Diabetes, Metabolic Syndrome and Obesity

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

TyG-WC Index as a Superior Predictor of Hyperuricemia Risk in the Hypertensive Population: A Prospective Cohort Study

Qin Zhang[1,*], Jian Liu[2,*], Ruize Zhang[3], Changfen Wang[4], Yanyan Song[5], Xi Wang[2], Fanling Zeng[6]

[1]Department of Cardiology, Xi Chang People's Hospital, Xi Chang, Sichuan Province, 615000, People's Republic of China; [2]Department of Cardiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, 400016, People's Republic of China; [3]Dougherty Valley High School, San Ramon, CA, 94582, USA; [4]Department of Cardiology, People's Hospital of Qianxinan Prefecture, Guizhou Province, People's Republic of China; [5]Department of Endocrinology, Chongqing Jianshe Hospital, Chongqing, People's Republic of China; [6]Health Management Ctr, The First Affiliated Hospital of Chongqing Medical University, Chongqing, 400016, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xi Wang; Fanling Zeng, The First Affiliated Hospital of Chongqing Medical University, No. 1 Youyi Road, Yuzhong District, Chongqing, 400016, People's Republic of China, Email 201884@cqmu.edu.cn; zengfanling@hospital.cqmu.edu.cn

Objective: To evaluate the predictive value of the triglyceride-glucose waist circumference index (TyG-WC) for hyperuricemia (HUA) risk in the hypertensive population.

Methods: This prospective cohort study involved 831 hypertensive patients with normal uric acid levels, who underwent continuous health examinations for five years. Participants were categorized into four groups based on baseline TyG-WC quartiles, and the incidence of hyperuricemia was monitored in each group. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) for HUA incidence were calculated using Cox proportional hazards regression analysis. The predictive ability of various TyG indices for HUA was evaluated using receiver operating characteristic curves.

Results: After five years of follow-up, 117 participants developed HUA. The cumulative incidence of HUA was significantly higher in the highest TyG-WC quartile (Q4) compared to the lowest quartile (Q1). The TyG-WC index demonstrated the highest predictive value, with an area under the curve of 0.685 (95% CI: 0.635–0.734) compared to other obesity-related TyG indices. After adjusting for confounding factors, per standard deviation increase in the TyG-WC index was associated with a 1.28-fold higher risk of developing HUA (95% CI: 1.04–1.56, $P < 0.001$).

Conclusion: The TyG-WC index is a robust independent predictor of HUA risk in the hypertensive population. It provides a practical, reliable, and cost-effective tool for the early identification of high-risk individuals in this population.

Keywords: hypertension, hyperuricemia, TyG-WC index, insulin resistance, obesity

Introduction

Hyperuricemia (HUA) is a prevalent condition associated with metabolic syndrome, affecting millions of individuals worldwide. Recent epidemiological data suggest that approximately 14% of Chinese adults were affected by HUA between 2018 and 2019.[1] It has been well established that HUA is not only a primary cause of gout and kidney disorders but also significantly increases the risk of cardiovascular and metabolic diseases.[2,3] Moreover, HUA can lead to multi-organ damage, further underscoring its clinical importance.[4,5] In light of rapid socioeconomic development and lifestyle changes, the prevalence of HUA and its associated socioeconomic burden are on the rise, making the early identification of individuals at high HUA risk essential.

Insulin resistance (IR), a condition characterized by impaired glucose uptake and metabolism, has been closely linked to obesity, metabolic syndrome, hypertension, and cardiovascular diseases.[6] Notably, IR also plays a critical role in the

Received: 6 December 2024
Accepted: 14 February 2025
Published: 3 March 2025

pathogenesis of HUA.[7,8] The triglyceride-glucose (TyG) index, calculated from triglyceride and fasting glucose levels, has recently gained recognition as a reliable surrogate marker of IR.[9] Emerging research has demonstrated a clear correlation between the TyG index and HUA, indicating its potential as a predictive marker for HUA risk. More importantly, when combined with obesity-related measures, such as body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHR), the TyG index (eg, TyG-BMI, TyG-WC, TyG-WHR) shows even greater predictive power for insulin resistance than the TyG index alone.[10,11] Epidemiological studies have demonstrated a high prevalence of hyperuricemia among hypertensive patients, with a significant proportion of these individuals also exhibiting metabolic syndrome, including insulin resistance.[12,13] Therefore, it is essential to further investigate the relationship between the TyG index and HUA risk in hypertensive populations.

Although some cross-sectional studies have examined the relationship between the TyG index and HUA in hypertensive populations,[7,14] there remains a paucity of longitudinal research investigating the association between the TyG index, its derived obesity-related measures, and HUA risk. To address this gap, our prospective cohort study aims to assess the longitudinal association between the TyG-WC index and the risk of HUA in the hypertensive population. The results of this study will provide valuable insights into early detection and prevention strategies for high-risk individuals with hypertension.

Materials and Methods

This prospective cohort study was conducted on 1134 hypertensive patients who underwent annual physical examinations from 1 January 2017 to 31 December 2021. The exclusion criteria for the study were as follows: (1) individuals with hyperuricemia at baseline (serum uric acid levels > 420 μmol/L for both sexes); (2) those with renal insufficiency, urinary tract infections, or other severe illnesses; (3) patients with incomplete data on serum uric acid or TyG index; and (4) individuals lost to follow-up. After applying these criteria, a total of 831 patients (262 men and 569 women) were included in the final analysis. Detailed information on participant selection and exclusion is presented in Figure 1. Participants were categorized into four groups based on the quartiles of their baseline TyG-WC index levels: Q1 (TyG-WC index ≤670.85, n = 208), Q2 (671.11 ≤ TyG-WC index ≤ 736.17,n = 208), and Q3 (736.27 ≤ TyG-WC index ≤ 804.10,n = 208), Q4 (TyG-WC index ≥805.60, n = 207) (Figure 1).

Data Collection and Definition

In our study, general personal information was collected by trained nurses through standardized patient-completed forms, which included but were not limited to age, sex, and the use of medications such as antihypertensive agents, anti-diabetic

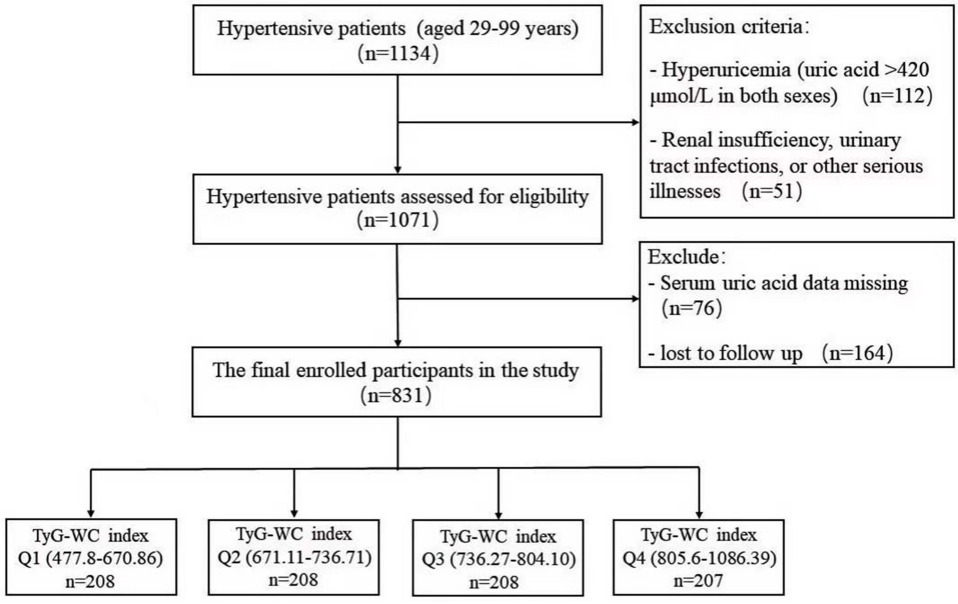

Figure 1 Flowchart of the study population.

agents, and lipid-lowering agents. Blood pressure was measured following standard official protocols, including systolic blood pressure (SBP) and diastolic blood pressure (DBP). Anthropometric measurements were performed by experienced research staff using uniform instruments. The height and weight of all participants were measured in an upright position with light clothing and bare feet, with an error range not exceeding 0.1 cm or 0.1 kg. Waist circumference was measured at the midpoint between the upper edge of the iliac bone and the lower edge of the twelfth rib, with a measurement error not exceeding 0.1 cm. Fasting venous blood samples were collected from participants in the morning and analyzed by laboratory technicians using automated biochemistry analyzers and corresponding reagents, in accordance with established procedures. The relevant laboratory indicators reported included aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine (Cr), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG), and uric acid (UA).

Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or the use of antihypertensive drugs and/or a self-reported history of hypertension. According to the latest guideline for the diagnosis and management of hyperuricemia and gout in China, HUA is diagnosed when serum uric acid (SUA) is>420 μmmol/L (7 mg/dL), regardless of gender. Other indexes were calculated using the following formulas: TyG = Ln [TG (mg/dL) × FPG (mg/dL) / 2]; BMI (kg/m^2) = Weight(kg) / Height^2(m^2); TyG-BMI = TyG (mg/dL) × BMI (kg/m^2); TyG-WC = TyG (mg/dL) × WC(cm); WHR=WC(cm)/Height(cm).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (version 25) and R (software version 4.4.0). Continuous variables with a normal distribution were presented as the mean ± standard deviation (SD), while non-normally distributed variables were expressed as the median with interquartile ranges (quartile 1 - quartile 3). Categorical variables were presented as frequencies (percentages). Analysis of variance (ANOVA) was used to compare the means of baseline characteristics, with pairwise comparisons performed using the least significant difference method. Continuous variables were compared using one-way ANOVA for normally distributed data, while the Kruskal–Wallis test was applied for non-normally distributed data. Categorical variables were expressed as numbers and percentages, and comparisons between groups were performed using the chi-squared test or Fisher's exact test.

Receiver operating characteristic (ROC) curve analysis and the area under the curve (AUC) were used to evaluate the discriminative ability of TyG, TyG-BMI, and TyG-WC for predicting HUA risk. Cumulative survival estimates were calculated using the Kaplan–Meier method and compared using the Log rank test. Univariate and multivariate Cox proportional hazards regression analyses were used to evaluate the relationship between the TyG-WC index and future HUA risk. Risk factors that were statistically significant in the univariate analysis ($P < 0.05$) or clinically significant were selected as covariates in the multivariate Cox model. The TyG-WC index was analyzed both as a categorical variable (using the lowest quartile as the reference) and as a continuous variable (per one SD increment), with results expressed as hazard ratios (HRs) and 95% confidence intervals (CIs). Three distinct models were developed: Model 1, which included no adjustments for covariates; Model 2 was adjusted for age, sex, and BMI; and in Model 3, we adjusted for the covariates in Model 2 as well as BUN, Cr, HDL-C, UA, and the use of antihypertensive drugs. In these models, TyG-WC quartiles were treated as ordinal variables, and the P value for the trend was subsequently calculated. Subgroup analysis was conducted to explore the association between the scaled TyG-WC index and HUA risk in different subgroups, the p-value for interaction was obtained with a likelihood ratio test comparing the main regression analysis with the interaction model. Finally, multivariate-adjusted Cox restricted cubic spline (RCS) analysis was used to further investigate the dose-response relationship between the TyG-WC index and HUA risk.

Results

Baseline Characteristics of Patients

A total of 831 eligible participants were included in the present study. The baseline characteristics of all participants according to the TyG-WC index quartile are shown in Table 1. The mean age was 68 ± 13.6 years, and 68.5% were

Table 1 Baseline Characteristics of Subjects

Variables	TyG-WC				P value
	Q1 (N=208) (477.8–670.86)	Q2 (N=208) (671.11–736.17)	Q3 (N=208) (736.27–804.10)	Q4 (N=207) (805.60–1086.39)	
Demographics					
Age, years	68.39±13.39	67.15±14.11	66.86±13.07	66.68±13.96	0.572
Gender					<0.001
Men	19 (9.1%)	50 (24%)	79 (38%)	114 (55.1%)	
Women	189 (90.9%)	158 (76%)	129 (62%)	93 (44.9%)	
BMI, kg/m^2	21.74±2.21	23.77±1.90	25.30±2.03	27.09±2.82	<0.001
WC, cm	73.04±5.70	81.55±1.90	86.28±4.25	93.62±6.58	<0.001
WHR	0.47±0.04	0.52±0.03	0.54±0.03	0.58±0.05	<0.001
SBP, mmHg	137.14±19.07	143.19±17.53	145.41±18.23	147.05±18.29	<0.001
DBP, mmHg	75.67±12.44	80.77±11.80	82.56±13.80	83.86±13.48	<0.001
Laboratory values					
AST, U/L	18.00(13.00,22.00)	18.00(15.00,23.75)	22.00(16.00,29.75)	24.00(17.00,35.00)	<0.001
ALT, U/L	23.00(19.00,27.00)	21.00(18.00,26.00)	22.00 (19.00,27.00)	23.00(19.00,29.00)	0.045
ALB, g/L	44.95±2.79	45.26±3.00	45.62±3.35	45.83±2.90	0.017
BUN, mmol/L	5.40(4.70,6.20)	5.25(4.50,6.28)	5.1(4.40,6.20)	5.50(4.60,6.70)	0.303
Cr, mmol/L	62.00(55.00,69.00)	62.00(55.00,75.00)	66.00(56.25,78.00)	70.00(57.00,85.00)	<0.001
TC, mmol/L	4.89±0.93	4.81±0.89	4.76±1.09	5.02±1.10	0.044
TG, mmol/L	0.98(0.77,1.30)	1.30(1.02,1.61)	1.54(1.23,2.09)	2.28(1.55,3.12)	<0.001
HDL-C, mmol/L	1.73±0.39	1.52±0.32	1.39±0.32	1.24±0.30	<0.001
LDL-C, mmol/L	2.87±0.80	2.96±0.79	2.98±1.02	3.15±1.01	0.018
FPG, mmol/L	5.30(5.00,5.80)	5.60(5.20,6.00)	5.70(5.30,6.50)	6.00(5.40,6.90)	<0.001
UA, μmol/L	280.35±56.61	299.35±62.54	314.04±59.97	337.14±58.30	<0.001
TyG	8.39±0.41	8.66±0.36	8.92±0.44	9.38±0.63	<0.001
Medications					
Antihypertensive agents	155(75%)	156(75%)	158(76%)	144(69%)	0.37
Anti-diabetic agents	35(17%)	49(24%)	44(21%)	42(20%)	0.39
Lipid-lowering agents	94(45%)	112(54%)	86(42%)	91(44%)	0.063

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HUA, hyperuricemia; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TyG, triglyceride and glucose index; UA, uric acid; WC, waist circumference; WHR,waist-to-height ratio.

women. With the increase of TyG-WC index, BMI, waist circumference, waist-to-height ratio, systolic blood pressure, diastolic blood pressure, AST, creatinine, triglycerides, fasting plasma glucose, and uric acid levels showed an upward trend (P<0.05). In addition, the proportion of males in the high TyG-WC group was significantly higher than that in the low TyG-WC group (P<0.001).

Follow-up results

After a follow-up period of five years, 117 participants developed HUA. Figure 2A illustrates the cumulative incidence of HUA across the four TyG-WC quartiles. Notably, the incidence of HUA was remarkably low in the Q1 group. However, a significant increase in the occurrence of HUA was observed as participants progressed to the Q2 and Q3 groups. When the TyG-WC index reached Q4, the incidence of HUA rose sharply, indicating a significant escalation in the risk of HUA as the TyG-WC index increased.

Predictive Values of TyG-WC Index for the Incidence of HUA

The ROC curve was plotted to measure the predictive power of TyG, TyG-BMI, TyG-WHR, and TyG-WC for HUA (Figure 2B). Table 2 shows the predicted values of HUA. In ascending order, the predictive values of the variables for HUA were as follows: Tyga [95% CI, 0.574–0.683; AUC = 0.628], TyG-BMI (95% CI,0.606–0.707; AUC = 0.656), and

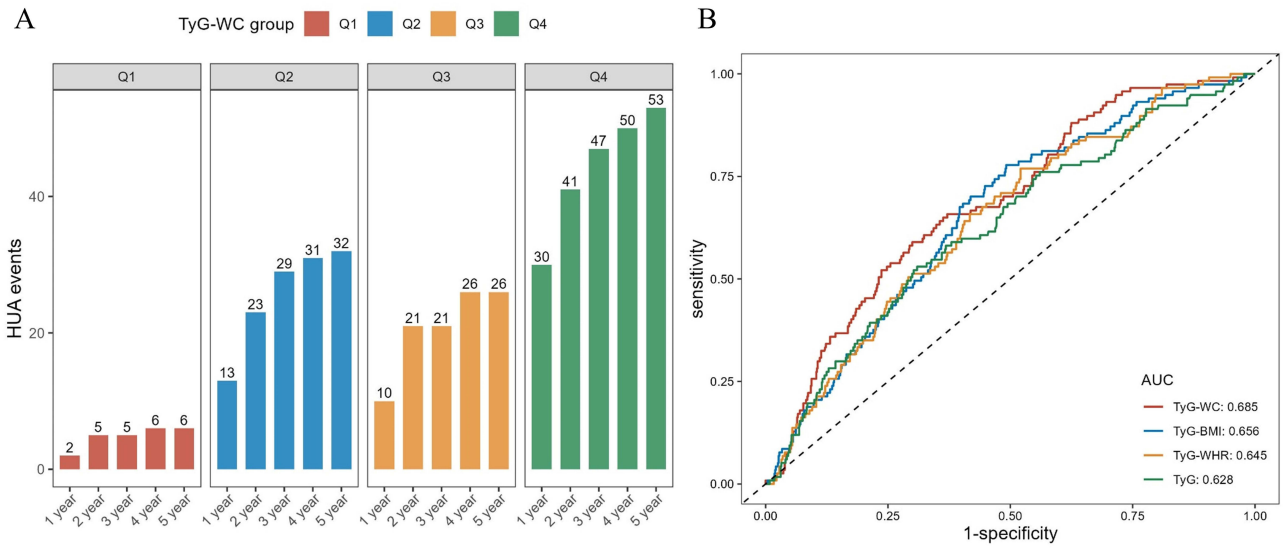

Figure 2 Cumulative incidence of hyperuricemia events according to triglyceride-glucose waist circumference index (TyG-WC) quartile (**A**). Receiver operating characteristic (ROC) curve analysis for the predictive value of TyG-related indices for hyperuricemia (**B**).

TyG-WC (95% CI, 0.635–0.734; AUC =0.685). These results indicate that combining the TyG index with obesity-related markers enhances its predictive value for HUA. Among these, TyG-WC demonstrated the highest predictive value, with a specificity of 0.700 and a sensitivity of 0.590.

Association Between TyG-WC Index and HUA Risk

Over a median follow-up period of five years, a total of 117 (14.1%) HUA events were recorded. Kaplan–Meier survival analysis revealed a significant difference in HUA risk among the TyG-WC quartile groups (Log rank test P < 0.0001), although no significant difference was observed between quartiles Q2 and Q3 (Figure 3A). Consequently, the cumulative risk of HUA in quartiles Q2, Q3, and Q4 was aggregated. Figure 3B illustrates that the HUA risk in Q1 was significantly lower than that of the combined group (Log rank test P < 0.0001).

Table 3 shows the variables associated with the risk of HUA in the univariate Cox regression model. The univariate analysis indicated that in all participants, TyG-WC index, age, sex(female), BMI, WC, BUN, Cr, TG, HDL-C, and UA were crucial factors for HUA risk. The HR of the TyG-WC index for the incidence of HUA was infinitely close to 1.00 (95% CI 1.00–1.01, P< 0.001), then in multivariate Cox regression analysis, the TyG-WC index was scaled. The effect sizes of the association between TyG-WC and the incidence of HUA in the general hypertensive population are listed in Table 4. As a crude model, Model 1 showed that the TyG-WC index was positively related to the incidence of HUA. In Model 2, for each 1-SD increase in TyG-WC, the risk of HUA increased 1.51-fold (HR = 1.51, 95% CI 1.26–1.80, P< 0.001) after adjusting for sex and age. In Model 3, the fully

Table 2 AUC of TyG, TyG-BMI, TyG-WC, and TyG-WHR for Predicting HUA

Variables	AUC	95% CI	Sensitivity	Specificity
TyG	0.628	0.574–0.683	0.530	0.690
TyG-WHR	0.645	0.593–0.696	0.769	0.479
TyG-BMI	0.656	0.606–0.707	0.778	0.508
TyG-WC	0.685	0.635–0.734	0.590	0.700

Abbreviations: AUC, area under the curve; BMI, body mass index; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; WC, waist circumference; WHR, waist-to-height ratio; TyG, triglyceride-glucose index.

https://doi.org/10.2147/DMSO.S509721

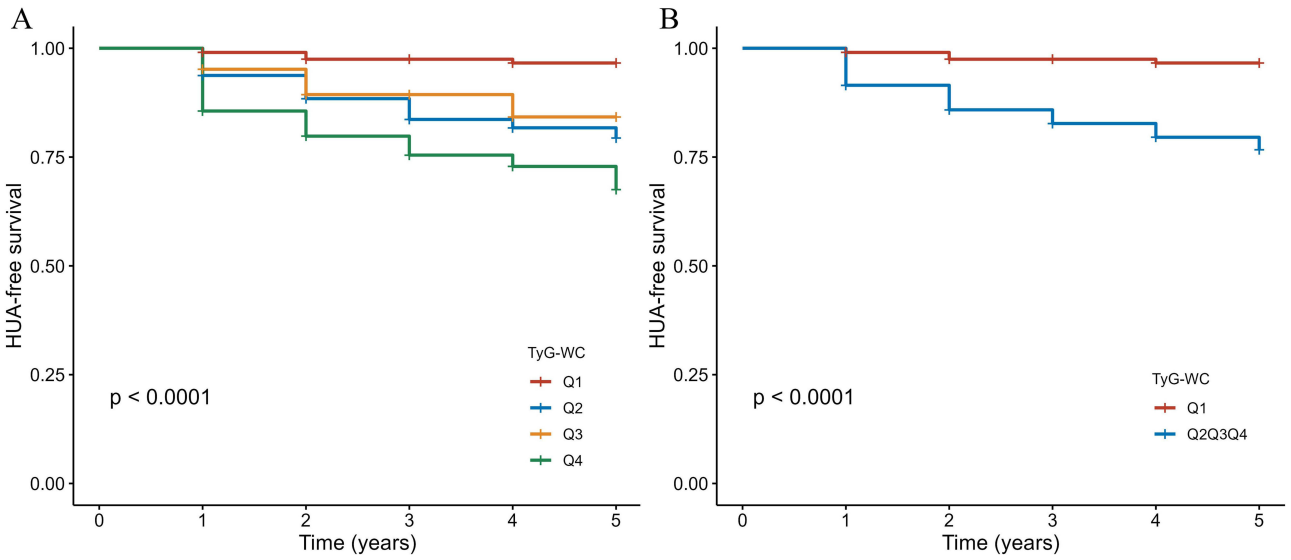

Figure 3 Kaplan-Meier analysis for hyperuricemia (HUA) incidence according to (**A**) TyG-WC quartiles, and (**B**) Q2, Q3, and Q4 were combined.

adjusted HR (95% CI) for the incidence of HUA in all subjects (including sex, age, BUN, Cr, HDL-C, UA, and use of antihypertensive agents) was 1.28 (95% CI 1.04–1.56, P<0.001) for each 1-SD increase in TyG-WC. To enhance the model's predictive capacity for HUA risk, the continuous variable TyG-WC was categorized into quartiles. In Model 3, the risk of HUA was found to be elevated in the Q2, Q3, and Q4 groups compared to the Q1 group,

Table 3 Univariate Cox Regression Model Showing Variables Associated With HUA Risk

Variables	Hazard Ratio	95% CI	P value
TyG-WC	1.00	1.00–1.01	<0.001
Age	1.02	1.00–1.03	0.03
Sex (Female)	0.36	0.25–0.52	<0.001
BMI	1.12	1.06–1.19	<0.001
WC	1.05	1.03–1.07	<0.001
SBP	1.00	0.99–1.01	0.69
DBP	1.00	0.99–1.01	0.86
BUN	1.14	1.07–1.21	<0.001
CR	1.00	1.00–1.01	<0.001
TC	0.86	0.72–1.04	0.12
TG	1.12	1.06–1.18	<0.001
HDL-C	0.37	0.22–0.61	<0.001
LDL-C	0.96	0.79–1.18	0.71
FPG	1.03	0.91–1.16	0.62
UA	1.02	1.02–1.03	<0.001
Antihypertensive agents	0.72	0.49–1.06	0.10
Anti-diabetic agents	0.74	0.51–1.07	0.11
Lipid-lowering agents	0.58	0.34–1.00	0.05

Abbreviations: BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HUA, hyperuricemia; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TyG, triglyceride-glucose index; TyG-WC, triglyceride-glucose waist circumference index; UA, uric acid; WC, waist circumference.

Table 4 Association Between TyG-WC and HUA Risk in Different Models

	Model 1 Hazard Ratio (95% CI)	P value	Model 2 Hazard Ratio (95% CI)	P value	Model 3 Hazard Ratio (95% CI)	P value
TyG-WC(1-SD increase)	1.63 (1.39, 1.92)	<0.001	1.51(1.26,1.80)	<0.001	1.28(1.04,1.56)	<0.001
TyG-WC Quartile						
Q1	Ref	<0.001	Ref	<0.001	Ref	<0.001
Q2	5.91(2.47, 14.1)	<0.001	5.42(2.26,13.00)	<0.001	4.94(1.97,12.40)	<0.001
Q3	4.77(1.96, 11.6)	<0.001	3.93(1.60,9.66)	0.003	3.25(1.24,8.51)	0.017
Q4	10.20 (4.39, 23.70)	<0.001	7.72(3.25,18.3)	<0.001	5.22(2.03,13.50)	<0.001
P for trend	1.70 (1.42, 2.03)	<0.001	1.55(1.28,1.87)	<0.001	1.31(1.07,1.61)	0.010

Notes: Model 1: unadjusted; Model 2: adjusted for age, sex, and body mass index (BMI); Model 3: adjusted for age, sex, body mass index (BMI), blood urea nitrogen (BUN), creatinine (Cr), high-density lipoprotein cholesterol (HDL-C), uric acid (UA), and use of antihypertensive agents.

demonstrating a general trend of increasing risk associated with higher TyG-WC index values. Specifically, the hazard ratios were as follows: Q1 vs Q2: HR 4.94 [95% CI 1.97–12.40]; Q3: HR 3.25 [95% CI 1.24–8.51]; Q4: HR 5.22 [95% CI 2.03–13.50]; with a P for trend < 0.001.

Figure 4A illustrates the relationship between the TyG-WC index and HUA risk as stratified by age, gender, and medications. In gender subgroups, the association is significantly different between females and males. Per 1-SD increase of TyG-WC index is associated with a 1.81-fold higher risk in females, while 1.22-fold in males, with an interaction p-value of 0.025. In other subgroups, no significant differences were found between the TyG-WC index and the HUA risk. Figure 4B reveals the dose-response relationship in the fully adjusted restricted cubic spline regression model with 4 knots, no nonlinear relationship was observed in the TyG-WC index and the risk of HUA.

Discussion

This prospective cohort study employed a systematic evaluation of three TyG-related indices, which serve as proxies for insulin resistance, to ascertain their predictive capacity for the development of HUA in hypertensive patients over five years. The findings of the study indicated a consistent and independent correlation between TyG-related indices and the likelihood of developing HUA, with the TyG-WC index demonstrating a superior predictive capacity. In particular, a one-standard-deviation elevation of the TyG-WC index was found to be associated with a 1.28-fold increase in the incidence of HUA, after adjusting all confounding variables. This is the inaugural cohort study to evaluate the predictive value of

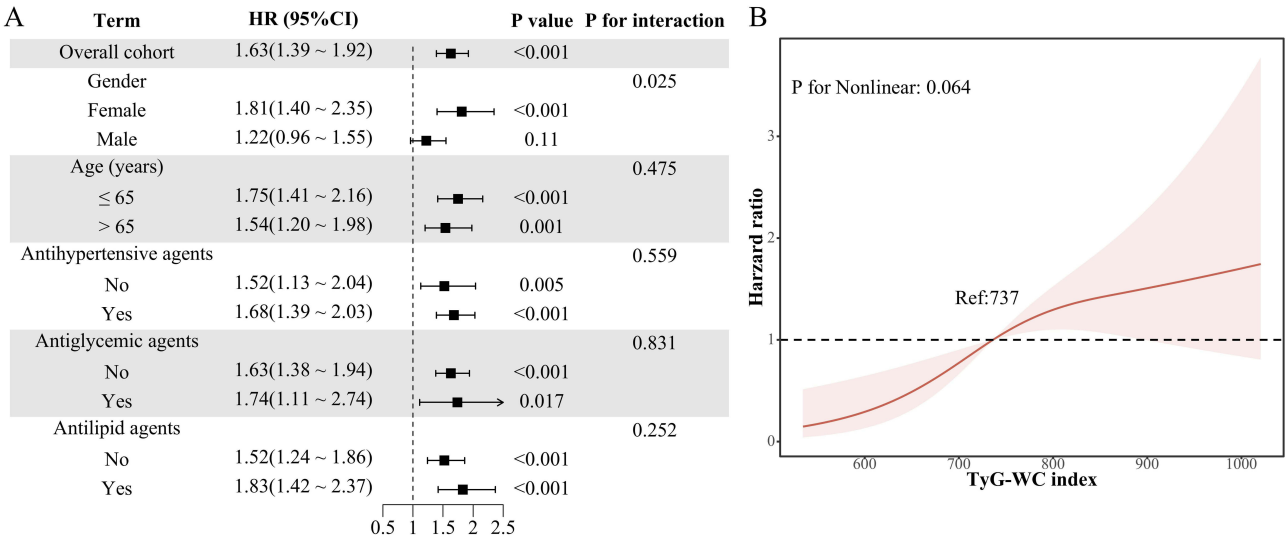

Figure 4 Subgroup analysis (**A**) and dose-response relationship between TyG-WC index and the risk of developing hyperuricemia (**B**).

https://doi.org/10.2147/DMSO.S509721

TyG-related indices for HUA risk in a hypertensive population. Our findings emphasized the significant contribution of hypertension and insulin resistance to the pathogenesis of HUA and also reinforced the value of these indices as a convenient tool for the early identification of individuals at risk of developing HUA.

HUA has been linked to the morbidity and mortality of various cardiovascular diseases.[15–17] Several factors, including age, gender, genetics, stress, metabolic disorders, and medications, have been identified as influencing uric acid levels.[18] It is noteworthy that there is a complex interplay between HUA and blood pressure. A prospective study from the Framingham cohort, which involved 3329 participants, demonstrated that HUA is associated with a 1.17-fold increased risk of developing hypertension.[19] Another prospective study found a positive correlation between HUA and hypertension risk across different genders and races.[20]

Furthermore, a nationally representative study revealed that the prevalence of HUA in the hypertensive population is significantly higher than in the general population, reaching 28.00%.[21] This underscored the urgency for early identification and management of high-risk hypertensive patients. To date, few longitudinal studies have investigated the long-term risk of HUA in patients with hypertension. The current study included 831 hypertensive patients with normal uric acid levels, and the prevalence of HUA was found to be 14.1% after a five-year follow-up period. The complex interrelation between HUA and hypertension may involve several mechanisms, including the activation of the renin-angiotensin system, insulin IR, heightened inflammatory responses, and an increase in oxidative stress.[22,23] Among these factors, IR may be of particular significance.

Substantial clinical and basic research supports the bidirectional relationship between IR and HUA.[24–27] Compensatory hyperinsulinemia following IR stimulates renal Na-H exchange and reduces uric acid excretion. In addition, the inflammatory cascade triggered by IR can impair liver function, disrupt purine metabolism, and increase the activity of xanthine oxidoreductase, which catalyzes uric acid synthesis.[28] In turn, a study showed that pancreatic beta cell dysfunction in the early stages of type 2 diabetes is associated with elevated uric acid levels.[29] Uric acid can cause IR and inflammation by promoting oxidative stress in adipocyte mitochondria and reducing nitric oxide bioavailability.[30,31] Similarly, metabolic abnormalities are more prevalent among hypertensive patients than in the general population. A significant positive linear correlation was identified between systolic blood pressure and HOMA-IR in both prediabetes and normoglycemia.[32] These findings suggest that IR may be a critical factor in the relationship between hypertension and HUA. The TyG index offers a more straightforward, cost-effective, and reliable alternative to traditional methods such as the high-insulin glucose clamp (HEC) and the homeostasis model assessment of IR (HOMA-IR).[33–35] Therefore, using the TyG index to quantitatively assess insulin resistance is a highly feasible approach for guiding the prevention and treatment of HUA in clinical practice.

Compelling evidence has demonstrated that the TyG index holds significant predictive and prognostic value in cardiovascular and metabolic diseases.[36] In this study, we compared the predictive ability of three indicators TyG, TyG-BMI, and TyG-WC for HUA risk. The AUCs for each indicator were 0.628, 0.656, and 0.685 respectively. While all three indicators were correlated with HUA risk, the TyG index combined with obesity measures showed a relatively higher predictive ability, with TyG-WC demonstrating the strongest predictive value. Additionally, it was identified that there is a mediating effect of obesity in the relationship between the TyG index and HUA, with BMI, waist circumference, and hip circumference partially mediating the association.[23] This finding further supported the validity of using the TyG index in combination with obesity-related measures to predict HUA.

Strengths and Limitations

This study has several strengths: (1) it is a prospective cohort study focused on a hypertensive population; (2) confounding factors were rigorously adjusted; (3) the analysis is based on physical examination data, incorporating obesity measures (BMI, WC, WHR) and lipid profiles, which enhances the reliability of the results; and (4) effect sizes were calculated for different gender groups. However, study limitations should also be acknowledged. First, our data lacks information on socioeconomic status, dietary habits, and alcohol consumption, which are unrecorded factors that could act as residual confounders and potentially bias the results. Second, this study is based on physical examination data from a hypertensive population in a single region, leading to selection bias that limits the generalizability of the findings to the broader population. Third, we did not directly measure the HOMA-IR in the study population, preventing

a direct comparison between the TyG index and traditional markers of insulin resistance. Therefore, further studies with more comprehensive data and robust experimental designs are needed to support our conclusions.

Conclusion

In conclusion, our study demonstrates that the TyG-WC index is a superior independent predictor of HUA risk in hypertensive patients. This index offers a convenient, reliable, and cost-effective approach for the early identification of high-risk individuals with hypertension.

Abbreviations

HUA, hyperuricemia; TyG index, triglyceride-glucose index; BMI, body mass index; WC, waist circumference, WHR waist-to-height ratio; IR, insulin resistance.

Data Sharing Statement

Datasets generated during the current study are not publicly available but are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (approval number: 2018-035). Informed consent was obtained in writing from all participants or their legal guardians.

Acknowledgments

Thanks for the data provided by the Health Management Center of the First Affiliated Hospital of Chongqing Medical University. We are also grateful to Dr. Dongying Zhang for her valuable suggestions and discussions, without her help, this work would never have been possible.

Author 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.

Funding

There is no funding to report.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wang L, Peng W, Zhao Z, et al. Prevalence and treatment of diabetes in China, 2013–2018. *JAMA*. 2021;326(24):2498–2506. doi:10.1001/jama.2021.22208
2. Wang H, Zhang H, Sun L, Guo W. Roles of hyperuricemia in metabolic syndrome and cardiac-kidney-vascular system diseases. *Am J Transl Res*. 2018;10(9):2749–2763.
3. Katsiki N, Dimitriadis GD, Mikhailidis DP. Serum uric acid and diabetes: from pathophysiology to cardiovascular disease. *Curr Pharm Des*. 2021;27(16):1941–1951. doi:10.2174/1381612827666210104124320
4. Borghi C, Rosei EA, Bardin T, et al. Serum uric acid and the risk of cardiovascular and renal disease. *J Hypertens*. 2015;33(9):1729–41; discussion1741. doi:10.1097/hjh.0000000000000701
5. Targher G, Byrne CD, Tilg H. NAFLD and increased risk of cardiovascular disease: clinical associations, pathophysiological mechanisms and pharmacological implications. *Gut*. 2020;69(9):1691–1705. doi:10.1136/gutjnl-2020-320622

6. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc Diabetol*. 2018;17(1):122. doi:10.1186/s12933-018-0762-4
7. Liu XZ, Xu X, Zhu JQ, Zhao DB. Association between three non-insulin-based indexes of insulin resistance and hyperuricemia. *Clin Rheumatol*. 2019;38(11):3227–3233. doi:10.1007/s10067-019-04671-6
8. Galindo-Yllu BM, Rojas-Humpire R, Toro-Huamanchumo CJ, Gutierrez-Ajalcriña R, Soriano AN. Serum uric acid is associated with metabolic syndrome and insulin resistance among health personnel from Peru. *J Nutr Metab*. 2021;2021:9933319. doi:10.1155/2021/9933319
9. Mazidi M, Katsiki N, Mikhailidis DP, Banach M. The link between insulin resistance parameters and serum uric acid is mediated by adiposity. *Atherosclerosis*. 2018;270:180–186. doi:10.1016/j.atherosclerosis.2017.12.033
10. Bala C, Gheorghe-Fronea O, Pop D, et al. The association between six surrogate insulin resistance indexes and hypertension: a population-based study. *Metab Syndr Relat Disord*. 2019;17(6):328–333. doi:10.1089/met.2018.0122
11. Ramírez-Vélez R, Pérez-Sousa M, González-Ruíz K, et al. Obesity- and lipid-related parameters in the identification of older adults with a high risk of prediabetes according to the American Diabetes Association: an Analysis of the 2015 health, Well-Being, and Aging Study. *Nutrients*. 2019;11(11):2654. doi:10.3390/nu11112654
12. Ma M, Liu H, Yu J, et al. Triglyceride is independently correlated with insulin resistance and islet beta cell function: a study in population with different glucose and lipid metabolism states. *Lipids Health Dis*. 2020;19(1):121. doi:10.1186/s12944-020-01303-w
13. Janczura M, Dropinski J, Gielicz A, et al. Potential roles of psychological and oxidative stress in insulin resistance: a cohort-based study. *Diabetol Metab Syndr*. 2020;12:58. doi:10.1186/s13098-020-00566-8
14. Shi W, Xing L, Jing L, Tian Y, Liu S. Usefulness of triglyceride-glucose index for estimating hyperuricemia risk: insights from a general population. *Postgrad Med*. 2019;131(5):348–356. doi:10.1080/00325481.2019.1624581
15. Martillo MA, Nazzal L, Crittenden DB. The crystallization of monosodium urate. *Curr Rheumatol Rep*. 2014;16(2):400. doi:10.1007/s11926-013-0400-9
16. Gustafsson D, Unwin R. The pathophysiology of hyperuricaemia and its possible relationship to cardiovascular disease, morbidity and mortality. *BMC Nephrol*. 2013;14:164. doi:10.1186/1471-2369-14-164
17. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. *N Engl J Med*. 2008;359(17):1811–1821. doi:10.1056/NEJMra0800885
18. Lanaspa MA, Ishimoto T, Li N, et al. Endogenous fructose production and metabolism in the liver contributes to the development of metabolic syndrome. *Nat Commun*. 2013;4:2434. doi:10.1038/ncomms3434
19. Sundström J, Sullivan L, D'Agostino RB, Levy D, Kannel WB, Vasan RS. Relations of serum uric acid to longitudinal blood pressure tracking and hypertension incidence. *Hypertension*. 2005;45(1):28–33. doi:10.1161/01.HYP.0000150784.92944.9a
20. Mellen PB, Bleyer AJ, Erlinger TP, et al. Serum uric acid predicts incident hypertension in a biethnic cohort: the atherosclerosis risk in communities study. *Hypertension*. 2006;48(6):1037–1042. doi:10.1161/01.Hyp.0000249768.26560.66
21. Wang L, Chao J, Zhang N, et al. A national study exploring the association between triglyceride-glucose index and risk of hyperuricemia events in adults with hypertension. *Prev Med Rep*. 2024;43:102763. doi:10.1016/j.pmedr.2024.102763
22. Ponticelli C, Podestà MA, Moroni G. Hyperuricemia as a trigger of immune response in hypertension and chronic kidney disease. *Kidney Int*. 2020;98(5):1149–1159. doi:10.1016/j.kint.2020.05.056
23. Sun J, Sun M, Su Y, et al. Mediation effect of obesity on the association between triglyceride-glucose index and hyperuricemia in Chinese hypertension adults. *J Clin Hypertens*. 2022;24(1):47–57. doi:10.1111/jch.14405
24. Han T, Lan L, Qu R, et al. Temporal relationship between hyperuricemia and insulin resistance and its impact on future risk of hypertension. *Hypertension*. 2017;70(4):703–711. doi:10.1161/hypertensionaha.117.09508
25. Zong J, Sun Y, Zhang Y, et al. Correlation between serum uric acid level and central body fat distribution in patients with type 2 diabetes. *Diabetes Metab Syndr Obes*. 2020;13:2521–2531. doi:10.2147/dmso.S260891
26. Dawson J, Wyss A. Chicken or the egg? Hyperuricemia, insulin resistance, and hypertension. *Hypertension*. 2017;70(4):698–699. doi:10.1161/hypertensionaha.117.09685
27. Adachi SI, Yoshizawa F, Yagasaki K. Hyperuricemia in type 2 diabetic model KK-A(y)/Ta mice: a potent animal model with positive correlation between insulin resistance and plasma high uric acid levels. *BMC Res Notes*. 2017;10(1):577. doi:10.1186/s13104-017-2897-x
28. Facchini F, Chen YD, Hollenbeck CB, Reaven GM. Relationship between resistance to insulin-mediated glucose uptake, urinary uric acid clearance, and plasma uric acid concentration. *JAMA*. 1991;266(21):3008–3011. doi:10.1001/jama.1991.03470210076036
29. Simental-Mendía LE, Simental-Mendía E, Rodríguez-Morán M, Guerrero-Romero F. Hyperuricemia is associated with the increase of insulin release in non-obese subjects with normal glucose tolerance. *Endocr Res*. 2017;42(1):1–5. doi:10.3109/07435800.2016.1155597
30. Baldwin W, McRae S, Marek G, et al. Hyperuricemia as a mediator of the proinflammatory endocrine imbalance in the adipose tissue in a murine model of the metabolic syndrome. *Diabetes*. 2011;60(4):1258–1269. doi:10.2337/db10-0916
31. Lanaspa MA, Sanchez-Lozada LG, Choi YJ, et al. Uric acid induces hepatic steatosis by generation of mitochondrial oxidative stress: potential role in fructose-dependent and -independent fatty liver. *J Biol Chem*. 2012;287(48):40732–40744. doi:10.1074/jbc.M112.399899
32. Quesada O, Claggett B, Rodriguez F, et al. Associations of insulin resistance with systolic and diastolic blood pressure: a study from the HCHS/SOL. *Hypertension*. 2021;78(3):716–725. doi:10.1161/hypertensionaha.120.16905
33. Wang T, Lu J, Shi L, et al. Association of insulin resistance and β-cell dysfunction with incident diabetes among adults in China: a nationwide, population-based, prospective cohort study. *Lancet Diabetes Endocrinol*. 2020;8(2):115–124. doi:10.1016/s2213-8587(19)30425-5
34. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *J Clin Endocrinol Metab*. 2010;95(7):3347–3351. doi:10.1210/jc.2010-0288
35. Minh HV, Tien HA, Sinh CT, et al. Assessment of preferred methods to measure insulin resistance in Asian patients with hypertension. *J Clin Hypertens*. 2021;23(3):529–537. doi:10.1111/jch.14155
36. Tao LC, Xu JN, Wang TT, Hua F, Li JJ. Triglyceride-glucose index as a marker in cardiovascular diseases: landscape and limitations. *Cardiovasc Diabetol*. 2022;21(1):68. doi:10.1186/s12933-022-01511-x