

Body mass index influence the association between triglyceride-glucose index and atherosclerosis in community population: the cardiometabolic risk in Chinese (CRC) study

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Abstract

Background: Cardiovascular disease (CVD) is an universal problem in modern society. Atherosclerosis is the leading cause of CVD resulting in high rate of mortality in the population. The study aimed to examine the association of triglyceride-glucose (TyG) index, a novel marker of insulin resistance, with atherosclerosis in Chinese adults, and the effects of different body mass index (BMI) levels on this relationship.

Methods: The study samples were from a community-based health examination survey in central China. A total of 4729 apparently healthy Chinese men and women were included. TyG index was calculated as $\ln[\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$. Parameters of vascular damage, including carotid-femoral pulse wave velocity (cfPWV), carotid-radial pulse wave velocity (crPWV), carotid-dorsalis pedis pulse wave velocity (cdPWV) were measured.

Results: After adjustment for conventional risk factors, TyG index was significantly associated with peripheral arterial stiffness ($\text{cdPWV} > 10.57 \text{ cm/s}$ or $\text{crPWV} > 11.12 \text{ cm/s}$), however, TyG index was not associated with central arterial stiffness, measured by cfPWV. Moreover, we found significant interactions between TyG index and BMI in relation to crPWV and cdPWV. Risk for crPWV and cdPWV elevation was significantly decreased across increasing quartiles of TyG index under different BMI levels ($P < 0.001$). There was a dose-response relationship of TyG index with crPWV and cdPWV in the normal-weight and overweight groups, with the most obvious in the normal-weight individuals. However, the dose-response relationship was not existed among the obesity group where the increase of TyG index did not significantly rise the risk of high crPWV and cdPWV.

Conclusions: TyG index, a simple measure reflecting insulin resistance, might be useful to early identify individuals at a high risk of developing atherosclerosis. Increased BMI weakened the effect of TyG index on crPWV and cdPWV, indicating that the value of TyG index in assessing the risk of atherosclerosis in obese people maybe easily ignored, however, TyG index can better reflect the risk of atherosclerosis in normal-weight adults.

Background

Cardiovascular diseases (CVDs) are a class of chronic non-communicable diseases with the highest incidence of premature death [1]. Atherosclerosis (AS) is the main cause of morbidity and mortality in CVDs, and abnormal blood lipids and blood glucose are one of the main risk factors of AS [2–3]. Various risk factors can lead to the increase of elastic fibrosis collagen fibers, and eventually lead to the decrease of arterial elasticity and increased stiffness by inducing endothelial dysfunction, inflammation and vascular smooth muscle proliferation [4–5]. Although AS is clinically present primarily in middle-aged and older adults, it is now recognized that the disease has a long insidious duration and begins early in life. Early identification of high-risk groups for AS and early intervention with preventive measures can slow the progression of AS and delay the occurrence of CVDs.

Pulse wave velocity (PWV) is one of the indicators for evaluating AS [6]. It is the most commonly used non-invasive measure of arterial stiffness and can be used as an indicator for reflecting AS and predicting cardiovascular events [7]. PWV measured at different sites can reflect the atherosclerotic alterations at central (e.g. carotid-femoral pulse wave velocity (cfPWV)) or peripheral arteries (e.g. carotid-dorsalis pedis pulse wave velocity (cdPWV) and carotid-radial pulse wave velocity (crPWV)) [8]. Studies have shown that insulin resistance (IR) plays an important role in the development of AS [9]. Triglyceride-glucose (TyG) index combines both levels of triglycerides and fasting glucose, and it has been reported to be significantly correlated with IR and a reliable surrogate marker of IR [10].

With the change in lifestyle, the prevalence of overweight and obesity is increasing rapidly, reaching global epidemic proportions [11–12]. It is well known that obesity is closely related to a variety of metabolic diseases, such as type 2 diabetes, hypertension, dyslipidemia, AS and CVDs [13–14]. Body mass index (BMI) is widely used to define obesity and it appears to be the most commonly employed metric used for stratifying obesity in clinical practice [15–16]. Goossens et al. believed that when BMI exceeded 18.5 kg/m², BMI was positively correlated with risk factors for cardiovascular and metabolic diseases [17]. However, a large population-based study recently showed that TyG index is a better indicator of metabolic risks in people with normal BMI levels [15]. In particular, there is still a certain degree of AS risk in non-obese people, which cannot be explained by previous obesity-related indicators, we guess TyG index could provide a certain possibility for the solution of this problem. Meanwhile, whether there is an interaction between BMI and TyG index that jointly affects the occurrence and development of AS has not been clarified.

Hence, the aim of this study was to investigate whether TyG index is associated with cfPWV, crPWV and cdPWV in apparently healthy Chinese adults, as well as the influence of BMI on the relationship, which is of great significance for the early screening of high-risk population, the control of the occurrence and development of AS, and the reduction of morbidity and mortality of CVDs.

Materials And Methods

1. Study population

In the Cardiometabolic Risk in Chinese (CRC) Study, we performed a community-based health examination survey for subjects (aged 19–90 years) who were randomly selected from residents living in the urban area of central China. For the present study, we included adult men and women who were successfully measured for PWVs, Blood pressure (BP), BMI, neck circumference (NC), waist circumference (WC), age, serum uric acid (SUA) and other metabolic markers. The exclusion criteria included the history of vascular disease, diabetes mellitus, hyperlipidemia, coronary heart disease, chronic inflammatory disease, acute and chronic liver and kidney failure. Meanwhile, anemia, cancer, pregnancy and various immune diseases were also excluded. In addition, we excluded people who did not undergo PWVs determination. In total 4729 men and women were included in the final analyses. There was not significant difference in basic characteristics such as age, education, and anthropometrics

between individuals included in the analyses and those who were excluded. Written consents were obtained from all the participants. The study was reviewed and approved by the ethics committee of the Central Hospital of Xuzhou, Affiliated Hospital of Medical School of Southeast University, China.

2. Assessment of PWVs

CfPWV, cdPWV and crPWV in subjects at rest were measured using Complior device (Artech-Medical, Pantin, France) that allowed pulse wave recording and automatic calculation of PWVs with 2 transducers. The pulse wave of the carotid and femoral arteries was analyzed, estimating the delay with respect to the ECG wave and calculating the PWV. CdPWV and crPWV were obtained in a similar way, with the pulse wave being measured simultaneously in the right radial, dorsum of foot and right carotid arteries. Three maxima and three minima were removed from 16 consecutive electrocardiogram gated waveforms. For analysis, we averaged 10 waveforms. PWV was based on the distance/time ratio (meters/second) and calculated as the path length divided by the transit time and expressed as m/s [8]. The subjects were divided into four groups according to their PWV levels, with highest PWV quartile set as risk of high PWVs [38–39].

3. Assessment of biomarkers

Venous blood sample was drawn from all subjects after an overnight fast (10 h). After blood was drawn, samples were allowed to clot at room temperature for 1–3 h and serum was separated. Immediately after clotting, serum was separated by centrifugation for 15 min at 3000 r.p.m. Fasting blood samples were collected for measurement of fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and SUA. Participants underwent a 75-g oral glucose tolerance test (OGTT). Blood samples were drawn at 120 minutes after the glucose or carbohydrate load. All biochemical assays were determined enzymatic ally on an auto analyzer (Type 7600, Hitachi Ltd, and Tokyo, Japan). Hemoglobin A1c (HbA1c) was measured by high-performance liquid chromatography (HPLC; HLC-723G7 hemoglobin HPLC analyzer, Tosoh Corp.) analysis according to the standardized method. TyG index was calculated as $\ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$.

4. Anthropometric measures

Body weight was recorded to the nearest 0.1 kg with the participants wearing light indoor clothing and no shoes. Height was recorded to the nearest 0.5 cm without shoes using a standardized wall-mounted height board. BMI was calculated as weight (in kilograms) divided by height (in meters) squared. According to Chinese guidelines for overweight and obesity, the BMI criteria (< 24.0 , $24.0 - < 28.0$, $\geq 28.0 \text{ kg/m}^2$) was used to classify individuals as normal-weight, overweight, and obese, respectively [37]. NC (cm) was measured with head erect and eyes facing forward, horizontally at the upper margin of the laryngeal prominence with a flexible tape [18]. Waist circumference (cm), an index of total abdominal fat, was measured at the mid-point between the lowest rib margin and the iliac crest. BP was measured after the subject had rested for at least 5 minutes with a mercury manometer by doctors. Three measurements, 60 seconds apart, were taken. The mean of the three measurements was used for analysis.

5. Statistical analysis

Data management and statistical analysis were performed using SPSS version 22.0 (SPSS Inc, Chicago, USA) and stata version 14.0 (StataCorp, College Station, Texas, USA). Categorical variates were summarized as frequency (percentage). Continuous variates were summarised as mean values \pm standard deviation (SD). Comparisons of metabolic indexes under the quartile of TyG index were performed using ANOVA. Chi-square test was employed to tell the differences of categorical variates between groups. Multivariate logistic regression was employed to determine the independent association between TyG index and risk of high PWVs and adjust for covariates including age, sex, BMI, BP, LDL, HbA1c, SUA and heart rate (HR). With the increase of TyG index, the dose-response plot of high crPWV and cdPWV risk under different BMI levels was analyzed by generalized linear equations using stata version 14.0. The results were shown as odds ratios (ORs) and 95% confidence intervals (95% CI). The interactions between TyG index and BMI were assessed by introduction of cross-product term in the regression models. $P < 0.05$ were considered statistically significant.

Results

1. The characteristics of the study participants by TyG index levels

The baseline clinical and biochemical characteristics for the 4729 participants according to quartile categories based on baseline TyG index levels were shown in Table 1. Positive relationships between the TyG index and crPWV, cfPWV, cdPWV, BMI, NC, WC, age, SBP, DBP, 2 h OGTT, HbA1c, TC, LDL-C, SUA and HR were observed, but a negative relationship existed between TyG index and HDL-C ($P < 0.05$).

2. Association between TyG index and markers of central and peripheral arterial stiffness

The subjects were divided into two groups according to their PWV levels where $cdPWV > 10.57$ cm/s, $cfPWV > 11.51$ cm/s, $crPWV > 11.12$ cm/s were set as PWV increase. Table 2 displays the associations of risk of high PWVs with TyG index in quartiles. After adjustment for sex, age and BMI, TyG index levels were significantly associated with an increasing trend of high cdPWV, cfPWV and crPWV risks ($P < 0.001$). Further adjustment for SBP, DBP, LDL-C, HbA1c, SUA and HR in Model2 attenuated the association between TyG index and cfPWV ($P = 0.112$), while the relationship of TyG index and the risk of high cdPWV and crPWV remained, which reflected the stiffness of peripheral arteries ($P < 0.001$).

3. Relationship of TyG index with crPWV and cdPWV under different BMI levels

We further evaluated the interaction between TyG index and BMI on crPWV and cdPWV (Table 3). The subjects were divided into three subgroups according to their BMI levels, and it was found that TyG index

and BMI had significant interaction with crPWV and cdPWV (both $P < 0.001$). The association was more pronounced in people with $BMI < 24 \text{ kg/m}^2$ ($P < 0.001$). Risk for crPWV and cdPWV elevation was significantly decreased across increasing quartiles of TyG index under different BMI levels (both $P < 0.001$). Taking quartile 1 of the TyG index as the reference group, the adjusted odds ratios (ORs) for increased risk of crPWV and cdPWV were significantly higher in quartile 4 of TyG index among the normal BMI group (OR = 1.950 and 2.951, respectively). Similar results can be seen in the overweight group, while in the obesity group, the increased risk of crPWV and cdPWV elevation decreased significantly compared to the normal and overweight groups.

We also examined the dose-response relationship of TyG index with high crPWV and cdPWV risk under different BMI levels (Fig. 1 and Fig. 2). After adjustment for age, sex, SBP, DBP, FPG and TC, we found that the dose-response relationships between TyG index and risk of high crPWV and cdPWV could be seen in the normal and overweight groups, with the most obvious in the normal individuals. However, the dose-response relationship was not existed among the obesity group where increased TyG index did not significantly raise the risk of high crPWV and cdPWV.

Discussion

In this study, we found positive association between TyG index and risk of peripheral arterial stiffness (cdPWV $> 10.57 \text{ cm/s}$ or crPWV $> 11.12 \text{ cm/s}$). However, TyG index were not associated with central arterial stiffness, measured by cfPWV. Moreover, we found significant interactions between TyG index and BMI in relation to crPWV and cdPWV.

Several previous studies have shown that TyG index was associated with CVDs [19–20], and the detrimental effects of high TyG index might occur at early stage of AS [21–22]. In a recent cross-sectional study, it was found that TyG index was independently related to brachial ankle PWV (baPWV) in Korean subjects [23]. However, it is not clear whether TyG index specifically affect central or peripheral arterial stiffness because baPWV may be influenced by both sites [24]. Our results suggest that high TyG index are more likely to affect peripheral arterial stiffness, while its effect on central arterial stiffness is mild. Poon et al. [40] conducted a cross-sectional and cohort follow-up study on 2571 middle-aged and elderly people from the American community, and found that higher TyG index was associated with higher cfPWV in cross-sectional study. However, high aortic stiffness was not caused by faster annual rate of log-Homeostasis model of assessment-insulin resistance (HOMA-IR) or log-TyG in the follow-up study. The discrepancy between the results of their cross-sectional study and ours maybe caused by different study population, ethnic and sample size. In spite of this, our sample size is larger, and their long-term follow-up study verifies our study results. Therefore, the role of TyG index in aortic wall remodeling should be further studied in the future.

Several mechanisms may be underlying the associations of high TyG index and AS. Firstly, we suspect it may have something to do with IR. IR not only consists of a decrease in insulin's ability to process glucose, but also of impaired lipid oxidative utilization [25]. And the decrease of the secretion of insulin by beta cells inevitably leads to a decrease in the amount of functional insulin, which then could cause a decrease of the body's ability to process glucose and blood lipids [26]. The above two aspects will cause the body to show a state of hyperglycemia and hyperlipidemia [26]. The content of free fatty acids in the blood increases, enters non-adipose tissue and further synthesizes triglycerides and deposits, which could result in abnormal lipid metabolism and amplifies the basic metabolic disorders characterized by IR, leading to the occurrence of AS [27]. At present, TyG index is known as a surrogate marker of IR [28–30], and previous studies had proved that IR was closely related to PWV [9]. Therefore, we speculated that IR may play a crucial role in the occurrence of AS, which was mediated by TyG index. Secondly, most previous studies had suggested that AS was only associated with excessive lipid accumulation [27]. However, recent advances suggest that AS is a multifactorial and multigenic inflammatory condition in the arterial wall [31–32]. Some of the major risk factors for the development of AS, including hyperglycemia, dyslipidemia, and hyperinsulinemia, along with hypertension, smoking, and physical inactivity, are classified as metabolic syndrome, persistent presence of various atherogenic molecules instigates a hypoxic environment along with oxidative stress [33]. These changes could contribute towards enhanced ROS production in the cells, which activating and augmenting various inflammatory pathways, leading to the occurrence and development of AS [34]. Therefore, we speculated that TyG index may mediate the occurrence of AS through inflammation and oxidative stress.

The association between TyG index and AS under different BMI levels remained unclear. It is well known the association between BMI and AS [35]. Interestingly, our study found that there was an interaction between TyG index and BMI, which jointly affected AS. With the increase of BMI, the contribution of TyG index to the increase of crPWV and cdPWV decreased gradually. The adverse effect of TyG index on arterial stiffness was more obvious in people of normal weight than in obese population suggesting that TyG index could better reflect the risk of AS in people of normal weight. Further analysis showed that there was a dose-response relationship of TyG index with crPWV and cdPWV at different BMI levels, and the dose-response relationship was more obvious in individuals with BMI < 24 kg /m². TyG index performed better in lean individuals probably because it was different from HOMA-IR, which mainly reflected muscle IR, while HOMA-IR reflected IR in the liver [25, 36]. A study about the association between TyG index and AS suggested that the TyG index may function in non-diabetic elderly populations through a different pathway from HOMA-IR [40]. Meanwhile, Lamb et al. [21] conducted a cross-sectional study of 473 postmenopausal women in Greek population, and found that TyG index was significantly better than metabolic syndrome in predicting subclinical AS in the population of postmenopausal lean women. More specifically, TyG index in lean postmenopausal women was significantly correlated with carotid intima media thickness, carotid atherosclerotic plaque formation, and aortic hardness as measured by PWV, which was similar to our findings.

To our knowledge, studies about the interactions of BMI and TyG index on AS in general population of Chinese adults are lacking. There are some limitations that should be considered in the cross-sectional study. First, causality between the TyG index and AS cannot be assured with certainty owing to the cross-sectional design. Second, our study was performed among Chinese adults, the result might not be applicable to other ethnicities. Third, the sample size was relatively small. In addition, the participants in our study were enrolled based on a community health examination survey, and thus the generalizability of the results may be limited. Further investigation on larger sample of subjects and longitudinal studies are needed to establish the causality between TyG index and AS.

Conclusion

In conclusion, TyG index is significantly associated with AS in healthy Chinese adults. Increased BMI weakened the effect of TyG index on AS, indicating that TyG index might be a useful marker for predicting AS among normal-weight people. As an alternative to IR, TyG index can help to identify those individuals (i.e., normal-weight people) who could be mistaken for not having a high risk of AS. In addition to traditional high-risk groups, the preventive measures against this high TyG index subgroup (i.e., normal-weight population) may have important clinical implications for reducing cardiovascular risk.

Abbreviations

CVD

cardiovascular disease

TyG

triglyceride-glucose

BMI

body mass index

cfPWV

carotid-femoral pulse wave velocity

crPWV

carotid-radial pulse wave velocity

cdPWV

carotid-dorsalis pedis pulse wave velocity

AS

atherosclerosis

PWV

pulse wave velocity

IR

insulin resistance

NC

neck circumference

WC

waist circumference

SUA

serum uric acid

FPG

fasting plasma glucose

TC

total cholesterol

TG

triglycerides

HDL-C

high-density lipoprotein

LDL-C

low density lipoprotein

OGTT

75-g oral glucose tolerance test

HbA1c

hemoglobin A1c

baPWV

brachial-ankle pulse wave velocity

HOMA-IR

homeostasis model of assessment-insulin resistance

Declarations

Authors' contributions

JL, HFG, YW^a, QQQ, XYM, XKL were responsible for patient recruitment, data acquisition and/or analysis. JL, HFG, YW^a, QQQ, XYM, XZ, WX, TTW, PL contributed to study design. JL, HFG, YW^a, QQQ, XYM, XKL, YW^b, FT contributed to statistical analysis and drafting of the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

Not applicable.

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Ethics approval and consent to participate

The study was reviewed and approved by the ethics committee of the Central Hospital of Xuzhou, Affiliated Hospital of Medical School of Southeast University, China. All subjects gave informed written consent for study participation.

Consent for publication

All authors approved the current version of the manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

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References

1. da Silva A, Caldas APS, Hermsdorff HHM, et al. Triglyceride-glucose index is associated with symptomatic coronary artery disease in patients in secondary care. *Cardiovasc Diabetol.* 2019;18:89.
2. Peng J, Luo F, Ruan G, et al. Hypertriglyceridemia and atherosclerosis. *Lipids Health Dis.* 2017;16:233.
3. Ruscitti P, Margiotta DPE, Macaluso F, et al. Subclinical atherosclerosis and history of cardiovascular events in Italian patients with rheumatoid arthritis: Results from a cross-sectional, multicenter GIRRCS (Gruppo Italiano di Ricerca in Reumatologia Clinica e Sperimentale) study. *Med (Baltim).* 2017;96:e8180.
4. Deng W, Tang T, Hou Y, et al. Extracellular vesicles in atherosclerosis. *Clin Chim Acta.* 2019;495:109–17.
5. Vallée A, Yannoutsos A, Temmar M, et al. Determinants of the aortic pulse wave velocity index in hypertensive and diabetic patients: predictive and therapeutic implications. *J Hypertens.* 2018;36:2324–32.
6. Kim HL. Pulse Wave Velocity in Atherosclerosis. *Front Cardiovasc Med.* 2019;6:41.
7. Chiha J, Mitchell P, Gopinath B, et al. Prediction of Coronary Artery Disease Extent and Severity Using Pulse Wave Velocity. *PLoS One.* 2016;11:e0168598.

8. Liang J, Wang Y, Li H, et al. Neck circumference and early stage atherosclerosis: the cardiometabolic risk in Chinese (CRC) study. *Cardiovasc Diabetol*. 2014;13:107.
9. Insulin resistance, lipotoxicity, type 2 diabetes and atherosclerosis: the missing links. The Claude Bernard Lecture 2009 *Diabetologia*. 2010;53:1270–87.
10. Su WY, Chen SC, Huang YT, et al. Comparison of the Effects of Fasting Glucose, Hemoglobin A, and Triglyceride-Glucose Index on Cardiovascular Events in Type 2 Diabetes Mellitus. *Nutrients* 2019; 11.
11. Kim CS, Ko SH, Kwon HS, et al. Prevalence, awareness, and management of obesity in Korea: data from the Korea national health and nutrition examination survey (1998–2011). *Diabetes Metab J*. 2014;38:35–43.
12. Barazzoni R, Bischoff S, Boirie Y, et al. Sarcopenic Obesity: Time to Meet the Challenge. *Obes Facts*. 2018;11:294–305.
13. Gadde KM, Martin CK, Berthoud HR. Obesity: Pathophysiology and Management. *J Am Coll Cardiol*. 2018;71:69–84.
14. Neeland IJ, Poirier P. Cardiovascular and Metabolic Heterogeneity of Obesity: Clinical Challenges and Implications for Management. *Circulation*. 2018;137:1391–406.
15. Lee SH, Han K, Yang HK, et al. Identifying subgroups of obesity using the product of triglycerides and glucose: the Korea National Health and Nutrition Examination Survey, 2008–2010. *Clin Endocrinol (Oxf)*. 2015;82:213–20.
16. Kommuri NV, Zalawadiya SK, Veeranna V, et al. Association between various anthropometric measures of obesity and markers of subclinical atherosclerosis. *Expert Rev Cardiovasc Ther*. 2016;14:127–35.
17. The Metabolic Phenotype in Obesity. Fat Mass, Body Fat Distribution, and Adipose Tissue Function. *Obes Facts*. 2017;10:207–15.
18. Liang J, Teng F, Liu X, et al. Synergistic effects of neck circumference and metabolic risk factors on insulin resistance: the Cardiometabolic Risk in Chinese (CRC) study. *Diabetol Metab Syndr*. 2014;6:116.
19. Jin JL, Cao YX, Wu LG, et al. Triglyceride glucose index for predicting cardiovascular outcomes in patients with coronary artery disease. *J Thorac Dis*. 2018;10:6137–46.
20. Mao Q, Zhou D, Li Y, et al. The Triglyceride-Glucose Index Predicts Coronary Artery Disease Severity and Cardiovascular Outcomes in Patients with Non - ST - Segment Elevation Acute Coronary Syndrome. *Dis Markers* 2019; 2019: 6891537.
21. Lambrinoudaki I, Kazani MV, Armeni E, et al. The TyG Index as a Marker of Subclinical Atherosclerosis and Arterial Stiffness in Lean and Overweight Postmenopausal Women. *Heart Lung Circ*. 2018;27:716–24.
22. Alizargar J. Comparison of Carotid Ultrasound Indices and the Triglyceride Glucose Index in Hypertensive and Normotensive Community - Dwelling Individuals: A Case Control Study for Evaluating Atherosclerosis. *Medicina (Kaunas)* 2018; 54.

23. Won KB, Park GM, Lee SE, et al. Relationship of insulin resistance estimated by triglyceride glucose index to arterial stiffness. *Lipids Health Dis.* 2018;17:268.
24. Liang J, Li Y, Zhou N, et al. Synergistic effects of serum uric acid and cardiometabolic risk factors on early stage atherosclerosis: the cardiometabolic risk in Chinese study. *PLoS One.* 2012;7:e51101.
25. Kelley DE. Skeletal muscle triglyceride. An aspect of regional adiposity and insulin resistance. *Diabetes Care.* 2001;24:933–41.
26. Wainwright P. Bidirectional Relationships and Disconnects between NAFLD and Features of the Metabolic Syndrome. *Int J Mol Sci.* 2016;17:367.
27. Lewis GF, Carpentier A, Adeli K. Disordered fat storage and mobilization in the pathogenesis of insulin resistance and type 2 diabetes. *Endocr Rev.* 2002;23:201–29.
28. Kang B, Yang Y, Lee EY, et al. Triglycerides / glucose index is a useful surrogate marker of insulin resistance among adolescents. *Int J Obes (Lond).* 2017;41:789–92.
29. Unger G, Benozzi SF, Perruzza F. Triglycerides and glucose index: a useful indicator of insulin resistance. *Endocrinol Nutr.* 2014;61:533–40.
30. Guerrero-Romero F, Villalobos-Molina R, Jiménez-Flores JR, et al. Fasting Triglycerides and Glucose Index as a Diagnostic Test for Insulin Resistance in Young Adults. *Arch Med Res.* 2016;47:382–7.
31. Wolf D. Immunity and Inflammation in Atherosclerosis. *Circ Res.* 2019;124:315–27.
32. Ali L, Schnitzler JG. Metabolism. The road to inflammation and atherosclerosis. *Curr Opin Lipidol.* 2018;29:474–80.
33. Varghese JF, Patel R. Novel Insights in the Metabolic Syndrome-induced Oxidative Stress and Inflammation-mediated Atherosclerosis. *Curr Cardiol Rev.* 2018;14:4–14.
34. Zhang X, Zhang JH, Chen XY, et al. Reactive oxygen species-induced TXNIP drives fructose-mediated hepatic inflammation and lipid accumulation through NLRP3 inflammasome activation. *Antioxid Redox Signal.* 2015;22:848–70.
35. van den Munckhof ICL, Holewijn S, de Graaf J. Sex differences in fat distribution influence the association between BMI and arterial stiffness. *J Hypertens.* 2017;35:1219–25.
36. Katsuki A, Sumida Y, Urakawa H, et al. Increased visceral fat and serum levels of triglyceride are associated with insulin resistance in Japanese metabolically obese, normal weight subjects with normal glucose tolerance. *Diabetes Care.* 2003;26:2341–4.
37. Sun H, Ren X, Chen Z, et al. Association between body mass index and mortality in a prospective cohort of Chinese adults. *Med (Baltim).* 2016;95:e4327.
38. Ohishi M, Tatara Y, Ito N, et al. The combination of chronic kidney disease and increased arterial stiffness is a predictor for stroke and cardiovascular disease in hypertensive patients. *Hypertens Res.* 2011;34:1209–15.
39. Yen CH, Hung CL, Lee PY, et al. Segmental arterial stiffness in relation to B-type natriuretic peptide with preserved systolic heart function. *PLoS One.* 2017;12:e0183747.

40. Poon AK, Meyer ML, Tanaka H, et al. Association of insulin resistance, from mid-life to late-life, with aortic stiffness in late-life: the Atherosclerosis Risk in Communities Study. *Cardiovasc Diabetol.* 2020;19:11.

Tables

Table 1. The clinical characteristics of participants under different levels of TyG index

Variables	TyG in quartiles				p for trend
	Q1	Q2	Q3	Q4	
	<3.97	3.97-5.92	5.93-9.3	≥9.3	
	1181	1184	1180	1184	
Carotid-femoral pulse wave velocity (cm/s)	10.03±1.56	10.09±1.47	10.31±1.57	10.41±1.59	<0.001
Carotid-radial pulse wave velocity (cm/s)	10.37±1.83	10.57±1.95	10.81±1.92	10.93±1.80	<0.001
Carotid-dorsalis pedis pulse wave velocity (cm/s)	9.35±1.41	9.51±1.49	9.77±1.54	9.93±1.46	<0.001
Neck circumference (cm)	48.08±13.14	47.85±12.57	49.69±13.01	48.86±12.66	0.002
Waist circumference (cm ²)	23.27±2.89	24.12±3.10	25.24±3.06	26.08±3.01	<0.001
Body mass index (kg/m ²)	34.55±3.72	35.18±3.45	36.00±3.61	36.66±4.14	<0.001
Systolic blood pressure (mmHg)	81.51±9.47	84.38±9.77	87.86±9.58	90.26±8.73	<0.001
Diastolic blood pressure (mmHg)	121.17±16.02	124.27±17.01	127.89±17.04	130.51±16.89	<0.001
Fasting glucose (mmol/l)	76.56±10.94	78.43±11.25	80.63±11.50	82.70±11.71	<0.001
Fasting insulin (mmol/l)	5.90±1.46	6.02±1.46	6.24±1.52	6.52±1.49	<0.001
Hemoglobin A1c (%)	5.21±0.39	5.26±0.40	5.31±0.40	5.36±0.40	<0.001
Total cholesterol (mmol/l)	4.64±0.79	4.92±0.80	5.17±0.86	5.40±0.98	<0.001
LDL-C (mmol/l)	1.42±0.30	1.32±0.28	1.22±0.26	1.05±0.24	<0.001
HDL-C (mmol/l)	2.69±0.66	2.99±0.64	3.22±0.71	3.03±0.88	<0.001
Uric acid (mmol/l)	265.02±69.98	285.36±73.28	307.99±76.87	330.76±83.82	<0.001
Heart rate (bpm)	69.76±10.37	70.05±9.99	70.68±10.29	71.22±10.02	0.002

Quantitative variables are shown as mean ± SD.

Abbreviations: crPWV, carotid-radial pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; cdPWV, carotid-dorsalis pedis pulse wave velocity; BMI, body mass index; NC, neck circumference; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; 2h OGTT, 2 hours blood glucose of oral glucose tolerance test; HbA1c, hemoglobin A1c; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SUA, serum uric acid; HR, heart rate; bpm, beats per minute.

Table 2. Associations of TyG index with central and peripheral arterial stiffness.

TyG in quartiles	Normal level	High level	Model1		Model2	
			OR	95%CI	OR	95%CI
$VV \square cm/s \square$	≤ 11.12	> 11.12				
Q1	971(82.2%)	210(17.8%)	1	1	1	1
Q2	927(78.3%)	257(21.7%)	1.36	1.096~1.689	1.22	0.881~1.690
Q3	835(70.8%)	345(29.2%)	1.889	1.528~2.334	1.937	1.401~2.678
Q4	814(69.8%)	370(31.3%)	2.148	1.732~2.664	1.767	1.273~2.453
<i>p</i> for trend	<0.001		<0.001		<0.001	
$VV \square cm/s \square$	≤ 11.51	> 11.51				
Q1	954(80.8%)	227(19.2%)	1	1	1	1
Q2	923(78.0%)	261(22.0%)	1.346	1.079~1.680	1.054	0.755~1.472
Q3	880(74.6%)	300(25.4%)	1.447	1.161~1.804	1.213	0.865~1.702
Q4	844(71.3%)	340(28.7%)	1.944	1.556~2.429	1.276	0.908~1.795
<i>p</i> for trend	<0.001		<0.001		0.112	
$VV \square cm/s \square$	≤ 10.57	> 10.57				
Q1	942(79.8%)	239(20.2%)	1	1	1	1
Q2	923(78.0%)	261(22.0%)	1.143	0.929~1.405	1.075	0.814~1.420
Q3	861(73.0%)	319(27.0%)	1.606	1.307~1.973	1.489	1.121~1.976
Q4	820(69.3%)	364(30.7%)	2.015	1.635~2.484	1.586	1.190~2.112
<i>p</i> for trend	<0.001		<0.001		<0.001	

el1:adjusted sex age BMI

el2:adjusted sex age BMI ,SBP ,DBP ,LDL, HbA1c, SUA and HR

Abbreviations: crPWV, carotid-radial pulse wave velocity; cfPWV, carotid-femoral pulse wave velocity; cdPWV, carotid-dorsalis pedis pulse wave velocity; TyG: triglyceride-glucose; OR, odds ratio; CI, confidence interval.

Table 3. The relationship of TyG index with crPWV and cdPWV under different BMI levels

TyG in quartiles						
OR [95% C.I.]						
BMI (kg/m ²)	Q1	Q2	Q3	Q4	<i>p</i> for trend	<i>p</i> for interaction
<24	1	1.081 (0.809~1.446)	1.457 (1.056~2.009)	1.950 (1.338~2.843)	<0.001	<0.001
[24~28)	1	1.167 (0.794~1.716)	1.042 (0.717~1.515)	1.702 (1.171~2.474)	0.003	
≥28	1	0.568 (0.202~1.598)	1.291 (0.503~3.310)	1.571 (0.617~4.000)	0.006	
<24	1	1.267 (0.898~1.787)	2.118 (1.485~3.021)	2.051 (1.373~3.063)	<0.001	<0.001
[24~28)	1	1.368 (0.903~2.073)	1.696 (1.149~2.503)	2.347 (1.602~3.438)	<0.001	
≥28	1	1.267 (0.513~3.125)	1.174 (0.494~2.792)	1.189 (0.508~2.785)	0.944	

Abbreviations: crPWV, carotid-radial pulse wave velocity; cdPWV, carotid-dorsalis pedis pulse wave velocity; TyG: triglyceride-glucose; BMI, body mass index; OR, odds ratio; CI, confidence interval.

Analysis was adjusted for age, sex, SBP, DBP, FPG and TC.

Figures

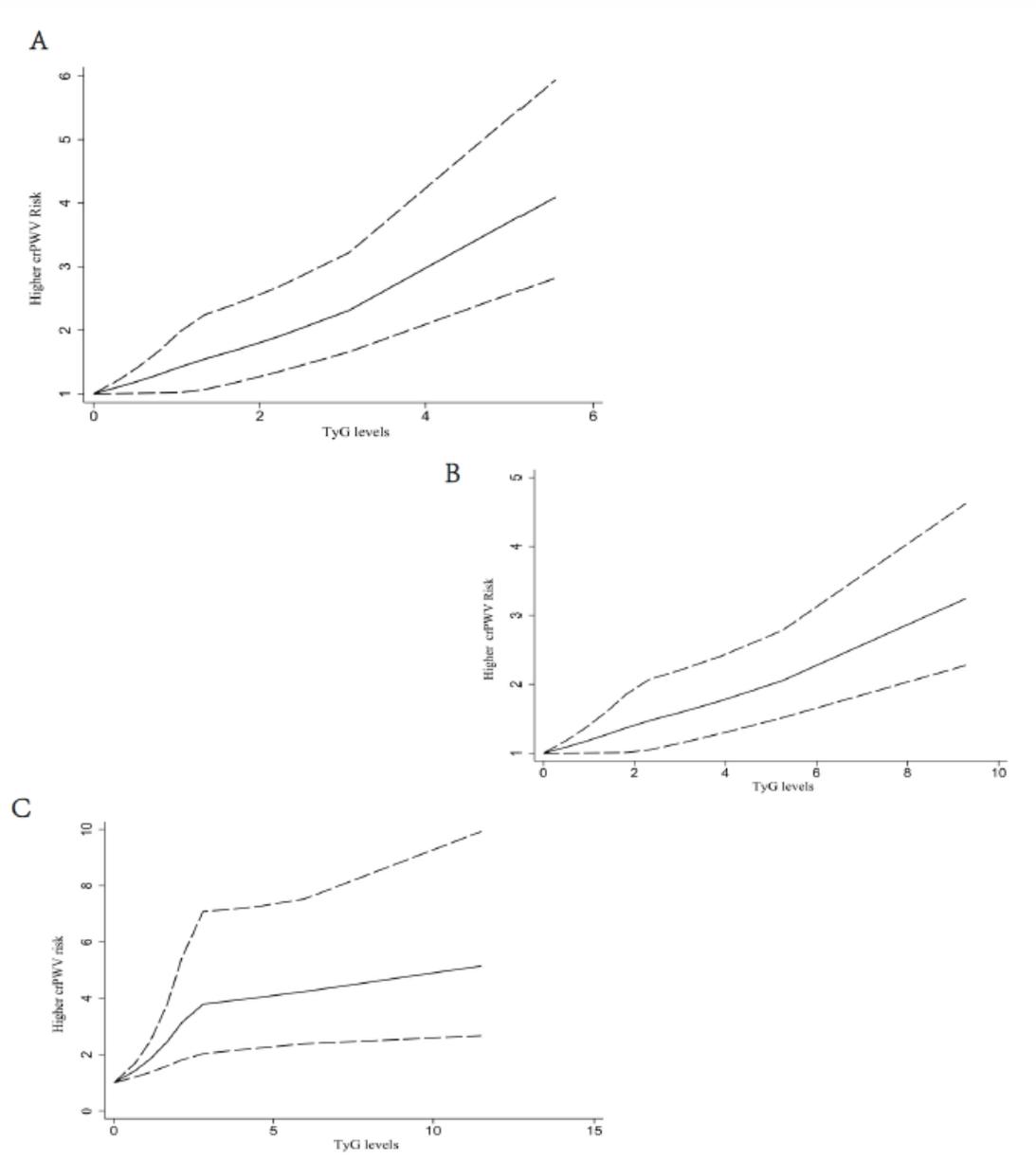


Figure 1

Dose-response relationship between TyG index and high crPWV risk under different BMI levels (A: BMI < 24 kg/m², B: 24 kg/m² ≤ BMI < 28 kg/m², C: BMI ≥ 28 kg/m²). Analysis was adjusted for age, sex, SBP, DBP, FPG and TC. Abbreviations: crPWV, carotid-radial pulse wave velocity; TyG: triglyceride-glucose; BMI, body mass index.

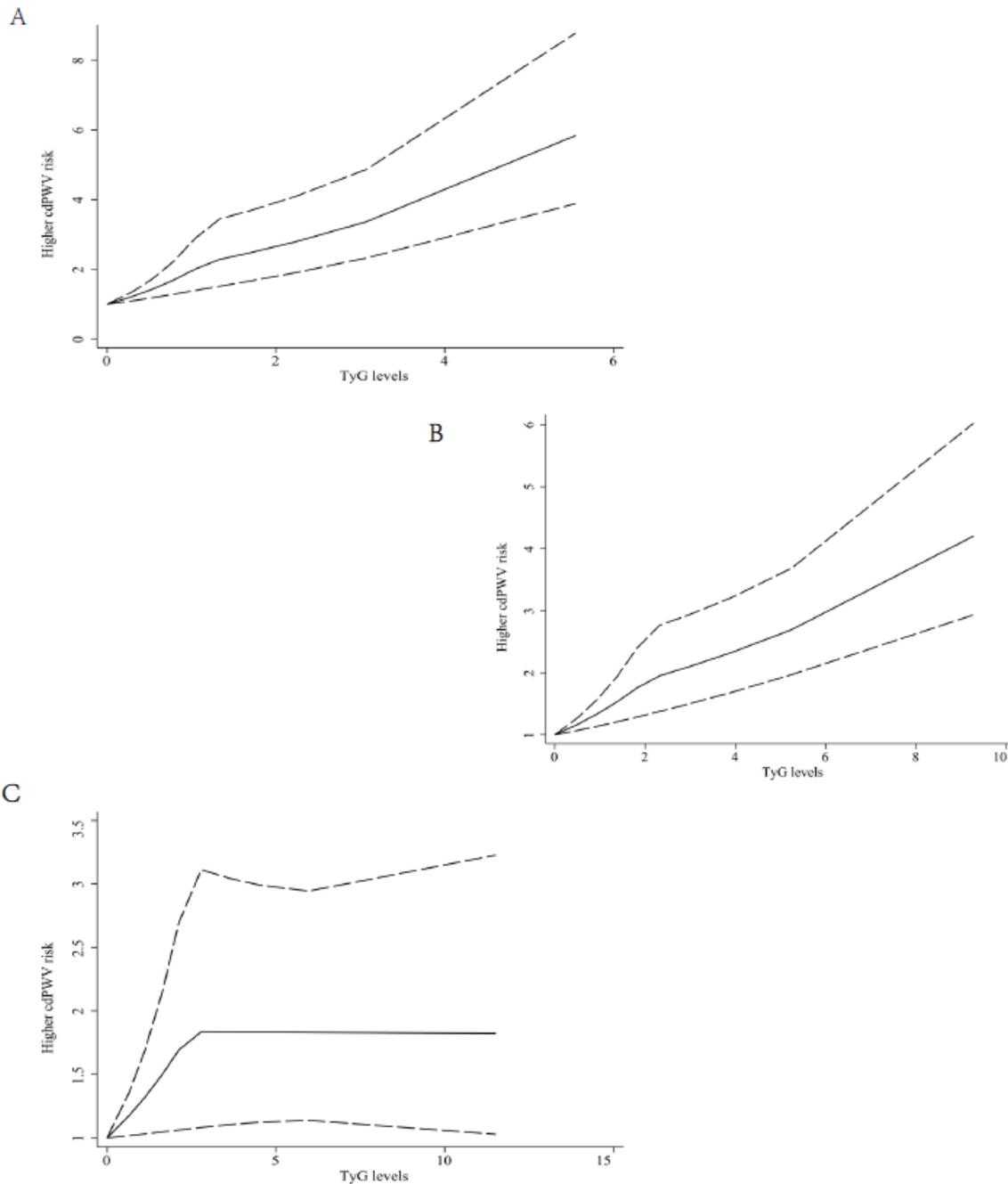


Figure 2

Dose-response relationship between TyG index and high cdPWV risk under different BMI levels (A: BMI < 24 kg/m², B: 24 kg/m² ≤ BMI < 28 kg/m², C: BMI ≥ 28 kg/m²). Analysis was adjusted for age, sex, SBP, DBP, FPG and TC. Abbreviations: cdPWV, carotid-dorsalis pedis pulse wave velocity; TyG: triglyceride-glucose; BMI, body mass index.