The triglyceride glucose index: a novel and effective surrogate marker to identify alanine aminotransferase levels

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Research Article

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Abstract

***Introducton**:* The triglyceride glucose index (TyG) has been proposed as a marker of insulin resistance or type 2 diabetes mellitus (T2DM). Risk of serum alanine aminotransferase (ALT) levels is increased in T2DM patients. We aimed to evaluate the association between TyG index and elevated ALT.

***Methods**:* A multicenter, cross-sectional study was conducted in China from Northeast China Rural Cardiovascular Health Study (NCRCHS), and 11,573 adults with complete data were included.

***Results**:* TyG index was positively associated with the prevalence of elevated ALT. Frequency of elevated ALT increased from the lowest to the top quartile of TyG in both sexes (p for trend <0.001). Compared with the participants in the lowest quartile of TyG, the adjusted odds ratio and 95% CIs for elevated ALT were 1.71 (1.32-2.21) and 2.46 (1.90-3.19) for those in the third and the fourth quartile of TyG (p<0.001). Compared with the first quartile of TyG, participants in the top quartile of TyG had more than 2 times risk for elevated ALT (2.38-times for men and 2.22-times for women, respectively, p<0.001). According to the ROC analysis, the optimal cut-off point of TyG for elevated ALT was 8.69 and 8.96 for men and women, respectively.

***Conclusions**:* TyG index is effective to identify individuals at risk for elevated ALT. TyG thresholds of 8.69 for men and 8.96 for women was highly sensitive for detecting elevated ALT subjects. Findings from this study underscore that TyG index may be suitable as a surrogate marker for abnormal liver enzymes in Chinese adults.

Highlights

1. TyG index is effective to identify individuals at risk for elevated ALT.

2. The article shows the optimal cut-off point of TyG for identifying elevated ALT.

3. TyG index is suitable as a biomarker for identification chronic hepatic diseases.

Background

Chronic liver disease is becoming a major health hazard over the world. The major cause of chronic liver disease is nonalcoholic fatty liver disease (NAFLD), which encompasses a spectrum of hepatic pathologies ranging from simple hepatic steatosis to steatohepatitis and cirrhosis [1 2]. Among the liver enzymes, serum alanine aminotransferase (ALT) is most relevant to liver fat content and considered as a reliable and sensitive marker of NAFLD [3–5]. Elevated ALT is associated with a range of health outcomes, such as all-cause mortality, metabolic disorders and cardiovascular diseases [6–8]. Furthermore, NAFLD is considered as the liver manifestation of metabolic syndrome (MetS) [9–11] and elevated ALT is positively associated with MetS [12].

Triglyceride glucose (TyG) index, the product of triglycerides (TG) and fasting plasma glucose (FPG) levels, has been recommended as a novel and effective surrogate marker for insulin resistance and type 2 diabetes

mellitus [13–15]. Moreover, TG and FPG are key components of MetS, which are overproduced by the fatty liver [16]. We speculate that the TyG index may be associated with chronic liver disease.

Recently, the association between the TyG index and liver steatosis has been demonstrated in 50 asymptomatic women from Mexico [17], and TyG is demonstrated effective to identify individuals at risk for NAFLD [18]. However, the confirmed diagnosis of NAFLD is invasive procedure such as liver biopsy, and a probable diagnosis can also be made based on the patient's elevated ALT level. Serum ALT levels > 40 U/L usually represent liver damage in the general population [19]. The blood collection of ALT level is simple and could be impractical in large-scale, population-based epidemiological studies. In addition, serum ALT level appears to be one liver enzyme that is most relevant to liver fat content and is used as a simple marker for NAFLD and chronic liver disease in large-scale screening studies [20 21]. To our best knowledge, whether the TyG index is able to identify elevated ALT level in general population has not been investigated. Therefore, we aimed to explore the relationship between TyG index and elevated ALT concentration in a large-scale Chinese population.

Methods

Study population

We conducted a cross-sectional study from July 2012 to August 2013 in rural areas of Liaoning Province, which is called Northeast China Rural Cardiovascular Health Study (NCRCHS). A representative sample aged ≥ 35 years was selected to describe the prevalence, incidence and natural history of cardiovascular risk factors. The study adopted a multi-stage, stratified randomly cluster-sampling scheme. In the first stage of sampling, 3 counties (Zhangwu, Dawa, and Liaoyang County) were randomly selected to represent south, east and north of Liaoning province. 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 were randomly selected from each township. In total, 26 rural villages were finally included. All eligible permanent residents aged ≥ 35 years from each village were selected for participation (a total of 14,016 participants). 11,956 individuals agreed and completed this cross-sectional study and the response rate was 85.3%. Approval for the NCRCHS was obtained from the Ethics Committee of China Medical University (Shenyang, China, ethical approval number: AF-SDP-07-1, 0–01). All participants provided written informed consent and all procedures were performed in accordance with the ethical standards. If the participants were illiterate, their proxies wrote the informed consents for them. In this study, we used data of baseline and only participants with complete data were included, making a final sample size of 11,573 (5,357 men and 6,216 women).

Data Collection

Data was collected during a single clinic visit by cardiologists and trained nurses using a standard questionnaire by face-to-face interview. Before the survey was performed, we invited all eligible investigators to attend the organized training. The training contents included the purpose of this study, how to administer the questionnaire, the standard method of measurement, the importance of standardization, and the study procedures. A strict test was evaluated after this training, only those who scored perfectly on the test could become investigators. During data collection, our inspectors had further instructions and support.

Data on demographic characteristics, lifestyle risk factors, medical history, were obtained by interview with a standardized questionnaire. There was a central steering committee with a subcommittee for quality control. Current smokers were defined as people who were currently smoking and current drinkers were defined as people who were currently drinking. Physical activity included occupational and leisure-time physical activity. Occupational and leisure-time physical activity were merged and regrouped into the following three categories: 1) low—subjects who reported light levels of both occupational and leisure-time physical activity, 2) moderate—subjects who reported moderate or high levels of either occupational or leisure-time physical activity and 3) high—subjects who reported a moderate or high level of both occupational and leisure-time physical activity [22].

Blood Pressure Measurements

According to American Heart Association protocol, blood pressure was measured three times in a sitting position at 2-min intervals after at least 5 min of rest in a quiet room with the use of an automatic electronic sphygmomanometer (HEM-741C; Omron, Tokyo, Japan). Two doctors checked the calibration of the Omron device using a standard mercury sphygmomanometer every month under the British Hypertension Society protocol [23]. The mean of three BP measurements was taken and used in all analyses.

Anthropometric Measurements

Standing height and weight were measured to the nearest 0.1 cm and 0.5 kg using a wall-mounted stadiometer and an automated balance. Waist circumference (WC) was measured at the minimum circumference between iliac crest and the rib cage in standing position at the end of normal expiration using a non-elastic tape. The body mass index (BMI) was calculated using the formula weight (kg)/height^2 (m^2). TyG index: Ln [TG (mg/dL) × FPG (mg/dL)/2] [13].

Biochemical Measurements

Fasting (12 h overnight) blood samples were collected by venepuncture in EDTA tubes. Plasma was subsequently separated and frozen at − 20°C within 1 h for testing at a central, certified laboratory after collection. Fasting plasma glucose (FPG), plasma total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), serum uric acid (SUA), serum ALT and other biochemical parameters were analyzed enzymatically on an Olympus AU640 auto analyzer (Olympus, Kobe, Japan). All laboratory equipment was calibrated and blinded duplicate samples were used.

Definition of Elevated Serum ALT

Elevated serum ALT level was defined as ALT > 40 U/L [24].

Statistical Analysis

Continuous variables were expressed as mean values and standard deviation (SD), whereas categorical variables were described as frequencies and percentages. Continuous variables and categorical variables were compared between men and women, normal ALT and elevated ALT group, and quartiles of TyG index by using Analysis of Variance (ANOVA) test and $\chi 2$-test analyses. Quartiles of TyG index were created. Logistic regression was used to estimate the odds ratios (ORs) and 95% CIs for elevated ALT levels per quintile of

TyG after adjustment for confounding factors, the lowest quintile was set as reference. We used the area under the receiver-operating characteristic curve (AUC) and 95% confidence intervals (CIs) to assess the discriminatory power of TyG index to assess the risk for elevated ALT level. The sensitivity, specificity, and Youden index of TyG were calculated, and the optimal cut-off value of TyG index for identifying elevated ALT was derived from the point with the maximum Youden index. All statistical analyses were performed using SPSS version 19.0 software (SPSS Inc, Chicago, Illinois, USA), and $P < 0.05$ indicated statistical significance.

Results

Characteristics of the study population

Table 1 showed the baseline characteristics of participants according to sex and ALT level (ALT ≤ 40 and ALT > 40). Data were analyzed for 11,573 adults (5,357 men and 6,216 women). In this population, the mean age was 53.8 ± 10.6 years and mean ALT level was 22.5 ± 18.4 U/L. There were 860 participants diagnosed as elevated ALT, with a prevalence of 7.4%. Compared to normal ALT individuals, subjects with elevated ALT were more likely to have a higher percentage of current drinking, and higher levels of SBP, DBP, FPG, TC, TG, LDL-C, and serum uric acid levels, but lower HDL-C levels (all $P < 0.001$). Moreover, participants with elevated ALT levels had a heavier weight, taller height, greater WC, and higher BMI (all $P < 0.001$). Notably, the median value of TyG index was significantly elevated in subjects with elevated ALT in contrast to those with normal ALT ($P < 0.001$).

Table 1
Baseline Characteristics of the Study Subjects. (N = 11573)

Variables	Men	Women	p	ALT ≤ 40U/L	ALT > 40U/L	p	Total
	n = 5357	n = 6216		n = 10713	n = 860		n = 11573
Age, yr	54.4 ± 10.8	53.4 ± 10.3	< 0.001*	54.1 ± 10.6	51.0 ± 9.4	< 0.001*	53.8 ± 10.6
Race(Han), %	5071(94.7)	5897(94.9)	0.324	10148(94.7)	820(95.3)	0.471	10968(94.8)
Current smoking status, %	3056(57.0)	1030(16.6)	< 0.001*	3757(35.1)	329(38.3)	0.063	4086(35.3)
Current drinking status, %	2434(45.4)	183(2.9)	< 0.001*	2333(21.8)	284(33.0)	< 0.001*	2617(22.6)
Physical activity, %			< 0.001*			0.641	
Low	1209(22.6)	2232(35.9)		3192(29.8)	249(29.0)		3441(29.7)
Moderate	3851(71.9)	3628(58.4)		6912(64.5)	567(65.9)		7479(64.6)
High	297(5.5)	356(5.7)		609(5.7)	44(5.1)		653(5.6)
SBP, mm Hg	143.7 ± 22.6	140.1 ± 24.0	< 0.001*	141.5 ± 23.5	144.8 ± 22.1	< 0.001*	141.8 ± 23.5
DBP, mm Hg	83.8 ± 11.8	80.6 ± 11.5	< 0.001*	81.7 ± 11.7	85.9 ± 12.0	< 0.001*	82.1 ± 11.8
Weight, kg	68.6 ± 11.1	60.3 ± 10.1	< 0.001*	63.5 ± 11.0	71.5 ± 13.3	< 0.001*	64.1 ± 11.4
Height, cm	166.4 ± 6.3	155.6 ± 6.1	< 0.001*	160.4 ± 8.2	163.5 ± 8.3	< 0.001*	160.6 ± 8.2
WC, cm	83.8 ± 9.8	81.3 ± 9.7	< 0.001*	82.0 ± 9.7	88.0 ± 10.1	< 0.001*	82.4 ± 9.8
BMI, kg/m^2	24.7 ± 3.5	24.9 ± 3.8	0.061	24.7 ± 3.6	26.7 ± 4.2	< 0.001*	24.8 ± 3.7

Data are expressed as the mean ± SD or as n (%).

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; TC, total cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; TyG, triglyceride glucose; ALT, alanine aminotransferase.

*p < 0.001, #p < 0.05.

Variables	Men	Women	p	ALT ≤ 40U/L	ALT > 40U/L	p	Total
	n = 5357	n = 6216		n = 10713	n = 860		n = 11573
TC, mmol/L	5.2 ± 1.0	5.3 ± 1.1	< 0.001*	5.2 ± 1.1	5.5 ± 1.3	< 0.001*	5.2 ± 1.1
TG, mmol/L	1.7 ± 1.6	1.6 ± 1.3	0.145	1.6 ± 1.4	2.3 ± 2.1	< 0.001*	1.6 ± 1.5
HDL-C, mmol/L	1.4 ± 0.4	1.4 ± 0.3	0.645	1.4 ± 0.4	1.3 ± 0.4	< 0.001*	1.4 ± 0.4
LDL-C, mmol/L	2.9 ± 0.8	3.0 ± 0.8	< 0.001*	2.9 ± 0.8	3.1 ± 0.9	< 0.001*	2.9 ± 0.8
FPG, mmol/L	6.0 ± 1.7	5.9 ± 1.6	0.004#	5.9 ± 1.6	6.1 ± 1.6	< 0.001*	5.9 ± 1.6
Serum uric acid, umol/L	333.7 ± 83.5	255.8 ± 67.8	< 0.001*	288.1 ± 82.6	338.9 ± 97.8	< 0.001*	291.9 ± 84.9
TyG	8.7 ± 0.7	8.7 ± 0.6	< 0.001*	8.7 ± 0.7	9.1 ± 0.7	< 0.001*	8.7 ± 0.7
ALT, U/L	25.6 ± 22.7	19.7 ± 13.1	0.903	19.0 ± 7.4	65.6 ± 43.4	< 0.001*	22.5 ± 18.4
Data are expressed as the mean ± SD or as n (%).							
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; TC, total cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; TyG, triglyceride glucose; ALT, alanine aminotransferase.							
*p < 0.001, #p < 0.05.							

Study participants' characteristics according to quartiles of TyG index

Table 2 showed the study participants' characteristics according to TyG index quartiles. The TyG index quartiles were as follows: <8.25, 8.25–8.64, 8.64–9.10, and ≥ 9.10. Serum ALT levels increased linearly with the increasing TyG index (P for trend < 0.001). From quartile 1 to quartile 4 of TyG index, subjects had significantly higher levels of weight, WC, BMI, SBP, DBP, TC, TG, LDL-C, FPG, and serum uric acid, while lower level of HDL-C (P for trend < 0.001 for all).

Table 2
Baseline characteristics of study participants stratified by quartiles of TyG index.

Variables	Q1 (< 8.25)	Q2 (8.25–8.64)	Q3 (8.64–9.10)	Q4 (≥ 9.10)	p for trend
	n = 2539	n = 2997	n = 3173	n = 2864	
Age, yr	51.0 ± 10.6	53.7 ± 10.6	55.1 ± 10.5	55.1 ± 10.1	< 0.001*
Race(Han), %	2386(94.0)	2842(94.8)	3016(95.1)	2724(95.1)	0.217
Current smoking status, %	870(34.3)	1048(35.0)	1150(36.2)	1018(35.5)	0.450
Current drinking status, %	607(23.9)	635(21.2)	710(22.4)	665(23.2)	0.085
Physical activity, %					< 0.001*
Low	579(22.8)	872(29.1)	1008(31.8)	982(34.3)	
Moderate	1843(72.6)	1975(65.9)	1982(62.5)	1679(58.6)	
High	117(4.6)	150(5.0)	183(5.7)	203(7.1)	
SBP, mm Hg	135.0 ± 21.6	138.9 ± 22.7	143.6 ± 23.6	148.7 ± 23.5	< 0.001*
DBP, mm Hg	78.4 ± 10.9	80.6 ± 11.4	83.0 ± 11.6	85.7 ± 11.9	< 0.001*
Weight, kg	60.6 ± 9.7	62.2 ± 10.8	64.6 ± 11.2	68.8 ± 11.8	< 0.001*
Height, cm	161.1 ± 7.9	160.3 ± 8.1	160.4 ± 8.2	160.7 ± 8.5	0.003#
WC, cm	77.6 ± 8.5	80.4 ± 9.2	83.4 ± 9.5	87.9 ± 9.0	< 0.001*
BMI, kg/m^2	23.3 ± 3.2	24.1 ± 3.6	25.0 ± 3.6	26.6 ± 3.5	< 0.001*
TC, mmol/L	4.7 ± 0.9	5.1 ± 0.9	5.4 ± 1.0	5.8 ± 1.2	< 0.001*
TG, mmol/L	0.7 ± 0.1	1.0 ± 0.2	1.5 ± 0.3	3.2 ± 2.2	< 0.001*
HDL-C, mmol/L	1.6 ± 0.4	1.5 ± 0.4	1.4 ± 0.3	1.2 ± 0.3	< 0.001*
LDL-C, mmol/L	2.5 ± 0.6	2.8 ± 0.7	3.1 ± 0.8	3.2 ± 0.9	< 0.001*
FPG, mmol/L	5.3 ± 0.6	5.5 ± 0.6	5.8 ± 1.0	7.0 ± 2.7	< 0.001*

Data are expressed as the mean ± SD or as n (%).

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; TC, total cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; TyG, triglyceride glucose; ALT, alanine aminotransferase.

*p < 0.001, #p < 0.05.

Variables	Q1 (< 8.25)	Q2 (8.25–8.64)	Q3 (8.64–9.10)	Q4 (≥ 9.10)	p for trend
	n = 2539	n = 2997	n = 3173	n = 2864	
Serum uric acid, umol/L	263.4 ± 71.8	278.0 ± 77.6	298.3 ± 83.7	324.5 ± 91.9	< 0.001*
TyG	7.9 ± 0.2	8.4 ± 0.1	8.8 ± 0.1	9.6 ± 0.5	< 0.001*
ALT, U/L	19.3 ± 22.7	20.3 ± 15.4	22.4 ± 14.6	27.5 ± 19.8	< 0.001*
Data are expressed as the mean ± SD or as n (%).					
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; TC, total cholesterol; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FPG, fasting plasma glucose; TyG, triglyceride glucose; ALT, alanine aminotransferase.					
*p < 0.001, #p < 0.05.					

Prevalence of elevated ALT categorized by quartiles of TyG index for both sexes

As shown in Fig. 1, the prevalence of elevated ALT increased from quartile 1 to quartile 4 of TyG index in both genders (P for trend < 0.001). The proportions of elevated ALT from quartiles 1–4 of TyG index were 4.9%, 6.5%, 11.4% and 18.8% for men, 2.5%, 3.7%, 4.3% and 8.5% for women, respectively. Moreover, data showed that men had higher prevalence of elevated ALT than women in all of the quartiles of TyG index.

Association between the TyG index and elevated ALT risk

With increasing TyG quartile, risk for elevated ALT increased substantially in the general population and both genders (Table 3). After adjusting for age, The ORs and 95%CIs for elevated ALT were progressively increased across quartiles of TyG index. Further adjustment for age, race, weight, height, WC, BMI, smoking, drinking, SBP, DBP, and serum uric acid, in general population and men, compared to the lowest quartile, the quartile3-4 remained significantly associated with elevated ALT. However, in women, only the top quartile of TyG index was associated with elevated ALT. The adjusted ORs (95%CIs) for elevated ALT were 1.71(1.32–2.21) and 2.46(1.90–3.19) among subjects in the third and the fourth quartile of TyG, as compared to persons in the first TyG quartile (p < 0.001).

Table 3
Odds ratios (ORs) and 95% CIs for elevated ALT according to quartile (Q) of TyG in the study subjects.

Quartiles of TyG	Age-adjusted model			Multivariable model		
	OR	95% CI	P	OR	95% CI	P
Total						
Q1	1.00	——	——	1.00	——	——
Q2	1.53	1.17-2.00	0.002#	1.25	0.95–1.64	0.107
Q3	2.57	2.00-3.29	< 0.001*	1.71	1.32–2.21	< 0.001*
Q4	4.82	3.80–6.11	< 0.001*	2.46	1.90–3.19	< 0.001*
Men						
Q1	1.00	——	——	1.00	——	——
Q2	1.46	1.04–2.05	0.031#	1.16	0.82–1.65	0.392
Q3	2.64	1.94–3.60	< 0.001*	1.82	1.32–2.51	< 0.001*
Q4	4.47	3.32–6.02	< 0.001*	2.38	1.72–3.30	< 0.001*
Women						
Q1	1.00	——	——	1.00	——	——
Q2	1.56	1.01–2.41	0.044#	1.30	0.84–2.02	0.240
Q3	1.94	1.27–2.98	0.002#	1.34	0.87–2.08	0.186
Q4	4.06	2.71–6.09	< 0.001*	2.22	1.44–3.42	< 0.001*
Abbreviations: TyG, triglyceride glucose.						
Multivariable model: adjusted for age, sex, race, weight, height, BMI, WC, smoking, drinking, physical activity, SBP, DBP, and serum uric acid.						
*p < 0.001, #p < 0.05.						

We also assessed the relationship between elevated ALT and per-unit increase in TyG index for both genders (Fig. 2). With per-unit increase of TyG index, the risk of elevated ALT increased 1.55-times (95%CI 1.35–1.77) for men and 1.59-times (95%CI 1.32–1.91) for women, respectively. Among four age groups, the elevated ALT was significantly associated with TyG index in middle and older age groups (ORs, 95%CIs: 1.66, 1.32–2.09 for 35-44y; 1.65, 1.37–1.99 for 45-54y; 1.48, 1.20–1.82 for 55-64y). However, we didn't find association between elevated ALT with per-unit increase of TyG index in subjects of ≥ 65 year old.

Diagnostic accuracy of TyG index for elevated ALT

The discriminatory power of TyG index in the prediction of elevated ALT was detected in both sexes. The results of ROC analyses and AUCs with their corresponding 95%CIs for TyG were shown in Fig. 3 (AUC =

0.667, 95%CI 0.643–0.691 for men, AUC = 0.637, 95%CI 0.604–0.671 for women). The best TyG value for identification of elevated ALT was 8.69 (sensitivity 0.702, specificity 0.562) for men and 8.96 (sensitivity 0.529, specificity 0.701) for women.

Discussion

This population-based cross-sectional study suggested an increased risk of elevated ALT levels with increasing TyG index in general Chinese population. To our best knowledge, this study is the first to demonstrate a significant association between TyG index and elevated ALT after adjustment for potential confounders. We also assessed the relationship between elevated ALT and per-unit increase in TyG index for both genders. In addition, the discriminatory power of TyG index in the prediction of elevated ALT was detected and the optimal cut-off point of TyG for the identification of elevated ALT was suggested. Thus, TyG index could be a simple and clinically effective surrogate marker to identify elevated ALT.

In the present study, the TyG index was positively associated with elevated ALT as anticipated. Elevated ALT is not only considered as a consequence of hepatocytes damage as a result of NAFLD, but also a cardiometabolic risk factor, associated with type 2 diabetes mellitus, metabolic syndrome [5 12 25]. Moreover, recent studies reported that elevated serum level of ALT was marker of inflammation and oxidative stress, which could lead to insulin resistance and further promote excessive accumulation of triglycerides in liver [25 26]. TG and FPG are key components of metabolic syndrome, which are overproduced by the fatty liver. Thus, we speculated that there existed an association between a novel index, the triglyceride glucose index and elevated ALT level.

TyG index, a biomarker related to IR, can be used in clinical practice and large-scale, population-based health screening because measuring TG and FPG is inexpensive and routine. Our data suggested that TyG was positively associated with elevated ALT. This result was not surprising because the TyG index, derived from TG and FPG, two crucial metabolic variables altered in fatty liver, and highly correlates with insulin resistance, which was the key pathogenesis of NAFLD.

Recently, TyG index has been used as excellent surrogate marker to identify IR and T2DM [13 27]. Moreover, a new published study demonstrated that the TyG index, a simple measure reflecting insulin resistance, might be useful to early identify individuals at a high risk of developing a cardiovascular event [28]. The present study showed that higher level of TyG index had a positive relationship with elevated ALT level the general Chinese population. Importantly, Guerrero-Romero et al. [13] indicated that TyG index could reflect hepatic insulin resistance due to its correlation with composition of liver fat. In recent years, the TyG index has attracted more attention. In fact, previous studies showed that the TyG index had an independent association with liver steatosis in chronic hepatitis C patients and NAFLD patients [29 30]. Another study also indicated that the TyG index was effective to screen simple steatosis and was superior to other indices for NAFLD [17].

In this study, we determined in a large Chinese population that thresholds of TyG $\geq$ 8.69 and 8.96 for men and women was effective enough to identify elevated ALT individuals. The cut-off values were similar to that of 8.5 in another Chinese study which evaluated the TyG and NAFLD [18], but quite different from the finding

of 4.58 by Simental-Mendia [17]. Our study indicated that the TyG index was closely associated with elevated ALT. The reason for this may be explained that in subjects with higher level of TyG index, excessive accumulation of triglycerides in the liver, which may lead to hepatic insulin resistance. Then, as a result of hepatic insulin resistance, FPG and LDL-C were overproduced, which could make the fat composition in the liver, further led to ALT levels elevation and chronic liver diseases.

Study strengths and limitations: The strengths of this study are its population-based design, large sample size, and the first evaluation of the associations of the TyG index with elevated ALT level in general Chinese population. These data are particularly important in the case of rural Chinese population who has relatively poor living standard and health resources. Several limitations in this study need to be acknowledged. First, because of its cross-sectional design, we were unable to determine whether or not there was a causal association. Thus, the obtained associations in this study should be considered with caution. Second, there are known causes of elevated liver enzyme levels that were not tested in our study, such as chronic viral hepatitis and other illnesses, and the possibility still exists that unmeasured confounders may explain part of the association.

Conclusions

We validated the effectiveness of the TyG index in identifying individuals at risk for elevated ALT level in a large sample of Chinese participants. We determined that the optimal cut-off point of TyG for identifying elevated ALT level was 8.69 and 8.96 for men and women. Our findings have important clinical and epidemiological research implications. The TyG index is an easy-to calculate and effective biomarker for identification elevated ALT level and risk for chronic hepatic diseases in general population.

Abbreviations

TyG
Triglyceride glucose index
ALT
Alanine aminotransferase
T2DM
Type 2 diabetes mellitus
NAFLD
Nonalcoholic fatty liver disease
MetS
Metabolic syndrome
FPG
Fasting plasma glucose
TC
Plasma total cholesterol
TG
Triglycerides

LDL-C
Low-density lipoprotein cholesterol
HDL-C
High-density lipoprotein cholesterol
SUA
Serum uric acid
WC
Waist circumference
BMI
Body mass index

Declarations

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Contributions

Yingxian Sun and Xingang Zhang designed this study and assisted in manuscript writing, Haiyue Yu and Xueyao Zhang analyzed and interpreted the participants data. Yu Hua wrote the manuscript as a major contributor. Shuang Chen and Xingang Zhang critically revised the manuscript. All authors read and approved the final manuscript.

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Ethics declarations

Ethics approval and consent to participate

Approval for the NCRCHS was obtained from the Ethics Committee of China Medical University (Shenyang, China, ethical approval number: AF-SDP-07-1, 0-01).

Consent for publication

All participants provided written informed consent and all procedures were performed in accordance with the ethical standards. If the participants were illiterate, their proxies wrote the informed consents for them.

Competing interests

The authors report no relationships that could be construed as a conflict of interest.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

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Figures

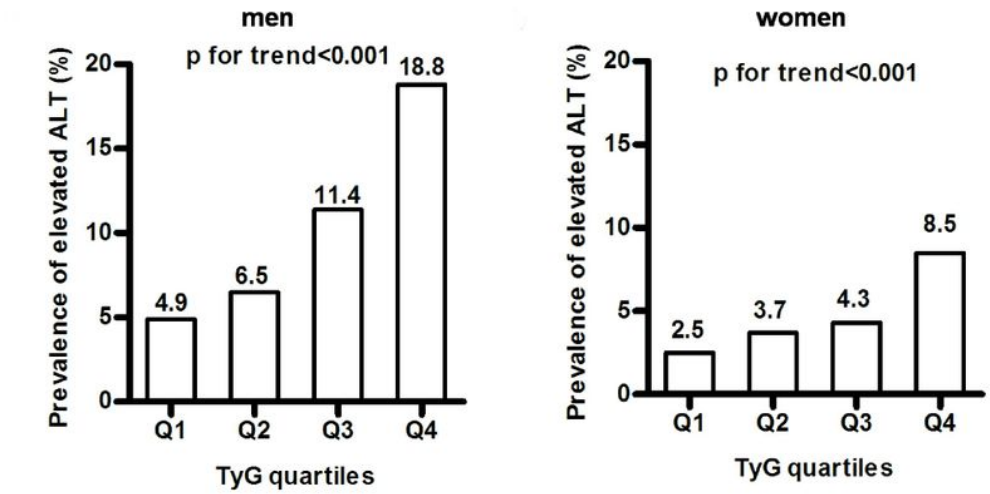


Figure 1

Frequency of elevated ALT according to the quartiles of TyG among the study subjects.

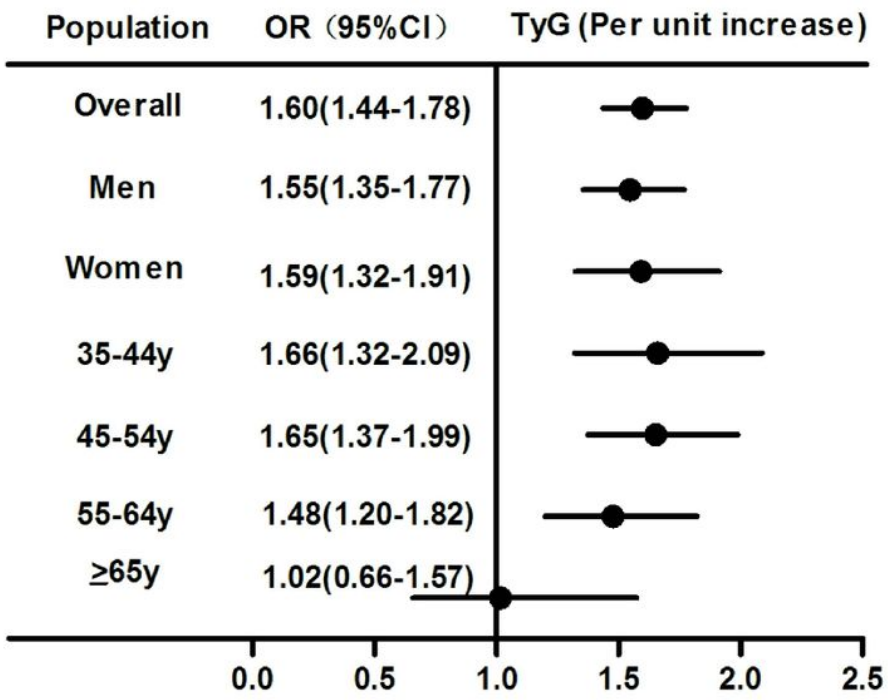
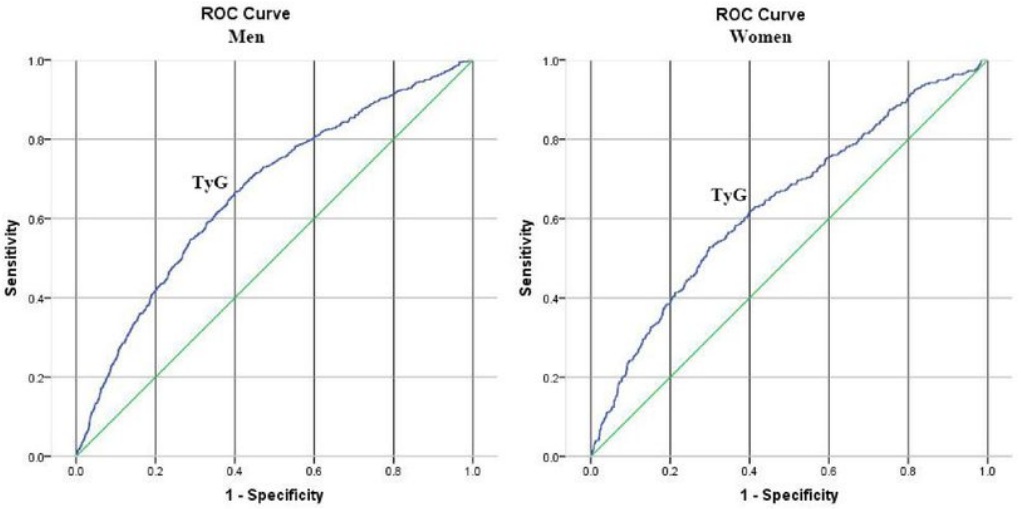


Figure 2

Association of elevated ALT and TyG index by sex and/or age groups.



Men		Women	
AUC	95%CI	AUC	95%CI
0.667	0.643-0.691	0.637	0.604-0.671

Figure 3

ROC curves for TyG index for predicting elevated ALT among men and women.