



Temporal relationship between body mass index and triglyceride-glucose index and its impact on the incident of hypertension

Yanxia Xie ^{a,1}, Rongrong Guo ^{a,1}, Zhao Li ^b, Xiaofan Guo ^b, Guozhe Sun ^b, Zhaoqing Sun ^c, Jia Zheng ^a, Yingxian Sun ^{c,**}, Liqiang Zheng ^{a,*}

^a Department of Clinical Epidemiology, Library, Department of Health Policy and Hospital Management, Shengjing Hospital of China Medical University, 36 Sanhao Street, Heping District, Shenyang, 110004, PR China

^b Department of Cardiology, The First Affiliated Hospital of China Medical University, 155 Nanjing Street, Heping District, Shenyang, 110001, PR China

^c Department of Cardiology, Shengjing Hospital of China Medical University, 36 Sanhao Street, Heping District, Shenyang, 110004, PR China

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KEYWORDS

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Abstract *Background and aims:* Obesity and insulin levels can influence each other by metabolism. However, their temporal sequences and influence on hypertension are generally unknown, especially in Chinese adults. Recently, some scholars have proposed that triglyceride-glucose index (TyG) is an important indicator of insulin resistance. The study aims to describe the relationship between body mass index (BMI) and TyG index and its impact on hypertension. *Methods and results:* A total of 4081 adults (56.33% women) without antihypertensive, hypoglycemic or lipid-lowering medications were selected for the present study. Measurements of BMI and TyG index were obtained twice from 2012 to 2017. Cross-lagged panel analysis was used to describe the temporal sequences between BMI and TyG index, and the effect of their temporal relationship patterns on hypertension was explored through mediation analysis. After adjusting for confounding factors (age, sex, ethnicity et al.), the cross-lagged path coefficient from baseline BMI to follow-up TyG ($\rho_2 = 0.135, P < 0.001$) was significantly greater than the path coefficient from baseline TyG to follow-up BMI ($\rho_1 = 0.043, P < 0.001$), and $P < 0.001$ for the difference between ρ_1 and ρ_2 . Furthermore, the sensitivity analyses between women and men revealed identical findings. In addition, TyG index mediation effect on BMI-hypertension was estimated to be 38.45% ($P < 0.001$) in total population, 25.24% in women and 57.35% in men.

Conclusion: These results provided evidence that the temporal relationship between BMI and insulin resistance is reciprocal and a higher BMI precedes hyperinsulinemia in Chinese adults. This relationship plays an essential role in the development of hypertension, while there is a difference between women and men.

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* Corresponding author. Fax: +86 24 83282346.

** Corresponding author. Fax: +86 24 83282346.

E-mail addresses: sunyingxian12@126.com (Y. Sun), liqiangzheng@126.com (L. Zheng).

¹ Yanxia Xie and Rongrong Guo contributed equally to this work.

Introduction

Obesity and insulin resistance are considered to be an important physiological and pathological basis for diabetes, hypertension and the development of many cardiovascular diseases. Previous studies indicating the trajectories of hypertension in the general population, often revealing that it is frequently preceded by insulin resistance and obesity [1–3]. A number of studies have found that the strong correlation between obesity and insulin resistance plays a vital role in the occurrence of hypertension [4–6]. In general, insulin treatment leads to weight gain in diabetics [7], and on the contrary, obesity results in hyperinsulinemia [8]. Previous study also has shown that based on pathological physiology and metabolism, obesity and insulin levels can influence each other [9]. Although insulin resistance is generally considered to be an important contact between obesity and hypertension, there is no compelling evidence for the temporal relationship between obesity and insulin resistance in population studies. Currently, the high insulin-positive glucose clamp test is the “gold standard” to the evaluation of insulin resistance, however, this method is complicated, expensive, and not widely available in clinical practice [10]. In recent years, some scholars have proposed triglyceride-glucose index (TyG) as an important indicator of insulin resistance, which is fasting blood glucose and triglyceride synthesis index [11,12]. For this reason, TyG index was applied instead of insulin resistance in this study to explore the temporal relationship with BMI.

In addition, BMI and insulin levels have been extensively reported in relation to hypertension [1,3]. However, limited studies have prospectively examined the extent to which obesity is associated with hypertension through insulin resistance, especially in the Chinese population.

Using a longitudinal cohort from the Northeast China Rural Cardiovascular Health Study (NCRCHS), the aim of this study was to apply cross-lagged panel analysis to describe the temporal sequences between BMI and TyG index and apply mediation analysis to explore the impact of their temporal relationship patterns on hypertension.

Methods

Study population

Methods of this study have been described elsewhere [13]. The present study applied ‘NCRCHS’, which is a large-scale epidemiological follow-up study in Liaoning Province, located in northeast China. From January 2012 to August 2012, a representative sample aged ≥ 35 years from 3 towns (a total of 26 rural villages) was selected, focusing on describing the prevalence, incidence and natural history of cardiovascular risk factors. The present study applied a multi-stage, stratified random-cluster sampling scheme. In the first stage, 3 counties (Dawa, Zhangwu, and Liaoyang County) were selected to represent the eastern, southern, and northern regions of Liaoning province in

China. In the second stage, one town was randomly selected from each county (a total of 3 towns). In the third stage, 8–10 rural villages from each town were randomly selected (a total of 26 rural villages). Participants that were pregnant, had malignant tumors and/or mental disorders were excluded from the present study. All eligible permanent residents aged ≥ 35 years from each village were invited to participate in the study (a total of 14,016 potential participants). Of the 14,016 potential participants, 11,956 participants agreed to participate in the present study (response rate of 85.3%).

All subjects in the current study were invited to return for follow-up from August 2015 to January 2016. Of the 11,956 subjects, 2076 were refused or were lost to follow-up, and 9880 (82.6%) agreed and completed the follow-up survey. The present study was selected from those not taking antihypertensive, hypoglycemic and lipid-lowering drugs, including 4081 individuals. The inclusion process of subjects is presented in Fig. 1.

The research has been approved by Ethics Committee of China Medical University, based on the declaration of Helsinki. All participants provided the written informed consent.

Measurements

At baseline and follow-up, all data were collected by cardiologists and trained nurses using a standard questionnaire by face-to-face interview during a single clinic visit. All eligible investigators were invited to attend an organized training session prior to the survey. The training included the purpose of this study, how to administer the questionnaire, the standard measurement methodology, the importance of standardization, and the study procedures. A strict test was conducted following completion of this training, and only those who scored perfectly on the test were allowed to serve as investigators. Further instruction and support was provided by the inspector during data collection.

A standardized questionnaire was used to collect demographic variables (sex, age, and ethnicity), lifestyle risk factors (smoking, drinking status and salt intake), history of heart disease and any medication used in the two weeks prior to the survey. Currently smoking has been defined as at least one cigarette per day and for at least one year [13]. Alcohol consumption was defined as the weekly consumption of beer, wine and hard liquor, converted into mL of alcohol. Current drinking was defined as more than 1 drink/day for women and more than 2 drinks/day for men during the last year [13]. In rural areas of China, 84% of consumed salt is added during cooking or as a preservative of foods prepared in the fall season for consumption through the spring season (salted foods). The researchers questioned the participants' addition of salt to daily meals as well as the amount of salt used in salted foods and then calculated the total salt consumed by the family per year divided by the number of family members to achieve an estimate of the individual salt intake per year [14]. Weight

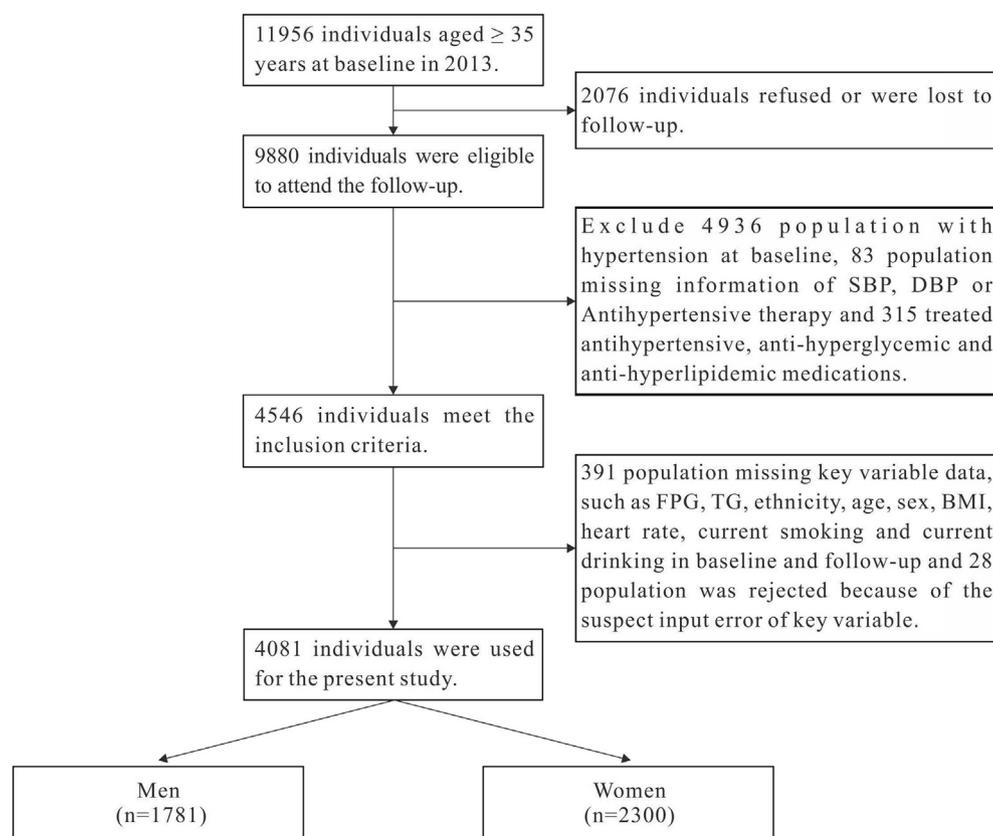


Figure 1 Flow chart of participant recruitment and derivation of the population used in the final analysis. Abbreviation: SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting blood glucose.

and height of each individual were measured to the nearest 0.1 kg and 0.1 cm, respectively, with participants in lightweight clothing and without shoes. Body mass index (BMI) was calculated as weight (kg)/height (m)².

According to the American heart association protocol, the blood pressure (BP) of each participant was measured three times at least 2 min after a rest of at least 5 min using a standardized automatic electronic BP measuring instrument (HEM-907), which has been confirmed by British hypertensive association [14]. Participants were advised to avoid exercise and drink alcohol for at least 30 min prior to BP measurement. During the measurements, participants were requested to rest in a chair for at least 5 min with their arms comfortably on the flat surface at the heart level. For each subject, three readings of measured BP were recorded, and the average of the BP readings was then calculated for final analysis. The hypertension was defined as systolic BP (SBP) ≥ 140 mmHg or diastolic BP (DBP) ≥ 90 mmHg or taking antihypertensive drugs in the last two weeks.

Subjects were instructed fasting for 12 h prior to the screening. Blood samples were obtained from an ante-cubital vein using BD Vacutainer tubes containing EDTA (Becton, Dickinson and Co., Franklin Lakes, NJ, USA). Then serum was subsequently isolated from whole blood serum and stored in the -20 freezer for testing at the center of

the certification laboratory. Fasting plasma glucose (FPG) and triglyceride (TG) were analyzed using automatic analyzer (Olympus AU640 automatic analyzer, Olympus Corp., Kobe, Japan). All laboratory equipment have been calibrated, and samples were repeated with blind samples. The triglyceride-glucose (TyG) index was calculated as the \ln [fasting TG (mmol/L) * FPG (mmol/L) * 0.5 * 159.37] [15].

In particular, data collection for each participant was obtained at the same location on the same day, both baseline and follow-up.

Statistical methods

The continuous variables were taken as the mean and standard deviation (SD) and compared with the student's t-test. The categorical variables were expressed as the ratio of frequency and Pearson's χ^2 -tests for independent proportions.

To examine the 1-directional association of whether BMI (TyG) at baseline predicted future risk of hypertension, we constructed a logistic regression model in which incident hypertension was the dependent variable and baseline TyG (BMI) was the independent variable. The potential baseline confounders was adjusted for baseline age, ethnicity and sex, SBP, DBP, family history of

hypertension, cigarette smoking, alcohol dinking, salt intake and self-reported history of diabetes. Prior to multivariate linear regression analysis, all preliminary variables were included in the OLS (least squares) model to test multicollinearity, and the variance expansion factor (VIF) was applied to examine the multicollinearity problem between independent variables.

Longitudinal changes in BMI and TyG index were measured at two-time points that can be modelled by cross-lagged panel designs. Cross-lagged panel design has been introduced in many articles [16–18]. The cross-lagged panel analysis is a form of path analysis, which also examines the reciprocal, longitudinal relationships between a set of inter-related variables [19]. Figure 2 shows the current model used in the analysis of the concept of a simplified version. The path with ρ_1 describes the effect of baseline TyG on follow-up BMI, and the path with ρ_2 describes the effect of baseline BMI on follow-up TyG. Prior to perform cross-lagged path analysis, the baseline and follow-up values of BMI, TyG were adjusted for age, sex, heart rate, current smoking, current drinking and duration of follow-up (months) in regression analyses and save residual, and then standardized it with z-transformation (mean = 0; standard deviation = 1). These analyses were conducted by IBM SPSS statistical software version 22.0. The cross-lagged model was established, and the path coefficients were estimated by SPSS Amos 22.0 (IBM Inc., Chicago, IL, USA). The model fits were evaluated by the χ^2 goodness-of-fit test and Comparative Fit Index (CFI). The difference between ρ_1 and ρ_2 derived from Z value was examined using Fisher Z test. The individual ρ_1 or ρ_2 shows a directional relationship between BMI and TyG index, and the difference between ρ_1 and ρ_2 suggests stronger evidence for their temporal relationship. $P < 0.05$ was considered statistically significant, and all P values were 2 sided.

Once the temporal relationship had been established, the mediation model was constructed to examine the impact of the association between BMI and TyG on

hypertension. In this model, X was predictor, M was mediator, hypertension is the outcome; predictor and mediator were determined by the cross-lagged path analysis. The simplified mediation model is presented in Fig. 3, which involved three models, including Model $Y = \beta_{Tot}X$ (β_{Tot} = total effect), Model $M = \beta_1X$ (β_1 = indirect effect 1), Model $Y = \beta_2M + \beta_{Dir}X$ (β_2 = indirect effect 2, β_{Dir} = direct effect). The proportion of the mediation effect was calculated using the formula: Mediation effect (%) = $(\beta_1 \times \beta_2 / \beta_{Tot}) \times 100\%$. Mediation analysis was performed by SPSS Amos 22.0 (IBM Inc., Chicago, IL, USA), adjusted for age, sex, heart rate, current smoking, current drinking and duration of follow-up (months).

In addition, sensitivity analyses were conducted for gender differences between men and women.

Results

During a median of 2.42 years of follow-up, 671 participants developed new hypertension, and the incidence of hypertension was 67.92 per 1000 person-years. Table 1 displays the characteristics of study subjects at baseline and follow-up. The differences in study variables were compared between sex groups. Age, current smoking, current drinking, heart rate, TG, FPG, TyG, SBP, and DBP differed significantly at baseline and follow-up between sex groups. There were no significant sex differences between BMI and ethnicity at baseline and follow-up.

The prospective associations of baseline BMI with incident hypertension and follow-up TyG are shown in Table 2. Based on the fact that all independent variables do not have collinearity, the results indicated that a higher level of BMI was significantly associated with a higher level of TyG ($\beta = 0.552, P < 0.001$) and marginal significantly associated with an increased risk of hypertension (OR = 1.025, 95%CI, 0.998–1.053, $P = 0.068$), after adjusting for baseline age, ethnicity and sex, SBP, DBP,

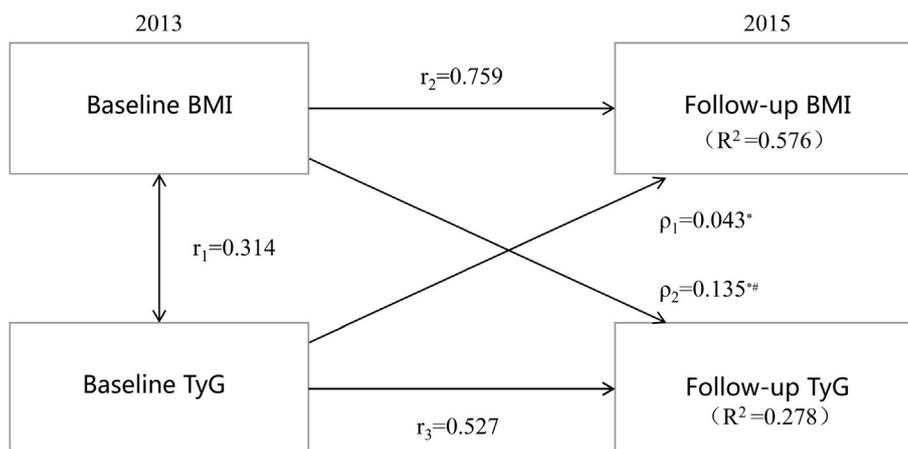


Figure 2 Cross-lagged path analysis of BMI and TyG index (n = 4081), adjusted for age, ethnicity, sex, current smoking, current drinking, heart rate and follow-up months. r_1 = synchronous correlations; r_2, r_3 = tracking correlations; ρ_1, ρ_2 = cross-lagged path coefficients; R^2 = variance explained. *, represent coefficients different from 0, $P < 0.001$. #, $p < 0.001$ for difference between ρ_1 and ρ_2 . Goodness-of-fit: CFI = 0.970.

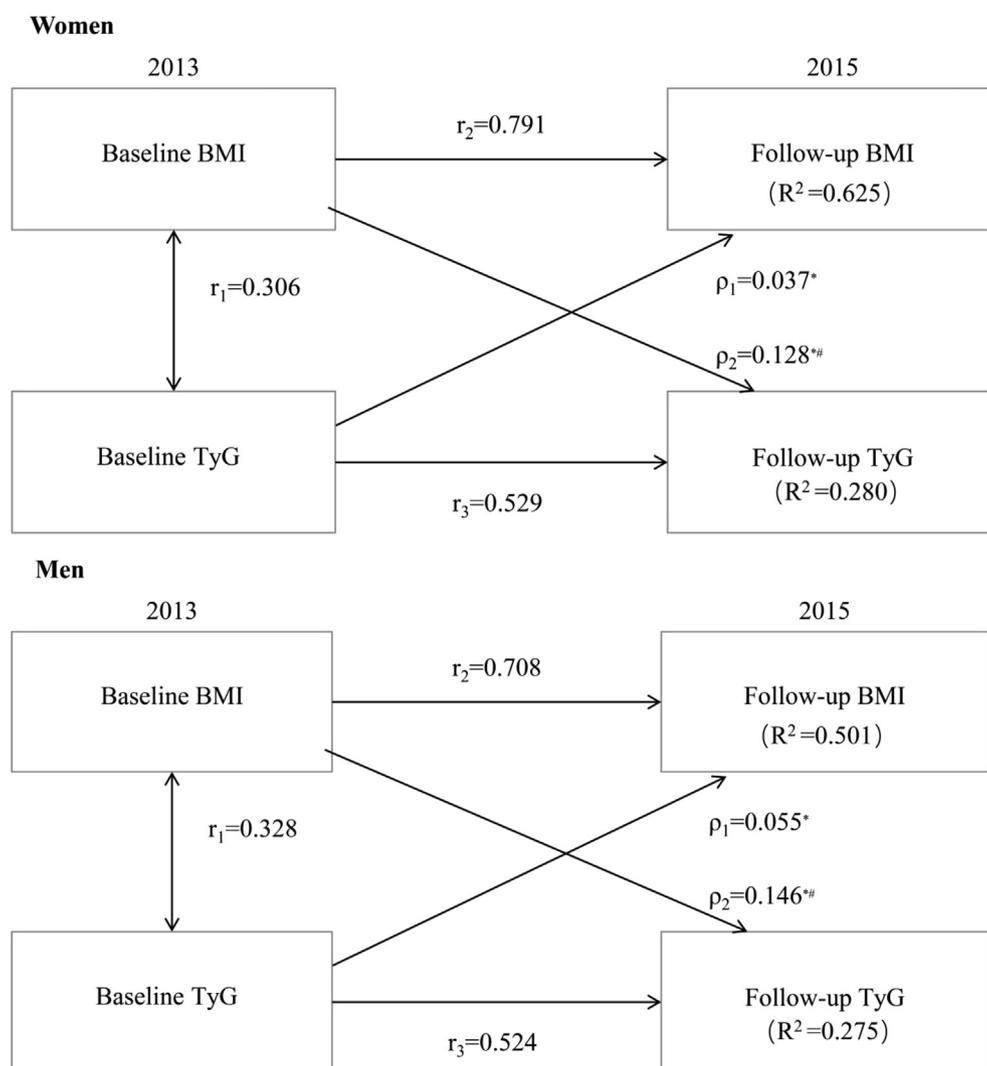


Figure 3 Sensitivity analysis of Cross-lagged path analysis of BMI and TyG index in men ($n = 1781$) and women ($n = 2300$), adjusted for age, ethnicity, sex, current smoking, current drinking, heart rate and follow-up months. r_1 = synchronous correlations; r_2 , r_3 = tracking correlations; ρ_1 , ρ_2 = cross-lagged path coefficients; R^2 = variance explained. *, represent coefficients different from 0, $P < 0.001$ #, $P < 0.001$ for difference between ρ_1 and ρ_2 . Goodness-of-fit: men: CFI = 0.958; women: CFI = 0.980.

family history of hypertension, cigarette smoking, alcohol dinking, salt intake and self-reported history of diabetes and TyG.

The prospective associations of baseline TyG with incident hypertension and follow-up BMI are shown in Table 3. After adjusting for baseline age, ethnicity and sex, SBP, DBP, family history of hypertension, cigarette smoking, alcohol dinking, salt intake and self-reported history of diabetes and BMI, the results showed that a higher level of TyG was significantly associated with a higher level of BMI ($\beta = 0.005$, $P = 0.022$) and an increased risk of hypertension (OR = 1.005, 95%CI, 1.001–1.010, $P = 0.016$).

Figure 2 shows the cross-lagged path analysis of BMI and TyG in the total population. Both of the path coefficients ρ_1 (0.043) and ρ_2 (0.135) were significantly different from 0 ($P < 0.001$). The ρ_2 from baseline BMI to follow-up TyG was greater than the ρ_1 from baseline TyG to follow-up BMI ($P < 0.001$). The χ^2 test for model-fitting showed a difference between the hypothesized model and

the observed data with $P < 0.001$, which was probably related to the high sensitivity to large sample size. The other model-fitting parameter CFI was 0.97, indicating a proper fit in the models based on the standard criterion of 0.90 for CFI. Furthermore, the sensitivity analyses between women and men showed similar outcomes [(Women, $\chi^2 = 73.404$, $P < 0.001$; CFI = 0.980; $\rho_1 = 0.037$, $P = 0.005$; $\rho_2 = 0.128$, $P < 0.001$; ρ_1 vs ρ_2 , $P < 0.001$) and (Men, $\chi^2 = 102.268$, $P < 0.001$; CFI = 0.958; $\rho_1 = 0.055$, $P = 0.001$; $\rho_2 = 0.146$, $P < 0.001$; ρ_1 vs ρ_2 , $P < 0.001$)] (Fig. 3).

As shown in Fig. 4, the mediation model had displayed the mediation effect of follow-up TyG on the baseline BMI to hypertension in the total population. The standardized total effect of TyG on hypertension was 0.08611, and the standardized direct effect was 0.053. The indirect effect had included indirect effect 1 and 2, and the former was greater than the latter at level $P < 0.001$. With the overall indirect effect being 0.03311 (0.301×0.110), the

Table 1 Descriptive data of study variables in baseline and follow-up by sex (n = 4081).

Characteristic	Women (n = 2300)	Men (n = 1781)	P Value
Baseline			
Age, years	49.63 ± 9.26	51.12 ± 10.05	<0.001
Ethnicity, %			
Han	94.8	94.8	
Mongolian	2.1	2.0	
Other	3.1	3.2	0.751
Current smoking, %	17.0	67.2	0.001
Current drinking, %	2.8	46.6	<0.001
Heart rate (times/min)	78.56 ± 12.01	74.59 ± 11.48	<0.001
TG (mmol/L)	1.36 ± 0.92	1.46 ± 1.49	<0.001
FPG (mmol/L)	5.45 ± 0.69	5.60 ± 0.98	<0.001
TyG ^a	1.21 ± 0.56	1.26 ± 0.63	0.001
SBP (mmHg)	132.67 ± 18.78	138.31 ± 19.30	<0.001
DBP (mmHg)	77.96 ± 9.75	81.58 ± 10.44	<0.001
BMI ^b (kg/m ²)	24.35 ± 3.62	24.39 ± 3.36	0.653
Follow-up			
Age (years)	53.78 ± 9.55	55.64 ± 10.36	<0.001
Ethnicity, %			
Han	94.4	94.3	
Mongolian	2.8	2.7	
Other	2.8	3.0	0.751
Current smoking, %	17.3	67.7	<0.001
Current drinking, %	5.3	55.3	<0.001
Heart rate (times/min)	75.56 ± 10.99	73.49 ± 11.69	<0.001
TG (mmol/L)	1.60 ± 1.16	1.72 ± 1.58	<0.001
FPG (mmol/L)	5.45 ± 1.04	5.77 ± 1.50	<0.001
TyG ^a	1.29 ± 0.60	1.36 ± 0.67	<0.001
SBP (mmHg)	129.09 ± 19.37	136.44 ± 19.77	<0.001
DBP (mmHg)	76.98 ± 10.46	81.60 ± 11.56	<0.001
Hypertension, %	59.0	70.5	<0.001
BMI ^b (kg/m ²)	24.55 ± 3.71	24.48 ± 3.39	0.414

Abbreviations: TG, Triglycerides; FPG, fasting blood glucose; TyG, triglyceride-glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, Body mass index.

^a TyG = ln [fasting TG (mmol/L) * FPG (mmol/L) *0.5*159.37].

^b BMI = Weight (kg)/height (m)².

percentage of the total effect mediated by follow-up TyG was estimated at 38.45% (0.03311/0.08611). However, the sensitivity analyses between women and men indicated the mediation effect values are quite different, that is the difference TyG index mediation effect on BMI-hypertension [(Women, $\beta_1 = 0.290$, $P < 0.001$; $\beta_2 = 0.078$, $P < 0.001$; Mediation effect (%) = 25.24%) and (Men, $\beta_1 = 0.318$, $P < 0.001$; $\beta_2 = 0.148$, $P < 0.001$; Mediation effect (%) = 57.35%)](Fig. 5).

Discussion

The most striking observation from the present study was that TyG is associated with risk of incidence hypertension and the temporal relationship between BMI and TyG index is reciprocal. In addition, the model further showed that BMI preceded TyG index, TyG index mediation effect on BMI-hypertension was estimated to be 38.45% in total population, and there is the difference TyG index

Table 2 Prospective associations of baseline BMI with follow-up TyG and incident HT.

Baseline	Follow-up TyG		Incident HT	
	β (95%CI)	P-value	β (95%CI)	P-value
Model 1				
BMI	0.560 (0.421–0.698)	<0.001	1.039 (1.014–1.065)	0.002
Model 2				
BMI	0.547 (0.407–0.687)	<0.001	1.061 (1.035–1.088)	0.001
Model 3				
BMI	0.552 (0.408–0.697)	<0.001	1.025 (0.998–1.053)	0.068

Model 1: adjusted for baseline TyG.

Model 2: adjusted for factors in model 1 and baseline age, ethnicity and sex.

Model 3: adjusted for all variables in model 1 plus baseline SBP, DBP, family history of hypertension, cigarette smoking, alcohol drinking, salt intake and self-reported history of diabetes.

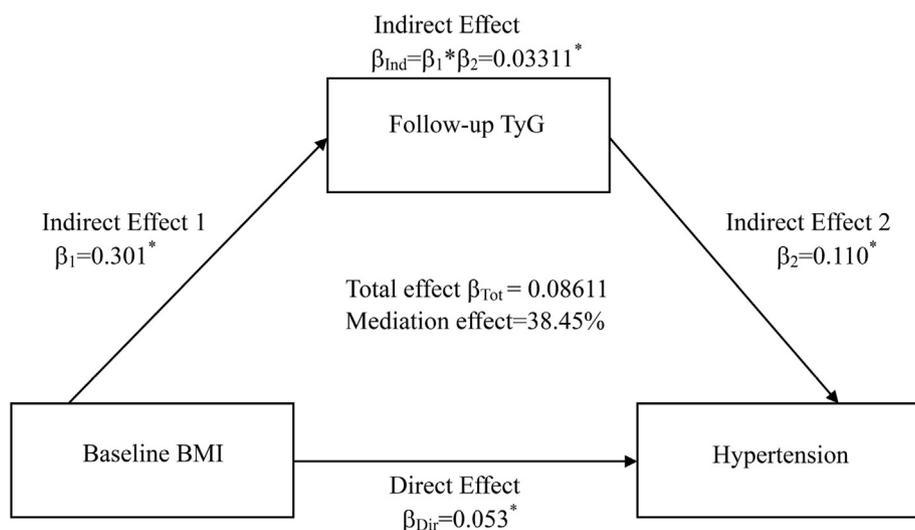
Table 3 Prospective associations of baseline TyG with follow-up BMI and incident HT.

Baseline	Follow-up BMI		Incident HT	
	β (95%CI)	<i>P</i> -value	β (95%CI)	<i>P</i> -value
Model 1				
TyG	0.005 (0.001–0.009)	0.025	1.007 (1.003–1.011)	0.001
Model 2				
TyG	0.005 (0.001–0.009)	0.019	1.007 (1.002–1.011)	0.003
Model 3				
TyG	0.005 (0.001–0.009)	0.022	1.005 (1.001–1.010)	0.016

Model 1: adjusted for baseline BMI.

Model 2: adjusted for factors in model 1 and baseline age, ethnicity and sex.

Model 3: adjusted for all variables in model 1 plus baseline SBP, DBP, family history of hypertension, cigarette smoking, alcohol drinking, salt intake and self-reported history of diabetes.

**Figure 4** Mediation effect of TyG index on the BMI-hypertension association ($n = 4081$). *, represent coefficients different from 0, $P < 0.001$.

mediation effect on BMI-hypertension between women and men (25.24% and 57.35%, respectively).

While the strong correlation between insulin resistance and obesity in children and adults has been well documented [10,20–22], the time relationship between insulin resistance and obesity at various ages is not completely elucidated, especially in the general population of rural adults in China. Although the Bogalusa Heart Study (BHS) from the American population indicates that higher BMI levels precede hyperinsulinemia during childhood [23], the existing data for Chinese adults are limited, and it is not consistent with whether the increase in obesity is earlier than insulin levels, or conversely, or this relationship is bidirectional [7–9]. The present study attempted to prove the temporal relationship between BMI and insulin resistance in adults. Previous studies have mostly used the traditional longitudinal analysis model, which failed to fully explain causality [7–10,17–19]. The present study explored the temporal relationship between BMI and insulin in a prospective cohort of rural adults in the Chinese through a cross-lagged path analysis model. The results of the study indicated that BMI and TyG index had a mutual effect and increased BMI at baseline preceded increased

TyG at follow-up. This result is consistent with the conclusion of the Bogalusa Heart Study.

The pathophysiological mechanisms underlying the temporal association between BMI and insulin resistance have been early elucidated [24,25]. The adipose tissue expandability hypothesis holds that obesity is a key factor leading to type 2 diabetes. When the fat tissue expands to the limit, the fatty tissue stops to store energy efficiently, and the fat starts to accumulate in other tissues. The accumulation of heterotopic lipids in non-fat cells can cause lipid damage, including apoptosis, inflammation and insulin resistance. Another theory is that after the onset of obesity, due to the decrease of glucose transporter (GLUT₄) and hepatic glucokinase (GK) in adipose tissue, there are insulin and peroxisome proliferator-activated receptor γ (PPAR) responsive components in both enzymes. Therefore, the decrease of GLUT₄ and GK causes a decrease in the use of glucose. On the other hand, changes in leptin, tumor necrosis factor (TNF- α), and corresponding receptors in adipose tissue may also affect GLUT₄ and GK activity. This leads to insulin resistance.

Insulin resistance induced by obesity, which is a major risk factor for hypertension [4–6,26,27]. It is possible for

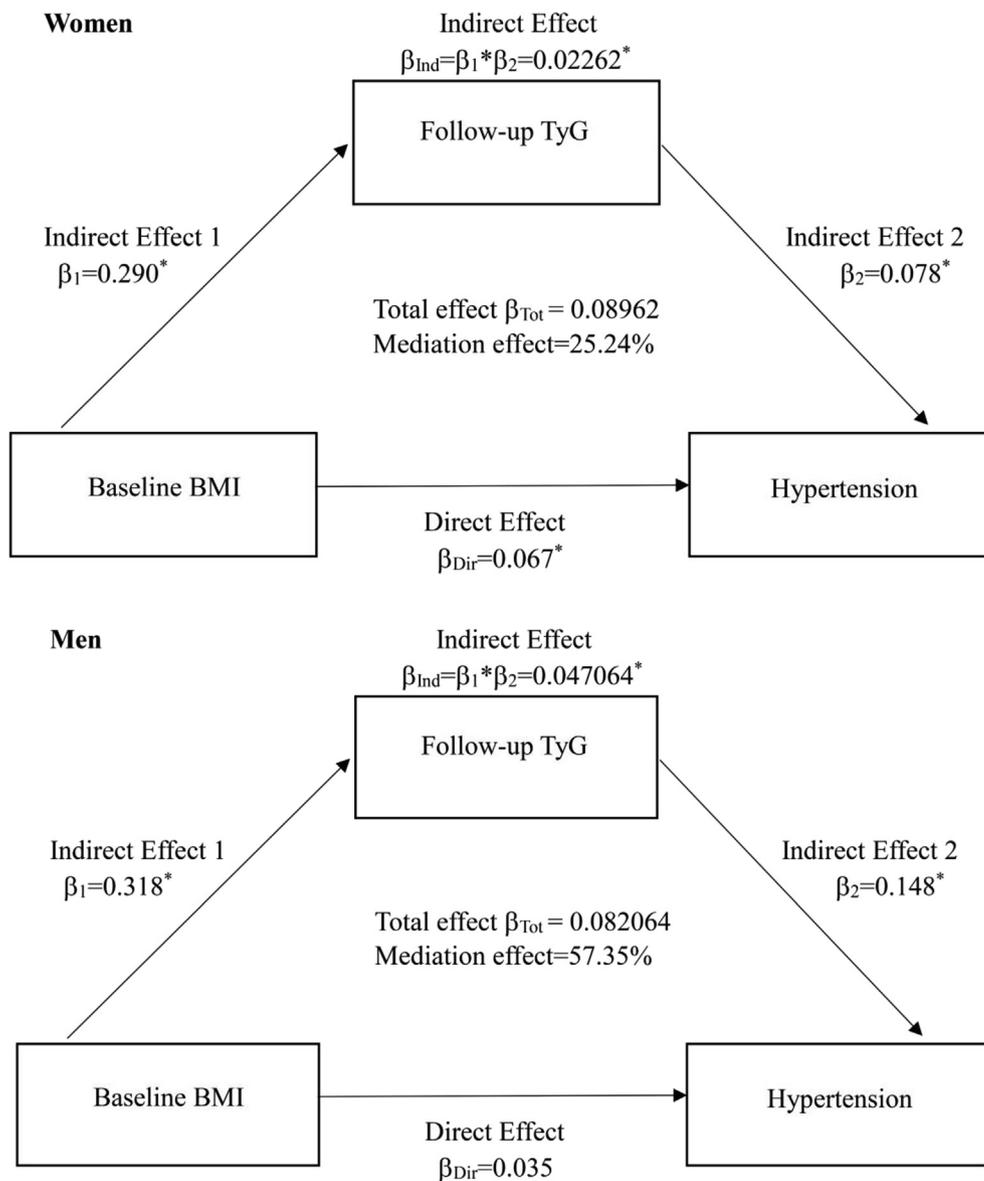


Figure 5 Sensitivity analysis of mediation effect of TyG index on the BMI-hypertension association in men (n = 1781) and women (n = 2300) *, represent coefficients different from 0, P < 0.001.

obesity and insulin resistance to increase BP through the various mechanism, including 1) affect renal sodium metabolism, 2) increase the activity of the sympathetic-adrenal system, 3) affect vasoactive substances. Based on the above mechanism, insulin resistance is considered as an important role between obesity and hypertension [28–30]. However, there is a lack of data on the mediation effect of insulin resistance on obesity-associated hypertension, especially in general Chinese adults. In the present study, the BMI-to-TyG index directionality was first established in the cross-lagged analysis models, and then the temporal patterns were linked to hypertension. The results of the present causal mediation analysis showed that the BMI-hypertension association was partially mediated by TyG index (38.45%). However, the sensitivity analyses between women and men revealed the mediation effect values are quite different, that is the difference TyG

index mediation effect on BMI-hypertension (25.24% in women and 57.35% in men). It has been reported that androgenic sex hormones contributed to the variance in insulin resistance [31] and estrogen deficiency appears to be associated with an increased risk for the development of most of the clinical features comprising hypertension [32]. This mechanism can be explained precisely by the difference between the mediation effect between men and women.

In the present study, we used a cross-lagged analysis to explore the temporal relationship between BMI and TyG index. Although, Hamaker EL et al. shows that if stability of constructs is to some extent of a trait-like, time-invariant nature, the autoregressive relationships of the cross-lagged panel model fail to adequately account for temporal relationship [33]. The TyG and BMI used in our research vary with time. All of the subjects were not treated

antihypertensive, hypoglycemic or lipid-lowering drugs. Such a population better reflect the relationship between BMI and TyG index as normal physiological conditions. Another strength of the present study was based on a prospective population-based sample with data on BMI and TyG index on two-time points, and the relatively large sample size increased the statistical power of our analysis.

However, our study had some limitations that need to be considered. Firstly, the TyG index was used to substitute insulin levels for insulin resistance. However, this scientific fact may be more reflected in the use of insulin. Secondly, our average follow-up time was 28.74 months, if the follow-up time is longer, the result of a temporal relationship between BMI and TyG index may be more credible. Thirdly, our study only collected data at two time points, the lack of an intermediate point data to make our mediation analysis of a major limitation. Finally, the study sample only included rural adults in Liaoning province; further research are required to validate the results in a larger population and more representative groups in the future.

In conclusion, the findings of the current study suggested that BMI and TyG index revealed a mutual effect, and the BMI preceded TyG index. The mediation effect of TyG index on the relationship of BMI with hypertension accounted for 38.45 percent of total effect in total population while there was an obvious difference TyG index mediation effect on BMI-hypertension between women and men. Our study provides direct evidence for the temporal relationship between BMI and insulin resistance. This study would provide important additional insights into the pathophysiological mechanisms of BMI and insulin resistance to hypertension, further provide a scientific basis for future clinical practice.

Author contributions

Yanxia Xie and Rongrong Guo contributed to the study's conception and drafted the manuscript. Zhao Li and Xiaofan Guo acquired the data. Guozhe Sun, Zhaoqing Sun and Jia Zheng contributed to the data cleaning and management. Yingxian Sun and Liqiang Zheng contributed to the study's design and conception.

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Ethical approval

The research has been approved by the Ethics Committee of China Medical University, based on the declaration of Helsinki.

Informed consent

Informed consent was obtained from all individual patients included in the study.

Conflict of interest

All authors approved the manuscript and there is no conflict of interests.

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