Original Article

The lipid accumulation product (LAP) association with hyperuricemic hypertension in the China Health and Nutrition Survey: A cross-sectional study

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Background and Objectives: Previous studies have explored the relationship between lipid accumulation product (LAP) and hypertension or hyperuricemia. However, the association between LAP and hypertension with hyperuricemia (HWH) is inconclusive. Therefore, we aimed to evaluate the association between LAP and HWH. **Methods and Study Design:** A total of 7897 participants aged 18 to 75 years from the 2009 wave of the China Health and Nutrition Survey were included in this study. General linear regression models were built to assess the association of LAP with systolic blood pressure (SBP), diastolic blood pressure (DBP), and uric acid (UA) concentrations. Logistic regression models were used to estimate the association between LAP and HWH risk, restricted cubic splines (RCS) were used to analyze the dose-response relationship between them. **Results:** The prevalence of HWH was significantly higher in men (7.63%) than in women (1.99%) (χ^2=142; p<0.001). After adjustment for potential confounders, LAP scores were positively correlated with SBP, DBP, and UA concentrations in both genders (all p-trend <0.01). Compared with participants in the lowest quartile of LAP, those in the highest quartile had a higher risk of HWH [OR (95% CI)=12.2 (7.22-20.5) for men, OR (95% CI)=14.5 (3.50-60.2) for women]. The RCS results suggested a nonlinear relationship between the continuous change of LAP and HWH risk after adjustment for confounding factors in each gender (p for nonlinearity <0.001). **Conclusions:** Our findings suggest that higher LAP scores was strongly associated with greater HWH risk in Chinese adults.

Key Words: lipid accumulation product, hypertension with hyperuricemia, the China Health and Nutrition Survey

INTRODUCTION

Hypertension (HTN), which is significantly associated with many chronic diseases, including stroke, diabetes, overweight/obesity, has been demonstrated to be a leading risk factor for the global burden of disease.[1-3] Similarly, hyperuricemia (HUA) is also closely related to higher rates of several chronic metabolic disorders, such as gout, chronic kidney disease (CKD), obesity, and cardiovascular diseases (CVDs).

In recent years, some synergistic effects of HTN and HUA on promoting the development and progression of renal dysfunction, CVDs, impaired glucose regulation, subclinical atherosclerosis, CKD, overweight or obesity have been vitally recognized.[1,2,4,5] It is well known that HTN is an important comorbidity of HUA. A retrospective study found that HTN was the only comorbidity of HUA in India.[6] A multicenter cross-sectional epidemiological study in France found that chronic HUA led to the accumulation of monosodium urate crystals in tissues, which can lead to gout, and the main co-morbidity of gout was HTN (53.8%).[7] In addition, a large cross-sectional population study shown that the prevalence of HTN was 36.6% among participants with HUA in Japan.[8] Meanwhile, several studies have focused on the prevalence of HUA in patients with HTN. The study in Japan have also shown that the prevalence of HUA was 22.1% among 17961 participants with HTN.[8] It has been reported that the average prevalence of HUA in patients with HTN was 31.2% in Taiwan.[9] Some researchers found that among patients with essential hypertension, the proportion of patients with HUA was 45.8%.[10] Moreover, some studies have shown that HTN patients were more vulnerable to HUA than normotensives,[4] and vice versa.[11] Therefore, increasing attention has been directed towards hypertension with hyperuricemia (HWH), and the prevention and management of HWH are major public health challenge worldwide to be addressed.

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Obesity, a complex disease influenced by environmental and genetic factors, has become more and more common all over the world. Previous studies have shown that overweight or obesity, especially excessive visceral fat accumulation, is an important risk factor for HTN and HUA.[3,12] The magnetic resonance imaging (MRI) and computed tomography (CT) are considered as the gold measures for evaluating visceral adiposity. However, due to the expensive cost and radiation risks, MRI and CT are limited to use in routine clinical practices. In recent years, lipid accumulation product (LAP) based on waist circumference (WC) and triglyceride (TG) has been proposed as a reliable indicator of the central lipid accumulation to discriminate central and peripheral obesity.[13,14] Previous epidemiological studies have shown that increased LAP was associated with various diseases, such as diabetes,[15] CVDs,[16] stroke,[17] HTN,[18] HUA.[19] However, there is no study that has analyzed the association between LAP and HWH.

Therefore, this study aimed to assess the association between LAP and HWH. It is extremely important to prevent the prevalence of HWH and guide overweight or obese individuals in managing their health.

METHODS

Study population

All data used in this study were obtained from the China Health and Nutrition Survey (CHNS). The details of this database have been presented elsewhere.[20] The survey was approved by institutional review boards at the Carolina Population Center at the University of North Carolina (Chapel Hill, NC), and the National Institute for Nutrition and Health, and the Chinese Center for Disease Control and Prevention (Beijing, China). All participants provided informed consent upon entering the survey. Up to now, ten waves (1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, 2015) of the survey have been completed. Considering that blood samples were only available in the wave of 2009, data from the 2009 CHNS survey were obtained for analysis.

A total of 9733 individuals aged 18 to 75 years were potentially eligible for this study. We excluded participants with the following missing information: anthropometric data (weight, height, WC, hip circumference (HC)), hypertension information (individuals with missing blood pressure data, missing previously diagnosed hypertension data and using antihypertensive drugs data), blood biochemical values (uric acid (UA), TC, TG, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)), and lifestyle (smoking and drinking). Finally, 7897 participants (3670 men and 4227 women) were included in this study (as shown in Figure 1).

Anthropometric and serum biochemical measurements

Weight, height, WC, and HC were measured by well-trained examiners under private and comfortable conditions following the standard protocols.[21] BMI was computed as weight (kg) divided by the square of height (m^2). Waist to height ratio (WHtR) was calculated as WC (cm) divided by height (cm), and waist to hip ratio (WHR) was calculated as WC (cm) divided by HC (cm). LAP was computed as the following formulas.[14]

LAP for men = (WC [cm] - 65) x (TG concentration [mmol/L])

LAP for women = (WC [cm] - 58) x (TG concentration [mmol/L])

The collection, transport and storage of serum samples, as well as the detection of biochemical parameters (TC, TG, LDL-C, HDL-C, UA), have been described in other

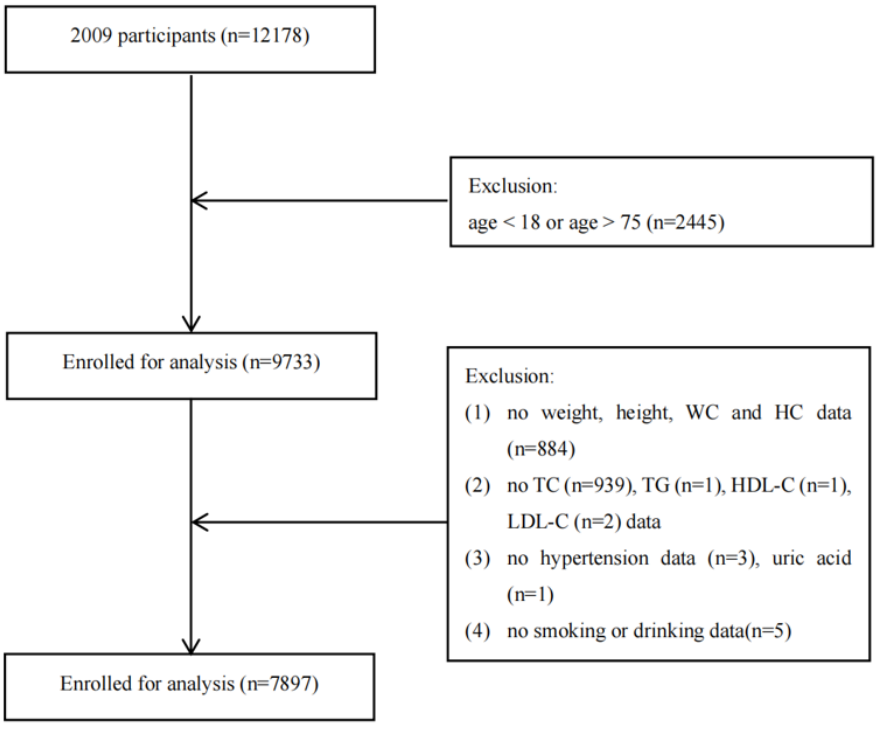

Figure 1. Flowchart of inclusion criteria for participants. WC: waist circumference; HC: hip circumference; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

studies.[21] Systolic blood pressures (SBP) and diastolic blood pressures (DBP) were measured in triplicate by trained professionals using mercury sphygmomanometers while the participants were in the sitting position, with an interval of 3–5 mins between the two measurements. The average of the three measurements was used for analysis in this study. The structured self-reported questionnaire was used to collect information on gender, age, living area (urban / rural), smoking (yes / no) and drinking (yes / no).

Definition of hypertension with hyperuricemia (HWH)

In the present study, individuals with HWH have to meet the following two criteria: (1) hyperuricemia: elevated serum UA (≥7 mg/dL in men and ≥6 mg/dL in women), (2) hypertension: SBP ≥140 mmHg and/or DBP ≥90 mmHg, or have been diagnosed as hypertension by a physician, or use of antihypertensive drugs. In this study, HTN was defined as those who meet the criteria for hypertension except those who also meet hyperuricemia criteria. Similarly, HUA was defined as those who meet the criteria for hyperuricemia except those who also meet hypertension criteria.

Statistical analyses

Continuous and categorical variables were presented as mean ± standard deviations (SDs) or counts (percentage), respectively. The chi-square test or t-test were used for pairwise comparisons. To estimate the association of LAP with blood pressure levels and UA concentrations, and risk of HWH, we constructed general linear regression models (SBP, DBP and UA concentrations) and logistic regression models (risk of HWH) with replicated analyses: original model without any adjustments (model 1), model 2 adjusted for socioeconomic factors (location, age), model 3 additionally adjusted for lifestyle factors (smoking status, alcohol consumption), model 4 further adjusted for TC concentrations. There was no linear relationship between LAP and TC by collinearity diagnostics. All the above statistical tests were carried out using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA). Restricted cubic splines (RCS) were used to detect the possible nonlinear dependency of the relationship between the risk of HWH and LAP levels, using 4 knots at prespecified locations according to the percentiles of the distribution of LAP (with cut points at 5, 35, 65 and 95th percentiles). R software version 4.2.0 was used to perform the above-mentioned dose-response analyses. All statistical tests were two-sided, and the p-value <0.05 was considered statistically significant.

RESULTS

Characteristics of the study population

According to the inclusion and exclusion criteria, a total of 7897 participants (3670 men and 4227 women) from the 2009 CHNS survey were included in this study. The overall prevalence of HTN, HUA and HWH was 22.2%, 7.45%, and 4.61%, respectively. The prevalence of HWH for men was higher than women (p<0.001). In both genders, compared with control participants, HWH participants were more likely to be older and urban residents. In addition, HWH participants tended to have higher values of TC, TG, SBP, DBP, UA, BMI, WC, WHR, WHtR, LAP, and lower concentrations of HDL-C (p<0.001). However, higher concentrations of LDL-C were observed in women with HWH, but not in men with HWH (p>0.05). In both genders, compared with HTN participants or HUA participants, HWH participants were also more tend to have higher values of LAP (p<0.001). The detailed demographic and biochemical characteristics of individuals were shown in Table 1.

Associations of LAP with blood pressure and UA concentrations

General linear regression was used to describe the relationship between the levels of LAP (quartile (Q)1, Q2, Q3, and Q4) and SBP, DBP, and UA concentrations for men and women in Table 2. For both genders, the levels of LAP scores were positively associated with SBP, DBP and UA concentrations in a dose-response manner (all p-trend <0.001) after progressive adjustment for potential confounders including living site, age, smoking, drinking, and TC. For men, compared with the reference group (Q1), those with the highest quartile showed significantly higher levels of SBP (by 8.78 mmHg, 95% CI: 7.21, 10.3; p-trend <0.001), DBP (by 7.12 mmHg, 95% CI: 6.08, 8.17; p-trend <0.001) and UA (by 1.66 mg/dL, 95% CI: 1.50, 1.83; p-trend <0.001). Similarly, compared with women who had the lowest quartile of LAP score, those with the highest quartile of LAP scores showed significantly higher levels of SBP (by 11.02 mmHg, 95% CI: 9.36, 12.7; p-trend <0.001), DBP (by 7.45 mmHg, 95% CI: 6.41, 8.49; p-trend <0.001) and UA (by 1.21 mg/dL, 95% CI: 1.10, 1.33; p-trend <0.001).

Associations of LAP with risk of HWH

We also applied logistic regression models to explore the association between LAP and the prevalence of HWH, and OR (95% CI) of all models were shown in Table 3. After adjustment for all potential confounders, the results exhibited that the levels of LAP scores were extremely, positively associated with the prevalence of HWH (all p-trend <0.001). In men, compared to the lowest quartile group of LAP scores, those with the highest quartile had a significantly higher risk of HWH (OR: 12.2; 95% CI: 7.22, 20.5; p-trend <0.001). The same association was also found in women individuals (OR: 14.5; 95% CI: 3.50, 60.2; p-trend <0.001).

Dose-response relationship between LAP and HWH

Based on the stratification of gender, we used RCS model with 4 knots to perform the relationship between LAP and HWH risk. Nonlinear dose-response association was found in the association between LAP and the risk of HWH (all p value of nonlinear <0.001). The results showed that with the continuous change of LAP, the association strength of HWH increased nonlinearly with confounders being adjusted in men and women (Figure 2).

DISCUSSION

In this cross-sectional study, we found that LAP was significantly positively associated with blood pressure, UA concentrations and risk of HWH for men and women. Previous studies reported that HTN patients were more

Table 1. Demographic characteristics of participants

Variables	Men					Women				
	Control	HTN	HUA	HWH	*p*	Control	HTN	HUA	HWH	*p*
N	2117	778	495	280		3074	976	93	84	
Age (y)	46.4±13.7	55.8±11.6†	44.7±13.5†‡	54.8±12.0†§	<0.001	45.5±13.3	57.6±10.5†	51.6±12.2†‡	61.2±9.04†‡§	<0.001
urban [n (%)]	646 (55.0)	228 (19.4)	188 (16.0)†‡	112 (9.5)†‡	<0.001	972 (70.0)	347 (25.0)†	31 (2.2)	39 (2.8)†	0.006
Smoking [n (%)]	1325 (57.9)	492 (21.5)	306 (13.4)	164 (7.2)	0.557	106 (64.2)	49 (29.7)†	4 (2.4)	6 (3.6)	0.062
Drinking [n (%)]	1268 (56.5)	463 (20.6)	342 (15.2)†‡	170 (7.6)§	0.001	290 (76.1)	72 (18.9)†	11 (2.9)	8 (2.1)	0.189
Height (cm)	167±6.65	167±6.58	168±6.61‡	168±6.36	0.042	156±6.24	155±6.30†	156±6.21	155±6.32†	<0.001
Weight (kg)	63.4±10.4	67.4±11.4†	67.7±11.0†	73.1±11.9†‡§	<0.001	56.0±8.91	60.2±10.3†	59.2±9.44†	63.4±11.0†‡§	<0.001
HC (cm)	93.5±7.26	96.2±7.28†	95.6±7.44†	99.5±7.73†‡§	<0.001	93.2±7.66	97.3±7.86†	95.6±8.29†‡	100±8.52†‡§	<0.001
WC (cm)	81.9±9.49	87.4±10.3†	85.7±9.14†‡	92.2±9.35†‡§	<0.001	79.2±9.57	86.3±9.82†	83.4±9.98†‡	89.9±10.4†‡§	<0.001
BMI (kg/m^2)	22.6±3.12	24.2±3.43†	24.0±3.20†	25.9±3.45†‡§	<0.001	22.8±3.20	25.0±3.62†	24.3±3.58†	26.5±3.90†‡§	<0.001
WHR	0.88±0.06	0.91±0.07†	0.90±0.06†‡	0.93±0.05†‡§	<0.001	0.85±0.08	0.89±0.08†	0.87±0.07†	0.90±0.06†§	<0.001
WHtR	0.49±0.06	0.52±0.06†	0.51±0.05†‡	0.55±0.05†‡§	<0.001	0.51±0.06	0.56±0.06†	0.53±0.07†‡	0.58±0.07†‡§	<0.001
TC (mmol/L)	4.67±0.92	4.9±0.88†	5.08±1.04†‡	5.28±1.02†‡§	<0.001	4.77±0.98	5.17±1.02†	5.38±1.32†‡	5.58±1.14†‡	<0.001
TG (mmol/L)	1.36±0.84	1.57±0.92†	3.06±2.91†‡	3.08±2.49†‡	<0.001	1.34±0.86	1.76±1.13†	3.19±2.14†‡	3.27±2.53†‡	<0.001
LDL-C (mmol/L)	2.9±0.95	3.06±0.86†	2.76±1.09†‡	3.01±1.18§	<0.001	2.93±0.91	3.28±1.01†	2.9±1.32‡	3.25±1.91†§	<0.001
HDL-C (mmol/L)	1.42±0.43	1.41±0.46	1.26±0.52†‡	1.27±0.95†‡	<0.001	1.50±0.38	1.45±0.60†	1.23±0.39†‡	1.24±0.37†‡	<0.001
SBP (mmHg)	117±10.3	143±16.9†	118±9.54‡	141±15.4†§	<0.001	114±11.8	145±17.9†	117±11.5‡	145±17.6†§	<0.001
DBP (mmHg)	76.6±7.14	92.1±10.1†	78.1±6.72†‡	92.3±11.3†	<0.001	74.4±7.70	90.1±10.4†	74.6±7.51‡	90.9±12.3†§	<0.001
UA (mmol/L)	0.31±0.06	0.32±0.06†	0.51±0.15†‡	0.51±0.11†‡	<0.001	0.25±0.06	0.28±0.07†	0.48±0.07†‡	0.49±0.09†‡	<0.001
LAP (cm·mmol/L)	25.1±25.1	37.4±31.5†	69.7±81.7†‡	88.7±86.9†‡§	<0.001	30.6±28.3	52.0±42.3†	85.7±78.0†‡	106±90.9†‡§	<0.001

HTN: hypertension; HUA: hyperuricemia; HWH: hypertension with hyperuricemia; HC: hip circumference; TC: total cholesterol; TG: triglycerides; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; SBP: systolic blood pressures; DBP: diastolic blood pressures; UA: uric acid; BMI: body weight mass; WC: waist circumference; WHR: waist to hip ratio; WHtR: waist-to-height ratio; LAP: lipid accumulation product.

Categorical data were described as counts (percentage) and continuous data were described as mean ± SD. Since some eligible participants not had SBP or DBP data, SBP data were obtained from 6918 participants and DBP data were obtained from 6917 participants.

$^{\dagger}p<0.05$ vs. Control group.

$^{\ddagger}p<0.05$ vs. HTN group.

$^{\S}p<0.05$ vs. HUA group.

Table 2. Associations between the quintile (Q) of LAP scores and blood pressure, and uric acid.

Gender	Q1 (≤13.6)	Q2 (13.6-25.9)	Q3 (25.9-48.2)	Q4 (≥48.2)	*p*-trend
SBP					
Men					
Model 1	Ref	5.34 (3.74-6.94)	7.75 (6.13-9.36)	10.3 (8.71-11.9)	<0.001
Model 2	Ref	4.38 (2.89-5.86)	6.70 (5.19-8.20)	9.58 (8.09-11.1)	<0.001
Model 3	Ref	4.35 (2.86-5.83)	6.63 (5.12-8.14)	9.55 (8.05-11.0)	<0.001
Model 4	Ref	4.08 (2.59-5.58)	6.23 (4.69-7.76)	8.78 (7.21-10.3)	<0.001
Women					
Model 1	Ref	8.38 (6.72-10.0)	13.8 (12.2-15.5)	19.3 (17.6-21.0)	<0.001
Model 2	Ref	4.24 (2.70-5.79)	7.54 (5.97-9.11)	11.5 (9.90-13.2)	<0.001
Model 3	Ref	4.25 (2.71-5.79)	7.49 (5.92-9.06)	11.5 (9.88-13.1)	<0.001
Model 4	Ref	4.14 (2.60-5.69)	7.20 (5.61-8.79)	11.0 (9.36-12.7)	<0.001
DBP					
Men					
Model 1	Ref	3.30 (2.29-4.30)	5.75 (4.73-6.76)	8.19 (7.19-9.19)	<0.001
Model 2	Ref	3.01 (2.02-4.01)	5.41 (4.41-6.41)	7.94 (6.95-8.93)	<0.001
Model 3	Ref	2.92 (1.93-3.91)	5.26 (4.25-6.26)	7.82 (6.83-8.81)	<0.001
Model 4	Ref	2.68 (1.69-3.68)	4.89 (3.87-5.90)	7.12 (6.08-8.17)	<0.001
Women					
Model 1	Ref	4.45 (3.49-5.42)	7.16 (6.20-8.12)	10.3 (9.33-11.3)	<0.001
Model 2	Ref	3.13 (2.17-4.09)	5.13 (4.16-6.11)	7.80 (6.80-8.81)	<0.001
Model 3	Ref	3.13 (2.17-4.09)	5.10 (4.12-6.07)	7.80 (6.79-8.81)	<0.001
Model 4	Ref	3.05 (2.09-4.01)	4.88 (3.90-5.87)	7.45 (6.41-8.49)	<0.001
UA					
Men					
Model 1	Ref	0.25 (0.09-0.41)	0.60 (0.45-0.76)	1.92 (1.76-2.07)	<0.001
Model 2	Ref	0.27 (0.11-0.42)	0.62 (0.46-0.78)	1.92 (1.77-2.08)	<0.001
Model 3	Ref	0.26 (0.11-0.42)	0.61 (0.45-0.77)	1.92 (1.76-2.07)	<0.001
Model 4	Ref	0.18 (0.02-0.33)	0.48 (0.32-0.64)	1.66 (1.50-1.83)	<0.001
Women					
Model 1	Ref	0.24 (0.14-0.35)	0.59 (0.48-0.69)	1.47 (1.37-1.58)	<0.001
Model 2	Ref	0.16 (0.05-0.27)	0.46 (0.35-0.57)	1.32 (1.21-1.43)	<0.001
Model 3	Ref	0.16 (0.05-0.26)	0.46 (0.35-0.57)	1.32 (1.21-1.43)	<0.001
Model 4	Ref	0.13 (0.03-0.24)	0.40 (0.29-0.51)	1.21 (1.10-1.33)	<0.001

SBP: systolic blood pressures; DBP: diastolic blood pressures; UA: uric acid.
Model 1 without any adjustments, model 2 adjusted for socioeconomic factors (location, age), model 3 additionally adjusted for lifestyle factors (smoking status, alcohol consumption), model 4 further adjusted for TC concentrations.

Table 3. Multivariable-adjusted odds ratios (and 95% CIs) of HWH according to quintile (Q) of LAP scores

Gender	Q1 (≤13.6)	Q2 (13.6-25.9)	Q3 (25.9-48.2)	Q4 (≥48.2)	*p*-trend
Men					
Model 1	Ref	2.17 (1.19-3.95)*	4.84 (2.81-8.35)*	14.4 (8.64-23.8)*	<0.001
Model 2	Ref	2.08 (1.14-3.81)*	4.59 (2.66-7.94)*	14.6 (8.73-24.3)*	<0.001
Model 3	Ref	2.07 (1.13-3.80)*	4.53 (2.62-7.83)*	14.4 (8.65-24.1)*	<0.001
Model 4	Ref	1.97 (1.07-3.61)*	4.14 (2.39-7.18)*	12.2 (7.22-20.5)*	<0.001
Women					
Model 1	Ref	2.28 (0.44-11.8)	4.90 (1.08-22.2)*	32.7 (7.99-134)*	<0.001
Model 2	Ref	1.48 (0.28-7.69)	2.63 (0.58-12.0)	16.1 (3.90-66.7)*	<0.001
Model 3	Ref	1.48 (0.29-7.70)	2.64 (0.58-12.1)	16.2 (3.91-66.9)*	<0.001
Model 4	Ref	1.48 (0.28-7.69)	2.52 (0.55-11.5)	14.5 (3.50-60.2)*	<0.001

Model 1 without any adjustments, model 2 adjusted for socioeconomic factors (location, age), model 3 additionally adjusted for lifestyle factors (smoking status, alcohol consumption), model 4 further adjusted for TC concentrations.
*$p<0.05$.

vulnerable to HUA than normotensives. A study in Central and Eastern Europe found that even among 3206 patients who had been treated for high blood pressure, a shockingly high rate of 25% developed HUA.[22] In the adolescent population, approximately 25-60% of untreated patients with essential hypertension and most patients with recent onset also developed HUA.[23] Hypertension may be a risk factor for HUA,[24] but the underlying mechanism is unclear. However, more epidemiology studies suggest a strong association between high serum UA con-

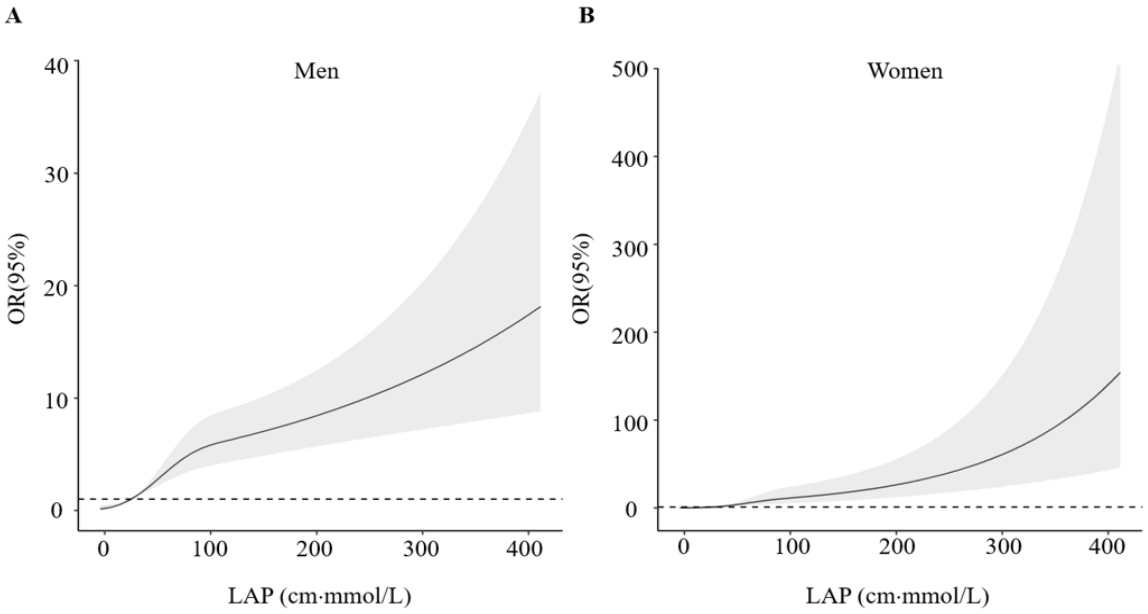

Figure 2. Dose-response analysis using restricted cubic spline model for the association between LAP and HWH risk. (A) men; (B) women. The solid lines and the shaded areas represent the estimated ORs and their 95% confidence intervals, respectively. The model adjusted for age, location, smoking, drinking, and TC. LAP: lipid accumulation product; HWH: hypertension with hyperuricemia; ORs: odds ratios; TC: total cholesterol.

centrations and the presence or the development of HTN.[5,25,26] The mechanism is mainly regulated by molecular signals, such as oxidative stress, intracellular urate activity, insulin resistance, inflammatory response, endothelial dysfunction, sympathetic overactivity, endoplasmic reticulum stress.[5,26-28] In addition, a large cross-sectional population study in Japan found that the prevalence of HWH was 4.6% among 85286 participants.[8] This is very similar to the prevalence of HWH in this study population. What's more, previous studies have shown that HWH had greater adverse effects on human health than HTN or HUA alone, such as exacerbated retinopathy and increased the risk of cardiovascular disease.[29,30] Therefore, it is extremely important to explore a fast, convenient and accurate method to improve the prevention and self-management of HWH.

Obesity is characterized by adipose tissue dysfunction and contributed to increased visceral adipose tissue, insulin resistance, elevated renin-angiotensin-aldosterone system activity, elevated pro-inflammatory factors, elevated leptin and reduced adiponectin.[31] Obesity, especially central lipid accumulation, is a risk factor for HTN and HUA. The main mechanisms by which obesity promotes the development and progression of HTN are: insulin resistance, elevated leptin and reduced adiponectin. Insulin resistance promotes the renin-angiotensin-aldosterone system which increases the risk of atherosclerosis and HTN.[32] The elevated secretion of leptin by adipose tissue activates the renal sympathetic nerves, followed by increased sodium, water retention, and increased renin secretion, thereby increasing blood pressure. Adiponectin, another adipocytokine synthetized by adipose tissue, has a potential protective role in the regulation of blood pressure. The reduced secretion of adiponectin can result in abnormal blood pressure levels and even HTN. The mechanisms by which obesity increases the risk of HUA are mainly through two pathways: insulin resistance affects the excretion of renal and the reabsorption of uric acid, and the lipolysis of visceral adipose tissue increases the burden of decomposition of free fatty acids in the liver, accelerating purine metabolism and promoting the production of uric acid.[33] Some studies had shown that obesity also is an important risk factor for HWH. It was found that obesity or overweight was a risk factor for HUA in pediatric patients with primary hypertension.[34] And among participants with primary hypertension, patients with HUA were more likely to be obese compared to patients with normal serum uric acid.[10] Therefore, we decided to explore an excellent method that could help individuals to predict HWH risk by describing obesity or visceral adipose accumulation. Although MRI and CT scans are the gold standard for measuring body fat distribution, they are expensive and have radiation exposure, making them inaccessible for basic public health applications.

Fortunately, the anthropometric index may provide us with a way forward. Especially, LAP was a new anthropometric index based on WC and TG, considered with central fat distribution and body lipid level. It may have an accurate ability to describe the visceral fat accumulation, due to lipid metabolism is closely related to body fat distribution. In recent years, many studies have focused on the relationship between LAP scores and HTN or HUA, respectively. Some researchers have demonstrated that LAP had a strong positive association with risk of HTN in men and women.[18,35-38] However, other different results were shown in a few studies. For example, a epidemiology study in China showed that LAP had a stronger association than BMI with risk of HTN in Mongolian men, but not in women.[39] A study from the nationwide Thai National Health Examination Survey 2009 found that WHtR was a more excellent measurement than LAP in assessing the association between visceral fat and hypertension in middle-aged and elderly Thais.[40] M Kaneva

and R Bojko found that age factor should be considered when the reference and cut-off values for LAP are defined for predicting hypertension.[41] Some studies also found that gender disparities should be considered in predicting HTN.[18,36,38] Therefore, the reason for this controversy may be gender, ethnic, regional and age differences among different study populations. Certainly, in recent 5 years, several studies have shown that LAP was positively correlated to risk of HUA for both sexes.[19,42-44] However, there is no study to explore the relationship between LAP and HWH. According to the results of the above studies, LAP may be associated with HWH, but this idea needs to be further studied. Therefore, this is also a novelty of this study. Our study found that LAP was positively associated with SBP, DBP, UA concentrations and risk of HWH. This result suggested that the mechanism, HWH had greater adverse effects on human health than HTN or HUA alone, may be closely related with obesity, especially lipid metabolism.

There are strengths in the present study. First, our study is the first to examine the association between LAP and risk of HWH. Second, considering gender disparities, this study applied sex subgroup analysis. Thirdly, the samples in the present study were obtained from partly national representative study, and all operations were carried out in accordance with unified standard procedures, so the results could reflect the real situations. However, some limitations have been found in our study. First, age stages and national minority factors were not taken into account, which may lead to different metabolism and the results of this study may not be applicable. Second, because of the cross-sectional study design, we could not investigate the longitudinal dynamic association between changes in LAP scores and progression of HWH, so the causal relationship between LAP and HWH is undetermined. Third, the number of HWH patients may not be enough which impacts the conclusion of the study. In the future, a large and longitudinal cohort study which considering age and ethnic factors would help to assess the predictive relationship between LAP and risk of HWH. What's more, HTN and HUA are known as risk factors for CVDs, diabetes and CKD.[1,2,4,5,45,46] Therefore, HTN and HUA can be taken as mediate factors to study the relationship between LAP and longer-term disease outcomes (CVDs, diabetes and CKD) in subsequent studies. In addition, the combined and independent effects of LAP, TC, blood glucose and other factors will also be considered in the mediation analysis.[47]

In conclusion, LAP has a strong positive relationship with HWH risk in men and women and there was an adjusted dose-response association between continuous LAP and risk of HWH.

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AUTHOR DISCLOSURES

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