65.34mg/g vs 48.30mg/g) in HTGW group. A previous study showed that increased vulnerability of the glomerular microcirculation to elevated systemic blood pressure is postulated to contribute to adverse effects of obesity on the kidney [43]. Consistent with our findings, there was a strong association between the HTGW phenotype and decreased eGFR risk found in participants with hypertension in a cross-sectional study among Chinese participants [44]. In another human study, increased systolic blood pressure was associated with a greater increase in albuminuria in obese people [45]. The probable mechanism of this phenomenon was the association between obesity and fatty kidney disease [46]. The term "fatty kidney", first appearing in the literature in 1883 [47], suggests that hyperlipidaemia is the cause of the characteristic renal lipid accumulation and nephrotoxicity [46]. Obesity itself is associated with increased renal tubular sodium reabsorption followed by initial hyper filtration and a subsequent gradual decline in the estimated glomerular filtration rate [10]. Adipocytes are able to secrete all components of the RAAS and are upregulated in obesity [48]. Therefore, the kidney is not just a victim but rather an active co-conspirator in metabolic syndrome. Given the substantial burden of chronic kidney disease worldwide, our findings emphasize the importance of early intervention to protect against kidney damage caused by obesity in individuals with hypertension, particularly in areas where prevalence of hypertension is increasing more rapidly. In subgroup analyses, the positive association were found in the

older, current smoking and subjects with type 2 diabetes. The strongest association were found in smoking subgroup. Previous evidence has shown that aging, smoke status and diabetes were strong risk factors for HMOD in Chinese obesity population [49]. Consistence with other studies, aging, diabetes, current smoker were the obvious risk factors of diseases caused by hypertension [50]. Several limitations in this study need to be considered. First, the temporal and causal relationship could not be assessed with a cross-sectional design. Further prospective studies are needed to test these results and potential mechanisms. Second, the definition of HTGW is currently diverse, and there is no specialized cutoff set for Chinese populations. Third, although multiple variables were adjusted, other confounding factors, such as diet may exist. Fourth, data on left ventricular septal thickness was not available to be able to study the relationship of LVH quantitatively. However, we could include qualitative analysis of LVH (yes/no) assessed by echocardiography, which add value to previous studies in Mets where only electrocardiographic parameters were used. Additionally, current guidelines do not recommend quantitative assessment of LVH in this setting [51]. Future investigations covering more elderly subjects (≥80 years) or those younger than 40 years and the rural population are warranted.

Conclusion

In summary, a strong association was observed between HTGW and HMOD in a middle- aged to elderly population of Shanghai, China. Both genders with HTGW were more likely to have HMOD than those with NTNW. And male hypertensive patients were more vulnerable to face the LVH than female if they were high TG and elevated waist circumference. Hence, more attention should be given to TG concentration and waist circumference in clinical screening and intervention. Furthermore, future large-scale prospective studies for uncertain sex-specific associations and other potential mechanisms are still essential.

Author Contributions

In this study, X. Y and G. X., were mainly responsible for the writing of the article, C. L. and L. L. Q. were mainly responsible for research, S. Y. and W.S. J. were mainly responsible for data entry, G.P. and T. D. were mainly responsible for data calculation and correction, and W. X and Z.F.F were mainly responsible for the final data results and additional experiments. The authors would like to thank all the participants for this article.

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Institutional Review Board Statement: The study protocol (No. LWEC2020024) was approved by the Ethics Committee of the Shanghai Ruijin Hospital, Luwan branch, Shanghai Jiao Tong University School of Medicine. These subjects provided written informed consent and the study protocol was approved by the institute's committee on human research.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study

Data Availability: The raw data supporting the conclusions of this manuscript will be made available by the authors, without undue reservation, to any qualified researcher.

Conflicts of Interest: The authors declare no conflicts of interest.

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