High triglyceride glucose index is more closely associated with hypertension than lipid or glycemic parameters in elderly individuals: a cross-sectional survey from the Reaction Study.

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Abstract

**Background:** Both lipid and glucose abnormalities are associated with hypertension (HTN). However, it is unclear whether triglyceride-glucose (TyG) index is associated with HTN. Therefore, the aim of this study is to investigate the association of TyG index and HTN and compare the discriminative power of TyG index, lipid, glycemic parameters for the risk of HTN in the elderly individuals.

**Methods:** The present study was nested in a longitudinal (REACTION) study from May 2011 to December 2011, which was designed to demonstrate the association of abnormal glucose metabolism with the risk of cancer in the Chinese population. 43591 participants were recruited in this cross-sectional study. TyG index were divided into 5 groups: <20% group, the 20-39% group, the 40-59% group, the 60-79% group and the ≥80% group according quartile division of the subjects. Three multivariate logistic regression models were used to evaluate the association between TyG v.s lipid parameters, glycemic parameters and HTN.

**Results:** Multivariate logistic regression analysis shows that compared with lipid and glycemic parameters, TyG index remains significantly associated with HTN in either total subjects or subjects separated into men and women (odds ratio (OR) 1.33, 95% confidence interval (CI) 1.18-1.51, p<0.0001 in total subjects; OR 1.39, 95% CI 1.11-1.74, p=0.0042 in men; OR 1.28, 95% CI 1.11-1.49, p=0.0010 in women). In stratified analysis, elevated TyG index is significantly associated with HTN in the subgroup of oldest age (≥65) (OR 1.67, 95% CI 1.30-2.14, p <0.0001), obesity (Body mass index (BMI) ≥28 kg/m²) (OR 1.85, 95% CI 1.29-2.66, p 0.0009) or lower estimated glomerular filtration rate (eGFR) (<90 mL/ (min·1.73 m²)) (OR 1.72, 95% CI 1.33-2.21, p <0.0001).

**Conclusion:** TyG index is significantly associated with HTN and shows the superior discriminative ability for HTN compared with lipid and glycemic parameters in the Chinese elderly population.

**Background**

Hypertension (HTN) is one of the most prevalent cardiovascular risk factors, with over 34% of males and 28% of women aged ≥ 25 years being affected globally by raised blood pressure. With 20% of the world’s population, China represents a large portion of this burden, where HTN and blood pressure-related cardiovascular diseases (CVDs) are major public health challenges. HTN prevalence has risen
in recent decades, resulting in an increase of blood pressure-related morbidity and mortality. It is well known that both lipid and glucose abnormalities are associated with HTN. It is reported that dyslipidemia has been in 50-80% of hypertensive patients. Dyslipidemia, comprising elevated triglyceride (TG), high cholesterol (TC), increased low-density lipoprotein cholesterol (LDL-C), and decreased high-density lipoprotein cholesterol (HDL-C), are independently associated with HTN or other CVDs risk factors. There are renewed interests engendered by epidemiological and genetic evidence proving that increased TG, remnant TC, or TG-rich lipoproteins as an additional cause of CVDs and all-cause mortality. Similarly, HTN and type 2 diabetes (T2DM) are common causes of morbidity, both constitute risk factors for CVDs and might be engaged in similar genetic and environmental risk factors. It is reported that elevated plasma glucose is a steady and independent predictor of HTN. Some modern antidiabetic drugs are also capable to lower both office and ambulatory blood pressure. This can contribute to the favorable effect on some clinical endpoints, most importantly the reduction of congestive heart failure and cardiovascular mortality.

The main pathogenetic pathways linking T2DM, dyslipidemia and HTN are thought to be through insulin resistance (IR) and increased activity of the sympathetic nervous system and of the renin-angiotensin-aldosterone system, as well as increased renal sodium reabsorption. The association between IR and risk of incident HTN was shown in a recent meta-analysis of 11 studies, suggesting that IR could be employed as an adjunctive tool to identify individuals at potential risk for HTN. Glucose clamp technique is the gold standard for IR measurement initially proposed by De Fronzo. However, such direct diagnostic tests have considerably high costs and low availability for epidemiologic use.

In recent years, triglyceride-glucose (TyG) index is arising as an ideal substitution for IR. It is calculated as \( \ln \left[ \text{fasting plasma glucose (FBG)} \left( \text{mg/dl} \right) \times \text{TG} \left( \text{mg/dl} \right)/2 \right] \). This measurement merely requests simple lab tests like TG and plasma glucose, which can be obtained highly cost-effective and time-efficient. Additionally, TyG index has been revealed to determine IR in a more appropriate way than other substitutional index like HOMA-IR, which was compared with the gold standard method for
IR. Previous studies showed that TyG index is closely associated with HTN, artery stiffness and coronary artery calcification. Furthermore, TyG index can well predict coronary artery disease severity and cardiovascular outcomes. The association between TyG index and T2DM was also demonstrated in Spain, China and Korea.

However, studies are limited, which involve the association between TyG index and HTN and comparison of the discriminative abilities of TyG index, lipid, glycemic parameters for the risk of HTN. Therefore, our study intends to explore the association of TyG index with HTN and compare the discriminative power of TyG index, lipid, glycemic parameters for HTN in the elderly individuals in China.

Methods

Study subjects

The present study assessed 45130 participants aged over 40 years from a longitudinal REACTION study (Risk Evaluation of cAncers in Chinese diabeTic Individuals), including seven regional centers (Gansu, Guangdong, Henan, Hubei, Liaoning, Shanghai, and Sichuan), from May 2011 to December 2011. Previous history of related chronic diseases, using ACEI/ARB medicines, lipid-lowering drugs, missed data and/or included outliers were exclusion criteria in the study. Finally, 43591 participants were recruited. (Fig. 1)

Before the investigation, the clinicians were well trained for questionnaire and data collection. The present study was approved by the Committee on Human Research at Rui-Jin Hospital affiliated with the School of Medicine, Shanghai Jiao Tong University and all participants recruited have signed informed consents before data collection.

Clinical Data And Biochemical Indicators

The subjects received the following examinations: a standardized questionnaire, anthropometric measurements, blood collection, and a standard 75-goral glucose tolerance test (OGTT) or standard meal test. The same trained clinicians carried out standard questionnaires which included demography, lifestyle, history of diabetes, stroke, coronary heart disease (CHD), HTN and dyslipidemia as well as the medication history including the use of drugs. All data were maintained corresponding to established standard methods by the same well-trained clinicians. Physical
examination items including height, weight, waist circumference, hip circumference, blood pressure, and heart rate. Height was measured in bare feet accurate to 0.01 m. Weight was measured in light clothes accurate to 0.1 kg. Waist circumference and hip circumference were measured to an accuracy of 0.01 m by the same staff. Waist circumference/hip circumference (WHR), was accurate to 0.01. Body mass index (BMI), was calculated as weight/height\(^2\). After at least 5-minute rest, blood pressure was measured seated three times with an interim of 1 minute, using an OMRON electronic blood pressure monitor. The average blood pressure was calculated and used for analysis. The estimated glomerular filtration rate (eGFR) was determined by the modified MDRD equation: \( \text{eGFR} = 186 \times \left( \frac{\text{serum creatinine} \times 0.011}{\text{age}^{0.203}} \right) \times (0.742 \text{ if female}) \times 1.233. \)

\[\text{TyG (mg/dl)}^2 = \ln[\text{FBG (mg/dl)} \times \text{TG (mg/dl)}] / 2.\]

75 g OGTT or standard meal test
After overnight fasting for at least 12 hours, the first fasting blood samples were obtained for FBG measurement. Standard 75 g glucose solution was given to the individuals without T2DM history, while standard meals containing 100 g carbohydrates were given to the individuals with T2DM history. Blood samples for glucose measurement were obtained at 120 minutes after either 75 g OGTT or standard meal test. FBG and 2 h post-load blood glucose (PBG) were measured by
Hexokinase method on autoanalyzer.

TG, TC, HDL-C, LDL-C, alanine transferase (ALT), aspartate transferase (AST), serum creatinine (Cr) and gamma-glutamyl transferase (GGT) were measured by chemiluminescent on autoanalyzer.

Glycosylated hemoglobin (HbA1c) was measured by high pressure liquid chromatography.

Definition Of Variables
TyG index was divided into 5 groups: <20% group, the 20–39% group, the 40–59% group, the 60–79% group and the ≥80% group according quartile division of the subjects. As Chinese guideline for the management of dyslipidemia in adults (revised in 2016) suggests, lipid parameters were categorized as follows: 1. TG: normal: <1.7 mmol/L, borderline high: 1.7–2.3 mmol/L, high: ≥2.3 mmol/L; 2. TC: normal: <5.2 mmol/L, borderline high: 5.2–6.2 mmol/L, high: ≥6.2 mmol/L; 3. HDL-C: low risk: ≥1.0 mmol/L, high risk: <1.0 mmol/L; 4. LDL-C: ideal < 2.6 mmol/L, borderline high: 3.4–4.1 mmol/,
high: \( \geq 4.1 \) mmol/L. According to the WHO guidelines, T2DM was defined as FBG \( \geq 7.0 \) mmol/L, or PBG \( \geq 11.1 \) mmol/L, or self-reported history of T2DM. HTN was defined as systolic blood pressure (SBP) \( \geq 140 \) mmHg or diastolic blood pressure (DBP) \( \geq 90 \) mmHg, or self-reported history of HTN. Participants were divided into three groups according to their smoking frequency: no: never or have already quit smoking; occasional: smoking less than once a week or less than 7 cigarettes weekly; frequently: smoking one or more cigarettes daily for at least a half year. Similarly, participants were divided into three groups according to their alcohol intake frequency: no: never or have already quit drinking; occasional: drinking less than once a week; frequently: drinking more than once a week for at least a half year. Stroke including all subtypes was determined according to a subject’s self-report, including a history of language or physical dysfunction lasting over 24 hours and ischemic or hemorrhagic stroke by imageological diagnosis. CHD events was defined as any self-report history of hospital-admitted myocardial infarction or angina, or coronary revascularization. CVDs was also according to a subject’s self-report, including history of CHD, stroke, or myocardial infarction.

**Statistical analysis**

Empower(R) (www.empowerstats.com, X&Y Solutions Inc., Boston, MA) and R (http://www.Rproject.org) were employed to perform the statistical analyses. The odds ratio (OR) and the 95% confidence intervals (CI) were calculated. P values < 0.05 (2-sided) was considered to indicate statistical significance.

Variables were presented as means ± standard deviation (SD) if normal distribution. And if they are not, they were presented as median (Q1-Q3), or n (%). Difference between continuous variables were compared using Kruskal-Wallis test. The percentage difference between groups was compared using \( \chi^2 \) test. Three multivariate logistic regression models were built to identify the association between TyG v.s lipid parameters, PBG, HbA1c and HTN. Model 0 was not adjusted for any confounding factors, while Model 1 was adjusted for age and sex. Model 2 was further adjusted for age; center; sex; history of CVDs; history of T2DM; hypoglycemic drugs; SBP; DBP; BMI; ALT; AST; WHR; eGFR; smoking habits, drinking habits. Stratified analyses were conducted by the different level of age (G1: <55, G2: 55–65, G3: \( \geq 65 \)), BMI (underweight: <18.5 kg/m\(^2\); normal weight: 18.5–24 kg/m\(^2\); overweight: 24–28 kg/m\(^2\),
obesity: BMI of $\geq 28 \text{ kg/m}^2$) and eGFR (G1: $<90 \text{ mL/ (min} \cdot 1.73 \text{ m}^2$), G2: $\geq 90 \text{ mL/ (min} \cdot 1.73 \text{ m}^2$)).

Subjects were stratified into subgroups to separately explore the underlying relevant factors which might affect the relationship between TyG index and HTN.

**Results**

**Characteristics of study population by HTN**

The study includes 43591 participants (Table 1), of whom 18293 (40.5%) had HTN. Compared to non-hypertensive participants, the hypertensive ones were older, possessing larger BMI, less frequently smokers, less frequently drinker, with a higher mean SBP and DBP, with a higher heart rate, with a less favorable metabolic profile (FBG, PBG, HbA1c, AST, ALT, GGT, TC, TG), lower levels of eGFR, and had a higher frequency of CVDs and T2DM).
Table 1
Characteristics of study population by HTN

|                | No HTN                  | HTN                  | P-value |
|----------------|-------------------------|----------------------|---------|
| N              | 25298                   | 18293                | <0.001  |
| Age, years     | 55.41 (50.05–60.73)     | 60.89 (55.38–68.15)  | <0.001  |
| BMI, kg/m²     | 23.46 (21.47–25.67)     | 25.33 (23.23–27.64)  | <0.001  |
| SBP, mmHg      | 121.00 (112.00–130.00)  | 149.00 (140.00–162.00)| <0.001  |
| DBP, mmHg      | 73.00 (68.00–79.00)     | 85.00 (77.00–92.00)  | <0.001  |
| HR             | 78.00 (71.00–86.00)     | 79.00 (72.00–88.00)  | <0.001  |
| FBG, mmol/L    | 5.40 (5.02–5.91)        | 5.77 (5.29–6.58)     | <0.001  |
| PBG, mmol/L    | 7.00 (5.81–8.84)        | 8.29 (6.60–11.24)    | <0.001  |
| HbA1c, %       | 5.80 (5.60–6.20)        | 6.00 (5.70–6.50)     | <0.001  |
| ALT, U/L       | 14.00 (10.00–20.00)     | 16.00 (12.00–22.00)  | <0.001  |
| AST, U/L       | 20.00 (16.00–24.00)     | 21.00 (17.00–25.00)  | <0.001  |
| GGT, U/L       | 19.00 (14.00–28.00)     | 23.00 (16.00–35.00)  | <0.001  |
| TC, mmol/L     | 1.24 (0.90–1.79)        | 1.52 (1.08–2.17)     | <0.001  |
| TG, mmol/L     | 4.93 (4.21–5.68)        | 5.14 (4.38–5.88)     | <0.001  |
| LDL-C, mmol/L  | 2.84 (2.28–3.45)        | 2.99 (2.40–3.61)     | <0.001  |
| HDL-C, mmol/L  | 1.31 (1.09–1.55)        | 1.25 (1.06–1.47)     | <0.001  |
| eGFR, mL/ (min·1.73 m²) | 96.85 (93.10–100.56)     | 92.98 (88.31–96.85)  | <0.001  |
| Sex, (%)       |                         |                      | <0.001  |
| Male           | 6918 (27.35%)           | 6201 (33.90%)        |         |
| Female         | 18380 (72.65%)          | 12092 (66.10%)       |         |
| Drinking, (%)  |                         |                      | <0.001  |
| Never          | 18643 (73.69%)          | 14023 (76.66%)       |         |
| Occasional     | 5278 (20.86%)           | 2883 (15.76%)        |         |
| Frequently     | 1377 (5.44%)            | 1387 (7.58%)         |         |
| Smoking, (%)   |                         |                      | <0.001  |
| Never          | 21443 (84.76%)          | 15779 (86.26%)       |         |
| Occasional     | 862 (3.41%)             | 495 (2.71%)          |         |
| Frequently     | 2993 (11.83%)           | 2019 (11.04%)        |         |
| CVDs, (%)      |                         |                      | <0.001  |
| Yes            | 681 (2.69%)             | 1690 (9.24%)         |         |
| No             | 24617 (97.31%)          | 16603 (90.76%)       |         |
| T2DM, (%)      |                         |                      | <0.001  |
| Yes            | 22723 (89.82%)          | 14226 (77.77%)       |         |
| No             | 2575 (10.18%)           | 4067 (22.23%)        |         |

Data were mean±SD or median (IQR) for skewed variables or numbers (proportions) for categorical variables.

HTN: hypertension; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; FBG: fasting plasma glucose; PBG: 2 h post-load blood glucose; HbA1c: glycosylated hemoglobin; ALT: alanine transferase; AST: aspartate transferase; GGT: gamma-glutamyl transferase; TG: triglyceride; TC: high cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; eGFR: lower estimated glomerular filtration rate; CVD: cardiovascular disease; T2DM: type 2 diabetes.

Association Of Tyg Index, Glycemic, Lipid Parameters With Htn

Multiple logistic regression models that consider separately each index and their individual components as predictors of HTN are constructed. Table 2 shows OR and 95% CI of HTN with the groups of TG, TC, HDL-C, LDL-C, TyG quartiles, HbA1c and PBG in the total population within 3
different models. As seen in the Table 2, every index is significantly associated with HTN in the non-adjusted model. However, after further adjustments in Model II, only fourth and fifth quartiles of TyG (fourth quartile: OR 1.33, 95% CI 1.18-1.51, p < 0.0001; fifth quartile: OR 1.26, 95% CI 1.11-1.44, p = 0.0005), HDL-C ≥ 1 mmol/L (OR 1.28, 95% CI:1.15-1.42, P = 0.0005), TG ≥ 1.7 mmol/L (1.7 ≤ TG<2.3 mmol/L: OR 1.25, 95% CI 1.13-1.38, P < 0.0001; TG ≥ 2.3 mmol/L: OR 1.19, 95% CI 1.07-1.31, P = 0.0007) and PBG ( OR 1.02, 95% CI 1.00-1.03, p = 0.0117) remain significantly associated with HTN whereas TC, HDL-C, LDL-C, HbA1c are not.

Table 2

| Variable        | Non−adjusted | Adjust I | Adjust II |
|-----------------|--------------|----------|----------|
|                 | OR (95% CI)  | P−value  | OR (95% CI) | P−value |
|                 | P−value      |          | P−value   |
|                  |              |           |           |          |
| TG, mmol/L      |              |           |           |          |
| <1.7            | 1.0          | 1.0       | 1.0       |
| ≥1.7, <2.3      | 1.72 (1.63, 1.81) <0.0001 | 1.63 (1.55, 1.72) <0.0001 | 1.25 (1.13, 1.38) <0.0001 |
| ≥2.3            | 1.99 (1.89, 2.10) <0.0001 | 2.01 (1.91, 2.12) <0.0001 | 1.19 (1.07, 1.31) 0.0007 |
| TC, mmol/L      |              |           |           |          |
| <5.2            | 1.0          | 1.0       | 1.0       |
| ≥5.2, <6.2      | 1.28 (1.23, 1.34) <0.0001 | 1.25 (1.19, 1.31) <0.0001 | 0.94 (0.86, 1.02) 0.1432 |
| ≥6.2            | 1.46 (1.39, 1.55) <0.0001 | 1.39 (1.31, 1.48) <0.0001 | 0.90 (0.81, 1.01) 0.0620 |
| HDL−C, mmol/L   |              |           |           |          |
| ≥1              | 1.0          | 1.0       | 1.0       |
| <1              | 1.18 (1.13, 1.25) <0.0001 | 1.15 (1.09, 1.22) <0.0001 | 1.28 (1.15, 1.42) <0.0001 |
| LDL−C, mmol/L   |              |           |           |          |
| <3.4            | 1.0          | 1.0       | 1.0       |
| ≥3.4, <4.1      | 1.31 (1.25, 1.37) <0.0001 | 1.24 (1.18, 1.31) <0.0001 | 1.00 (0.91, 1.09) 0.9455 |
| ≥4.1            | 1.48 (1.39, 1.57) <0.0001 | 1.39 (1.30, 1.48) <0.0001 | 1.02 (0.90, 1.15) 0.7711 |
| TYG in transform Q5 |         |           |           |          |
| Q1              | 1.0          |          | 1.0       |
| Q2              | 1.54 (1.44, 1.64) <0.0001 | 1.41 (1.31, 1.51) <0.0001 | 1.06 (0.94, 1.20) 0.3362 |
| Q3              | 2.02 (1.89, 2.15) <0.0001 | 1.76 (1.64, 1.88) <0.0001 | 1.10 (0.98, 1.24) 0.1173 |
| Q4              | 2.80 (2.62, 2.98) <0.0001 | 2.36 (2.21, 2.53) <0.0001 | 1.33 (1.18, 1.51) <0.0001 |
| Q5              | 3.79 (3.55, 4.04) <0.0001 | 3.32 (3.10, 3.55) <0.0001 | 1.26 (1.11, 1.44) 0.0005 |
| HbA1c, %        | 1.30 (1.27, 1.33) <0.0001 | 1.19 (1.16, 1.21) <0.0001 | 0.95 (0.91, 1.00) 0.0639 |
| PBG, mmol/L     | 1.11 (1.10, 1.12) <0.0001 | 1.08 (1.07, 1.09) <0.0001 | 1.02 (1.00, 1.03) 0.0117 |

Model 0: Adjusted for no confounding factors;
Model 1: Adjusted for age and gender;
Model 2: age; center; sex; history of CVDs; history of T2DM; hypoglycemic drugs; SBP; DBP; BMI; ALT; AST; WHR; eGFR; smoking habits, drinking habits.

Table 3 shows similar results in subjects separated into men and women: 1.male: third and fourth quartiles of TyG (third quartile: OR 1.27, 95% CI 1.02-1.59, p = 0.0309; fourth quartile: OR 1.39, 95% CI 1.11-1.74, p = 0.0042), HDL-C (OR 1.36, 95% CI:1.16-1.58, p < 0.0001) and TG ≥ 1.7 mmol/L ( 1.7
\(\leq TG \leq 2.3\) mmol/L: OR 1.22, 95% CI 1.02–1.47, \(p = 0.0336\) are all associated with HTN; 2. female: fourth and fifth quartiles of TyG (fourth quartile: OR 1.28, 95% CI 1.11–1.49, \(p = 0.0010\); fifth quartile: OR 1.25, 95% CI 1.07–1.47, \(p = 0.0057\), HDL-C (OR 1.20, 95% CI: 1.04–1.39, \(p < 0.0001\)), TG \(\geq 1.7\) mmol/L (1.7 \(\leq TG \leq 2.3\): OR 1.24, 95% CI 1.10–1.40, \(p = 0.0003\); TG \(\geq 2.3\) mmol/L: OR 1.18, 95% CI 1.04–1.33, \(p = 0.0098\)) and PBG (OR 1.03, 95% CI 1.01–1.05, \(p = 0.0023\)) are associated with HTN.

### Table 3

| Variable       | Male                      | Female                     |
|----------------|---------------------------|-----------------------------|
|                 | OR (95% CI) P−value       | OR (95% CI) P−value         |
| TG, mmol/L     |                           |                             |
| \(<1.7\)       | 1.0                       | 1.0                         |
| \(\geq1.7, <2.3\) | 1.22 (1.02, 1.47) 0.0336  | 1.24 (1.10, 1.40) 0.0003    |
| \(\geq2.3\)    | 1.14 (0.96, 1.36) 0.1377  | 1.18 (1.04, 1.33) 0.0098    |
| TC, mmol/L     |                           |                             |
| \(<5.2\)       | 1.0                       | 1.0                         |
| \(\geq5.2, <6.2\) | 0.89 (0.76, 1.04) 0.1454  | 0.95 (0.86, 1.06) 0.3689    |
| \(\geq6.2\)    | 0.98 (0.78, 1.24) 0.8749  | 0.87 (0.77, 0.99) 0.0289    |
| HDL−C, mmol/L  |                           |                             |
| \(\geq1\)      | 1.0                       | 1.0                         |
| \(<1\)         | 1.36 (1.16, 1.58) \(<0.0001\) | 1.20 (1.04, 1.39) 0.0128   |
| LDL−C, mmol/L  |                           |                             |
| \(<3.4\)       | 1.0                       | 1.0                         |
| \(\geq3.4, <4.1\) | 0.99 (0.83, 1.18) 0.9088  | 1.00 (0.89, 1.11) 0.9433    |
| \(\geq4.1\)    | 1.15 (0.89, 1.48) 0.2941  | 0.97 (0.84, 1.11) 0.6651    |
| TyG ln transform Q5 |                     |                             |
| Q1             | 1.0                       | 1.0                         |
| Q2             | 1.05 (0.85, 1.32) 0.6358  | 1.05 (0.91, 1.22) 0.4763    |
| Q3             | 1.27 (1.02, 1.59) 0.0309  | 1.01 (0.88, 1.17) 0.8498    |
| Q4             | 1.39 (1.11, 1.74) 0.0042  | 1.28 (1.11, 1.49) 0.0010    |
| Q5             | 1.19 (0.95, 1.51) 0.1376  | 1.25 (1.07, 1.47) 0.0057    |
| HbA1c, %       | 0.91 (0.84, 0.99) 0.0259  | 0.98 (0.92, 1.04) 0.5076    |
| PBG, mmol/L    | 1.00 (0.98, 1.02) 0.8036  | 1.03 (1.01, 1.05) 0.0023    |

Model 2: Adjusted for age; center; history of CVDs; history of T2DM; hypoglycemic drugs; SBP; DBP; BMI; ALT; AST; WHR; eGFR; smoking habits, drinking habits.

### Associations between TyG index and HTN in individuals with LCL-C < 2.6 mmol/L or HDL-C > 1.0 mmol/L

As Chinese guideline for the management of dyslipidemia in adults (revised in 2016)\(^32\) suggests, population are categorized into two groups, LDL-C < 2.6 mmol/L (ideal value) and HDL-C \(\geq 1.0\) mmol/L (low risk value). As Table 4 shows, high TyG levels (the fourth and fifth quantile) are still significantly associated with HTN even when LDL-C or HDL-C is well controlled (When LDL-C is well controlled: the forth quartile of TyG: OR 1.26, 95% CI 1.10–1.44, \(p = 0.0026\); the fifth quartile of TyG: OR 1.24, 95% CI
When HDL-C is well controlled: the forth quartile of TyG: OR 1.28, 95% CI 1.09–1.50, p = 0.0007; the fifth quartile of TyG: OR 1.27, 95% CI 1.06–1.51, p = 0.0026). Moreover, medium and high TG levels (≥ 1.7 mmol/L), high HDL-C levels (≥ 1 mmol/L) and PBG also remain associated with HTN when LDL-C or HDL-C is well controlled. The associations are not statistically significant in HbA1c or other lipid parameters.

Table 4

| Variable       | HDL−C>1.0mmol/L OR (95% CI) P−value | LDL−C<2.6mmol/L OR (95% CI) P−value |
|----------------|------------------------------------|------------------------------------|
| TG, mmol/L     |                                    |                                    |
| <1.7           | 1.0                                 | 1.0                                 |
| ≥1.7, <2.3     | 1.24 (1.11, 1.39) 0.0001            | 1.19 (1.06, 1.34) 0.0040            |
| ≥2.3           | 1.19 (1.05, 1.33) 0.0048            | 1.12 (0.99, 1.28) 0.0772            |
| TC, mmol/L     |                                    |                                    |
| <5.2           | 1.0                                 | 1.0                                 |
| ≥5.2, <6.2     | 0.97 (0.88, 1.06) 0.4546            | 0.99 (0.89, 1.10) 0.8933            |
| ≥6.2           | 0.94 (0.83, 1.05) 0.2736            | 0.96 (0.85, 1.09) 0.5788            |
| HDL−C, mmol/L  |                                    |                                    |
| ≥1             | –                                   | 1.0                                 |
| <1             | –                                   | 1.26 (1.05, 1.50) 0.0125            |
| LDL−C, mmol/L  |                                    |                                    |
| <3.4           | 1.0                                 | –                                   |
| ≥3.4, <4.1     | 1.00 (0.90, 1.11) 0.9993            | –                                   |
| ≥4.1           | 1.04 (0.92, 1.18) 0.5327            | –                                   |
| TyG ln transform Q5 |                        |                                    |
| Q1             | 1.0                                 | 1.0                                 |
| Q2             | 1.03 (0.90, 1.17) 0.6633            | 1.09 (0.93, 1.29) 0.2728            |
| Q3             | 1.05 (0.92, 1.20) 0.4438            | 1.12 (0.95, 1.31) 0.1734            |
| Q4             | 1.26 (1.10, 1.44) 0.0007            | 1.28 (1.09, 1.50) 0.0026            |
| Q5             | 1.24 (1.07, 1.44) 0.0042            | 1.27 (1.06, 1.51) 0.0080            |
| HbA1c, %       | 0.97 (0.92, 1.03) 0.3249            | 0.99 (0.93, 1.05) 0.6697            |
| PBG, mmol/L    | 1.02 (1.00, 1.03) 0.0086            | 1.02 (1.01, 1.04) 0.0043            |

Adjusted for age; center; sex; history of CVDs; history of T2DM; hypoglycemic drugs; SBP; DBP; BMI; ALT; AST; WHR; eGFR; smoking habits, drinking habits.

Associations between TyG index and HTN for stratified subgroups of age, BMI and eGFR

Stratified analyses were conducted in the different subgroups to further validate the abovementioned results, shown in Table 5. The present study suggested that compared with participants with lower TyG level, subjects with higher TyG level (the fourth and fifth quartile) are more closely associated with HTN in the older age (≥ 55 years), higher level of BMI (≥ 24 kg/m²) and both eGFR subgroups. To
be noted, these association is most significant in the subjects that both in the subgroup of forth quartile of TyG and the subgroup of oldest age (≥ 65 years) (OR 1.67, 95% CI 1.30-2.14, p < 0.0001), obesity (BMI ≥ 28 kg/m²) (OR 1.85, 95% CI 1.29-2.66, p 0.0009) or lower eGFR (< 90 mL/ (min·1.73 m²)) (OR 1.72, 95% CI 1.33-2.21, p < 0.0001).

Table 5
Associations of TyG quartiles with HTN for different levels of age, BMI, eGFR

| Variable | AGE<55 OR (95% CI) | AGE≥55, <65 OR (95% CI) | AGE≥65 OR (95% CI) | BMI <18.5 OR (95% CI) | BMI≥18.5, <24 OR (95% CI) | BMI≥24, <28 OR (95% CI) | BMI≥28 OR (95% CI) | eGFR<90 OR (95% CI) | eGFR≥90 OR (95% CI) |
|----------|------------------|---------------------|------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
|          | P-value           | P-value             | P-value           | P-value             | P-value             | P-value             | P-value             | P-value             | P-value             |
| TG, mmol/L |                  |                     |                  |                     |                     |                     |                     |                     |                     |
| <1.7     | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| ≥1.7, <2.3 | 1.23 (1.01, 1.48) | 0.0348              | 1.16 (1.00, 1.34) | 0.0470              | 1.44 (1.18, 1.76)   | 0.0004              | 1.09 (0.37, 3.19)   | 0.8769              | 1.23 (1.04, 1.45)   | 0.0161              |
| ≥2.3     | 1.13 (0.93, 1.36) | 0.2135              | 1.21 (1.04, 1.40) | 0.0111              | 1.15 (0.93, 1.42)   | 0.1872              | 0.11 (0.01, 1.29)   | 0.0788              | 0.95 (0.80, 1.14)   | 0.6042              |
| TC, mmol/L |                  |                     |                  |                     |                     |                     |                     |                     |                     |
| <5.2     | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| ≥5.2, <6.2 | 0.90 (0.77, 1.05) | 0.1798              | 0.98 (0.86, 1.11) | 0.7541              | 0.92 (0.78, 1.09)   | 0.3530              | 1.33 (0.65, 2.69)   | 0.4344              | 0.91 (0.79, 1.04)   | 0.1637              |
| ≥6.2     | 0.89 (0.72, 1.10) | 0.2962              | 0.85 (0.72, 0.99) | 0.0405              | 1.06 (0.85, 1.33)   | 0.6183              | 0.85 (0.34, 2.10)   | 0.7236              | 0.83 (0.70, 0.98)   | 0.0305              |
| HDL−C, mmol/L |              |                     |                  |                     |                     |                     |                     |                     |                     |
| ≥1      | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| <1      | 1.50 (1.23, 1.82) | 0.0001              | 1.34 (1.14, 1.57) | 0.0004              | 1.03 (0.85, 1.26)   | 0.7484              | 0.81 (0.20, 3.38)   | 0.7756              | 1.25 (1.04, 1.51)   | 0.0164              |
| LDL−C, mmol/L |              |                     |                  |                     |                     |                     |                     |                     |                     |
| <3.4    | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| ≥3.4, <4.1 | 1.09 (0.91, 1.30) | 0.3674              | 0.99 (0.87, 1.14) | 0.9010              | 0.93 (0.76, 1.12)   | 0.4351              | 1.92 (0.88, 4.22)   | 0.1033              | 0.97 (0.83, 1.13)   | 0.6814              |
| ≥4.1    | 0.97 (0.76, 1.23) | 0.7791              | 0.98 (0.82, 1.16) | 0.7966              | 1.20 (0.93, 1.55)   | 0.1623              | 1.04 (0.34, 3.21)   | 0.9470              | 0.99 (0.82, 1.21)   | 0.9540              |
| TYG ln transform Q5 |      |                     |                  |                     |                     |                     |                     |                     |                     |
| Q1      | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| Q2      | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| Q3      | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| Q4      | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
| Q5      | 1.0              | 1.0                 | 1.0              | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 | 1.0                 |
Q2 | 1.03 (0.83, 1.27) | 1.04 (0.87, 1.26) | 1.14 (0.89, 1.46) | 1.62 (0.80, 3.27) | 0.95 (0.80, 1.13) | 1.14 (0.93, 1.40) | 1.24 (0.84, 1.81) | 1.13 (0.88, 1.45) | 1.04 (0.91, 1.20) | 0.5523
| 0.7970 | 0.6479 | 0.2946 | 0.1760 | 0.5580 | 0.2142 | 0.2775 | 0.3386 |

Q3 | 0.98 (0.79, 1.22) | 1.04 (0.86, 1.25) | 1.36 (1.07, 1.74) | 0.97 (0.39, 2.40) | 1.08 (0.91, 1.29) | 1.07 (0.87, 1.30) | 1.42 (0.98, 2.05) | 1.36 (1.06, 1.74) | 1.02 (0.89, 1.18) | 0.7273
| 0.8431 | 0.0126 | 0.9520 | 0.3835 | 0.3386 | 0.5208 |

Q4 | 1.28 (1.02, 1.60) | 1.20 (1.00, 1.45) | 1.67 (1.30, 2.14) | 1.68 (0.60, 4.67) | 1.17 (0.97, 1.41) | 1.34 (1.10, 1.64) | 1.85 (1.29, 2.66) | 1.72 (1.33, 2.21) | 1.23 (1.07, 1.42) | 0.0037
| 0.0308 | 0.0515 | <0.0001 | 0.3203 | 0.1018 | 0.0041 | 0.0009 |

Q5 | 1.18 (0.93, 1.50) | 1.23 (1.00, 1.50) | 1.37 (1.05, 1.79) | 0.62 (0.12, 3.21) | 0.95 (0.77, 1.18) | 1.35 (1.09, 1.66) | 1.84 (1.27, 2.66) | 1.42 (1.08, 1.87) | 1.23 (1.06, 1.43) | 0.0074
| 0.1727 | 0.0448 | 0.0221 | 0.5669 | 0.6473 | 0.0051 |

HbA1c, % | 0.95 (0.86, 1.05) | 0.98 (0.91, 1.05) | 0.93 (0.85, 1.03) | 1.10 (0.80, 1.51) | 0.97 (0.90, 1.05) | 0.95 (0.88, 1.02) | 0.89 (0.78, 1.01) | 0.96 (0.88, 1.05) | 0.98 (0.93, 1.03) | 0.4295
| 0.2888 | 0.5363 | 0.1578 | 0.5456 | 0.4689 | 0.1600 |

PBG, mmol/L | 1.02 (0.99, 1.05) | 1.02 (1.00, 1.04) | 1.01 (0.99, 1.04) | 0.99 (0.89, 1.11) | 1.01 (0.99, 1.04) | 1.02 (1.00, 1.05) | 1.01 (0.98, 1.05) | 1.02 (1.00, 1.05) | 1.02 (1.00, 1.05) | 0.0180
| 0.1858 | 0.0430 | 0.4088 | 0.9122 | 0.2281 | 0.0278 |

Adjusted for age; center; sex; history of CVDs; history of T2DM; hypoglycemic drugs; SBP; DBP; BMI; ALT; AST; WHR; eGFR; smoking habits, drinking habits.

Our study also shows that people with borderline high TG level (≥ 1.7, < 2.3 mmol/L) are associated with HTN either in all age subgroups, normal and overweight subgroups (BMI ≥ 18.5 kg/m², < 28 kg/m²) and both eGFR subgroups. Meanwhile, people with high TG level (≥ 2.3 mmol/L) are associated with HTN either in the medium age (≥ 55, < 65 years) subgroup, overweight and obesity subgroups (BMI ≥ 28 kg/m²) and both eGFR subgroups. People with lower HDL-C level (< 1 mmol/L) are associated with HTN either in younger and medium age subgroups (< 65 years), normal and overweight subgroups (BMI ≥ 28 kg/m²) and both eGFR subgroups. People with lower HDL-C level (< 1 mmol/L) are associated with HTN either in younger and medium age subgroups (< 65 years), normal and overweight subgroups (BMI ≥ 18.5 kg/m², < 28 kg/m²) or higher eGFR (≥ 90 mL/ (min·1.73 m²)) subgroup. TC (≥ 6.2 mmol/L) subgroup is associated with HTN only in medium age subgroup (≥ 55, < 65 years) or higher eGFR (≥ 90 mL/ (min·1.73 m²)) subgroup. Slight association between PBG and HTN is observed only in medium age, overweight and higher eGFR subgroups. However, no apparent association is observed in HbA1c stratified subgroups. When comparing the OR of TyG, lipid and glycemic parameters, the OR of TyG stands the most, indicating that TyG can be a better discriminator of HTN.

Discussion
Main findings
As far as we know, this is the first study to investigate the associations of TyG index, glycemic, lipid parameters with HTN in a Chinese general population with large sample, multicenter survey.
Following are the main findings of this study: (1) TyG index is significantly associated with HTN and remains significant after LDL-C or HDL-C was well controlled and the association of TyG index with HTN is stronger than lipid or glycemic parameters. (2) HDL-C, TG and PBG are also associated with HTN, but are inferior than TyG index. (3) Further stratification shows that people with larger BMI (≥ 24 kg/m²), older age (≥ 65) and lower eGFR (< 90 mL/ (min·1.73 m²)) have higher risks of HTN when TyG index is in high levels (the fourth and fifth quartile). Therefore, TyG index is a better discriminator for the risk of HTN compared with lipid and glycemic parameters.

Glycemic Parameters And Htn

It was shown in previous studies that patients with CVDs can be benefited from better glycemic control. These researches have put their focus on the average levels and ideal targets of FPG and HbA1c for the most part. However, it is found in this study only slight association between HTN and PBG and no apparent association between HTN and HbA1c levels, even in subjects with older age, larger BMI or lower eGFR. There are potential limitations existing in the assessment of these two glycemic parameters. Although elevated glucose concentration has been treated as a regulable cardiovascular risk factor, FPG only serves as a less effective predictor of cardiovascular outcomes. HbA1c is recommended as the most reliable parameter in short-term evaluation of glycemic control, but substantial differences have been uncovered between HbA1c and average glycemic level. Especially, similar average glycemic levels could yield considerable discrepancies in HbA1c levels because glucose metabolism and hemoglobin glycation rate might vary corresponding to different individuals.

Lipid Parameters And Htn

Dyslipidemia remains as a conventional risk factor for CVD including atherosclerosis, particularly in the general population. Little research has been carried out on the association between lipid parameters and HTN. A 6.4 years follow-up study of 5971 middle-eastern women reported that the predictive value between TG, HDL-C, TG/HDL-C and HTN were most significant among several lipid parameters. Studies on adolescents also reached similar conclusion. Although ACC/AHA and ESC/EAS guidelines has recommended LDL-C to be the most crucial lipid risk factor and therapeutic goal for
CVDs, LDL-C is not effectively indicative in our study. Moreover, Assmann et al. have proved that the number of clinical events is still alarming regardless of currently desirable LDL-C lowering therapies. In fact, even if LDL-C or HDL-C is well controlled, higher TyG index or hypertriglyceridemia is still significantly associated with HTN in our study.

**The Mechanisms Between Tyg Index And Uacr**

Although the relevant pathophysiological mechanisms responsible for the association between TyG index and HTN is unclear, several studies suggested the possible mechanism by which IR might affect elevating blood pressure. In recent years, several studies revealed that TyG index was closely associated with IR and recommended TyG index as a surrogate index of IR. Theoretically, IR is an essential pathological element involved in metabolic syndrome and a risk factor for the elevated blood pressure. Numerous studies suggested that excess visceral fat represented the cause of metabolic abnormalities leading to increased IR and cardiometabolic risk, including risk of HTN.

Therefore, the measurement of IR is valuable in indicating HTN development. Our finding shows that TyG index, an emerging measurable substitution of IR, is independently associated with HTN after various confounding factors adjustment, which are consistent with previous studies. IR-compensatory hyperinsulinemia can generate overactivation of carotid body, bringing on an escalation in sympathetic nervous system activity, further prompting the adrenaline and norepinephrine’s secretion, and eventually result in cardiac output increases and peripheral vascular resistance. The vascular smooth muscle may be thickened in high concentrated catecholamine, inducing HTN development. Moreover, blood pressure could be also elevated by IR through the activation of the renin-angiotensin-aldosterone system and the increase in endothelin synthesis. Such increase may contract the blood vessels, decrease the prostacyclin (PGI2) and prostaglandin E2 (PGE2) circulated in vessels which are supposed to be dilated by them, and finally proliferate the vascular smooth muscle, contributing HTN development.

Interestingly, in our study, it is firstly revealed that TyG index might be superior to mere glycemic or lipid parameters in associating HTN development. TyG index is applied in assessing the joint value of
TG and FPG because the two parameters are intensively interrelated. Hypertriglyceridemia remains to be one of the prevalent abnormalities in T2DM patients and its association with increased risk of CVDs has been fully demonstrated. TG might prompt formation of atherosclerotic plaque while glycemic level might be involved in endothelial cells and platelet dysfunction. Their values in association with HTN might be better interpreted when they were considered as a whole. Our study shows that TyG index helps to identify potential risks in the individuals who would otherwise be neglected. The clinicians usually put their focus merely on individuals with high FBG or TG. Such conventional clinical practice might possibly miss out some potential risk groups whose FBG and TG are in the normal or borderline ranges.

Limitations
Our seven-region community-based samples, which representatively demonstrates the distribution of different regions in China, largely and positively influence the research. However, there are still limitations in our study. Firstly, we are not able to directly measure IR in our study population and to further compare the surrogate indices with direct markers of IR. Secondly, because the data of this research are from Chinese elderly individuals, it remains uncertain whether the findings can be applicable to other ethnic groups. Finally, as the feature of cross-sectional study, only associations rather causality can be established. More prospective studies are needed to identify causal relationship between TyG index and HTN.

Conclusion
To conclude, the results of our study reveals the significant association between TyG index and HTN in Chinese elderly individuals and it is superior to other lipid profiles and HbA1c and PBG. Therefore, we make a proposal that TyG index could be a more efficient, useful and simple index for the screening and managing HTN.

Abbreviations
HTN: hypertension; CVD: cardiovascular disease; T2DM: type 2 diabetes; IR: insulin resistance; OGTT: glucose tolerance test; CHD: coronary heart disease; WHR: waist circumference/hip circumference; BMI: body mass index; TyG: triglyceride-glucose; FBG: fasting plasma glucose; PBG: 2 h post-load blood glucose; HbA1c: glycosylated hemoglobin; TG: triglyceride; TC: high cholesterol; LDL-C: low-
density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; ALT: alanine transferase; AST: aspartate transferase; GGT: gamma-glutamyl transferase; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; eGFR: lower estimated glomerular filtration rate; PGI2: prostacyclin; PGE2: prostaglandin E2; OR: odds ratio; CI: confidence interval.

Declarations

Data Availability

The datasets used to support this study are not freely available due to participants’ privacy protection.

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Authors' contributions:

YM, JW and BZ contributed to the conception and design of the study. KC, WY, AW, WW, ZG, X T, LY, QW, ZL, GQ and LC recruited the subjects and supervised the study. JW and BZ analyzed the data. BZ wrote the initial draft of the paper. YM, JW and BZ contributed to the writing, reviewing, and revising of the manuscript.

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Figures
Participants from 7 centers of Reaction study: Liaoning 10140, Gansu 10026, Guangzhou 9743, Sichuan 8105, Shanghai 6821, Henan 1978, Hubei 995

A total of 45130 participants aged over 40 years were recruited.

Excluded participants:
1. Previous history of drugs used
   ACEI drugs (n=595)
   ARB drugs (n=1099)
   Lipid lowering drugs (n=421)
2. Related chronic diseases
   Kidney stones (n=1541)
   Nephrotic syndrome (n=17)
   Other chronic diseases (n=227)
   Other kidney diseases (n=228)
3. Participants without other complete data (n=1241)

Study population (n=43591)

Participants without hypertension (n=25298)
Participants with hypertension (n=18293)

Figure 1
Flow chart of the selection of study participants