

# Contribution of Different Phenotypes of Obesity to Metabolic Abnormalities from a Cross-Sectional Study in the Northwest China

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**Background:** This study has been conducted to explore the correlation between phenotypes of obesity and metabolic comorbidities.

**Methods:** This cross-sectional study recruited 14,724 adults aged  $\geq 18$  years with a randomized stratified sampling strategy. Obesity was classified into four types according to body mass index (BMI) and waist-to-height ratio (WHtR): normal weight with central obesity (NWCO) and without (NW) CO, and obese or overweight with (OBCO) and without (OB) central obesity. Uric acid (UA), fasting blood glucose (FBG), and lipid profile were measured.

**Results:** The prevalence of hyperuricemia in the 4 groups (NW, NWCO, OB and OBCO) was 3.7%, 5.6%, 8.7% and 12.4%, whilst the prevalence of hypertriglyceridemia was 13.4%, 27.4%, 30.3% and 43.7%, separately. The prevalence of hypo-high-density lipoprotein cholesterolemia (hypo-HDL emia) was 20.1%, 21.4%, 30.8% and 27.9%, while the prevalence of hyper-low-density lipoprotein cholesterolemia (hyper-LDL emia) was 9.8%, 24.4%, 12.3% and 27.9%. The prevalence of hypercholesterolemia was 11.2%, 23.5%, 14.7%, 28.5% and the prevalence of hyperglycemia was 9.7%, 22.6%, 18.5%, and 27.0%, respectively. The prevalence of hypertension was 6.9%, 13.1%, 14.7%, and 20.6%. For various metabolic abnormalities, OBCO have the highest risks compared with NW (hyperuricemia: adjusted OR (aOR)= 2.60; hypertriglyceridemia: aOR= 3.19; hypercholesterolemia: aOR= 1.48; hyper LDLemia: aOR= 2.21; hypo HDLemia: aOR= 1.42; hyperglycemia: aOR= 1.95; hypertension: aOR= 2.16). The risk of hyper LDLemia, hypercholesterolemia and hyperglycemia in the NWCO group was higher than that in the OB group (hyperLDLemia: aOR: 1.69 vs 0.97; hypercholesterolemia: aOR: 1.27 vs 1.24; hyperglycemia: aOR: 1.62 vs 1.28).

**Conclusion:** Different phenotypes of obesity are significantly associated with metabolic abnormalities. NWCO is more closely associated with hypercholesterolemia, hyperglycemia and hyper LDLemia. General obesity and central obesity have a synergistic effect on the diseases.

**Keywords:** obesity, central obesity, metabolic abnormalities, BMI, WHtR

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## Introduction

Obesity (OB) is a chronic disease caused by multiplex reasons including genetics, lifestyle and dysfunctional neurohormonal systems that manifested as excess weight and adiposopathy. According to WHO, the prevalence of obesity has tripled since 1975 with 1.9 billion overweight adults and 650 million obese adults.<sup>1</sup> The increasing trend in obesity prevalence has put a heavy burden on health care economics,

increasing risks for plenty of comorbidities such as cardiovascular disease (CVD),<sup>2</sup> heart failure,<sup>3</sup> liver disease, type 2 diabetes<sup>4</sup> and specific cancers.<sup>5</sup> The diagnosis of obesity is achieved by anthropometric methods, where waist circumference (WC) and waist/hip circumference ratio have been used as indicators of central obesity (CO), and body mass index ( $\text{kg}/\text{m}^2$ ) (BMI) has been used as general obesity indicators.<sup>6</sup> Recently, several studies indicated that waist-to-height Ratio (WHtR), as a new indicator of central obesity, is better and more effective to identify health risks in the overall population.<sup>7,8</sup> Considerable evidences showed that both BMI and WHtR were closely correlated to various kinds of metabolic abnormalities, including diabetes,<sup>9–11</sup> hypertension,<sup>12</sup> dyslipidemia<sup>13</sup> and hyperuricemia.<sup>14</sup> However, researches that comprehensively analyze the effects of different phenotypes of obesity on metabolic disorders are rare. In this study, we investigated the association between phenotypes of obesity and the metabolic comorbidities and evaluate the independent effects of obesity on different metabolic disorders in a large sample size of a northwest population from 2014 to 2017.

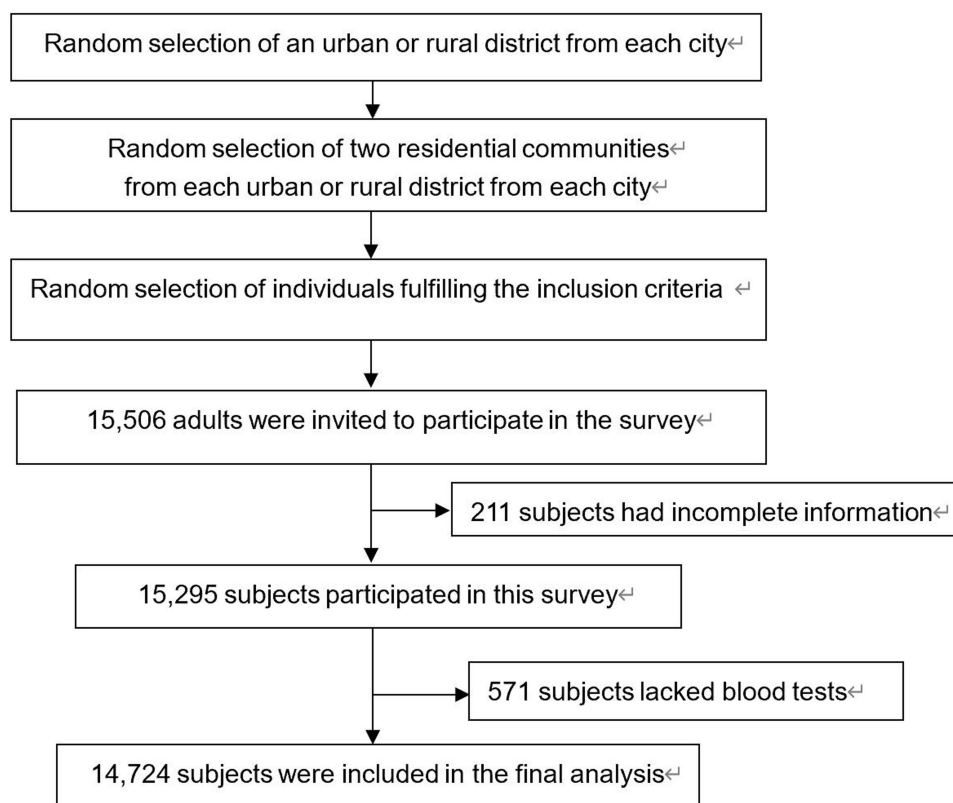
## Methods

### Subjects

This study was conducted in Northwest China including six provinces (Ningxia, Shanxi, Gansu, Xinjiang, Qinghai, Mongolia) between 2014–2017 by using a whole cluster stratified random sampling design. Subjects selected for inclusion: age 18 and above; local residence for at least 5 years; non-pregnant women. The study was approved by the Ethics Committee of Ningxia Medical University General Hospital and all procedures were performed in accordance with the ethical standards of the Committee and with the 1964 Helsinki declaration and its later amendments (The ethical approval code: 2,014,121). Participants were provided written informed consent after a detailed explanation. A total of 14,724 people were enrolled in this study. The sample screening process was illustrated in Figure 1.

### Data Collection and Anthropometry

A standardized questionnaire was conducted by professionally trained workers to collect the data, including sociodemographic data, regional location, lifestyle, and medical history. Physical examination and blood pressure



**Figure 1** The sample screening process.

were operated by doctors or medical students. Body mass index was calculated as weight in kilograms divided by the square of the height in meters. Waist-to-height ratio was calculated by dividing the WC by the subject's height. Blood pressure (BP) was measured three times after a resting period of at least 10 minutes, and the averages of three times were taken as the final value.

## Laboratory Measurements and Anthropometry

Participants were asked to fast for 8 hours overnight before venipuncture. The blood specimens were centrifuged, separated, and stored at 4 °C, and then transported to the Laboratory of General Hospital of Ningxia Medical University to process the laboratory assays. Uric acid (UA), fasting blood glucose (FBG), and lipid profile were quantified using routine laboratory analysis (Konelab, Espoo, Finland). Weight was measured when subject was minimally clothed without shoes using digital scales and recorded to the nearest 100g. Height was measured in a standing position, without shoes, using tape meter, while the shoulders were in a normal position. BMI was calculated as weight in kilograms divided by height in meters squared. WC was measured at the narrowest level and that of hip at the maximal level over light clothing, using unstretched tape meter, without any pressure to body surface, and was recorded to the nearest 0.1cm. WHtR was calculated as WC divided by height.

## Definitions of Obesity and Other Variables

Obesity is generally defined as a BMI  $\geq 30$  kg/m<sup>2</sup>, though a BMI  $\geq 27.5$  kg/m<sup>2</sup> defines obesity in Asian populations.<sup>15</sup> Based on the expert consensus on prevention and treatment of adult obesity in China, obesity is defined as a BMI  $\geq 28$ kg/m<sup>2</sup> which is closer to China's national conditions. Taking into account the different definitions of obesity, we divided the study population into overweight and obese people (BMI $\geq 24$ ) and normal weight people (BMI $<24$ ).<sup>16</sup> Central obesity was defined as WHtR  $\geq 0.5$ .<sup>7</sup> The phenotype of obesity was classified into the following four types according to general overweight or obesity and central obesity status: Normal weight with (NWCO) and without (NW) CO, and obese or overweight with (OBCO) and without (OB) central obesity. Definitions for metabolic abnormalities were listed as followings: hyperglycemia: fasting blood glucose (FBG)  $\geq 6.1$  mmol/L (110 mg/dL) and/or receiving current medication

for this condition; hypertension: systolic blood pressure  $\geq 140$ mmHg and/or diastolic blood pressure  $\geq 90$ mmHg and/or currently being on antihypertensive medications; hypertriglyceridemia (HTG): serum triglyceride  $\geq 1.7$ mmol/L (150 mg/dL) and/or receiving current medication; hypercholesterolemia (HC): serum cholesterol  $\geq 5.2$ mmol/L (200 mg/dL) and/or receiving current medication; hypo-high-density lipoprotein cholesterol (hypo HDLemia): serum HDL cholesterol  $< 1.0$ mmol/L (40 mg/dL) in men and  $< 1.3$ mmol/L (50mg/dL) in women; hyper-low-density lipoprotein cholesterol (hyper LDLemia): serum LDL-C  $\geq 3.4$ mmol/L (130 mg/dL); hyperuricemia (HUA): serum urate level  $\geq 420$   $\mu$ mol/L (7.0 mg/dl) in males and  $\geq 360$   $\mu$ mol/L (6.0 mg/dl) in females.<sup>17</sup> Smoking status was classified as regular heavy smoker (having smoked at least 100 cigarettes in one's lifetime and smoke  $\geq 20$  cigarettes/day), regular moderate smoker (having smoked at least 100 cigarettes in one's lifetime and smoke  $< 20$  cigarettes/day) and nonsmoker.<sup>18</sup> The location was divided into an urban or rural area. Income was divided into low, medium, and high levels with the average annual income of  $< 10,000$ ,  $< 50,000$  and  $\geq 50,000$  Yuan separately. Educational attainment was classified as elementary school and below, junior high school and above and college and above. Salt intake was classified as high ( $>10.0$  g/day), medium (6.0–10.0 g/day), and low ( $<6.0$  g/day).

## Statistical Analysis

All statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). The measurement data in this article can be approximated as normal distributed, and therefore are expressed as means  $\pm$  Standard deviation (Means  $\pm$  SDs). One-way analysis of variance (ANOVA) was used for the comparison of continuous variables amongst all groups, and the Post Hoc multiple comparison was further applied to obtain the difference between the other three obese groups and NW. A chi-square test was performed to investigate the distributions (%) and the association between obesity and possible associated factors. Variables that were significantly associated or known a priori from the literature were considered as covariance in subsequent analyses. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated by univariable and multivariable logistic regression to examine the association between obesity and metabolic disorders in a stepwise manner. For all measures, Two-tailed  $p < 0.05$  was considered as statistically significant.

## Results

### The Basic Characteristics of the Studied Population

The study included a total of 14,724 people from six provinces of the northwest China. Based on BMI and WHtR, participants were divided into NW ( $n = 6018$ ), NWCO ( $n = 1614$ ), OB ( $n = 1118$ ) and OBCO ( $n = 5974$ ). The prevalence of NWCO, OB and OBCO were 11.0%, 7.6%, and 40.6%, respectively. NW subjects were more likely to be young, well-educated, and have higher income. The participants in the NWCO group were more likely to be females, older, poorly educated and nonsmokers. Subjects in the OB group were more likely to be males, live in rural areas, have lower salt intake and insufficient income. OBCO participants were more likely to live in urban areas, have medium-high salt intake and smoke cigarettes heavily. Tibetans accounted for a higher proportion of OBCO, while Hui and Han people accounted for a large proportion of NWCO and OB, separately. The sociodemographic and lifestyle characteristics of all participants categorized by the patterns of obesity are presented in Table 1.

### The Prevalence of Metabolic Abnormalities and Serological Metabolic Indexes in Different Obese Phenotypes

As shown in Table 2, the prevalence of hyperuricemia in the 4 groups (NW, NWCO, OB, and OBCO) was 3.7%, 5.6%, 8.7%, and 12.4%, respectively. The prevalence of HUA in OBCO group was significantly higher than that of the NW group ( $p < 0.001$ ). The prevalence of hypertriglyceridemia was 13.4%, 27.4%, 30.3% and, 43.7% respectively. The prevalence of hypo-HDLemia was 20.1%, 21.4%, 27.9% and 30.8%, while the prevalence of hyper-LDLemia was 9.8%, 24.4%, 12.3% and 27.9%. The prevalence of hypercholesterolemia was 11.2%, 23.5%, 14.7% and 28.5%. In addition, the prevalence of hyperglycemia in the four groups was 9.7%, 22.6%, 18.5%, and 27.0% whilst the prevalence of hypertension was 6.9%, 13.1%, 14.7%, and 20.6%. It is found that the prevalence of metabolic abnormalities was remarkably higher in the other three groups than the NW group ( $p < 0.05$ ), with the highest occurrence in the OBCO group. Hyperuricemia, hypertriglyceridemia, hypertension, and hypo HDLemia seem to be more prevalent in OB group compared with NWCO. Hypercholesterolemia, hyper LDLemia and hyperglycemia was more epidemic in

NWCO compared with OB. The serum uric acid level and blood lipid level showed a consistent trend in each group.

### Association of Obesity Patterns with Different Metabolic Abnormalities

We then carried out stepwise logistic regression through different models to assess the risk of different obesity types for metabolic abnormalities. After univariate logistic regression, we analyzed a variety of influencing factors, including age, nationality, education, income, geographic region, lifestyle (smoking, salt intake), comorbidities (hyperglycemia, hyperuricemia, hypertension and dyslipidemia) and all the above factors were adjusted. For various metabolic abnormalities, people in the OBCO group have the highest risks without exception compared with the NW group (HUA: aOR= 2.60; HTG: aOR= 3.19,  $p < 0.001$ ; HC: aOR= 1.48,  $p < 0.001$ ; hyper LDLemia: aOR= 2.21,  $p < 0.001$ ; hypo HDLemia: aOR= 1.42,  $p < 0.01$ ; hyperglycemia: aOR= 1.95,  $p < 0.001$ ; hypertension: aOR= 2.16,  $p < 0.001$ ). However, the two different obesity phenotypes in the NWCO and OB groups have different contributions to the risk of metabolic abnormalities. The risk of hyper LDLemia, HC and hyperglycemia in the NWCO group was significantly higher than that in the OB group (hyper LDLemia: aOR:1.69 Vs 0.97; HC: aOR:1.27 Vs 1.24; hyperglycemia: aOR:1.62 Vs 1.28). Individuals of OB group had increased risks of HUA, HTG, hypo HDLemia, and hypertension as compared with NWCO group (HUA: aOR:2.24 Vs 1.61; HTG: aOR:2.69 Vs 2.18; hypo HDLemia: aOR:1.32 Vs 1.13; hypertension: aOR:1.78 Vs 1.32), as shown in Table 3.

## Discussion

The deleterious effects of obesity on health have been widely acknowledged. Obesity is a major risk factor for cardiovascular diseases, cancer and diabetes mellitus and substantially increases the risk of metabolic diseases.<sup>19</sup> In the past, substantive studies have explored the contribution of obesity to diseases by analyzing BMI, waist circumference and waist/hip ratio.<sup>20</sup> Research on the obesity phenotypes and metabolic abnormalities is scarce.

Waist circumference was viewed as a better predictor of abdominal visceral fat and used to be a regular measure of central obesity.<sup>21</sup> However, the cutoff values are differed by ethnicity, age, and sex.<sup>22,23</sup> Waist-to-height ratio is considered to be a more reasonable anthropometric measurement factor for assessing central obesity and is proposed for self-assessment or monitoring of CVD risk factors.<sup>24</sup> A systematic review has studied the predictive

**Table I** The Basic Characteristics of Studied Participants (n=14,724)

	NW	NWCO	OB	OBCO	P <sup>f</sup>
	N=6018, 40.8%	N=1614, 11.0%	N=1118, 7.6%	N=5974, 40.6%	
Age (yr) <sup>a</sup>	37.8±14.5	50.5±16.4	41.5±13.0	47.4±14.3	<0.001
Gender Female (% , n)	56.0%, 3373	58.9%, 951	43.3%, 484	44.7%, 2673	<0.001
Location Urban (% , n)	51.5%, 3099	50.4%, 813	43.6%, 488	56.5%, 3373	<0.001
Ethnicity Han Tibet Hui	76.8%,4622 11.2%,672 12.0%,724	84.0%, 1356 9.6%, 155 6.4%, 103	63.8%,713 7.7%,86 28.5%,319	73.2%, 4370 19.6%,1171 7.2%,433	<0.001
Smoking status <sup>b</sup> No Moderate Heavy	74.8%,4502 2.8%,171 22.3%,1345	76.4%,1233 2.5%,41 21.1%,340	70.8%,791 3.6%,40 25.75,287	68.2%,4074 3.3%,198 28.5%,1702	<0.001
Education College Junior Primary	35.8%,2155 43.5%,2620 20.7%,1243	21.0%,339 45.4%,732 33.6%,543	31.5%,352 36.0%,402 32.6%,364	23.4%,1397 48.1%,2874 28.5%,1703	<0.001
Income <sup>c</sup> High Medium Low	27.2%,1634 48.5%,2921 24.3%,1463	25.1%,405 47.7%,770 27.2%,439	24.2%,270 47.5%,531 28.4%,317	26.7%,1594 46.1%,2752 27.3%,1628	<0.001
Salt intake <sup>d</sup> High Medium Low	15.3%,922 65.4%,3935 19.3%,1159	18.0%,291 64.0%,1033 18.0%,290	17.1%,191 58.0%,648 25.0%,279	18.4%,1100 65.8%,3928 15.8%,943	<0.001
BMI (kg/m2) <sup>e</sup>	20.88±1.82	22.42±1.41	25.53±1.77	27.60±2.91	<0.001
WC (cm)	74.79±6.14	87.10±5.78	79.20±6.22	94.36±8.13	<0.001
WHtR	0.45±0.03	0.54±0.02	0.48±0.03	0.57±0.07	<0.001

**Notes:** <sup>a</sup>Age was expressed as mean ±standard deviation. <sup>b</sup>Never-smoker was defined as having smoked less than 100 cigarettes in one's lifetime; regular moderate smoker was defined as having smoked at least 100 cigarettes in one's lifetime and smoke less than 20 cigarettes per day; Regular heavy smoker was defined as having smoked at least 100 cigarettes in one's lifetime and smoke equal to or more than 20 cigarettes per day. <sup>c</sup>Income was divided into low, medium, and high levels with the average annual income of < 10,000, < 50,000 and ≥ 50,000 Yuan separately. <sup>d</sup>High salt intake was defined as daily intake>10 g/day; medium salt intake was defined as daily intake 6–10 g/day; low salt intake was defined as daily intake <6 g/day. <sup>e</sup>The body-mass index is the weight in kilograms divided by the square of the height in meters. <sup>f</sup>P-value from Chi-square test for categorical variable and from One-Way ANOVA for continuous variable for all the groups.

**Abbreviations:** NW, normal weight without central obesity; NWCO, normal weight with central obesity; OB, obese or overweight without central obesity; OBCO, obese or overweight with central obesity; BMI, body-mass index; WC, Waist circumference; WHtR, waist-to-height Ratio.

value of WHtR, WC and BMI for CVD, diabetes and related risk factors, and found that WHtR and WC are more probably reliable predictors than BMI.<sup>25</sup>

Therefore, we divided the population into different obesity phenotypes by WHtR and BMI, and further discovered the relationships between different phenotypes of obesity and metabolic comorbidities in Chinese adults. We found that all the metabolic comorbidities included was

significantly associated with NWCO, OB and OBCO, compared with NW. It has been shown that the OBCO group has the highest risk of suffering from various metabolic abnormalities, suggesting that central obesity and ordinary obesity have a superimposing effect. Compared with OB, NWCO has a relatively higher risk of hyperglycemia, HC and hyper LDLmia, after the adjustment of the sociodemographic factors, lifestyles and abnormal metabolisms.



**Table 2** The Prevalence of Metabolic Abnormalities and Serological Metabolic Indexes in Obese Phenotypes

%(95 CI)	NW	NWCO	OB	OBCO	P <sup>a</sup>
HUA	3.7(3.2–4.1)	5.6(4.5–6.7) <sup>d</sup>	8.7(7.0–10.3) <sup>d</sup>	12.4(11.6–13.2) <sup>d</sup>	<0.001
HTG	13.4(12.5–14.3)	27.4(25.2–29.6) <sup>d</sup>	30.3(27.6–33.0) <sup>d</sup>	43.7(42.7–44.9) <sup>d</sup>	<0.001
HC	11.2(10.4–12.0)	23.5(21.4–25.6) <sup>d</sup>	14.7(12.6–16.7) <sup>c</sup>	28.5(27.4–29.7) <sup>d</sup>	<0.001
L-HDL	20.1(19.1–21.1)	21.4(19.6–23.4) <sup>d</sup>	30.8%(28.1–35.0) <sup>d</sup>	27.9(26.7–29.0) <sup>d</sup>	<0.001
H-LDL	9.8(9.1–10.6)	24.4(22.3–26.6) <sup>d</sup>	12.3%(10.3–14.2) <sup>b</sup>	27.9(26.7–29.0) <sup>d</sup>	<0.001
Hyperglycemia	9.7(9.1–10.4)	22.6(20.7–24.4) <sup>d</sup>	18.5(16.7–20.5) <sup>d</sup>	27.0(25.8–28.3) <sup>d</sup>	<0.001
Hypertension	6.9(6.2–7.5)	13.1(11.5–14.8) <sup>d</sup>	14.7(12.6–16.7) <sup>d</sup>	20.6(19.6–21.7) <sup>d</sup>	<0.001
sUA <sup>e</sup> : mmol/L	266.6±79.3	278.1±83.7 <sup>c</sup>	297.8±91.2 <sup>c</sup>	310.8±96.9 <sup>c</sup>	<0.001
sTG <sup>e</sup> : mmol/L	1.19±0.91	1.55±1.24 <sup>c</sup>	1.62±1.32 <sup>c</sup>	1.95±1.42 <sup>c</sup>	<0.001
sTC <sup>e</sup> : mmol/L	4.05±0.96	4.52±1.14 <sup>c</sup>	4.18±1.01 <sup>b</sup>	4.69±1.26 <sup>c</sup>	<0.001
sHDL <sup>e</sup> : mmol/L	1.74±0.90	1.64±0.83 <sup>c</sup>	1.50±0.79 <sup>c</sup>	1.68±0.98 <sup>b</sup>	<0.001
sLDL <sup>e</sup> : mmol/L	2.45±0.97	2.89±1.22 <sup>c</sup>	2.61±0.82 <sup>b</sup>	3.16±1.42 <sup>c</sup>	<0.001
FBG <sup>e</sup> : mmol/L	4.87±1.13 <sup>c</sup>	5.33±1.72 <sup>c</sup>	5.17±1.60 <sup>c</sup>	5.43±1.62 <sup>c</sup>	<0.001

**Notes:** <sup>a</sup>P-value from Chi-square test or One-Way ANOVA for all groups. <sup>b</sup>Compared with the NW, the prevalence was significantly higher (P<0.05). <sup>c</sup>Compared with the NW, the prevalence was significantly higher (P<0.01). <sup>d</sup>Compared with the NW, the prevalence was significantly higher (P<0.001). <sup>e</sup>The value is expressed as mean ± standard deviation.

**Abbreviations:** NW, normal weight without central obesity; NWCO, normal weight with central obesity; OB, obese or overweight without central obesity; OBCO, obese or overweight with central obesity; HUA, hyperuricemia; HTG, hypertriglyceridemia; HC, hypercholesterolemia; L-HDL, hypo-high-density lipoprotein cholesterol; H-LDL, hyper-low-density lipoprotein cholesterol; CI, confidence intervals; FBG, fasting blood glucose.

**Table 3** The Correlation of Obesity Patterns with Different Metabolic Abnormalities

Odds Ratio (95% CI)					
		NW(ref)	NWCO	OB	OBCO
HUA	Model 1	1	1.55(1.21–1.99) <sup>c</sup>	2.49(1.95–3.19) <sup>d</sup>	3.71(3.18–4.34) <sup>d</sup>
	Model 2	1	1.88(1.44–2.45) <sup>d</sup>	2.42(1.87–3.13) <sup>d</sup>	3.61(3.05–4.26) <sup>d</sup>
	Model 3	1	1.61(1.29–2.01) <sup>d</sup>	2.24(1.79–2.82) <sup>d</sup>	2.60(2.34–3.02) <sup>d</sup>
HTG	Model 1	1	2.44(2.14–2.78) <sup>d</sup>	2.81(2.43–3.26) <sup>d</sup>	5.01(4.58–5.48) <sup>d</sup>
	Model 2	1	2.18(1.90–2.51) <sup>d</sup>	2.69(2.32–3.13) <sup>d</sup>	4.48(4.08–4.92) <sup>d</sup>
	Model 3	1	1.82(1.57–2.10) <sup>d</sup>	2.16(1.84–2.53) <sup>d</sup>	3.19(2.89–3.53) <sup>d</sup>
HC	Model 1	1	2.44(2.12–2.80) <sup>d</sup>	1.37(1.14–1.64) <sup>c</sup>	3.18(2.88–3.50) <sup>d</sup>
	Model 2	1	1.81(1.56–2.09) <sup>d</sup>	1.31(1.09–1.58) <sup>c</sup>	2.55(2.30–2.82) <sup>d</sup>
	Model 3	1	1.27(1.08–1.53) <sup>c</sup>	1.24(0.99–1.54) <sup>a</sup>	1.48(1.30–1.67) <sup>d</sup>
L-HDL	Model 1	1	1.29(1.13–1.46) <sup>d</sup>	1.77(1.53–2.04) <sup>d</sup>	1.54(1.41–1.67) <sup>d</sup>
	Model 2	1	1.23(1.07–1.41) <sup>c</sup>	2.08(1.80–2.41) <sup>d</sup>	1.78(1.62–1.95) <sup>d</sup>
	Model 3	1	1.13(0.98–1.30) <sup>a</sup>	1.32(1.17–1.70) <sup>d</sup>	1.42(1.28–1.57) <sup>d</sup>
H-LDL	Model 1	1	2.49(2.15–2.88) <sup>d</sup>	1.28(1.05–1.56) <sup>b</sup>	3.54(3.20–3.92) <sup>d</sup>
	Model 2	1	2.07(1.78–2.41) <sup>d</sup>	1.06(0.87–1.31) <sup>a</sup>	3.01(2.71–3.35) <sup>d</sup>
	Model 3	1	1.69(1.42–2.01) <sup>d</sup>	0.97(0.78–1.22) <sup>a</sup>	2.21(1.95–2.45) <sup>d</sup>
Hyperglycemia	Model 1	1	2.71(2.35–3.13) <sup>d</sup>	2.11(1.78–2.52) <sup>d</sup>	3.44(3.11–3.82) <sup>d</sup>
	Model 2	1	1.59(1.36–1.86) <sup>d</sup>	1.81(1.51–2.17) <sup>c</sup>	2.40(2.15–2.67) <sup>d</sup>
	Model 3	1	1.62(1.33–1.93) <sup>d</sup>	1.48(1.24–1.69) <sup>b</sup>	1.95(1.74–2.18) <sup>d</sup>
Hypertension	Model 1	1	2.05(1.72–2.44) <sup>d</sup>	2.33(1.92–2.82) <sup>d</sup>	3.52(3.13–3.96) <sup>d</sup>
	Model 2	1	1.48(1.23–1.78) <sup>d</sup>	2.00(1.64–2.44) <sup>d</sup>	2.70(2.39–3.06) <sup>d</sup>
	Model 3	1	1.32(1.10–1.59) <sup>c</sup>	1.78(1.46–2.17) <sup>d</sup>	2.16(1.90–2.46) <sup>d</sup>

**Notes:** <sup>a</sup>Take NW as reference value, P-value for odds ratio was not significantly different (P>0.05). <sup>b</sup>Take NW as reference value, P-value for odds ratio was significantly higher (P<0.05). <sup>c</sup>Take NW as reference value, P-value for odds ratio was significantly higher (P<0.01). <sup>d</sup>Take NW as reference value, P-value for odds ratio was significantly higher (P<0.001). Model 1: no adjustment. Model 2: adjusted with sex, location, age, ethnicity, smoking status, income, education and salt intake. Model 3: model 2 adjusted with the other metabolic abnormalities.

**Abbreviations:** NW, normal weight without central obesity; NWCO, normal weight with central obesity; OB, obese or overweight without central obesity; OBCO, obese or overweight with central obesity; HUA, hyperuricemia; HTG, hypertriglyceridemia; HC, hypercholesterolemia; L-HDL, hypo-high-density lipoprotein cholesterol; H-LDL, hyper-low-density lipoprotein cholesterol; CI, confidence intervals; FBG, fasting blood glucose.

In the present study, we find that the risk of hyperglycemia in NWCO is higher than that of OB group, which is consistent with the previous results,<sup>13,26–28</sup> suggesting that central obesity is more closely related to glucose metabolism. Excessive visceral fat is well known to be related with insulin resistance, dyslipidemia and inflammation.<sup>29</sup> A cross-sectional analysis conducted in China suggested that compared with people with normal weight without abdominal obesity, NWCO patients have higher insulin resistance (IR) and decreased insulin sensitivity (DIS).<sup>30</sup> Another study in Brazil reported that people with NWCO had a higher risk of IR and DIS.<sup>31</sup> Waist circumference was the strongest associated factor and indicator of adipose tissue insulin resistance compared with BMI.<sup>32</sup> Previous articles have inferred that obese individuals with normal weight usually have more lean mass, since this is the only way for individuals with large amounts of abdominal fat to keep BMI within the normal range. Therefore, obese people with normal weight not only have too much abdominal fat, but also decrease in muscle mass or muscle quantity, which may cause reduced energy consumption, poor aerobic fitness and metabolic disorders.<sup>33</sup>

Some previous studies have explored the influence of waist circumference, BMI, and waist circumference-to-height ratio on blood lipid profile.<sup>7,34</sup> WHtR has also been suggested to be significantly related to the risk of hyper LDLemia and HC, which supported our results.<sup>35</sup> Few articles have yet analyzed the effect of phenotypes of obesity on lipid in details. We found that the risk of hyper LDLemia is also significantly higher in the NWCO group than in the OB group. This result is in line with another study which found that abdominal obesity is the main driving factor of the secretion of hepatic VLDL particles, and therefore causes a significant increase in plasma VLDL concentration in women.<sup>36</sup> The results of another study on abdominal obesity suggest that central obesity is not related to LDL which is different from our results. It can be attributed to the different adjustments of the confounding factors and the geographical discrepancy of the included population.

Previous studies have confirmed that abdominal fat accumulation is associated with liver fat,<sup>37</sup> excessive production of very low-density lipoprotein (VLDL) in the liver, and decreased catabolism of apolipoprotein (apo) B in men.<sup>38</sup> The impaired catabolism of VLDL1-triglyceride is the most important determinant of the plasma triglyceride concentration in people with central obesity.<sup>39</sup> The specific molecular mechanism of abdominal obesity and hyper-LDLemia remains to be elucidated. LDL concentrations in

abdominal obesity populations should be given more attention as the reduction in mortality was mainly achieved by successful reduction of LDL-cholesterol.<sup>40</sup>

Lipid metabolism is very dynamic and depends on many factors, including concentrations of TG-rich lipoproteins, levels and function of HDL, energy expenditure, insulin levels and sensitivity and function of adipose tissues. The most significant contributing factor for obesity-related dyslipidemia is likely uncontrolled fatty acid released from adipose tissue, especially visceral adipose tissue, through lipolysis, which causes increased delivery of fatty acids to the liver and synthesis of very-low-density lipoprotein (VLDL).<sup>41</sup> We hypothesize that different obesity phenotypes may cause different lipid metabolism abnormalities due to the following factors: I. Different degrees of insulin resistance. Central obesity and hyperinsulinemia accompanying insulin resistance cause an excess production of VLDL, which is triglyceride-rich in the liver.<sup>42</sup> The enhanced lipolytic activity of visceral adipocytes may cause an increased free fatty acid flux to the liver and stimulate VLDL secretion. II. Difference in adipocyte size, white adipose tissue (WAT) and brown adipose tissue (BAT). Enlargement of adipocytes is related with an increase in lipolysis, leading to further increases in levels of circulating free fatty acids and their delivery to the liver to increase triglyceride synthesis.<sup>43</sup> The content of visceral adipose tissue is positively correlated with the number of VLDLs and LDLs, even when controlling for BMI and distribution of subcutaneous adipose tissue.<sup>44</sup> In addition, cholesterol in WAT was reported to efflux to HDL.<sup>45</sup> BAT has been identified as a key player in triglyceride clearance because thermogenesis of BAT consumes large amounts of fatty acids,<sup>46</sup> and BAT activation decreases cholesterol levels as well.<sup>47</sup> III. Diversity on apolipoprotein (apo) and lipid metabolism. Lipid metabolism is regulated by several enzymes and proteins acting as co-factors. Plasma apo C-III concentrations correlate positively with plasma TG.<sup>48</sup> Apoprotein B100 is necessary for the secretion of VLDL, IDL, and LDL.<sup>49</sup> Peripheral obesity and central obesity may have an impact on different apolipoproteins and consequently affect the content of various lipid components. Besides, the LDL receptor expression is found to be reduced in central obesity,<sup>50</sup> providing clues to the higher concentration of LDL in central obesity. IV. Inflammation and adipokines. Adipose tissue has a major endocrine function secreting multiple adipokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), interleukin-1 (IL-1), serum amyloid A (SAA) and adiponectin, and the number of adipose macrophages also play an important role in the development

of dyslipidemia. levels of plasma TNF- $\alpha$  are reported to be associated with the promotion of hepatic triglyceride synthesis and secretion,<sup>51</sup> as well as inhibition of lipoprotein lipase (LPL).<sup>52</sup> IL-6 is also related to hypertriglyceridemia.<sup>53</sup> Adiponectin have been suggested negatively correlated with triglycerides and positively correlated with HDL cholesterol.<sup>54</sup> Despite the above evidence, additional experiments targeting apolipoprotein, LDL-receptor, adipokines and inflammation are required to verify the hypothesis. The specific mechanism of BMI and WC on lipid metabolism needs to be further explored.

In this article, all types of obese patients have increased risks of hypertension and hyperuricemia compared with NW group, which fits well with many previous studies.<sup>13,14,55–57</sup> The increase in serum UA in obese individuals may be attributed to two factors: overproduction and poor renal excretion. Most obese patients have excess energy, which may result in over-production of purine. A study has shown that obese patients have reduced urinary urate excretion and clearance.<sup>58</sup> Furthermore, the accumulation of visceral fat causes a large quantity of plasma free fatty acids to flow into the liver to stimulate the synthesis of triglycerides, and then induce an associated overvoltage in the production of uric acid by activating the uric acid synthesis.<sup>59,60</sup> A Japanese study found that NWCO has a higher risk of hyperuricemia compared with OB.<sup>61</sup> Although our research has failed to reach unanimous conclusion, increasing studies suggest that the contribution of NWCO to the severity of certain diseases is even higher than that of ordinary obesity,<sup>62,63</sup> especially in cardiovascular disease<sup>33,64</sup> and mortality.<sup>65,66</sup>

The mechanisms of hypertension linked to obesity are complex. Our current understanding of pathophysiology is based on the sympathetic nervous system (SNS), kidney and adrenal function, endothelium, adipokine and insulin resistance. Obese subjects display signs of an augmented sympathetic nerve circulation and an increased rate of norepinephrine overflow.<sup>67,68</sup> The increased sympathetic outflow to the kidneys is also responsible for the increased retention of sodium.<sup>69</sup> Recent studies suggest that central renin-angiotensin system (RAS) is capable of modulating the effects of leptin on energy expenditure and blood pressure.<sup>70</sup> It has also been suggested that adiponectin plays a protective role against hypertension via an endothelium-dependent mechanism.<sup>71</sup> The role of insulin-mediated SNS stimulation in the pathogenesis of hypertension is supported by evidence that indicating concomitant decreases in BP

and SNS activity when insulin is lowered by low energy diets in obese patients.<sup>72</sup> Insulin also acts directly on the kidney to stimulate and enhance sodium reabsorption.<sup>73</sup>

Several limitations of the study need to be noted. First, the cross-sectional design of the study restricted the interpretation of the observed associations in terms of cause and effect. Second, in our research, we did not evaluate insulin resistance which is a core component of the pathophysiology of metabolic disorders. In addition, there is also a lack of data on physical activity. This may cause bias and weak interpretation of the results. Finally, our study is limited by geography and sample size. More prospective population-based research should be conducted.

In conclusion, we found that different phenotypes of obesity are markedly associated with hyperglycemia, hypertension, hyperuricemia and dyslipidemia. They are all independent risk factors for metabolic abnormalities despite of the phenotypes. Central obesity with normal weight is more closely associated with hypercholesterolemia, hyperglycemia and hyper LDLemia. General obesity and central obesity have a synergistic effect on the diseases.

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## Disclosure

The authors declare that they have no conflict of interest.

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