

# Correlation between non-insulin-based insulin resistance indexes and the risk of prehypertension: A cross-sectional study

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## Abstract

The authors aimed to characterize the relationships between non-insulin-based insulin resistance (IR) indexes and the risk of prehypertension, and to compare their abilities to identify prehypertension. The authors recruited 3274 adults who did not have hypertension and were not taking hypoglycemic or lipid-lowering medications. The triglyceride-to-high-density lipoprotein-cholesterol ratio (TG/HDL-C), fasting triglyceride and glucose index (TyG), and metabolic score for IR (METS-IR) were calculated. Bivariate Spearman's correlation analysis and multiple logistic analysis were used. The area under the receiver operating characteristic (ROC) curve was used to compare the ability of the three indexes to identify prehypertension. Systolic and diastolic blood pressure (BP) positively correlated with TG/HDL-C ( $r = .272, P < .001$ ), TyG ( $r = .286, P < .001$ ), and METS-IR ( $r = .340, P < .001$ ) in the entire cohort. Multiple logistic analysis showed that the proportion of prehypertension in the third and fourth quartiles of the TG/HDL-C (Q3 vs. Q1: odds ratio (OR) = 1.527, 95% confidence interval (CI): 1.243–1.988; Q4 vs. Q1: OR = 1.580, 95% CI: 1.231–2.028), TyG (Q3 vs. Q1: OR = 1.519, 95% CI: 1.201–1.923; Q4 vs. Q1: OR = 1.658, 95% CI: 1.312–2.614), and METS-IR (Q3 vs. Q1: OR = 1.542, 95% CI: 1.138–2.090; Q4 vs. Q1: OR = 2.216, 95% CI: 1.474–3.331) were significantly higher than in the lowest quartiles. The areas under the curves and 95% CIs for the identification of prehypertension were .647 (.628–.667) for TG/HDL-C, .650 (.631–.669) for TyG, and .683 (.664–.702) for METS-IR, respectively. Thus, non-insulin-based IR indexes (TG/HDL-C, TyG, and METS-IR) are significantly associated with the risk of prehypertension. Furthermore, METS-IR is better able to identify prehypertension than TG/HDL-C and TyG. These non-insulin-based IR indexes might assist with the prevention of hypertension in primary care and areas with limited medical resources.

## KEYWORDS

fasting triglyceride and glucose index, insulin resistance, metabolic score for insulin resistance, prehypertension, triglyceride-to-high-density lipoprotein-cholesterol ratio

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## 1 | INTRODUCTION

Prehypertension, also referred to as high-normal blood pressure (BP), is defined using a systolic BP of 120–139 mmHg and/or a diastolic BP of 80–89 mmHg,<sup>1,2</sup> and affects 25%–50% of adults worldwide.<sup>3</sup> According to the latest China Hypertension Survey, approximately 435.3 million people  $\geq 18$  years of age have prehypertension in mainland China.<sup>4</sup> Multiple prospective cohort studies and meta-analyses have demonstrated that individuals with prehypertension are at two- to three times higher risk of progression to chronic hypertension,<sup>5,6</sup> and at higher risks of coronary artery disease, stroke, and cardiovascular disease (CVD), when compared to normotensive individuals.<sup>7</sup> Hence, the early identification of individuals at high risk of prehypertension and targeted interventions are important for the prevention of hypertension and CVD. However, BP is not routinely measured in all health checkups. In addition, the use of additional simple, and reliable tools for the identification of prehypertension would supplement BP measurement and may be particularly important for the prevention of hypertension in the community.

Insulin resistance (IR), a common metabolic disorder, is associated with higher risks of hypertension<sup>8</sup> and prehypertension.<sup>9–11</sup> Therefore, the evaluation of insulin sensitivity might also be regarded as a means of screening for a high risk of prehypertension. However, the hyperinsulinemic euglycemic clamp (HEC), the gold-standard method of assessing insulin sensitivity, has some limitations, including its invasiveness, complexity, and the time it takes, which makes it impractical for use in the clinic and epidemiological studies.<sup>12</sup>

Recently, a number of non-insulin-based indexes have been developed to assess IR, including the triglyceride-to-high-density lipoprotein-cholesterol ratio (TG/HDL-C),<sup>13</sup> fasting triglyceride and glucose index (TyG),<sup>14</sup> and metabolic score for IR (METS-IR).<sup>15</sup> However, there have been few studies regarding the relationships between these indexes and prehypertension, and the published findings have been contradictory.<sup>16,17</sup> Therefore, we performed a cross-sectional study to characterize the relationships of TG/HDL-C, TyG, and METS-IR with prehypertension; and to compare their abilities to identify prehypertension in community-dwelling adults from Chengdu, southwest China.

## 2 | METHODS

### 2.1 | Study participants

We performed a cross-sectional study between January 2011 and December 2013. Adults of  $\geq 18$  years old were recruited at the Physical Examination Department, Pidu district People's Hospital, Chengdu, Sichuan Province, southwest China. Individuals with a history of hypertension and/or a mean clinic BP  $\geq 140/90$  mmHg were excluded, as were those taking hypoglycemic or lipid-lowering medications, because these factors notably influence fasting plasma glucose (FPG), triglyceride (TG), and cholesterol concentrations. The recruitment of participants is described in Figure 1. The study was conducted

according to the principles of the Declaration of Helsinki<sup>18</sup> and was approved by the ethics committee of West China Hospital, Sichuan University.

### 2.2 | Physical examination and collection of medical history

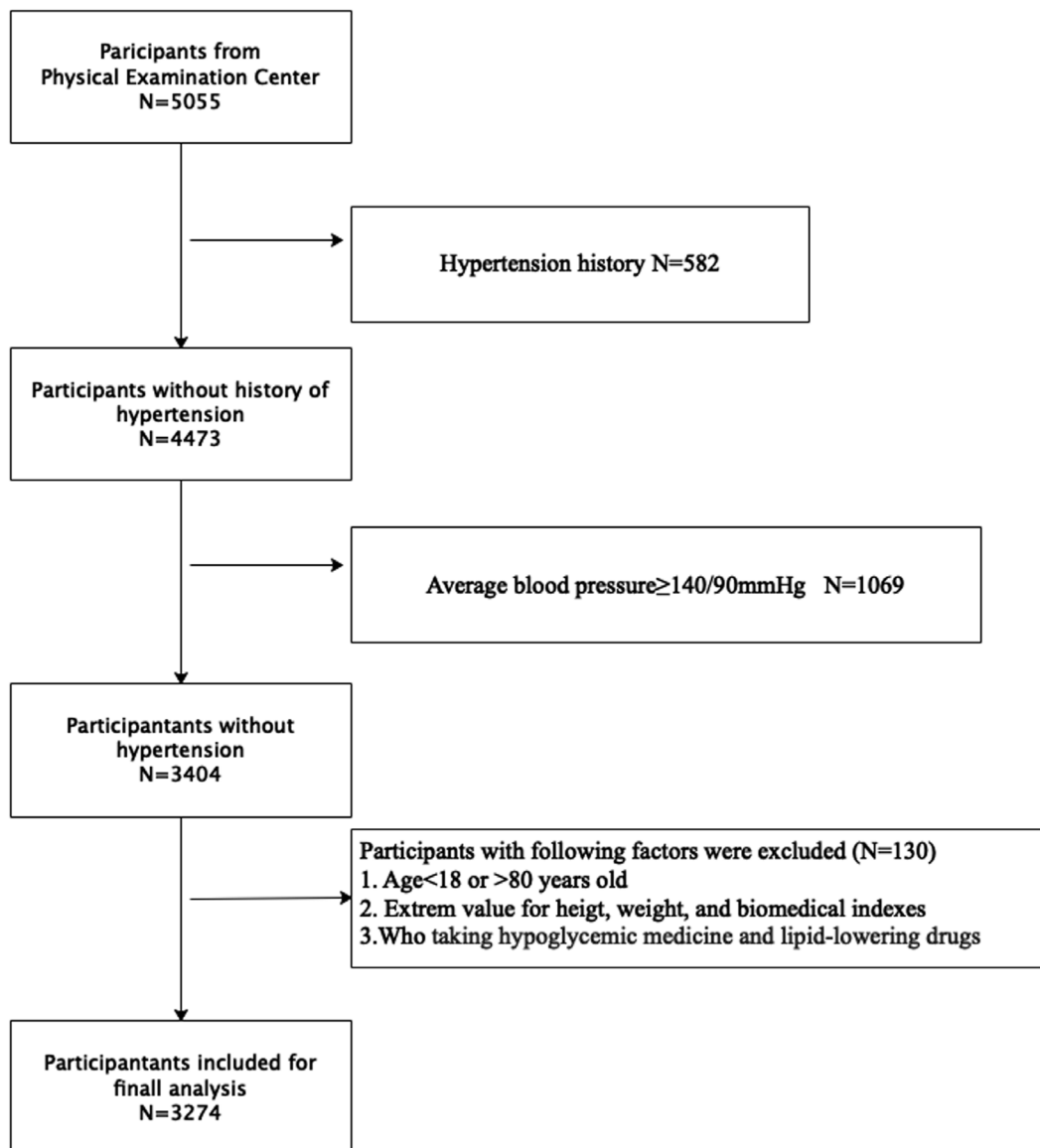
Information regarding the basic characteristics, medical history, and therapies for chronic diseases, including hypertension and diabetes mellitus (DM), was collected by well-trained investigators. Physical examinations (height, body mass, and BP) were conducted in a quiet room at a temperature of  $\sim 25^\circ\text{C}$ . Calibrated electronic sphygmomanometers (Omron HEM-7200, Kyoto, Japan) were used to measure BP in the clinic, after a 5-min rest. The systolic and diastolic BPs were measured three times using the right arm in a seated position, and the mean values were calculated. Blood samples were collected in the morning after 8 h of overnight fasting, and the FPG, TG, total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C) concentrations were measured using an automatic biochemical analyzer.

### 2.3 | Definitions

Hypertension was defined using a mean systolic BP  $\geq 140$  mmHg and/or a diastolic BP  $\geq 90$  mmHg, the use antihypertensive therapy, or a previous diagnosis of hypertension. Prehypertension was defined using an SBP of 120–139 mmHg and/or a DBP of 80–89 mmHg, without the use of an antihypertensive drug. Normal BP was defined using an SBP  $< 120$  mmHg and a DBP  $< 80$  mmHg.<sup>2</sup> DM was defined using a previous diagnosis or FPG  $\geq 7.0$  mmol/L this time.<sup>19</sup> Body mass index (BMI) was calculated as body mass/height<sup>2</sup> ( $\text{kg}/\text{m}^2$ ). The non-insulin-based IR indexes were calculated as follows: TG/HDL-C = TG (mg/dL)/HDL-C (mg/dL)<sup>13</sup>; TyG =  $\text{Ln}[\text{fasting TG (mg/dL)} \times \text{FPG (mg/dL)} / 2]$ <sup>14</sup>; and METS-IR =  $\text{Ln}[(2 \times \text{fasting FPG (mg/dL)} + \text{TG (mg/dL)}) \times \text{BMI} / (\text{Ln}[\text{HDL-C (mg/dL)}])]$ .<sup>15</sup>

### 2.4 | Statistical methods

SPSS 26.0 statistical software (IBM, Inc., Armonk, NY, USA) was used for the analyses. Continuous, normally distributed data are expressed as mean  $\pm$  standard deviation (SD), and non-normally distributed data are expressed as median [interquartile range (IQR)]. Categorical variables are expressed as frequency (%). Continuous datasets were compared using the independent-samples *t*-test or the Mann-Whitney *U* test, as appropriate, and the chi-square test was used to compare categorical datasets among the groups. Bivariate Spearman's correlation analysis was used to characterize the relationships between the non-insulin-based IR indexes and BP, and univariate logistic analysis



**FIGURE 1** Flow diagram for study participant inclusion

was used to identify risk factors for prehypertension. The participants were also categorized according to quartiles of the non-insulin-based IR indexes, with the lowest quartiles being used as the references. This categorization was performed as follows: quartile 1 (Q1):  $\leq .503$ , quartile 2 (Q2):  $.504-.759$ , quartile 3 (Q3):  $.760-1.217$ , and quartile 4 (Q4):  $\geq 1.218$  for TG/HDL-C; Q1:  $\leq 7.979$ , Q2:  $7.980-8.328$ , Q3:  $8.329-8.757$ , and Q4:  $\geq 8.758$  for TyG; and Q1:  $\leq 27.234$ , Q2:  $27.235-30.834$ , Q3:  $30.835-35.489$ , and Q4:  $\geq 35.490$  for METS-IR. Multiple logistic regression analysis was used to analyze the relationships between the quartiles of each non-insulin-based IR index with prehypertension, after adjustment for age, sex, BMI, smoking status, alcohol consumption status, and DM, using the forced entry method in the regression model. Finally, the area under the receiver operating characteristic (ROC) curve was used to compare the abilities of the indexes to identify prehypertension. Furthermore, the optimal cutoff value, Youden index (YI), positive predictive value (PPV), and negative predic-

tive value (NPV) were calculated for each index.  $P < .05$  was considered to represent statistical significance.

### 3 | RESULTS

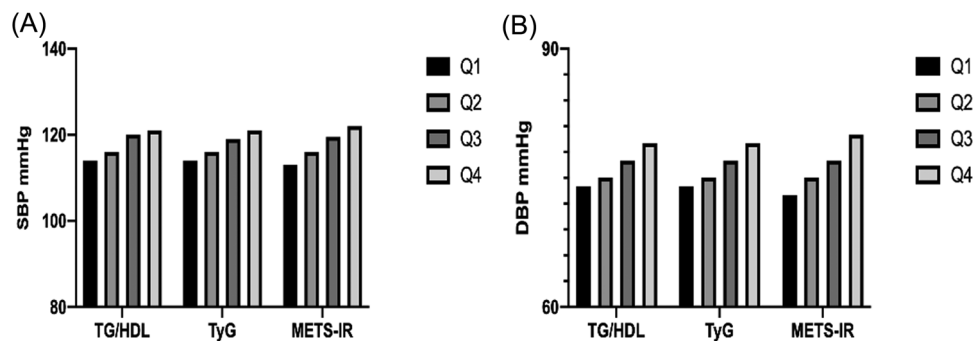
#### 3.1 | Basic characteristics of the participants

The baseline characteristics of the normotensive and prehypertensive participants are presented in Table 1. The age, height, body mass, BMI, SBP, DBP, FPG, TG, TC, LDL-C, TG/HDL-C, TyG, and METS-IR of the prehypertensive participants were higher than those of the normotensive participants. The proportions of men, smokers, alcohol consumers, and participants with DM were also higher in the prehypertension group. However, the HDL-C concentration of the normotensive participants was higher.

**TABLE 1** Clinical baseline of the normotensive and prehypertensive in this study

Variables	Normotension (N = 2081)	Prehypertension (N = 1193)	P value
Age, years	37.91 ± 11.36	44.01 ± 13.00	<.001
Male (%)	37.2% (775/2081)	63.7% (760/1193)	<.001
Smoking (%)	20.6% (429/2081)	31.9% (380/1193)	<.001
Alcohol (%)	28.4% (590/2081)	44.8% (534/1193)	<.001
DM (%)	.5% (11/2081)	2.1% (25/1193)	<.001
Height (cm)	162.46 ± 7.55	164.44 ± 7.93	<.001
Weight (kg)	57.80 ± 9.67	63.87 ± 10.77	.025
BMI (kg/m <sup>2</sup> )	21.50 (19.92–23.4)	23.43 (21.45–25.37)	<.001
SBP (mmHg)	113.29 ± 7.68	125.58 ± 7.13	<.001
DBP (mmHg)	72.24 ± 4.89	82.84 ± 3.50	<.001
FPG (mg/dl)	83.17 (75.94–90.41)	86.79 (79.56–94.02)	<.001
TG (mg/dl)	90.35 (66.43–126.66)	117.80 (84.15–168.03)	<.001
TC (mg/dl)	161.78 (144.02–182.82)	170.11 (150.19–191.51)	<.001
HDL-C (mg/dl)	58.30 (49.81–67.57)	52.90 (45.17–62.93)	<.001
LDL-C (mg/dl)	82.63 (69.15–100.82)	93.44 (76.61–110.79)	<.001
TG/HDL-C	.66 (.46–1.04)	.97 (.62–1.54)	<.001
TyG	8.22 (7.90–8.60)	8.55 (8.17–8.93)	<.001
METS-IR	29.43 (26.44–33.30)	33.63 (29.33–38.36)	<.001

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; 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, triglyceride and glucose index.



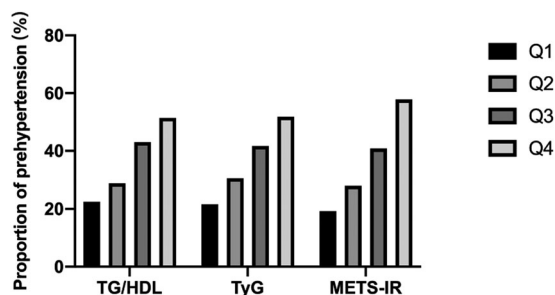
**FIGURE 2** The SBP and DBP levels by quartiles of TG/HDL-C, TyG, and METS-IR. Both SBP (A) and DBP (B) levels showed an increasing trend with increases across ascending quartiles of TG/HDL-C, TyG, and METS-IR (all  $P < .001$ ). SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; TyG, triglyceride and glucose index; METS-IR, metabolic score for insulin resistance; Q, quartile

### 3.2 | SBP, DBP, and the proportion of prehypertension, according to the quartiles of the non-insulin-based IR indexes

Both SBP and DBP tended to increase with the quartiles of TG/HDL-C, TyG, and METS-IR (all  $P < .001$ ). Similarly, the proportion of prehypertension increased with the quartiles of TG/HDL-C, TyG, and METS-IR (all  $P < .001$ ). These data are presented in Figures 2 and 3.

### 3.3 | Relationships between blood pressure and the non-insulin-based IR indexes

As shown in Table 2, SBP and DBP were positively associated with TG/HDL-C ( $r = .272$ ,  $P < .001$ ), TyG ( $r = .286$ ,  $P < .001$ ), and METS-IR ( $r = .340$ ,  $P < .001$ ) across the entire cohort. Similar relationships were also identified separately for men and women.



**FIGURE 3** The proportion of prehypertension by quartiles of TG/HDL-C, TyG, and METS-IR. The proportion of prehypertension showed an increasing trend with an increase across ascending quartiles of TG/HDL-C, TyG, and METS-IR (all  $P < .001$ ). TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; TyG, triglyceride and glucose index; METS-IR, metabolic score for insulin resistance; Q, quartile

### 3.4 | Relationships between the non-insulin-based IR indexes and prehypertension, according to univariate and multiple logistic analyses

Univariate logistic analysis (Table 3) showed that age (OR = 1.042,  $P < .001$ ), male sex (OR = 2.958,  $P < .001$ ), smoking (OR = 1.800,  $P < .001$ ), alcohol consumption (OR = 2.048,  $P < .001$ ), BMI (OR = 1.236,  $P < .001$ ), and DM (OR = 2.002,  $P < .001$ ) were associated with prehypertension in the participants. In addition, TG/HDL-C (OR = 1.446,  $P < .001$ ), TyG (OR = 2.370,  $P < .001$ ), and METS-IR (OR = 1.109,  $P < .001$ ), were positively associated with prehypertension. When TG/HDL-C, TyG, and METS-IR were analyzed as quartiles, using the lowest quartiles as the references, univariate analysis revealed that the proportion of prehypertension in the second, third, and fourth quartiles of TG/HDL-C, TyG, and METS-IR were significantly higher than those in the first quartiles. The specific odds ratios (ORs) and their 95% confidence intervals (CIs) are shown in Table 4. After adjustment for confounding factors, multiple logistic analyses showed that the proportion of prehypertension in the third and fourth quartiles of the TG/HDL-C (Q3 vs. Q1: OR = 1.527, 95% CI: 1.243–1.988; Q4 vs. Q1: OR = 1.580, 95% CI: 1.231–2.028), TyG (Q3 vs. Q1: OR = 1.519, 95% CI: 1.201–1.923; Q4 vs. Q1: OR = 1.658, 95% CI: 1.312–2.614), and METS-IR (Q3 vs. Q1: OR = 1.542, 95% CI: 1.138–2.090; Q4 vs. Q1: OR = 2.216, 95% CI: 1.474–3.331) were also significantly higher than

**TABLE 3** Univariate logistic analysis on clinical/laboratory parameters for prehypertension

Variables	Prehypertension	
	OR (95% CI)	P value
Age, years	1.042 (1.035–1.048)	<.001
Sex (male)	2.958 (2.552–3.429)	<.001
Smoking	1.800 (1.531–2.0116)	<.001
Drinking	2.048 (1.765–2.376)	<.001
BMI (kg/m <sup>2</sup> )	1.236 (1.203–1.269)	<.001
DM	2.002 (1.406–2.850)	<.001
TG/HDL-C	1.446 (1.331–1.571)	<.001
TyG	2.370 (2.086–2.694)	<.001
METS-IR	1.109 (1.095–1.123)	<.001

Abbreviations: BMI, body mass index; CI, confidence interval; DM, diabetes mellitus; HDL-c, high-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; OR, odds ratio; TG, triglyceride; TyG, triglyceride and glucose index.

those in the lowest quartiles (Table 4). These findings imply that high values of non-insulin-based IR indexes may be risk factors for prehypertension.

### 3.5 | ROC curve analysis of the predictive values of TG/HDL-C, TyG, and METS-IR for prehypertension

Figure 4 shows the ROC curves for the non-insulin-based IR indexes. Of these, METS-IR showed the greatest ability to identify prehypertension. When these indexes were analyzed according to sex, METS-IR remained the best index for the identification of prehypertension in men, but not in women. As shown in Table 5, the AUC for METS-IR for the identification of prehypertension was .683 (95% CI: .664–.702), which was significantly higher than those for TG/HDL-C (.647, 95% CI: .628–.667) and TyG (.650, 95% CI: .631–.669) across the entire cohort. After categorization according to sex, the METS-IR performed better than TG/HDL-C or TyG in men, with an AUC of .636 (95% CI: .608–.663). METS-IR also had the highest AUC in women (.646, 95% CI: .616–.677), although there was no significant difference between the METS-IR and TyG. The YI, PPV, and NPV for METS-IR confirmed its superior ability to identify prehypertension in the entire cohort (YI = .287,

**TABLE 2** Spearman correlation between TG/HDL-C, TyG, METS-IR, and blood pressure level

Variables	All subjects				Male participants				Female participants			
	SBP		DBP		SBP		DBP		SBP		DBP	
	r	P	r	P	r	P	r	P	r	P	r	P
TG/HDL-C	.272	<.01	.269	<.01	.121	<.01	.193	<.01	.197	<.01	.165	<.01
TyG	.286	<.01	.280	<.01	.151	<.01	.220	<.01	.247	<.01	.204	<.01
METS-IR	.340	<.01	.343	<.01	.191	<.01	.289	<.01	.260	<.01	.222	<.01

Abbreviations: DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; SBP, systolic blood pressure; TG, triglyceride; TyG, triglyceride and glucose index.

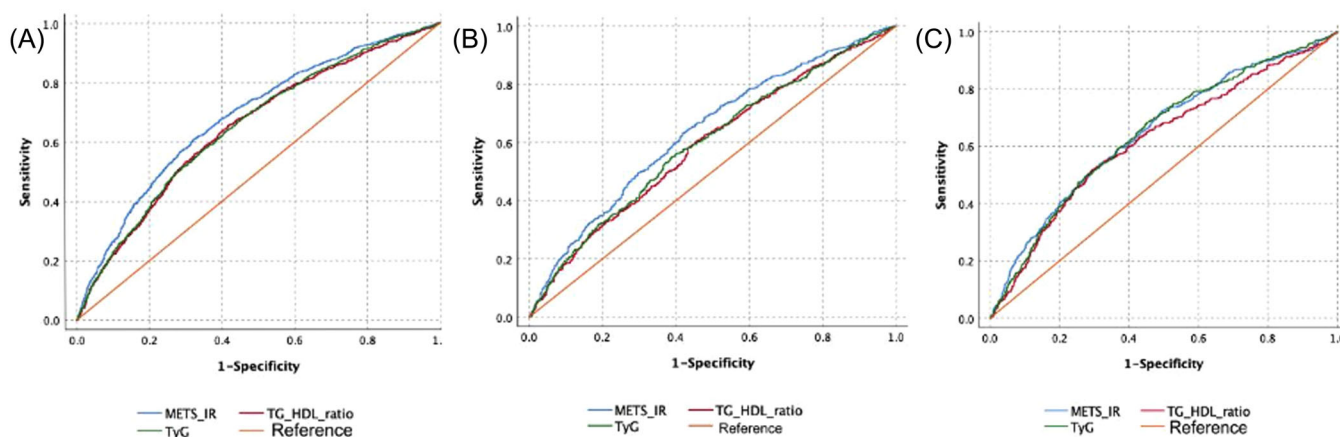
**TABLE 4** Association between the quartiles of TG/HDL-C, TyG, and METS-IR and risk of prehypertension

Variables	Quartile 1	Quartile 2	Quartile 3	Quartile 4
<b>Model 1</b>				
TG/HDL-C	1.000 (ref)	1.399 (1.119–1.749) <sup>*</sup>	2.607 (2.103–3.231) <sup>*</sup>	3.651 (2.948–4.521) <sup>*</sup>
TyG	1.000 (ref)	1.604 (1.283–2.005) <sup>*</sup>	2.549 (2.089–3.221) <sup>*</sup>	3.909 (3.151–4.849) <sup>*</sup>
METS-IR	1.000 (ref)	1.634 (1.296–2.060) <sup>*</sup>	2.905 (2.325–3.631) <sup>*</sup>	5.756 (4.607–7.190) <sup>*</sup>
<b>Model 2</b>				
TG/HDL-C	1.000 (ref)	1.041 (.820–1.321)	1.572 (1.243–1.988) <sup>*</sup>	1.580 (1.231–2.028) <sup>*</sup>
TyG	1.000 (ref)	1.199 (.945–1.520)	1.519 (1.201–1.923) <sup>*</sup>	1.658 (1.312–2.614) <sup>*</sup>
METS-IR	1.000 (ref)	1.176 (.905–1.528)	1.542 (1.138–2.090) <sup>*</sup>	2.216 (1.474–3.331) <sup>*</sup>

Model 1: unadjusted; Model 2: adjusted for age, sex, BMI, smoking, alcohol, DM.

Abbreviations: BMI, body mass index; DM, diabetes mellitus; HDL-c, high-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; TG, triglyceride; TyG, triglyceride and glucose index.

<sup>\*</sup>P value < .001.

**FIGURE 4** Receiver operative characteristic curves for distinguishing prehypertension by TG/HDL-C, TyG, and METS-IR. A: all subjects; B: male group; C: female group

PPV = .520, and NPV = .752) and in men (YI = .214, PPV = .577, and NPV = .640), compared to TG/HDL-C and TyG.

## 4 | DISCUSSION

In the present cross-sectional study, we have shown that the non-insulin-based IR indexes TG/HDL-C, TyG, and METS-IR are significantly associated with prehypertension. Of these, METS-IR performed better than TG/HDL-C and TyG for the identification of prehypertension, especially in men. Given that BP is not always routinely measured for three consecutive times during health checkups, the evaluation of non-insulin-based IR indexes might be useful for the identification of individuals at a high risk of prehypertension, and may be especially useful for those with normal clinic BP, providing an opportunity to introduce appropriate preventive strategies for hypertension. Thus, these non-insulin-based IR indexes might assist with the prevention of hypertension in primary care or areas with limited medical resources.

IR, a metabolic dysfunction characterized by impaired responses to insulin in organs and tissues, leading to defects in the uptake and use of glucose and glycogen synthesis,<sup>20</sup> is strongly predictive of CVD.<sup>21–23</sup> Epidemiological and basic science studies have shown that IR is associated with higher risks of hypertension and prehypertension,<sup>8,11</sup> which are mediated through an impairment in NO synthesis, and increases in the tissue activities of angiotensin II and aldosterone, oxidative stress, and sympathetic activity.<sup>24</sup> Therefore, the early identification of IR is very important for the prevention of hypertension.

The methods used for the evaluation of IR include HEC, insulin tolerance testing, insulin suppression testing, rapid insulin sensitivity testing, the homeostasis model assessment of IR index (HOMA-IR), the beta-cell function evaluation index (HOMA- $\beta$ ), and the quantitative insulin sensitivity check index (QUICKI index).<sup>12</sup> Of these, HEC, which was first developed by De Fronzo, is regarded as the gold-standard method of evaluating insulin sensitivity. However, it is time-consuming, complex, and invasive, which makes it impractical for use in epidemiological studies and health checkups. In addition, HOMA-IR, HOMA-

**TABLE 5** The ROC curves analysis of TG/HDL-C, TyG, and METS-IR index for discriminating prehypertension

Characteristics	TG/HDL-C	TyG	METS-IR	P <sub>1</sub> -value	P <sub>2</sub> -value	P <sub>3</sub> -value
<b>ALL</b>						
AUC (95% CI)	.647 (.628–.667)	.650 (.631–.669)	.683 (.664–.702)	.523	<.001	<.001
Cutoff value	.751	8.338	31.999			
YI	.238	.226	.287			
PPV	.474	.470	.520			
NPV	.747	.739	.752			
<b>Male</b>						
AUC (95% CI)	.589 (.561–.618)	.597 (.568–.625)	.636 (.608–.663)	.308	<.001	<.001
Cutoff value	.957	8.569	33.513			
YI	.149	.162	.214			
PPV	.541	.548	.577			
NPV	.598	.593	.640			
<b>Female</b>						
AUC (95% CI)	.620 (.589–.652)	.643 (.613–.673)	.646 (.616–.677)	.001	.045	.822
Cutoff value	.769	8.170	28.108			
YI	.224	.232	.230			
PPV	.363	.357	.396			
NPV	.815	.816	.801			

P<sub>1</sub>: comparison between TG/HDL-C and TyG; P<sub>2</sub>: comparison between TG/HDL-C and METS-IR; P<sub>3</sub>: comparison between TyG and METS-IR. Abbreviations: AUC, area under the curve; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; NPV, negative predictive values; PPV, positive predictive values; ROC, receiver operating characteristic; TG, triglyceride; TyG, triglyceride and glucose index; YI, Youden index.

$\beta$ , and QUICKI require the measurement of insulin. Although these methods use fasting data to predict pancreatic  $\beta$ -cell function,<sup>25</sup> they have the disadvantages of the necessity for laboratory testing and invasiveness, and are therefore not widely used in the general population, and especially in areas with limited resources.<sup>26</sup> Recently, some other indexes of IR, which are based on anthropometric and biochemical data, have been developed, and the values derived show good correlations with the results of HEC.<sup>14,15</sup> Therefore, these may represent suitable means of screening for IR in a primary care setting. These indexes have previously been used to predict diabetes,<sup>27</sup> hypertension,<sup>28,29</sup> arterial stiffness,<sup>30</sup> and cardiovascular mortality.<sup>31</sup>

Previous studies of the relationships between non-insulin-based IR indexes and prehypertension have been relatively few in number. A study by Zhang and colleagues of 32 124 normoglycemic adults showed that the risks of prehypertension in the highest quartiles of TyG and TG/HDL were 1.876 (95% CI: 1.713–2.055) and 1.575 (95% CI: 1.439–1.724) times higher than those in the lowest quartiles.<sup>16</sup> Furthermore, Jie and colleagues showed that METS-IR, but not TG/HDL or TyG, was significantly associated with prehypertension, and the OR for prehypertension in the highest quartile versus the lowest quartile was 2.223.<sup>17</sup> In the present study, all of the non-insulin-based IR indexes evaluated were found to be significantly associated with prehypertension. In addition, METS-IR had the highest AUC, YI, PPV, and NPV values for the discrimination of prehypertension of the three

indexes in the entire cohort and in men. Thus, METS-IR is better able to identify prehypertension than TG/HDL-C or TyG in the population as a whole and in men. The better performance of METS-IR in distinguishing prehypertension might be explained as follow. Bello-Chavolla and colleagues demonstrated that METS-IR had a good diagnostic performance for DM prediction, which was significantly higher than the TyG index and the TG/HDL-C.<sup>15</sup> Second, overweight/obesity, a common metabolic disorder worldwide, affects insulin and non-insulin-based means of estimating IR.<sup>32,33</sup> The addition of BMI to the formulas that are based on TG, glucose, and HDL-C increases the spectrum of explained variability of the model.<sup>15</sup> In the present cohort, participants with prehypertension had higher BMIs and a higher prevalence of overweight than normotensive participants. These factors might explain the superior ability of METS-IR to identify individuals with prehypertension.

The present study had some limitations. First, we used clinic BP measurements to distinguish normotension and prehypertension, rather than ambulatory BP, which might have led to the inclusion of some participants with masked hypertension. Second, TG/HDL-C, TyG, and METS-IR were developed in Caucasian and Mexican populations, and there are differences in the insulin secretory capacity of East Asian people and those of other ethnicities. Unfortunately, we did not measure plasma insulin concentration in this cohort, owing to the relatively large sample size and high cost of testing. Therefore, whether

these indexes are representative of IR in East Asian people should be assessed in future studies. Third, the present study was cross-sectional in nature, and therefore inferences regarding causal relationships between IR and prehypertension cannot be made. A prospective cohort study is urgently needed to better characterize the relationships of TG/HDL-C, TyG, and METS-IR with hypertension. In addition, the data were gathered at a health management center 10 years previously, and the family history of hypertension and lifestyles of the participants were not commonly recorded. Therefore, these factors could not be adjusted for in the multiple logistic analyses. Finally, the results may not be applicable to other ethnicities, because only Han Chinese people were studied.

## 5 | CONCLUSIONS

In conclusions, the non-insulin-based IR indexes TG/HDL-C, TyG, and METS-IR were significantly associated with the risk of prehypertension. Furthermore, METS-IR is a superior means of identifying prehypertension to TG/HDL-C and TyG. These non-insulin-based IR indexes might assist with the prevention of hypertension in primary care and areas with limited medical resources.

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## CONFLICT OF INTEREST

The authors declare that they have no competing interests to declare.

## CONSENT FOR PUBLICATION

All coauthors and participants have given their consent for publication of this article in *the journal of Clinical Hypertension*.

## AUTHOR CONTRIBUTIONS

Xin Zhang designed the study intellectual content, and wrote this initial manuscript. Chaoping Yu participated in original data acquisition. Runyu Ye carried out literature search and chart production. Xin Zhang, Runyu Ye, and Tianhu Liu undertook the statistical analysis and participated in manuscript preparation. Xiaoping Chen and Tianhu Liu revised the manuscript for important intellectual content and languages. All authors read and approved the final manuscript.

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