

Predictive Value of the Triglyceride-Glucose (TyG) Index for New-Onset Hypertension in Chinese Individuals Aged 45 and Above: A National Longitudinal Cohort Study from CHARLS

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Abstract: Triglycerides and glucose, key metabolic products in the human body, are linked to the onset of various chronic diseases. However, the relationship between the triglyceride-glucose (TyG) index and hypertension among middle-aged and elderly populations remains unclear. This study primarily aims to explore the association between the TyG index and the risk of developing hypertension in individuals aged 45 and older through a prospective cohort study approach. This research incorporated clinical data from 4,940 participants of the China Health and Retirement Longitudinal Study (CHARLS) spanning from 2011 to 2018. The TyG index was calculated for all participants using the formula $\ln [\text{triglycerides (mg/dL)} \times \text{plasma glucose (mg/dL)} / 2]$. Cox regression analysis was employed to assess the relationship between the TyG index and the onset of new hypertension, with adjustments made for pertinent variables. Participants were also stratified by demographic characteristics to further examine the consistency of the TyG index's relationship with new-onset hypertension. Over the 7-year observation period, 1,275 participants developed hypertension, accounting for 25.8% of the total cohort. Factors such as older age, higher body mass index, lower educational levels, and elevated TyG index were linked to a higher risk of developing hypertension. Significant correlations were observed between the TyG index and variables including participants' height, weight, BMI, residential area, smoking habits, alcohol consumption, diabetes, heart disease, blood glucose, blood lipids, and uric acid levels. The likelihood of developing hypertension increased progressively with higher TyG index values, indicating a positive correlation. This positive relationship was consistent across various demographic and health-related subgroups. Within this Chinese cohort, the TyG index is a valuable predictor of the risk for new-onset hypertension. Consequently, in the realm of primary hypertension prevention, individuals with hyperlipidemia and diabetes should be identified as high-risk and receive targeted interventions.

Keywords: TyG Index, Hypertension, CHARLS Database

1. Introduction

Hypertension is a prevalent cardiovascular condition characterized by elevated systemic arterial blood pressure and is one of the most common health issues in China. Chronic hypertension can induce functional and structural damage to vital organs, including the heart, brain, and kidneys^[1]. The etiology of hypertension remains ambiguous, with primary hypertension being the predominant type. Numerous risk factors contribute to hypertension, such as genetic predispositions, lifestyle choices, and dietary habits, all of which can elevate blood pressure and potentially lead to the disease. Research indicates that individuals with metabolic syndrome are at a significantly increased risk of developing new-onset hypertension, complicating blood pressure management^[2]. Consequently, this study seeks to uncover additional risk factors associated with hypertension to innovate strategies for its primary prevention.

In recent years, the Triglyceride-Glucose (TyG) index has emerged as a novel metabolic marker, garnering extensive attention. Derived from fasting blood glucose and triglyceride levels, the TyG index was initially introduced as a straightforward tool for evaluating insulin resistance. Current studies identify insulin resistance as a critical risk factor for hypertension, implicated through mechanisms such as heightened sympathetic nervous system activity, sodium and water retention, endothelial

dysfunction, and the promotion of inflammation and oxidative stress^[3]. As investigations continue, the link between the TyG index and hypertension is becoming more apparent. Notably, research, including that by Xu J and colleagues, has demonstrated a correlation between the TyG index and an increased likelihood of developing pre-hypertension or hypertension among individuals with normoglycemia in Japan^[4]. Despite these findings, the predominance of retrospective studies on this topic limits the ability to establish causality between the TyG index and hypertension. Thus, this study employs longitudinal data from the China Health and Retirement Longitudinal Study (CHARLS) to evaluate the causal relationship between the TyG index and new-onset hypertension.

2. Methods

2.1 Data Source

This study utilized data from the China Health and Retirement Longitudinal Study (CHARLS) database. In 2011, a multi-stage probability sampling method was employed to survey national baseline data, collecting representative population samples from 150 counties across 28 provinces, municipalities, and autonomous regions of China. The initial face-to-face Computer Assisted Personal Interviewing (CAPI) was completed in 2011-2012, with follow-ups conducted every two years thereafter. The survey included basic demographic data of respondents and their families, transfers among family members, respondents' health status, medical care and insurance, employment, income, expenditures, and assets^[5]. Researchers can download the CHARLS dataset from its homepage (<http://charls.pku.edu.cn/en>). The Peking University Institutional Review Board first approved CHARLS in 2008 (IRB0000105211, 015), and all participants signed informed consent forms.

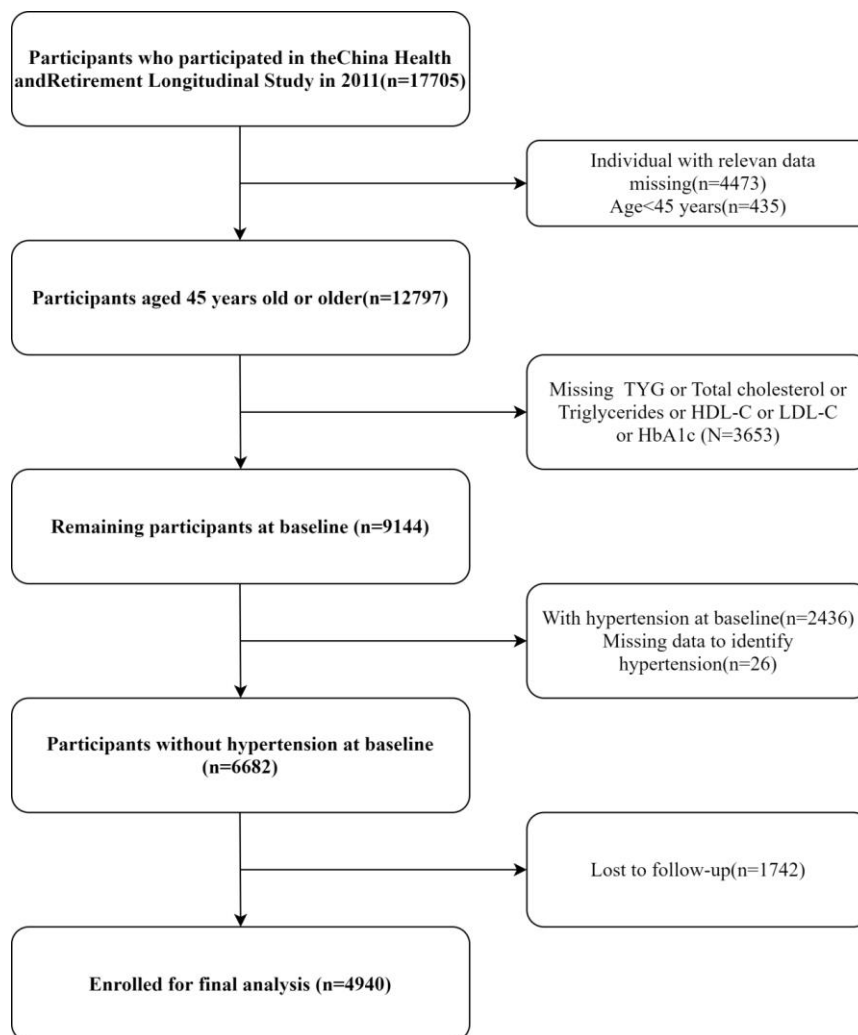


Figure 1: Flow diagram of study participants.

It is noteworthy that in 2011, researchers collected venous blood samples from participants who had fasted for at least 12 hours. All biomedical procedures were strictly performed by certified professionals. These samples were stored at an optimal temperature of 4 °C and immediately sent to the central laboratory in Beijing (You'anmen Clinical Laboratory Center of Capital Medical University) for advanced diagnostic assessments. The enzyme colorimetric method was used to precisely measure serum indices such as glucose concentration, triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).

Figure 1 illustrates the selection process for participants in this study. In the 2011 baseline survey, a total of 17,705 participants completed physical examinations and questionnaire assessments. This study excluded participants based on specific criteria: under the age of 45 (435 people), incomplete baseline data (4473 people), incomplete TyG index and lipid data (3653 people), diagnosed with hypertension in 2011 (2436 people), missing hypertension information (26 people), and lost to follow-up in 2018 (1742 people). The study used data collected in 2011 (Wave 1), 2013 (Wave 2), 2015 (Wave 3), and 2018 (Wave 4), strictly adhering to all relevant standards and recommendations specified by CHARLS.

2.2 Assessment of the TyG Index

The TyG index in this study was determined using the following formula: $\ln[\text{triglycerides (mg/dL)} * \text{plasma glucose (mg/dL)} / 2]^{61}$.

2.3 Assessment of New-Onset Hypertension

New-onset hypertension was defined as hypertension newly reported by the participant during the follow-up period. Staff asked participants the following survey question: "Has a doctor ever told you that you have the following chronic diseases?" If a participant checked hypertension, it indicated that the participant had developed hypertension during the follow-up period.

2.4 Assessment of Covariates

This study also extracted sociodemographic characteristics, lifestyle behaviors, and health conditions as covariates. Sociodemographic characteristics included age (in years), gender (male/female), height, weight, body mass index (BMI), marital status, educational level, and residential area (rural/urban). Lifestyle behaviors included smoking habits (non-smoker/smoker) and drinking status (non-drinker/drinker). Current health conditions included diabetes (yes/no), heart disease (yes/no), stroke (yes/no), and kidney disease (yes/no). Laboratory test results included blood glucose, creatinine, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, hemoglobin, and uric acid.

2.5 Statistical Analysis

The data for this study primarily came from the national CHARLS survey conducted from 2011 to 2018 over seven years. Initially, descriptive analysis was performed on participants included in the study. Continuous variables were analyzed using means, standard deviations (SD), or medians and interquartile ranges (IQR), while categorical variables were expressed as percentages (%). The t-test was used for continuous variables, and the chi-square test was used for categorical variables. The relationship between the TyG index and new-onset hypertension was analyzed using a multivariable Cox regression model. Subgroup analysis was conducted using stratified Cox regression analysis. Interaction analysis was utilized to determine whether sociodemographic factors, lifestyle behaviors, and health conditions moderated the relationship between the TyG index and new-onset hypertension.

All statistical analyses were performed using IBM SPSS Statistics 25.0 and Easy-R software. A p-value of <0.05 was considered statistically significant.

3. Results

3.1 Characteristics of Participants Divided by New-Onset Hypertension and TyG Index Quartiles

The final cohort for this study included 4,940 participants, of whom 1,275 developed new-onset hypertension. Table 1 displays the basic characteristics of participants grouped according to new-onset

hypertension status. Compared to those who did not develop hypertension, participants with new-onset hypertension were older, had a higher BMI, were more often unmarried, had lower education levels, and higher incidences of diabetes and heart disease. Additionally, they had higher levels of blood lipids, glucose, creatinine, and uric acid, with all these differences being statistically significant.

Table 1: Baseline characteristics of study participants according to Hypertension index. Data was shown as mean \pm standard deviation (SD) for continuous variables or frequency (percentage) for categorical variables.

Hypertension	No	Yes	P-value
N	3665	1275	
Age	57.57 \pm 8.56	59.58 \pm 8.91	<0.001
Gender			0.743
Remale	1977 (53.94%)	681 (53.41%)	
Male	1688 (46.06%)	594 (46.59%)	
Height, m	1.58 \pm 0.09	1.58 \pm 0.10	0.221
Weight, kg	56.95 \pm 10.68	59.62 \pm 11.37	<0.001
BMI, kg/m ²	22.88 \pm 8.33	25.80 \pm 68.05	0.011
Marry			0.002
No	332 (9.06%)	154 (12.08%)	
Yes	3333 (90.94%)	1121 (87.92%)	
Living area			0.125
Urban	1189 (32.44%)	384 (30.12%)	
Rural	2476 (67.56%)	891 (69.88%)	
Education			0.006
Primary lower	1661 (45.32%)	643 (50.43%)	
Primary	826 (22.54%)	283 (22.20%)	
Secondary	790 (21.56%)	236 (18.51%)	
Higher	388 (10.59%)	113 (8.86%)	
Drink			0.732
No	2411 (65.78%)	832 (65.25%)	
Yes	1254 (34.22%)	443 (34.75%)	
Smoke			0.961
No	2515 (68.62%)	874 (68.55%)	
Yes	1150 (31.38%)	401 (31.45%)	
Diabetes			0.032
No	3541 (96.62%)	1215 (95.29%)	
Yes	124 (3.38%)	60 (4.71%)	
Heart			<0.001
No	3411 (93.07%)	1148 (90.04%)	
Yes	254 (6.93%)	127 (9.96%)	
Stroke			0.381
No	3622 (98.83%)	1256 (98.51%)	
Yes	43 (1.17%)	19 (1.49%)	
Kidney			0.5
No	3476 (94.84%)	1203 (94.35%)	
Yes	189 (5.16%)	72 (5.65%)	
TyG quartiles			<0.001
Q1 (4.96 - 8.18)	983 (26.82%)	252 (19.76%)	
Q2 (8.18 - 8.54)	940 (25.65%)	295 (23.14%)	
Q3 (8.54 - 8.97)	902 (24.61%)	333 (26.12%)	
Q4 (8.96 - 11.99)	840 (22.92%)	395 (30.98%)	
Creatine, mg/dL	0.76 \pm 0.17	0.77 \pm 0.19	0.045
Total Cholesterol, mg/dl	190.93 \pm 36.79	196.37 \pm 40.07	<0.001
Triglycerides, mg/dl	120.35 \pm 85.69	137.43 \pm 97.83	<0.001
HDL-C, mg/dL	52.93 \pm 15.41	50.61 \pm 15.14	<0.001
LDL-C, mg/dl	114.84 \pm 33.14	118.81 \pm 36.32	<0.001
Hemoglobin, g/dl	5.19 \pm 0.68	5.33 \pm 0.87	<0.001
Uric Acid, mg/dl	4.26 \pm 1.15	4.45 \pm 1.23	<0.001
TyG	8.57 \pm 0.62	8.74 \pm 0.67	<0.001

Participants were also divided into four groups (Q1, Q2, Q3, Q4) based on the quartiles of the TyG index, and baseline data were collected. Table 2 shows the basic characteristics of the participants

according to the quartiles of the TyG index. The study found that the TyG index levels were significantly associated with height, weight, BMI, living area, smoking, drinking, diabetes, heart disease, blood sugar, blood lipids, and uric acid levels.

Table 2: Baseline characteristics of study participants according to tertiles of triglyceride glucose (TyG) index. Data was shown as mean + standard deviation (SD) for continuous variables or frequency (percentage) for categorical variables.

TyG quartiles	Q1 (4.96 - 8.18)	Q2 (8.18 - 8.54)	Q3 (8.54 - 8.97)	Q4 (8.96 - 11.99)	P-value
N	1235	1235	1235	1235	
AGE	58.15 ± 8.92	57.95 ± 8.64	58.47 ± 8.66	57.77 ± 8.53	0.225
Gender					<0.001
Female	578 (46.80%)	650 (52.63%)	712 (57.65%)	718 (58.14%)	
Male	657 (53.20%)	585 (47.37%)	523 (42.35%)	517 (41.86%)	
Height, m	1.58 ± 0.08	1.58 ± 0.09	1.57 ± 0.10	1.58 ± 0.08	0.006
Weight, kg	55.00 ± 9.71	56.59 ± 10.80	57.94 ± 11.35	61.04 ± 10.86	<0.001
BMI, kg/m ²	21.86 ± 3.17	22.65 ± 3.75	25.63 ± 70.34	24.41 ± 3.43	0.035
Marry					0.391
No	134 (10.85%)	115 (9.31%)	126 (10.20%)	111 (8.99%)	
Yes	1101 (89.15%)	1120 (90.69%)	1109 (89.80%)	1124 (91.01%)	
Living area					<0.001
Urban	345 (27.94%)	358 (28.99%)	403 (32.63%)	467 (37.81%)	
Rural	890 (72.06%)	877 (71.01%)	832 (67.37%)	768 (62.19%)	
Education					0.373
Primary lower	561 (45.43%)	569 (46.07%)	611 (49.47%)	563 (45.59%)	
Primary	274 (22.19%)	302 (24.45%)	253 (20.49%)	280 (22.67%)	
Secondary	269 (21.78%)	242 (19.60%)	249 (20.16%)	266 (21.54%)	
Higher	131 (10.61%)	122 (9.88%)	122 (9.88%)	126 (10.20%)	
Drink					0.001
No	764 (61.86%)	802 (64.94%)	857 (69.39%)	820 (66.40%)	
Yes	471 (38.14%)	433 (35.06%)	378 (30.61%)	415 (33.60%)	
Smoke					0.006
No	803 (65.02%)	841 (68.10%)	869 (70.36%)	876 (70.93%)	
Yes	432 (34.98%)	394 (31.90%)	366 (29.64%)	359 (29.07%)	
Diabe					<0.001
No	1215 (98.38%)	1207 (97.73%)	1199 (97.09%)	1135 (91.90%)	
Yes	20 (1.62%)	28 (2.27%)	36 (2.91%)	100 (8.10%)	
Heart					0.018
No	1152 (93.28%)	1154 (93.44%)	1136 (91.98%)	1117 (90.45%)	
Yes	83 (6.72%)	81 (6.56%)	99 (8.02%)	118 (9.55%)	
Stroke					0.712
No	1218 (98.62%)	1217 (98.54%)	1223 (99.03%)	1220 (98.79%)	
Yes	17 (1.38%)	18 (1.46%)	12 (0.97%)	15 (1.21%)	
Kidney					0.751
No	1169 (94.66%)	1163 (94.17%)	1174 (95.06%)	1173 (94.98%)	
Yes	66 (5.34%)	72 (5.83%)	61 (4.94%)	62 (5.02%)	
GLU, mg/dL	94.75 ± 13.93	100.49 ± 13.95	104.93 ± 18.00	128.78 ± 50.03	<0.001
Creatine, mg/dL	0.76 ± 0.16	0.76 ± 0.17	0.77 ± 0.18	0.77 ± 0.18	0.072
Total Cholesterol, mg/dl	178.76 ± 33.91	189.43 ± 33.49	194.89 ± 36.16	206.24 ± 41.57	<0.001
Triglycerides, mg/dl	58.99 ± 13.20	87.36 ± 14.15	121.82 ± 21.70	230.85 ± 118.56	<0.001
HDL-C, mg/dL	60.96 ± 15.44	55.64 ± 13.48	50.36 ± 13.80	42.39 ± 12.14	<0.001
LDL-C, mg/dl	108.50 ± 29.30	118.23 ± 30.60	121.99 ± 32.85	114.73 ± 40.78	<0.001
Hemoglobin, g/dl	5.07 ± 0.40	5.13 ± 0.53	5.18 ± 0.57	5.52 ± 1.13	<0.001
Uric Acid, mg/dl	4.16 ± 1.07	4.21 ± 1.16	4.32 ± 1.15	4.53 ± 1.27	<0.001
TyG	7.90 ± 0.26	8.37 ± 0.10	8.73 ± 0.12	9.47 ± 0.46	<0.001
New-onset hypertension, n (%)	252 (20.40%)	295 (23.89%)	333 (26.96%)	395 (31.98%)	<0.001

3.2 Relationship between the TyG Index and New-Onset Hypertension

Table 3 presents the results of the multivariable Cox regression analysis. The findings indicate that compared to the Q1 group, the incidence of hypertension in the highest TyG index quartile group (Q4) increased by 43% (OR 1.43; 95% CI 1.22, 1.68) in Model I, and by 44% (OR 1.44; 95% CI 1.23, 1.70) in Model II.

Table 3: Hazard ratios of triglyceride glucose (TyG) index for hypertension in participants

Adjust I model adjust for: gender, marry, age, education, height, weight.

Adjust II model adjust for: gender, marry, age, education, height, weight, rural, drink, smoke and BMI.

Variariable	N	HR (95% CI) P value		
		Crude model	Model I	Model II
TyG	4940	1.37 (1.26, 1.48) <0.0001	1.28 (1.17, 1.39) <0.0001	1.28 (1.18, 1.40) <0.0001
TyG quartiles				
Q1 (4.96 - 8.18)	1235	1	1	1
Q2 (8.18 - 8.54)	1235	1.17 (0.99, 1.38) 0.0663	1.12 (0.95, 1.33) 0.1723	1.12 (0.95, 1.33) 0.1762
Q3 (8.54 - 8.97)	1235	1.35 (1.15, 1.59) 0.0003	1.23 (1.04, 1.45) 0.0148	1.23 (1.05, 1.46) 0.0129
Q4 (8.97 - 11.99)	1235	1.64 (1.40, 1.92) <0.0001	1.43 (1.22, 1.68) <0.0001	1.44 (1.23, 1.70) <0.0001

3.3 Stratified Analysis Results

	N	HR(95%CI)	HR(95%CI)	P for interaction
Gender				0.4048
Female	2658	1.42 (1.27, 1.59)		
Male	2282	1.33 (1.18, 1.49)		
BMI				0.5571
<24	3202	1.30 (1.16, 1.47)		
≥24	1738	1.24 (1.10, 1.39)		
Age				0.8892
<60	3185	1.39 (1.25, 1.54)		
≥60	1755	1.37 (1.20, 1.56)		
Drink				0.7812
No	3243	1.36 (1.22, 1.51)		
Yes	1697	1.39 (1.22, 1.58)		
Smoke				0.4217
No	3389	1.40 (1.27, 1.54)		
Yes	1551	1.30 (1.12, 1.51)		
Diabetes				0.9669
No	4756	1.36 (1.25, 1.49)		
Yes	184	1.38 (1.04, 1.83)		
Heart				0.9736
No	4559	1.36 (1.25, 1.49)		
Yes	381	1.36 (1.05, 1.75)		
Stroke				0.0922
No	4878	1.36 (1.25, 1.47)		
Yes	62	2.28 (1.24, 4.20)		
Kidney				0.6964
No	4679	1.36 (1.26, 1.48)		
Yes	261	1.46 (1.06, 2.02)		

Figure 2: Stratified analyses of the association between triglyceride glucose (TyG) index and new-onset hypertension

To assess the stability of the positive correlation between the TyG index and new-onset hypertension, the study stratified participants based on sociodemographic characteristics, lifestyle behaviors, and health conditions. Figure 2 illustrates that the analysis of correlations within each

subgroup revealed that the positive correlation between the TyG index and new-onset hypertension remained unaffected across various factors in the subgroup analyses.

4. Discussion

This study was a longitudinal analysis of the relationship between the TyG index and the risk of new-onset hypertension in middle-aged and elderly Chinese populations. Higher TyG index values correlate with an elevated future risk of hypertension among middle-aged and elderly populations in China, and this relationship persists independently of most demographic characteristics, lifestyle behaviors, and health conditions.

Previous studies have established the TyG index as a reliable predictive marker for hypertension. For instance, Zhang et al. in a comprehensive cross-sectional study, discovered a significant association between elevated TyG levels and increased risks of pre-hypertension and hypertension among individuals with normal blood glucose levels^[6]. A meta-analysis of eight observational studies revealed that those in the highest quartile of the TyG index experienced a 53% increased risk of hypertension compared to those in the lowest quartile^[7]. Additionally, a nine-year prospective cohort study involving a healthy Chinese cohort demonstrated that high baseline TyG levels are independent predictors of hypertension development^[8]. These findings align with our study's conclusions, supporting the notion that high TyG index levels could heighten hypertension risk among China's middle-aged and elderly populations. Our longitudinal analysis indicates that individuals with higher TyG indices face a higher risk of hypertension compared to those with lower indices. These insights advocate for the integration of TyG index assessments into community health screenings and routine clinical practices to identify individuals at heightened risk of hypertension, enabling timely interventions that support primary prevention strategies.

Although the mechanisms linking the TyG index to hypertension are not yet fully understood, extensive research has explored the theoretical underpinnings of their association. The TyG index likely forecasts hypertension by indicating levels of insulin resistance (IR). IR may influence hypertension through the activation of the sympathetic nervous system. Notably, insulin abnormalities induced by IR are particularly significant in obese individuals and those with type 2 diabetes, leading to the overactivation of the sympathetic nervous system. This activation can induce vasoconstriction, heightened cardiac output, and fluid retention, subsequently elevating blood pressure. IR may also intensify the activity of the renin-angiotensin-aldosterone system (RAAS), crucial for maintaining fluid balance and blood pressure. Overstimulation of RAAS by IR can trigger physiological responses that increase blood pressure^[9]. Moreover, IR can aggravate hypertension by enhancing renal sodium reabsorption, which boosts fluid retention and blood volume, thereby raising blood pressure^[10]. This effect may be attributed directly to insulin's impact on renal tubules, influencing sodium channels and transporters^[11]. Additionally, IR can amplify the influence of variable risk factors for hypertension, such as hyperinsulinemia, hyperglycemia, dyslipidemia, inflammatory states, and arteriosclerosis^[12].

This study has several strengths. First, it utilized a large, nationally representative sample, enabling the generalization of results across China. Secondly, this longitudinal research contrasts with numerous cross-sectional studies by examining the relationship between the TyG index and the risk of new-onset hypertension, thereby enhancing the robustness of its conclusions.

However, the study also presents some limitations. Firstly, the follow-up duration was relatively brief, preventing the monitoring of the long-term relationship between the TyG index and hypertension. Secondly, the reliance on observational data may have introduced confounding factors, potentially leading to biased outcomes. Thirdly, the diagnosis of hypertension was based on self-reports provided by doctors, without comprehensive medical records, thus introducing a measure of bias. Nevertheless, the findings of this study significantly deepen the understanding of the TyG index's impact on hypertension.

This research provides new longitudinal evidence of a substantial link between the TyG index and the risk of new-onset hypertension among Chinese individuals aged 45 and older. Interventions targeting triglyceride and glucose levels may help reduce the incidence of hypertension and improve the overall health of the elderly population, thereby enhancing the effectiveness of primary hypertension prevention.

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