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Sex-Based Differences in the Associations Between Obesity- and Lipid-Related Indexes and Hyperuricemia Risk in Patients with Obesity

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Purpose: This study aimed to investigate the association of the triglyceride-glucose index (TyG) and its related parameters with the risk of hyperuricemia in patients with obesity of different sexes.

Patients and Methods: In this cross-sectional study, a total of 951 patients with obesity were included. They were divided into two groups based on their serum uric acid levels, and separate analyses were conducted for males and females. Binary logistic regression analysis using the backward likelihood ratio (LR) approach was performed to investigate the association between hyperuricemia and indicators related to obesity and lipids.

Results: Multivariate logistic regression analysis indicated that, across the overall population, higher quartiles of the TyG and TyG-BMI indexes were significantly associated with an increased risk of hyperuricemia (HUA) after adjusting for confounding factors. Specifically, in the fourth quartile of the TyG index, the odds ratio (OR) for HUA was 3.16 (95% confidence interval [CI]: 1.39–7.18), and for the TyG-BMI index, the OR was 4.06 (95% CI: 1.73–9.52) in the fully adjusted model. In sex-specific analyses, for males, those in the third quartile of the TyG-WC index had a higher likelihood of HUA (OR, 8.13; 95% CI, 2.28–29.01) compared to the lowest quartile. Among females, an elevated TyG index was significantly associated with increased HUA risk, with an OR of 5.13 (95% CI: 1.66–15.92) in the fourth quartile.

Conclusion: Sex-based differences exist regarding the risk factors for hyperuricemia in patients with obesity. An elevated TyG-WC index is linked to an increased risk in males, while an elevated TyG index is associated with an increased risk in females.

Keywords: Obesity-and lipid-related indexes, triglyceride glucose index, hyperuricemia, obesity

Introduction

Hyperuricemia, characterized by elevated serum uric acid (SUA) levels, is linked to disruptions in purine metabolism, excessive production, or inadequate excretion of uric acid.[1,2] With shifts in lifestyle and dietary habits, the prevalence of hyperuricemia has surged, affecting ~20.1% of the US population and 15.1% of the population in China.[3,4] This condition is not considered only a marker, but also a precursor, to a range of diseases—including coronary artery disease, cardiovascular disease, chronic kidney disease, obesity, diabetes, metabolic syndrome, and stroke.[5–11] Obesity, particularly morbid obesity, is strongly associated with higher SUA levels, highlighting the intricate relationship between body weight and uric acid metabolism.[12] The interplay between obesity and hyperuricemia is further complicated by the role of insulin resistance, which represents a key component of metabolic syndromes.

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The triglyceride-glucose index (TyG) index, introduced in 2008, serves as a reliable and straightforward clinical marker of insulin resistance, combining fasting plasma glucose and triglyceride levels.[13] It has been validated as a predictor for various health conditions—including hypertension, diabetes, cardiovascular disease, and diabetic retinopathy.[14–17] The clinical utility of the TyG index extends beyond its standalone value, as it shows enhanced predictive accuracy when combined with other indicators such as body mass index (BMI) or waist circumference.[18–20]

Despite the established links between obesity indexes such as BMI, glycated hemoglobin, total cholesterol, and triglycerides with SUA levels;[21] and the known associations between hyperuricemia and serum lipids and blood glucose levels;[22] comparative studies focusing on the predictive values of the TyG index and related parameters in patients with obesity are currently scares in the literature—particularly ones that are stratified by sex.

This study hypothesizes that the TyG index and its related parameters are significantly associated with the risk of hyperuricemia in patients with obesity, with notable sex-specific differences. We hope that its findings provide a nuanced understanding of the risk factors for hyperuricemia in the context of obesity, and contribute to the development of sex-specific preventive and therapeutic strategies for this patient population.

Material and Methods

Study Population

Medical examination data were collected from the Department of Endocrinology at Shanghai Tenth People's Hospital between January 2017 and October 2020. Initially, 3047 participants were enrolled. However, some were excluded based on the following criteria: (1) age <18 or >60 years, (2) BMI <28 or >40 kg/m^2, (3) lack of documented information on age and BMI, and (4) absence of SUA data. This study is a retrospective cohort study that focused on participants diagnosed with obesity and treated in the endocrine department. The inclusion criteria were as follows: participants aged 18–60 years with a BMI of ≥28 kg/m² and <40 kg/m². After applying these exclusion criteria, the final analysis included data from 951 patients, comprising 406 males and 565 females. A flowchart of the participant selection process is presented in Figure1.

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. As this was a retrospective study, obtaining informed consent from each patient was not required.

Diagnostic Criteria

Hyperuricemia is characterized by elevated blood uric acid (UA) levels. It is diagnosed when the SUA concentration is ≥ 420 μmol/L in men, or > 360 μmol/L in women.[23] In this study, participants were categorized into two groups based on their SUA levels: high UA (HUA) and non-HUA. Individuals in the HUA group were diagnosed with hyperuricemia. Obesity was defined as a BMI of ≥ 28 kg/m^2, according to the Asia-Pacific criteria established by the World Health Organization (WHO).[24]

Laboratory and Clinical Measurements

Blood samples were collected after a 12-hour fast. Biochemical parameters, including UA, fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL), were measured using the Alinity C analyzer (Abbott Laboratories, USA). HbA1c levels were determined using the Tosoh HLC-723 G11 (Tosoh Corporation, Japan), while fasting insulin (FINS) and fasting C-peptide (FCP) were analyzed on the Cobas e 601 (Roche Diagnostics, Switzerland). All instruments were calibrated and operated according to the manufacturers' protocols. Anthropometric data (weight, height, waist circumference(WC), and hip circumference(HC)) were collected following WHO's "Stepwise Approach to Surveillance" (STEPS) guidelines.[25] Weight and height were measured with participants in light clothing and without shoes, and WC and HC were taken using standardized anatomical landmarks. Blood pressure (BP) was measured using an automated BP monitor following American Heart Association (AHA) guidelines.[26] Participants were seated at rest for 5 minutes before measurements, with BP recorded three times on the left arm at one-minute intervals. The average of the three readings was used for analysis.

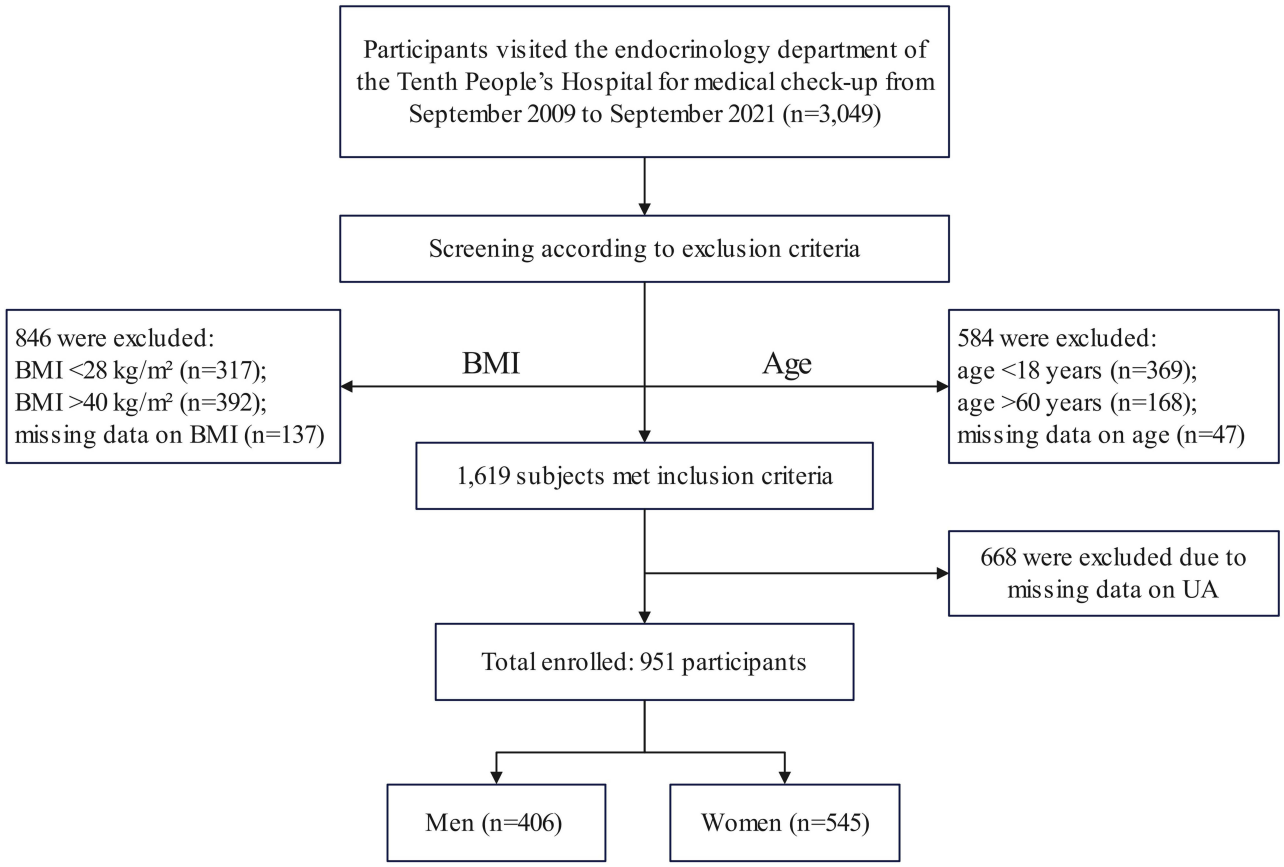

Figure 1 Flowchart of the study population.

It is important to note that the remaining 14 indicators require specific calculations. For example, BMI was calculated by dividing each participant's body mass (kg) by the square of their height (m). The waist-to-height ratio (WHtR) was determined by dividing the WC (m) by height (m), whereas the waist-to-hip ratio (WHpR) was calculated by dividing the WC (m) by HC (m). The body adiposity index (BAI) was calculated using WC and HC, while HC and height determined the abdominal volume index (AVI). LAP was calculated by subtracting a specific number (males: 65 cm, females: 58 cm) from WC and multiplying the result by TG. ABSI was determined through a comprehensive calculation involving WC, BMI, and height. The TyG index was calculated using TG and fasting glucose levels, whereas TyG-BMI, TyG-WC, TyG-WHtR, and TyG-WHpR were obtained by multiplying TyG by BMI, WC, TyG-WHtR, and WHpR, respectively. The TG/HDL cholesterol ratio was defined as TG divided by HDL cholesterol, and the triglyceride–total cholesterol body weight index (TCBI) was calculated using TG, TC, and weight. These calculations were performed using rigorous and well-established academic methods, in order to ensure the accuracy and reliability of the collected data.

All calculations for the 14 indexes were performed according to the following equations:

1. $\mathrm{BMI} = \mathrm{Weight}(kg)/\mathrm{height(m)}^2$
2. $\mathrm{WHtR} = \mathrm{WC(cm)}/\mathrm{height(cm)}$
3. $\mathrm{WHpR} = \mathrm{WC(cm)}/\mathrm{HC(cm)}$
4. $\mathrm{BAI} = \mathrm{HC(cm)}/\mathrm{height(cm)}^{1.5} - 18$[27]
5. $\mathrm{AVI} = [2 \times (\mathrm{WC(cm)})^2 + 0.7 \times (\mathrm{WC(cm)}) - \mathrm{height(cm)})^2]/1,000$[28]
6. $\mathrm{LAP} = (\mathrm{WC(cm)} - 65) \times \mathrm{TG(mmol/L)in\ males} = (\mathrm{WC(cm)} - 58) \times \mathrm{TG(mmol/L)in\ females}$[29]
7. $\mathrm{ABSI} = \mathrm{WC(m)}/[BMI^{2/3}(kg/\mathrm{m}^2) \times \mathrm{height}^{1/2}\mathrm{(m)}$[30]
8. $\mathrm{TyG\ index} = \mathrm{In}[\mathrm{TG(mg/dL)} \times \mathrm{FPG(mg/dL)}/2]$[13]

9. $\mathrm{TyG-BMI} = \mathrm{TyG\,index} \times \mathrm{BMI}(kg/m^2)$[31]
10. $\mathrm{TyG-WC} = \mathrm{TyG\ index} \times \mathrm{WC(m)}$
11. $\mathrm{TyG-WHpR} = \mathrm{TyG\ index} \times \mathrm{WHpR}$
12. $\mathrm{TyG-WHtR} = \mathrm{TyG\,index} \times \mathrm{WHtR}$
13. $\mathrm{TG/HDL\ ratio} = \mathrm{TG(mg/dL)/HDL(mg/dL)}$
14. $\mathrm{TCBI} = \mathrm{TG(mg/dL)} \times \mathrm{TC(mg/dL)} \times \mathrm{Weight(kg)}/1,000$[32]

Statistical Analysis

The Kolmogorov–Smirnov test was used to assess the normality of continuous variables. Normally distributed variables were reported as means (standard deviations), and compared between two groups using the Student's *t*-test. Skewed variables were presented as medians (interquartile range value), and differences between groups were analyzed using the Wilcoxon rank-sum test. Categorical variables were expressed as frequencies (percentages), and compared using the Chi-squared test. To account for multiple comparisons of categorical variables, we used Bonferroni correction. Spearman's rank correlation analysis was conducted to identify the factors associated with hyperuricemia. The Spearman correlation coefficient fell between −0.3 and −0.1 or 0.3 and 0.1, suggesting a modest correlation.

To screen for risk factors of hyperuricemia in patients with obesity, we conducted a bivariate logistic regression analysis. Variables with P-values of < 0.1 in the univariate analysis, as well as those considered clinically relevant, were further investigated in the multivariate analysis using backward selection, based on the likelihood ratio. A multivariate logistic regression model was then created to present the results as odds ratios (OR) with associated 95% confidence intervals (CIs). The models were defined as follows: Model 1 adjusted for age and heart rate; Model 2 further adjusted for HbA1c and FPG; and Model 3 included additional adjustments for TC, TG, HDL, LDL, BAI, and LAP. Statistical analyses were performed using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism 9. Statistical significance was set at two-tailed P-values of <0.05.

Results

Baseline Characteristics of the Total Population with Obesity

Table 1 presents the characteristics of the study participants according to sex-based differences. Of the 951 participants with obesity, 406 were men and 545 were women. The median patient age for both sexes was 31 years. The men had higher mean SUA levels and a higher prevalence of hyperuricemia compared to the women (459 umol/L vs 373 umol/L and 63.5% vs 55.2%, respectively). However, there were no significant differences between the sexes in terms of SP, DP, HR, HbA1c, FPG, 2h-PG, FINS, or FC-P levels. The men had higher TC, TG, and LDL levels; whereas the women had lower HDL levels.

Comparison of Obesity- and Lipid-Related Indexes Between the HUA Non-HUA Groups

Table 2 shows a comparison of the obesity- and lipid-related indexes between the HUA and non-HUA groups, stratified by sex. Patients with hyperuricemia of both sexes had significantly higher BMI, WC, and BAI values. Furthermore, the HUA group showed higher levels of TC, TG, and LDL, as well as lower levels of HDL, compared to the non-HUA group, in both sexes. In women, all obesity and lipid-related indexes differed significantly between the HUA and non-HUA groups. Significant differences were observed between the men in terms of TyG-WC, TyG-BMI, TG-HDL, TCBI, and LAP indicators (P<0.05).

Correlation of UA with Clinical Variables

The correlations between UA levels and various clinical variables were analyzed using Spearman's rank correlation analysis (Table 3). In the overall population, UA levels showed weak negative correlations with age and HDL, and weak positive correlations with BMI, WC, SP, TC, TG, LDL, BAI, TyG, TyG-WHtR, TyG-WHPR, TyG-WC, TyG-BMI, TGtoHDL, and LAP. Among the men, UA levels were weakly negatively correlated with age, HbA1c, FPG, HDL, and ABSI; and weakly

Table 1 Baseline Characteristics of Total Obesity Population

Variables	Total (N=951)	Man (N=406)	Woman (N=545)
Age(years)[b]	31 (10)	31 (9)	31 (11)
HR (beats/min)[b]	83 (16)	84 (18)	82 (15)
SP(mmHg)[b]	132 (22)	137 (23)	130 (21)
DP(mmHg)[b]	84 (15)	84 (16)	83 (15)
UA (umol/L)[a]	410(105)	459 (111)	373(83)
Hyperuricemia[c]	559(58.8)	258(63.5)	301(55.2)
Weight(Kg)[a]	97.0(15.0)	106.9 (13.9)	89.7(11.0)
Height(m)[b]	1.68 (0.14)	1.77 (0.08)	1.63(0.07)
BMI (kg/m^2)[b]	33.8(5.3)	34.4 (5.5)	33.5 (5.2)
WC(cm)[a]	108.0 (10.5)	112.9 (9.6)	104.3 (9.6)
HC(cm)[a]	112.5(7.7)	113.4(7.4)	111.8(7.9)
HbA1c (%)[b]	5.8(1.3)	5.9(1.6)	5.8 (1.2)
FPG (mmol/L)[b]	5.4(1.4)	5.3(1.5)	5.4(1.2)
2h-PG (mmol/L)[b]	7.7(4.2)	7.6(4.3)	7.9(4.0)
FINS (mU/L)[b]	23.1(16.9)	24.4(18.7)	22.1(15.7)
FC-P (ng/mL)[b]	3.76(1.6)	3.92(1.7)	3.63(1.5)
TC (mmol/L)[a]	4.9(1.1)	5.0(1.1)	4.9(1.0)
TG (mmol/L)[b]	1.7(1.1)	1.9(1.2)	1.5(1.0)
HDL (mmol/L)[b]	1.1(0.3)	1.0(0.3)	1.1(0.3)
LDL (mmol/L)[a]	3.0(0.9)	3.1(0.9)	3.0 (0.9)

Notes: Continuous data are presented as means (standard deviations) or medians (interquartile range value) based on the data distribution. Categorical data is presented as numbers-(percentages); [a]Data are means (standard deviations); [b]Data are medians (interquartile range value); [c]Data are numbers(percentage).

Table 2 Comparison Between Obesity- and Lipid-Related Indexes of Obesity Patients with HUA and Non-HUA Group

Variables	Total (N=951)		P-value	Man (N=406)		P-value	Woman (N=545)		P-value
	Non-HUA	HUA		Non-HUA	HUA		Non-HUA	HUA	
Obesity-related index									
BMI(kg/m^2)[a]	33.3(3.2)	34.3(3.2)	<0.001**	33.7(3.3)	34.8(3.2)	0.001**	33.1(3.1)	33.9(3.2)	0.002**
WC(cm)[a]	106.1(10.2)	109.7(10.5)	<0.001**	111.4(9.2)	113.8(9.7)	0.018*	102.7(9.4)	105.5(9.5)	0.001**
WHtR[a]	0.6(0.1)	0.6(0.1)	0.018*	0.6(0.1)	0.6(0.1)	0.420	0.6(0.1)	0.6(0.1)	0.022*
WHpR[a]	0.95(0.07)	1.0(0.1)	0.023*	1.0(0.1)	1.0(0.1)	0.383	0.9(0.1)	0.9(0.1)	0.211
ABSI[b]	7.96(0.67)	8.0(0.5)	0.939	8.1(0.5)	8.0(0.4)	0.038*	7.9(0.7)	7.9(0.6)	0.410
BAI[b]	22.47(5.93)	24.2(6.1)	<0.001**	24.2(6.3)	25.6(6.3)	0.016*	21.0(5.3)	22.1(4.7)	0.001**
AVI[a]	61.0(5.2)	61.6(5.4)	0.072	59.4 (4.5)	59.9(4.7)	0.281	62.0(5.4)	63.1(5.6)	0.027*
Lipid-related index									
TC (mmol/L)[b]	4.7(1.2)	5.0(1.2)	<0.001**	4.8(1.2)	5.1(1.2)	0.008**	4.7(1.2)	4.9(1.3)	0.026*
TG (mmol/L)[b]	1.5(1.1)	1.8(1.1)	<0.001**	1.7(1.1)	2.0(1.3)	0.002**	1.3(1.0)	1.7(1.0)	<0.001**
HDL (mmol/L)[b]	1.1(0.3)	1.0(0.3)	<0.001**	1.1(0.3)	1.0(0.3)	0.013*	1.2(0.3)	1.1(0.3)	0.003**
LDL (mmol/L)[b]	2.9(1.0)	3.1(1.1)	0.002**	3.0(1.1)	3.2(1.1)	0.022*	2.9(1.0)	3.1(1.2)	0.047*
Obesity- and lipid-related index									
TyG index[b]	8.8(1.0)	9.0(0.7)	0.001**	9.0(0.9)	9.1(0.7)	0.452	8.6(0.8)	8.9(0.7)	<0.001**
TyG-WHpR[a]	8.5(1.1)	8.7(1.3)	0.010*	9.1(1.0)	9.1(0.9)	0.432	8.2(1.1)	8.4(0.9)	0.033*
TyG-WHtR[a]	5.7(1.9)	5.8(0.6)	0.004**	5.8(0.7)	5.9(0.6)	0.449	5.6(0.8)	5.8(0.7)	0.004**

(*Continued*)

Table 2 (Continued).

Variables	Total (N=951)		P-value	Man (N=406)		P-value	Woman (N=545)		P-value
	Non-HUA	HUA		Non-HUA	HUA		Non-HUA	HUA	
TyG-WC[b]	9.4(1.4)	9.80(1.5)	<0.001**	10.0(1.6)	10.4(1.4)	0.004*	8.9(1.6)	9.4(1.5)	<0.001**
TyG-BMI[b]	295.6(53.2)	311.5(49.5)	<0.001**	303.4(56.5)	319.2(51.0)	0.030*	289.3(52.5)	307.5(50.3)	<0.001**
TG to HDL[b]	1.3(1.3)	1.7(2.1)	<0.001**	1.6(1.2)	2.0(1.7)	0.001**	1.1(1.1)	1.5 (1.10)	<0.001**
TCBI[b]	205.5(211.7)	281.3(217.4)	<0.001**	265.5(242.1)	364.3(256.5)	<0.001**	173.0(168.6)	234.2(227.7)	<0.001**
LAP[b]	64.7(53.3)	84.1 (57.7)	<0.001**	80.4(58.2)	96.7(68.4)	0.001**	58.1(47.5)	77.5(44.6)	<0.001**

Notes: Continuous data are presented as means (standard deviations) or medians (interquartile range value) based on the data distribution. [a]Data are means (standard deviations); [b]Data are medians (interquartile range value); The p-value represents the difference between the non-HUA group and the HUA group. **P<0.01, *P<0.05.

Table 3 Spearman Correlation of UA Levels with Clinical Variables

Variables	Total	Man	Woman
Age(years)	−0.25**	−0.27**	−0.23**
BMI	0.20**	0.20**	0.13**
WC	0.29**	0.17**	0.14**
HR (beats/min)	0.09*	0.09	0.17*
SP(mmHg)	0.11**	0.08	0.01
DP(mmHg)	0.06	0.03	0.04
HbA1c (%)	−0.09*	−0.31**	0.02
FPG (mmol/L)	−0.06	−0.19**	0.03
TC (mmol/L)	0.10**	0.11*	0.06
TG (mmol/L)	0.24**	0.15**	0.19**
HDL (mmol/L)	−0.24**	−0.16**	−0.17**
LDL (mmol/L)	0.11**	0.10*	0.06
ABSI	0.06	−0.10*	0.03
BAI	0.29**	0.17**	0.14**
AVI	−0.03	0.10*	0.11*
TyG index	0.16**	0.02	0.15**
TyG-WHpR	0.23**	0.02	0.13**
TyG-WHtR	0.16**	0.04	0.17**
TyG-WC	0.30**	0.12*	0.19**
TyG-BMI	0.24**	0.15**	0.19**
TG to HDL	0.27**	0.18**	0.20**
TCBI	0.27**	0.18**	0.12**
LAP	0.29**	0.19**	0.24**

Notes: Statistically significant values are indicated by **P<0.01, *P<0.05.

positively correlated with BMI, WC, TC, TG, LDL, BAI, AVI, TyG-WC, TyG-BMI, TG-to-HDL ratio, TCB index, and LAP. Among the women, UA levels showed weak negative correlations with age and HDL; and weak positive correlations with HR, TG, BAI, AVI, TyG, TyG-WHtR, TyG-WHPR, TyG-WC, TyG-BMI, TGtoHDL, and LAP.

Association of Clinical Variables with HUA

The results of our univariate logistic regression analysis are presented in Supplementary Table 1. As is shown in Figure 2, our multivariate logistic regression analysis (using backward LR methods) revealed significant associations between hyperuricemia and several risk factors. For the overall population, HR (OR, 1.02; 95% CI, 1.01–1.04; P=0.012), TyG

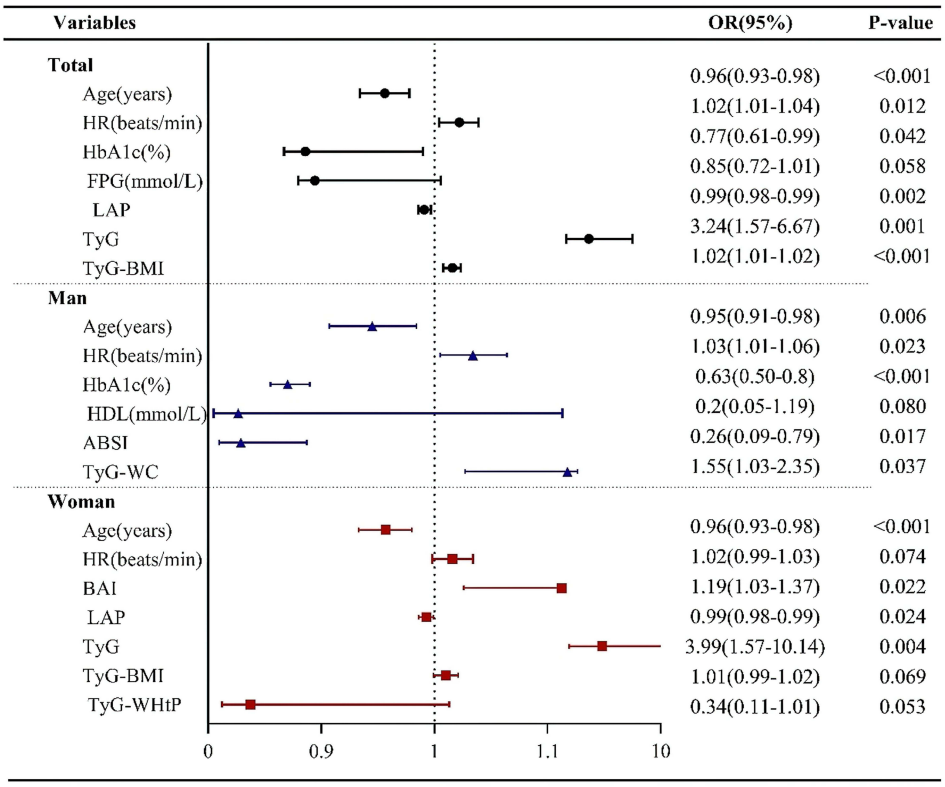

Figure 2 The forest plot shows the odds ratio of multivariate stepwise regression for hyperuricemia.

(OR, 3.24; 95% CI, 1.57–6.67; P=0.001), and TyG-BMI (OR, 1.02; 95% CI, 1.01–1.02; P<0.001) were positively correlated with the risk of HUA

In the male population, the occurrence of HUA was positively associated with HR (OR, 1.03; 95% CI, 1.01–1.06; P<0.001) and TyG-WC (OR, 1.55; 95% CI, 1.03–2.35; P=0.037). For females, HUA showed a positive association with BAI (OR,1.19; 95% CI, 1.03–1.37; P=0.022) and TyG (OR, 3.99; 95% CI, 1.57–10.14; P=0.002).

HUA Prevalence Across TyG-Related Index Quartiles

Figure 3 shows the distribution of HUA cases across the TyG, TyG-WC, and TyG-BMI quartiles in both sexes. In males, the prevalence of HUA was 58.1%, 64.6%, 70.7%, and 58.9% across the TyG index quartiles; 50.6%, 61.4%, 70.9%, and 64.0% across the TyG-WC quartiles; and 52.7%, 61.3%, 69.9%, and 68.5% across the TyG-BMI quartiles. In females, the prevalence of HUA was 37.6%,59.2%, 68.8%, and 56.9% across the TyG index quartiles; 41.0%, 52.1%, 67.2%, and 63.8% across the TyG-WC quartiles; and 43.2%, 52.4%, 58.4%, and 68.5% across the TyG-BMI quartiles.

Dose-Response Relationship Between TyG-Related Indexes and HUA Risk

Table 4 shows the ORs for HUA based on the quartiles of TyG-related indicators associated with the development of HUA. Multivariate-adjusted association analyses were initially adjusted for age and HR (model 1), further adjusted for HbA1c and FPG (model 2), and finally further adjusted for TC, TG, HDL, LDL, BAI, and LAP (model 3). In the overall population, compared to the first quartile, the other three quartiles of TyG and TyG-BMI were strongly associated with HUA (all P for trend <0.05). The adjusted relative risk of HUA increased with higher TyG levels and TyG BMI quartiles. For males, compared to the first quartile, the ORs (95% CIs) for TyG-WC in the third quartile were 2.39 (1.27–4.46) in the unadjusted model, 3.46 (1.69–7.08) in model 1, 5.32 (1.79–15.89) in model 2,

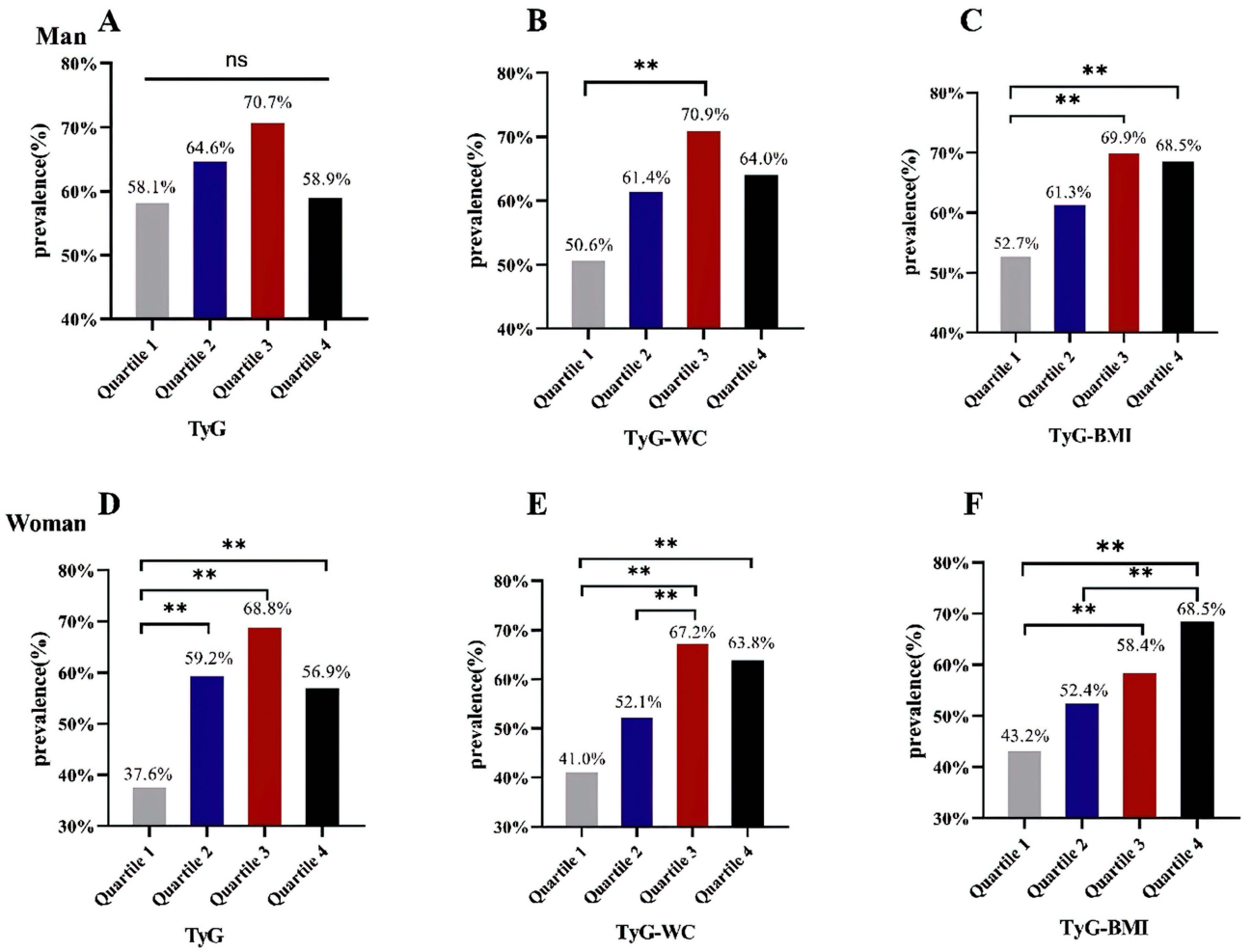

Figure 3 The constituent ratio of hyperuricemia cases across TyG-related index quartiles among men and women. (**A**) prevalence of HUA according to TyG quartiles in men; (**B**) prevalence of HUA according to TyG-WC quartiles in men; (**C**) prevalence of HUA according to TyG-BMI quartiles in man; (**D**) prevalence of HUA according to TyG quartiles in women; (**E**) prevalence of HUA according to TyG-WC quartiles in women; (**F**) prevalence of HUA according to TyG-BMI quartiles in women. ns P≥0.05, **P<0.01.

and 8.13 (2.28–29.01) in model 3. For females, compared to the first quartile, the ORs (95% CIs) for TyG in the fourth quartile were 2.19 (1.32–3.64) in the unadjusted model, 0.95 (0.93–0.97) in model 1, 2.89 (1.28–6.53) in model 2, and 5.13 (1.66–15.92) in model 3.

Table 4 Multivariable-Adjusted ORs and 95% Confidence Intervals of the TyG-Related Indexes Levels Associated with Hyperuricemia

Median[quartile]	Unadjusted	Model 1[a]	Model 2[b]	Model 3[c]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Total: TyG				
Q1 8.29[<8.53]	1(Ref)**	1(Ref)**	1(Ref)**	1(Ref)**
Q2 8.74[8.53–8.89]	1.85(1.27–2.70)**	1.66(1.10–2.52)*	1.48(0.86–2.55)	1.25(0.69–2.26)
Q3 9.12[8.89–9.33]	2.45(1.66–3.62)**	2.795(1.80–4.35)**	2.56(1.46–4.48)**	2.78(1.47–5.26)**
Q4 9.74[>9.33]	1.71(1.17–2.50)**	2.13(1.38–3.29)**	2.79(1.46–5.31)**	3.16(1.39–7.18)**
P for trend	0.005	<0.001	<0.001	0.002

(*Continued*)

Table 4 (Continued).

Median[quartile]	Unadjusted	Model 1[a]	Model 2[b]	Model 3[c]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
TyG-BMI				
Q1 260.72[<279.44]	1(Ref)**	1(Ref)**	1(Ref)**	1(Ref)**
Q2 293.43[279.44–304.84]	1.46(1.01–2.13)*	1.46(0.97–2.22)	0.92(0.53–1.60)	0.95(0.51–1.78)
Q3 316.72[304.84–331.52]	2.47(1.67–3.64)**	2.60(1.69–3.99)**	2.03(1.16–3.57)*	2.23(1.12–4.45)*
Q4 349.72[>331.52]	2.74(1.85–4.06)**	2.83(1.83–4.36)**	2.93(1.61–5.33)**	4.06(1.73–9.52)**
P for trend	<0.001	<0.001	<0.001	<0.001
Man: TyG-WC				
Q1 9.02[<9.52]	1(Ref)	1(Ref)**	1(Ref)**	1(Ref)**
Q2 9.93[9.52–10.28]	1.55(0.85–2.83)	1.35(0.69–2.62)	0.99(0.38–2.61)	1.07(0.37–3.05)
Q3 10.60[10.28–11.03]	2.38(1.27–4.46)**	3.457(1.69–7.08)**	5.32(1.79–15.89)**	8.13(2.28–29.01)**
Q4 11.63[>11.08]	1.73(0.94–3.19)	1.85(0.94–3.63)	2.59(0.94–7.15)	5.29(1.23–22.86)*
P for trend	0.044	0.021	0.019	0.010
Woman: TyG				
Q1 8.24[<8.44]	1(Ref)**	1(Ref)**	1(Ref)*	1(Ref)**
Q2 8.61[8.44–8.70]	2.41(1.45–4.00)**	2.40(1.39–4.16)**	2.17(1.10–4.29)*	1.90(0.90–3.99)
Q3 8.97[8.79–9.25]	3.66(2.17–6.18)**	4.58(2.54–8.28)**	2.91(1.44–5.88)**	4.80(2.03–11.35)**
Q4 9.60[>9.25]	2.19(1.32–3.64)**	0.95(0.93–0.97)**	2.89(1.28–6.53)*	5.13(1.66–15.92)**
P for trend	0.005	<0.001	0.012	0.002

Notes: *P<0.05 **P<0.01.

Discussion

This cross-sectional study revealed significant associations between the TyG index and the risk of developing HUA in patients with obesity, and clarified the differences in this relationship between males vs females. The TyG-WC index was found to be more strongly linked to hyperuricemia in men, whereas the TyG index itself was a key correlate in women. These findings highlight the value of considering sex-specific factors when evaluating the risk of hyperuricemia in patients with obesity.

Our results are consistent with a growing body of literature that highlights the role of obesity—particularly central obesity—in the pathogenesis of hyperuricemia.[33,34] The distribution of adipose tissue, whether visceral or subcutaneous, has been shown to influence uric acid metabolism differently, with visceral fat being more strongly associated with metabolic disorders.[33,35] The introduction of novel obesity indexes such as ABSI, BAI, LAP, and AVI provides a more nuanced understanding of adipose tissue distribution and its impact on metabolic health.[27,29,30,36] One comparative study examined the associations between 10 obesity-related indicators and hyperuricemia in a Taiwanese population, and found that LAP and VAI were the strongest predictors.[37] Another study found that VAI was an effective indicator for the prevalence of hyperuricemia among individuals without metabolic syndrome.[38] In addition, Zhang N. et al found that ABSI, WC, and WHtR were significantly associated with hyperuricemia in males and females.[39]

The TyG index, as a marker of insulin resistance, has been increasingly recognized for its value in predicting metabolic complications such as hyperuricemia.[40,41] Gu et al conducted a longitudinal study to examine the relationship of TyG and its derivatives with the risk of HUA in the general Chinese population.[42] Several previous studies have reported that TyG was positively associated with HUA in patients with diabetic kidney disease[43] and nonalcoholic fatty liver disease (NAFLD).[44] In addition, this index also holds potential for predicting hyperuricemia in patients with hypertension.[45] Liu et al indicated the potential of TG/HDLc and TyG to serve as independent risk indicators in the prevention of HUA.[46] Furthermore, obesity has been shown to play a partial mediating role in the association between the TyG index and hyperuricemia in Chinese adults with hypertension.[47] Despite these findings, there is currently

a scarcity of studies examining the role of the TyG in hyperuricemia within the context of obesity. The potential collinearity between obesity-related indicators and TyG derivatives has often been overlooked. Our study addressed this gap by using stepwise logistic regression to account for collinearity, thereby enhancing the identification of the most significant independent risk factors for hyperuricemia in patients with obesity.

We observed sex-based differences in terms of the risk of developing hyperuricemia in patients with obesity. Su et al also found that obesity-related indexes correlated with hyperuricemia, with a stronger association in women than in men.[37] This sex-based difference may be attributable to variations in fat distribution, glycolipid metabolism, and urate metabolism.[48] Men tend to have more visceral and hepatic adipose tissue, which is associated with higher metabolic risks; while women have higher amounts of peripheral or subcutaneous adipose tissue.[49,50] Furthermore, estrogen's protective effects may foster a more insulin-sensitive environment in women, influencing the TyG index's association with hyperuricemia.[51] These hormonal and metabolic factors, along with the differences in adipose tissue distribution, contribute to the distinct associations observed between the TyG index, TyG-WC index, and hyperuricemia risk across the sexes.

The main strengths of this study include our comprehensive assessment of 14 obesity indexes and their association with hyperuricemia in men and women with obesity. Although these analyses have made important discoveries, they were also subject to certain key limitations worth noting. First, the cross-sectional study design precludes any causal inferences or the establishment of predictive models for the risk of hyperuricemia. Second, our study's findings were limited by its reliance on a patient population recruited from a single clinical institution, which may limit the generalizability of our findings. Third, although our model was adjusted for a number of covariates, we did not have any access to data regarding dietary habits, physical activity, drug history, or family history—all of which are known to affect uric acid levels. Finally, SUA is derived from a single blood sample, and thus only reflects UA levels within a single individual at a certain point in time. Future systematic, large-scale, multicenter prospective studies are therefore warranted to fully elucidate how changes in uric acid levels are associated with various risk factors in patients with obesity.

Conclusion

This study revealed significant associations between all 14 obesity- and lipid-related indexes and the risk of hyperuricemia in patients with obesity. Notably, we observed sex-specific differences in the risk factors for hyperuricemia. Specifically, an elevated TyG-WC index was found to be associated with an increased risk of hyperuricemia in males, whereas an elevated TyG index was associated with an increased risk of hyperuricemia in females. These findings suggest the potential value of incorporating sex-specific approaches in clinical guidelines for managing hyperuricemia risk in obesity.

Abbreviations

SUA, Serum Uric acid; HR, Heart rate; SP, Systolic pressure; DP, Diastolic pressure; BMI, Body mass index; WC, Waist circumference; HC, Hip circumference; WHtR, Waist-height ratio; WHpR, Waist-hip ratio; BAI, Body adiposity index; AVI, Abdominal volume index; ABSI, A body shape index; LAP, Lipid accumulation product; FPG, Fasting plasma glucose; FINS, Fasting insulin; FCP, Fasting C-peptide; HbA1c, Glycated hemoglobin; TC, Total cholesterol; TG, Triglycerides; LDL, Low-density lipoprotein; HDL, High-density lipoprotein; TyG, Triglyceride-glucose index; TyG-WHpR, The product of TyG waist-to-hip ratio; TyG-WC, The product of TyG and waist circumference; TyG-BMI, The product of TyG and body mass index; OR, Odds ratio; CI, Confidence intervals.

Data Sharing Statement

The datasets generated during and analyzed during the current study are not publicly available due to the conditions of the ethical approval but are available from the corresponding author upon reasonable request.

Ethical Approval and Consent to Participate

The study has been approved by the Ethics Committee of Shanghai 10th People's Hospital (approval no. 2012-RES-05). Due to the retrospective design of the study, the requirement for informed consent was waived by the Ethics Committee, and all procedures were conducted in accordance with the ethical standards of the institution and the Declaration of Helsinki. As patient consent to review their medical records was not required by the Ethics Committee of Shanghai 10th People's Hospital, patient confidentiality was strictly maintained, with all data anonymized and securely handled.

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Consent to Publish

All authors gave their consent for publication.

Authors' Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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