


Association of three insulin resistance indices with hypertension and body weight among Uyghur adults in rural areas of Xinjiang, China

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Abstract

Obesity and insulin resistance are significant contributors to hypertension. There is a high prevalence of obesity among Uyghurs in the rural areas of Xinjiang, China. Therefore, this study aimed to explore the association between insulin resistance indices and hypertension according to different body weights in rural Uyghur residents of Xinjiang, China. A total of 12 813 local Uyghur residents were recruited for the study. Excluding those with incomplete data and those using antihypertensive, lipid-lowering, or glycemic drugs, 9577 permanent residents were eligible for the study. Three insulin resistance indicators were calculated: triglyceride to high-density lipoprotein cholesterol ratio, product of fasting triglyceride and glucose (TYG), and metabolic score for insulin resistance. Multivariate logistic regression analysis was performed to estimate the association between the three non-insulin-based insulin resistance indices and the risk of hypertension for different body weights. TYG was significantly associated with hypertension in the normal-weight group, particularly in women. In the obese group that was obese, all three indicators were associated with hypertension. Since TYG was associated with hypertension in the groups with normal weight and obesity, it may be useful as a reference indicator for insulin resistance. This indicator may provide a basis for the identification and management of hypertension risk among adults in the Uyghur population.

KEYWORDS

hypertension, insulin resistance indices, obesity

1 | INTRODUCTION

Hypertension is an important cause of cardiovascular disease and poses a serious health burden worldwide.¹ It is estimated that 31.1% of adults (1.39 billion) worldwide have hypertension.² The Chinese population accounts for 20% of the world's population, exerting an important impact on the worldwide prevalence of hypertension.³

Accumulating evidence suggests that insulin resistance (IR) plays a crucial role in the development of hypertension.^{4,5}

Traditional insulin-based IR assessment tools, such as the hyperinsulinemic/euglycemic clamp (HEC)⁶ and homeostasis model assessment of IR (HOMA-IR) index,⁷ are not widely used in primary clinical practice due to their invasiveness, complexity, low practicality, and poor reproducibility.^{8,9} Therefore, a simpler, more accurate, and

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practical IR index is needed to enable early screening for risk of hypertension.

Recent studies have focused on several non-insulin-based indicators of IR, such as the triglyceride (TG) and high-density lipoprotein cholesterol (HDL-c) ratio (TG/HDL-c), product of fasting TG and glucose level (TYG), and metabolic score of IR (METS-IR), which can be calculated using simple conventional biochemical indicators.¹⁰ Many clinical and epidemiological studies have shown an association between non-insulin-based IR indices and hypertension.^{11,12} However, these associations according to different body weights have not been reported in rural Uyghur residents of Xinjiang, China. Xinjiang is located in the far northwest of China and has a disadvantaged economic status. Insulin tests are expensive and difficult to perform in economically disadvantaged regions. Therefore, in rural areas of Xinjiang, it is necessary to identify a simple IR index that is significantly associated with hypertension. The characteristic diet of rural Uyghur residents is rich in salt, fat, and carbohydrates, leading to a high prevalence of obesity.¹³ Therefore, we aimed to explore the association between IR indicators and hypertension at different body weights. Especially in normal-weight individuals, these findings are expected to provide an important reference to reduce hypertension risk based on IR and provide a basis for the hierarchical management of hypertension and obesity.

2 | METHODS

2.1 | Study participants

A total of 12 813 Uyghur residents from the rural region of Xinjiang were recruited for this study, between 2016 and 2020. A multi-stage (prefecture-county-township-village Interview) stratified cluster random sampling method was used to select participants. The inclusion criteria were as follows: Uyghur residency for at least 6 months; and age ≥ 18 years. The exclusion criteria were as follows: self-reported use of antihypertensive, lipid-lowering, or glycemic drugs; and incomplete data. A total of 9577 individuals were included in this study. The participant inclusion process is illustrated in Figure 1.

This study was approved by the Ethics Committee. All participants provided informed consent.

2.2 | Interview

Each participant was interviewed in person. The interview included items on demographic characteristics (age, sex, occupation, and educational level), behavior and lifestyle (smoking and alcohol drinking), and disease history. Smoking was defined as currently smoking more than 100 cigarettes before the interview.¹⁴ Alcohol consumption was defined as drinking alcoholic beverages (beer, red wine, and white wine) at least twice a month or active continuous drinking.¹⁵

2.3 | Anthropometric and biochemical measurements

Trained examiners measured participant height, weight, and waist circumference (WC). Blood pressure was measured after a 5-min rest using an electronic sphygmomanometer (HEM-7051; Omron, Dalian, China), three times at 30-s intervals. The average value was noted. Overnight fasting blood samples were collected. Serum levels of fasting plasma glucose (FPG), total cholesterol (TC), TG, low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c) were measured using a biochemical autoanalyzer.

2.4 | Definitions

Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg according to the Guidelines for Prevention and Treatment of Hypertension in China (revised in 2018).¹⁶ Participants diagnosed with hypertension at the hospital were advised to provide diagnostic certificates. According to the regulations of the Working Group on Obesity in China,¹⁷ body mass index (BMI) values of 18.5–23.9 and ≥ 24.0 kg/m² are considered normal-weight and elevated-weight, respectively. Abdominal obesity and elevated-WC were both defined as a WC ≥ 85 cm in men and ≥ 80 cm in women. The waist-to-height ratio (WtHR) was defined as the WC divided by height. Non-insulin-based IR indices were calculated using the following formulae:

$$\text{TYG} = \text{Ln}[\text{fasting TG level (mg/dL)} \times \text{FPG level (mg/dL)} / 2]^{18}$$

$$\text{TG/HDL-c ratio} = \text{TG level divided by HDL-c level}^{19}$$

$$\text{METS-IR} = \text{Ln}[(2 \times \text{FPG level}) + \text{TG level}] \times \text{BMI} / (\text{Ln}[\text{HDL-c level}])^{20}$$

2.5 | Statistical analysis

Continuous variables are described as mean \pm standard deviation, while categorical variables are shown as number (percentage). Independent sample *t*-test and χ^2 test was used to compare the population mean and rate/ratio, respectively. Binary logistic regression was used to analyze the associations between the IR indices and hypertension. TYG, TG/HDL-c ratio, and METS-IR were classified into four quartiles, with the lowest quartile used as the reference. Model 1 was unadjusted; Model 2 was adjusted for age, educational level, occupation, smoking, alcohol drinking, and history of diabetes, hyperlipidemia, coronary heart disease, stroke, or kidney disease. Statistical significance was set at $p < 0.05$. STAR software (an online crowdsourcing platform in mainland China powered by www.wjx.cn) was used to establish the database, and IBM SPSS Statistics for Windows, Version 26.0. (Armonk, NY, USA: IBM Corp) was used for statistical analyses. Graphs were constructed using GraphPad Prism software, Version 8.0. (GraphPad Software, San Diego, California USA, www.graphpad.com).

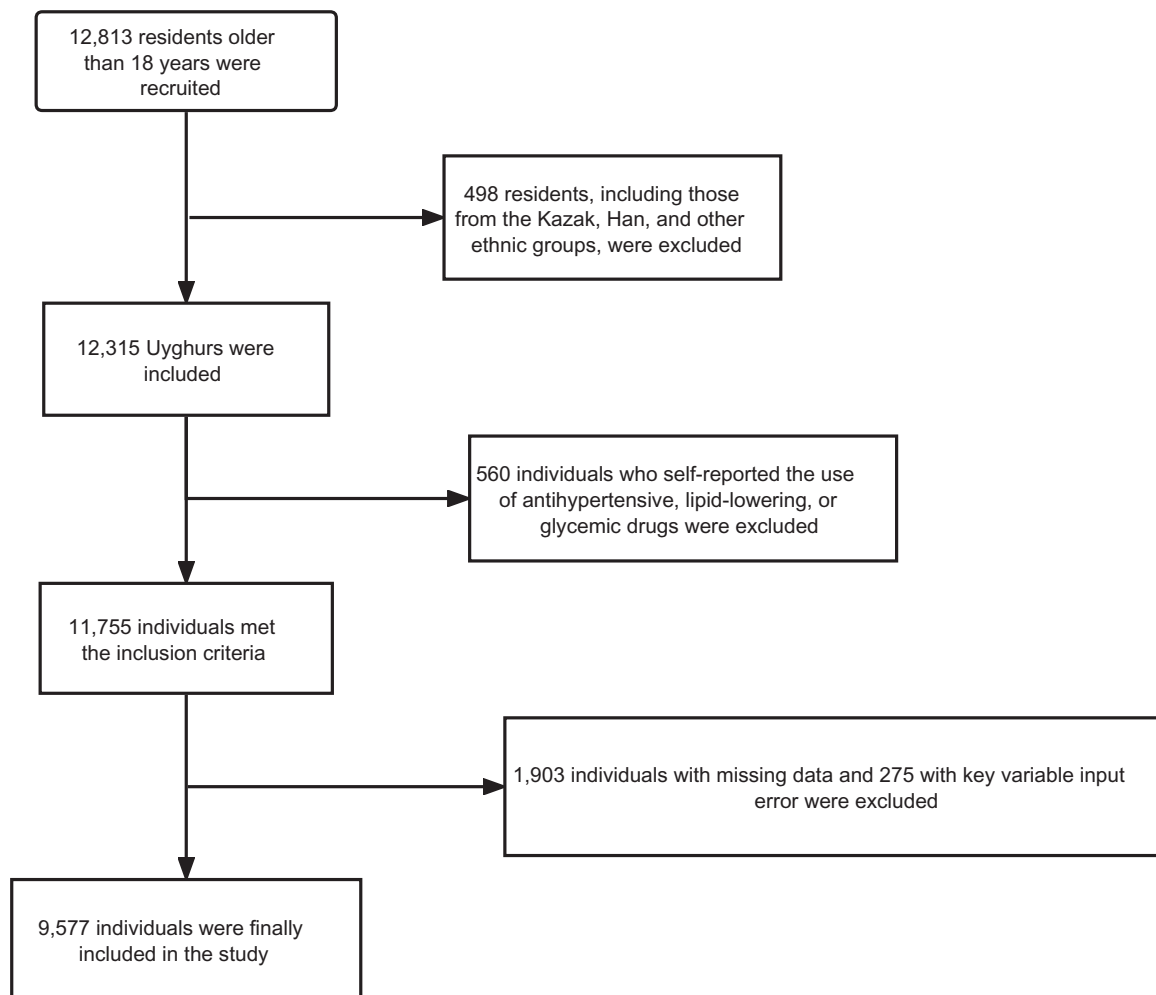


FIGURE 1 Flow chart of participant recruitment and selection process.

3 | RESULTS

3.1 | Population characteristics

This study included 9577 rural Uyghur residents. The participant inclusion process is illustrated in Figure 1. Overall prevalence of hypertension was 29.71%; 31.49% in males and 27.94% in females.

3.2 | Hypertension groups

People with hypertension (hypertension group) were older than those without (non-hypertension group) (mean \pm standard deviation, 52.85 \pm 13.92 vs. 42.55 \pm 12.37 years, respectively), and the different sexes showed the same results (mean \pm standard deviation: In males: 52.14 \pm 14.70 vs. 43.54 \pm 12.70 years; In females: 53.62 \pm 12.94 vs. 41.60 \pm 11.98 years, respectively). Body mass index, waist circumference; waist-to-height ratio, fasting plasma glucose, total cholesterol, triglyceride, low-density lipoprotein cholesterol, TG/HDL-c ratio, TYG, and METS-IR were significantly higher in the hypertension group than in

the non-hypertension group ($p < 0.001$). However, there was no significant intergroup difference in HDL-c level ($p = 0.534$, $p = 0.444$, and $p = 0.596$).

In the hypertension group, 5.66% of the participants had a high school degree or higher education level, 86.57% were farmers, and 12.27% were smokers. In the non-hypertension group, 8.65% of the participants had a high education level, 83.93% were farmers, and 14.84% were smokers. The prevalence of diabetes, hyperlipidemia, and coronary heart disease was higher in the hypertension than in the non-hypertension group ($p < 0.001$). The clinical characteristics of the participants are shown in Table 1.

3.3 | Weight, hypertension, and insulin resistance indices

The prevalence of hypertension increased with increasing non-insulin-based IR indices in the different weight groups (Figure 2). In the normal and elevated BMI group, the prevalence of hypertension showed a significant increasing trend in ascending quartiles of TYG, TG/HDL-c and

TABLE 1 Participant clinical characteristics according to hypertension

Characteristics	Overall (n = 9577)		Male (n = 4783)		Female (n = 4800)	
	Non-hypertension	Hypertension	Non-hypertension	Hypertension	Non-hypertension	Hypertension
Participant count	6732 (70.29)	2845 (29.71)	3277 (68.51)	1506 (31.49)	3459 (72.06)	1341 (27.94)
Age, years	42.55 ± 12.37	52.85 ± 13.92	43.54 ± 12.70	52.14 ± 14.70	41.60 ± 11.98	53.62 ± 12.94
BMI, kg/m ²	25.83 ± 4.48	28.25 ± 5.13	25.79 ± 4.20	27.61 ± 4.60	25.86 ± 4.73	28.97 ± 5.59
WC, cm	90.97 ± 13.55	98.26 ± 14.87	92.83 ± 13.04	98.19 ± 13.56	89.21 ± 13.77	98.33 ± 16.22
WHR	0.56 ± 0.09	0.61 ± 0.10	0.55 ± 0.08	0.59 ± 0.08	0.57 ± 0.09	0.63 ± 0.11
SBP, mmHg	119.89 ± 11.67	154.04 ± 18.34	121.06 ± 11.66	152.40 ± 17.21	118.78 ± 11.56	155.87 ± 19.36
DBP, mmHg	70.86 ± 8.99	87.11 ± 13.81	70.58 ± 9.18	86.34 ± 13.71	71.13 ± 8.81	87.96 ± 13.87
FPG, mmol/L	4.92 ± 2.04	5.42 ± 2.61	5.05 ± 2.32	5.46 ± 2.62	4.80 ± 1.72	5.36 ± 2.59
TC, mmol/L	4.64 ± 1.22	5.01 ± 1.37	4.73 ± 1.28	4.97 ± 1.48	4.55 ± 1.15	5.06 ± 1.25
TG, mmol/L	1.65 ± 1.26	2.03 ± 1.51	1.84 ± 1.40	2.11 ± 1.55	1.48 ± 1.07	1.95 ± 1.45
HDL-c, mmol/L	1.57 ± 0.63	1.58 ± 0.69	1.52 ± 0.62	1.53 ± 0.68	1.61 ± 0.65	1.63 ± 0.70
LDL-c, mmol/L	2.63 ± 0.83	2.82 ± 0.90	2.68 ± 0.84	2.80 ± 0.91	2.58 ± 0.82	2.83 ± 0.88
TG/HDL-c	2.78 ± 2.54	3.39 ± 3.18	3.19 ± 2.90	3.60 ± 3.09	2.38 ± 2.06	3.15 ± 3.26
TYG	8.54 ± 0.72	8.82 ± 0.75	8.66 ± 0.73	8.86 ± 0.77	8.42 ± 0.68	8.78 ± 0.73
High school or above	573 (8.65)	159 (5.66)	272 (8.42)	113 (7.58)	301 (8.86)	46 (3.49)
Farmers	5564 (83.93)	2431 (86.57)	2729 (84.20)	1286 (86.31)	2835 (83.68)	1145 (86.87)
Smoking	999 (14.84)	349 (12.27)	979 (29.90)	341 (22.67)	20 (0.58)	8 (0.60)
Drinking	303 (4.50)	143 (5.03)	293 (8.95)	141 (9.38)	10 (0.29)	2 (0.15)
Diabetes	73 (1.08)	80 (2.81)	35 (1.07)	33 (2.19)	38 (1.10)	47 (3.50)
Hyperlipidaemia	1961 (29.13)	1193 (41.93)	1154 (35.25)	668 (44.41)	807 (23.33)	525 (39.15)
Kidney disease	40 (0.59)	13 (0.46)	27 (0.82)	10 (0.66)	13 (0.38)	3 (0.22)
History of CVD ^a	139 (2.06)	163 (5.73)	50 (1.53)	56 (3.72)	89 (2.57)	107 (7.98)

Note: Values are shown as n (%) or mean ± standard deviation.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; TYG, product of fasting triglyceride and glucose; WC, waist circumference; WHtR, waist-to-height ratio.

^aIncluding coronary heart disease and stroke.

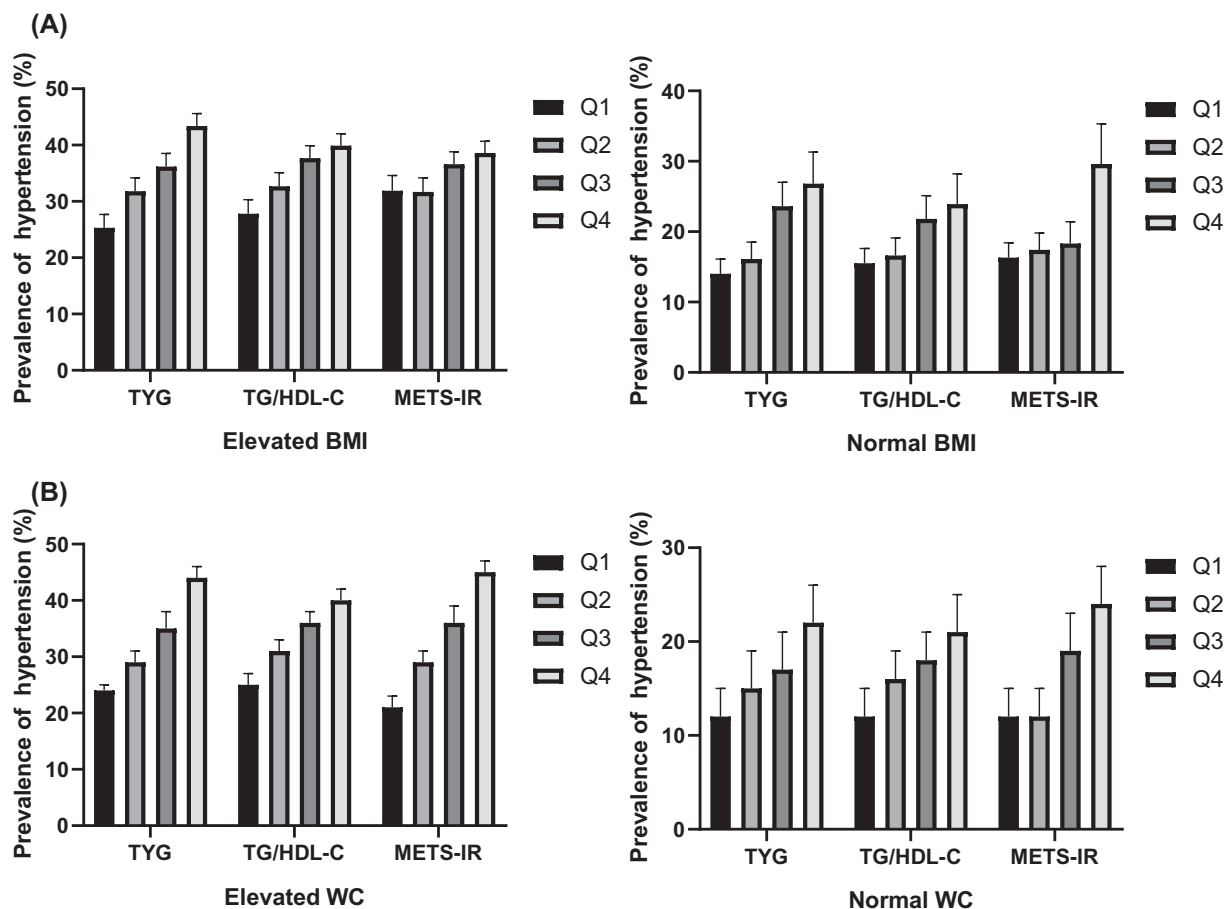


FIGURE 2 Prevalence of hypertension by quartiles of the three non-insulin-based IR indices, according to (A) BMI and (B) WC.

Note: BMI, body mass index; HDL-c, high-density lipoprotein cholesterol; IR, insulin resistance; METS-IR, metabolic score for insulin resistance; Q, quartile; TG, triglyceride; TYG, product of fasting triglyceride and glucose; WC, waist circumference. Normal BMI, 18.5–23.9 kg/m²; elevated BMI, ≥ 24.0 kg/m². Elevated WC, ≥ 85 cm in men and ≥ 80 cm in women.

METS-IR (Figure 2A). The same results were found in the normal WC and elevated WC groups (Figure 2B).

In the unadjusted logistic regression analysis Model 1, TYG, and METS-IR were associated with hypertension in the normal-weight group ($p = 0.001$). All three indicators were significantly associated with hypertension in the elevated BMI and -WC groups ($p < 0.001$). The results of the unadjusted binary logistic regression of Model 1 are shown in Figure S1.

After adjusting for confounders (as detailed in the methods) in the normal BMI group, the odds ratio (OR) for hypertension in the highest quartile of TYG was 1.776 (95% confidence interval [CI], 1.196–2.636; $p = 0.004$) overall, 3.063 (95% CI, 1.556–6.029; $p = 0.001$) in women, and 1.737 (95% CI, 1.058–2.852; $p = 0.029$) in men (Figure 3A). In the normal WC group, only TYG was associated with hypertension in women ($p = 0.001$). The OR for hypertension in the fourth quartile of TYG was 6.297 (95% CI, 2.032–19.521) in women (Figure 3B). All three indicators were significantly associated with hypertension in the elevated BMI and WC groups ($p < 0.001$). The ORs for hypertension in the highest quartile of the three non-insulin-based IR indices in Model 2 are shown in Figure 3.

The three cut-off points for TG/HDL-c ratio, TYG, and METS-IR in the different groups are shown in Table S1.

The number of participants with hypertension in each quartile is presented in Table S2.

The ORs for the continuous variables and the second and third quartiles are shown in Table S3.

The results of the multiple linear regression of the relationship between the three non-insulin-based IR indices and blood pressure, in the different BMI and WC groups, are shown in Table S4.

The clinical conditions of the different BMI and WC groups are presented in Table S5.

4 | DISCUSSION

In this cross-sectional study, we evaluated the association between three non-insulin-based IR indices and hypertension for different body weights. TYG was significantly associated with hypertension in the normal-weight group, particularly in women. In the group that was obese, all three indicators were associated with hypertension. TYG was

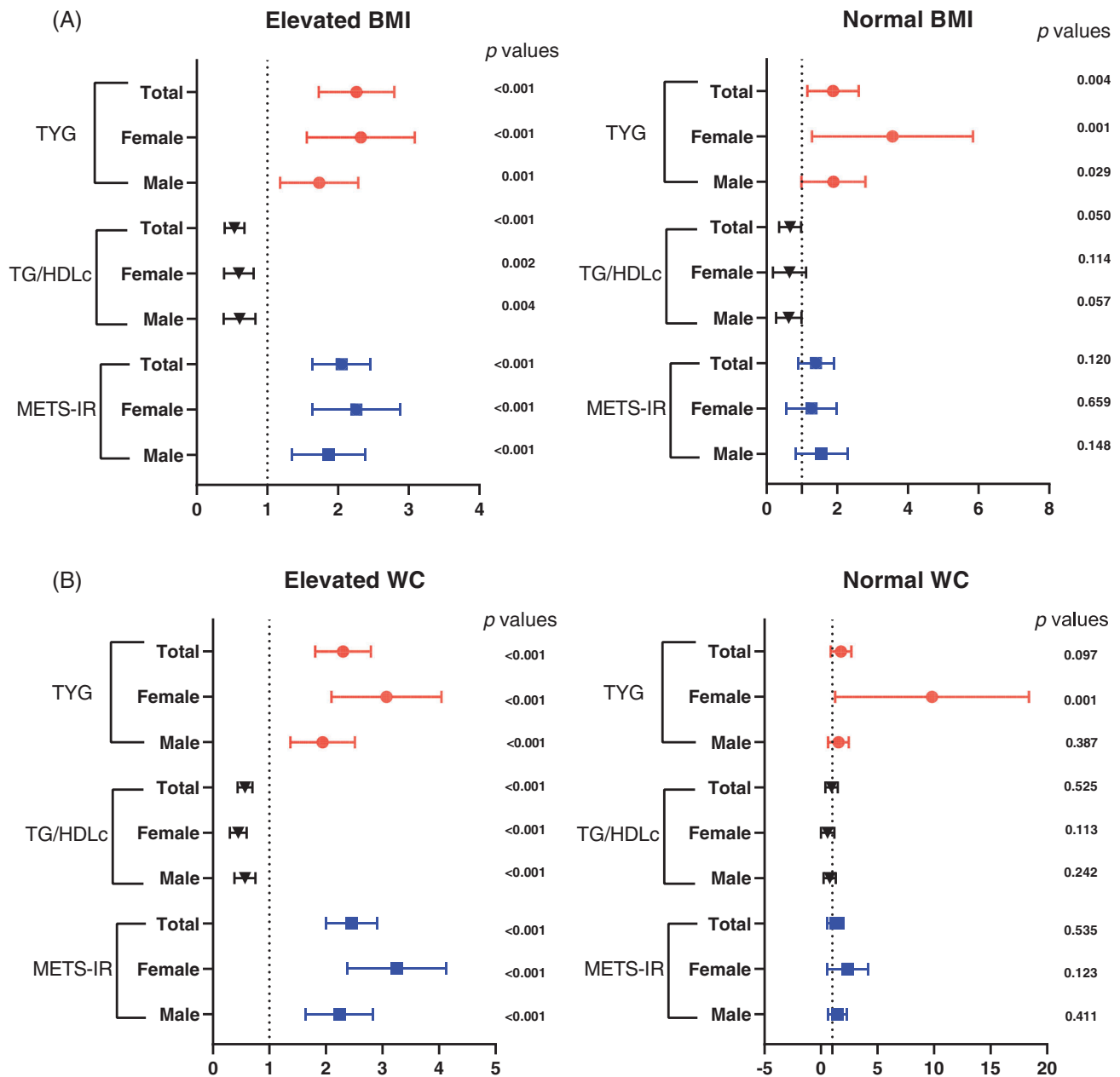


FIGURE 3 Odds ratios for hypertension in the highest quartiles of the three non-insulin-based IR indices in Model 2, according to (A) BMI and (B) WC.

Note: HDL-c, high-density lipoprotein cholesterol; IR, insulin resistance; METS-IR, metabolic score for insulin resistance; TG, triglyceride; TYG, product of fasting triglyceride and glucose.

associated with hypertension in both the groups with normal-weight and obesity. Therefore, TYG may be a potential reference indicator for hypertension risk screening in Uyghur adults.

Recently, several studies have shown that IR indices (TYG, TG/HDL-c ratio, and METS-IR) are clinically important for the prevention of hypertension and metabolic diseases. TYG has been proposed as a surrogate for IR, which correlates with the hyperinsulinemic/euglycemic clamp test result,²¹ homeostasis model assessment of IR index,¹⁹ fat distribution, and subclinical atherosclerosis.²² The TG/HDL-c ratio is

associated with hyperinsulinemia²³ and has been proposed as a simple marker of IR in clinical practice.²⁴ The METS-IR is a novel alternative IR index validated for essential hypercholesterolemia. It also has good diagnostic and predictive performance for detecting type 2 diabetes and prehypertension.²⁵

Previous studies explored the associations between hypertension, IR, and obesity. However, only a few have focused on the relationship between IR and hypertension at different body weights.²⁶ This study explored the association between three non-insulin-based IR

indices and hypertension according to body weight in the Uyghur > population.

We found that TYG was significantly associated with hypertension in the group with normal weight. Similar results were reported by a large cohort study in which TYG was significantly associated with subsequent risk of cardiovascular disease in individuals with normal weight.²⁷ TYG was also associated with cardiovascular risk factors in a cross-sectional study of children with normal weight and adolescents.²⁸ Another important finding of our study was that the association between TYG and hypertension in the group with normal weight was more common in women than in men, which is consistent with previous findings. A cohort study showed that IR was associated with the development of hypertension in women but not men.²⁹ This sex difference may be related to estrogen levels.³⁰ Our study found no differences in HDL-c level between the non- and hypertension groups in the rural Xinjiang population with normal weight. Therefore, HDL-c-related indicators, TG/HDL-c ratio, and METS-IR were not associated with hypertension in this population.

Current public health strategies focus on reducing the risk of hypertension in overweight and individuals who are obese. The risk of hypertension in individuals with normal weight is often ignored.³¹ Since metabolic abnormalities in individuals with normal weight are more likely to be overlooked, it is crucial to accurately identify IR to reduce the risk of hypertension in this population.

Our study demonstrated significant associations between the three non-insulin-based IR indices and hypertension in the group with obesity. This suggests that IR plays a more critical role in the development of hypertension in individuals who are obese than in individuals with normal weight. This result is consistent with those of previous reports.³² Obesity and hypertension are characterized by increased spill over from the kidneys.³³ Recent evidence has shown that IR, particularly in the presence of visceral fat, can stimulate and increase sodium and urate reabsorption at the tubular level, leading to increased blood pressure.³⁴ This may provide an etiological basis for the management of hypertension, specifically targeting IR-driven metabolic abnormalities among individuals who are obese. In our study, TYG was significantly associated with hypertension in participants who are obese. Therefore, the measurement of TYG in the whole population of rural areas of Xinjiang is of great significance for the management of hypertension.

To the best of our knowledge, this is the first large-scale population-based study to examine the relationship between three non-insulin-based IR indices and hypertension according to body weight in the rural areas of Xinjiang. This study provides a reference for screening for hypertension in rural residents of Xinjiang.

Our study had some limitations. First, it was a cross-sectional study; thus, it was not possible to determine the causal time series for the three indicators of hypertension. Second, we were unable to perform direct hyperinsulinemic/euglycemic clamp for IR measures. Third, there may be some recall bias in the self-reports of drug use. Therefore, further prospective studies are required to confirm our findings.

AUTHOR CONTRIBUTION

All authors were involved in developing the study design, data acquisition, data management, and interpretation of results. MYD wrote the manuscript. MRL, YYZ, HJ, RDS, and DYS proposed research ideas and designed research schemes. SXY, LSY, and HX helped establish the database and undertook all the statistical analysis of the data. GH involved in designing, editing, and review. All authors have approved the final version of this submission.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest associated with this work.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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