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The Application of Triglyceride-Glucose Index and Related Parameters in Diagnosing MAFLD in a Chinese population

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Abstract

Objective To explore the diagnostic value of TyG and its related parameters in MAFLD.

Design A cross-sectional study of local residents who attended medical checkups at the First Hospital of Nanping City, Fujian Medical University, between 2015 and 2017.

Setting One participation center.

Participants 2605 subjects met the inclusion exclusion criteria. Subjects were grouped according to whether they had MAFLD or not.

Results The TyG index and its related parameters are risk factors for the development of MAFLD (P<0.001). Restriction cube spline (RCS) analysis showed a significant dose-response relationship between the TyG index and MAFLD. The risk of developing MAFLD increases significantly with increasing levels of TyG. After adjusting for confounders, this relationship remains (*OR*: 4.89, 95%*CI*: 3.98-6.00). The areas under the ROC curves (AUC) of the TyG index for MAFLD detection were 0.793 (0.774-0.812). The AUCs of TyG-related parameters were improved, among which TyG-waist circumference (TyG-WC) showed the largest AUC for MAFLD detection (0.873, 95%*CI*: 0.860-0.887). In addition, the best cut-off value of the TyG-WC was 716.743 with a sensitivity and specificity of 88.7% and 71.4%, respectively.

Conclusion The TyG index is effective in identifying MAFLD, and the TyG-related parameters improved the identification and prediction of MAFLD, suggesting that TyG-related parameters, especially TyG-WC may be a useful marker for identifying MAFLD.

Keywords: Metabolic-associated Fatty Liver Disease; TyG; TyG Index-Related Parameters

Strengths and limitations of this study

We combined metabolic-related indices with TyG index to predict MFALD with a

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comprehensive index.

In this study, the latest diagnostic criteria were used for the diagnosis of MAFLD. Measurement error in self-reported dietary habits and other data in this study is unavoidable.

Introduction

Non-alcoholic fatty liver disease (NAFLD), with hepatic steatosis as the main pathological manifestation, can progress to cirrhosis and hepatocellular carcinoma(HCC)(1, 2), affecting approximately one-quarter of the adult population worldwide(3). In recent years, there has been increasing recognition of the inherent flaws in the term "non-alcoholic". It overemphasizes the presence or absence of alcohol use disorders and ignores the importance of metabolic risk for NAFLD progression. As such, an international panel of experts renamed NAFLD to metabolism-associated fatty liver disease (MAFLD) in 2020(4). MAFLD is used as a more appropriate disease designation to describe liver diseases associated with metabolic dysfunction(5). Due to its high global prevalence, it poses a serious threat to human health and a huge economic burden to society(6). Steatosis is a reversible condition in its early stages and can be addressed through behavioral changes(7, 8). For example, increasing physical activity and controlling energy intake are particularly effective interventions in the early stages of the disease(9, 10). However, the aggressive form of steatohepatitis can progress to fibrosis and eventually cirrhosis, which is irreversible damage(11). Due to the high prevalence of MAFLD and its progressive nature, the early detection of MAFLD is of great significance to enable the provision of early intervention, thus avoiding the progression of MAFLD(12).

Although the gold standard for identifying fatty liver disease (FLD) is still liver biopsy, it is unsuitable for large-scale epidemiological surveys because of its

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invasiveness, poor acceptability, cost, and sampling variability(12). Thus, it is necessary to develop a simple tool to identify MAFLD. Significant progress has been made in the noninvasive assessment of FLD in recent years, including fatty liver index (FLI) and hepatic steatosis index (HSI)(13). The FLI is a prevalent biomarker panel consisting of body mass index (BMI), waist circumference, triglycerides, and gamma-glutamyl transferase ($FLI=e^{0.953*\ln(TG)+0.139*BMI+0.718*\ln(GGT)+0.053*WC-15.745}/(1+e^{0.953*\ln(TG)+0.139*BMI+0.718*\ln(GGT)+0.053*WC-15.745})\times100$)(14). The HSI is a biomarker panel consisting of BMI, diabetes, and the alanine transaminase(ALT)/aspartate transaminase(AST) ratio (HSI=8*ALT/AST+BMI(+2 if type 2 diabetes, +2 if female))(15). However, the calculation process of both indices is more complicated and involves more traits and indicators. An ideal non-invasive test should be simple, easily accessible, cost-effective, and efficient, and allow easy visualization to detect and identify people at high risk of MAFLD(16). With such a test, large-scale population-wide screening and preventive programs in large populations would be possible. Prior studies have confirmed that insulin resistance (IR) is an important pathogenic mechanism in MAFLD(17). Homeostasis model assessment of insulin resistance (HOMA-IR) is the gold standard diagnostic method of IR and has an excellent diagnostic effect on MAFLD(18). However, HOMA-IR is costly, time-consuming, and complex, which limits its widespread implementation in large epidemiological investigations(19). TyG, a non-invasive index, calculated from fasting glucose and triglycerides, has been proposed as a reliable marker for IR in clinical practice(20). Since MAFLD is associated with IR and dyslipidemia, the TyG index is also considered a useful predictive marker for MAFLD(21). However, the results from epidemiological studies remained controversial(22). The longitudinal association between baseline TyG index and the risk of MAFLD was assessed in a cohort study conducted in Jiangsu,

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China, which included 2056 subjects(21). The results showed that the TyG index was independently associated with the risk of developing MAFLD (*HR*: 1.784, 95%*CI*: 1.383-2.302, *P*< 0.001)(21). A cross-sectional study in US adults also showed a positive association between the TyG index and the risk of MAFLD/NAFLD, as for MAFLD, TyG-WC presented the highest *OR* (*OR*: 28.435, 95%*CI*: 12.121-66.705)(23). However, the sample sizes of these studies were small, and more large prospective studies are needed to further validate the association between the two.

The present study aimed to investigate the association of the TyG index and its related parameters with MAFLD in a Chinese population and to assess their predictive efficacy for MAFLD.

Material and Methods

Study subjects and design

This cross-sectional study included 2605 subjects who underwent a physical examination and completed an abdominal ultrasound examination at Nanping First Hospital, Fujian Medical University (Nanping, China) between April 2015 and August 2017. The study protocol conformed to the ethical guidelines of the 1,975 Declaration of Helsinki (6th revision, 2008) and was approved by the Ethics Committee of Fujian Medical University(ethical approval number 2014096). All the participants provided their informed consent before the study started.

The inclusion criteria for participants in the current study were permanent residency in Nanping and age between 18 and 75 years and completed ultrasonography examination. The diagnosis of fatty liver disease (FLD) in this cohort was primarily based on ultrasonographic findings rather than a liver biopsy(24). This is because recent standardized criteria have significantly improved the diagnostic accuracy of ultrasonography so that even minor degrees of steatosis can be detected.

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Data collection and measure

Data on MAFLD risk factors were obtained through direct interviews with the help of a structured medical questionnaire. The risk factors included were age, gender, marital status, income, educational level, smoking, drinking, lifestyle, dietary habits, medical history, and family history of MAFLD. All subjects underwent a complete physical examination in the morning after an overnight fast. The clinical variables collected were height, weight, waist circumference (WC), hip circumference (HC), Waist-to-Hip Ratio (WHR), diastolic blood pressure (DBP), and systolic blood pressure (SBP), serum triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), and high-density lipoprotein (HDL), fasting plasma glucose (FPG), Gamma-glutamyltransferase (GGT) alanine transaminase(ALT), and aspartate aminotransferase (AST). All these variables were assessed using standard procedures (triglyceride: 1mmol/L=88.5mg/dL; fasting blood glucose: 1mmol/L=18mg/dL). Body mass index (BMI) was calculated as body weight/(height)^2. Food consumption was assessed with the help of a food frequency questionnaire, and total consumption was calculated by multiplying the frequency of food consumption by the amount of food consumed each time. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or the current use of anti-hypertensive medication. Diabetes was defined as fasting plasma glucose ≥7.0 mmol/L or the current use of hypoglycemic agents.

Triglyceride-Glucose Index and Related Parameters

The TyG index and its related parameters were calculated according to the previous studies(20, 24). The specific calculation formulas were as follows：

(1) TyG=(ln[triglyceride(mg/dL) × glucose(mg/dL)/2]);

(2) TyG-WC=TyG×WC;

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(3) TyG-BMI=TyG×BMI;

(4) TyG-WHR=TyG×WHR;

Diagnosis of MAFLD

MAFLD is diagnosed by ultrasound showing hepatic steatosis and having one of the following three criteria(3): (1) overweight or obesity (BMI ≥ 23.0kg/m^2); (2) type 2 diabetes mellitus (T2DM); and (3) metabolic dysregulation among non-overweight individuals (BMI < 23.0kg/m^2). Metabolic disorders include abnormalities in WC, blood pressure (BP), TG, HDL, prediabetes, HOMA-IR, and C-reactive protein (CRP). Non-overweight individuals meeting any two and more of the metabolic disorders are diagnosed as MAFLD.

Statistical Analyses

The baseline characteristics of subjects were analyzed using the Nonparametric Kruskal-Wallis test for non-normal continuous variables and the Chi-Square test for nominal variables. Continuous variables were expressed as median (interquartile range, IQR). Univariate and multivariate logistic regression methods were used to analyze the association of TyG and its related parameters with MAFLD risk. The restricted cubic spline (RCS) was used to explore the dose-response relationship between TyG and its related parameters and the risk of MAFLD. The predictive value of TyG and related parameters were compared using the area under receiver operating characteristic (AUROC).

All analyses were performed in R (version 4.2.1, R Foundation) software or Statistical Product and Service Solutions (SPSS) 26.0 software. All *P* values were based on the two-sided test, and $P<0.05$ was considered statistically significant.

Results

Baseline characteristics

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Demographic and lifestyle habits and clinical characteristics were detailed in Supplementary Tables 1 and 2. Of the 2605 participants, 726 were MAFLD patients, and the prevalence of MAFLD was 27.9%. The mean age of the participants was 45 years, and 56.5% of the subjects were male. Compared to those without MAFLD, subjects with MAFLD were more likely to be male, older, married, smokers, drinkers, tea drinkers, and have a history of diabetes or hypertension (all $P<0.05$). In addition, the subjects in both groups were different in terms of clinical detection indicators (SBP, DBP, TG, FPG, TC, GGT, HDL, BMI, WC, WHR, FLI, and HSI) (all $P<0.001$).

Association of MAFLD with TyG and its related parameters

The associations between MAFLD and TyG and its related parameters were mainly analyzed using the logistic regression model. In the crude model, TyG and its related parameters were positively correlated with MAFLD risk (Table 1). The positive correlations of TyG and its related parameters with MAFLD remained unchanged after adjusting for gender, age, marital status, and educational level in model 1 (each $P<0.001$). Model 2 further adjusted for variables such as smoking, drinking, and tea drinking based on model 1. The results remained unchanged (each $P<0.001$). Adding adjustments to some disease history indicators in model 3, the results remained similar.

The restricted cubic spline analyses were applied to interpret the dose-response relationships of TyG and its related parameters with MAFLD risk (Figure 1). The *OR*s of MAFLD increased with increasing TyG levels. the *OR*s of MAFLD also rose with the increasing TyG-BMI, TyG-WC, and TyG-WHR.

Assessment of the accuracy of TyG and its related parameters for the diagnosis of MAFLD

The ROC curve for the ability of TyG and its related parameters and traditional indicators to predict the risk of MAFLD were shown in Figure 2. And the performance

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of these models was detailed in Table 2. The AUROCs of TyG and its related parameters were greater than that of traditional indicators, including the HSI. The TyG-WC performed the highest AUROC (0.873, 95%*CI*: 0.860-0.887, *P*<0.001), compared with TyG-BMI (0.862, 95%*CI*: 0.847-0.876, *P*<0.001), TyG-WHR (0.836, 95%*CI*: 0.820-0.852, *P*<0.001). Compared with TyG, the accuracy of TyG-WC, TyG-BMI, and TyG-WHR were improved by 26.4%, 18.7%, and 12.5% (each *P*<0.001), respectively. The IDI values of TyG and its parameters were greater than 0. The detailed results were shown in Supplementary Table 3.

Discussion

In this cross-sectional study, different parameters were tested to predict the presence of MAFLD. A positive association was observed between the TyG index and its associated parameters with the risk of MAFLD. After adjusting for various confounding factors, the TyG index and its related parameters remained independent predictors of MAFLD. Advanced results from ROC curve analyses indicated that TyG-BMI, TyG-WC, and TyG-WHR, especially TyG-WC, had better diagnostic values than the TyG index alone for predicting MAFLD. More detailed discussions of those observations are presented below.

The diagnosis of MAFLD is based on histological (liver biopsy), imaging, and blood biomarker evidence of hepatic fat accumulation (hepatocellular steatosis) in combination with one of the following three conditions: overweight/obesity, type 2 diabetes mellitus, and metabolic dysfunction(25). Currently, abdominal ultrasonography is the primary method for diagnosing hepatic steatosis(26). However, the sensitivity of using ultrasound to diagnose fatty liver is limited. In subjects with BMI > 40 kg/cm², the performance of ultrasound detection is not high(27). Magnetic resonance spectroscopy (MRS) allows quantitative assessment of liver fat content, but

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it is expensive and requires special software, making it difficult to use widely in large epidemiological surveys. Many attempts were targeted at finding an appropriate marker for MAFLD. As a major metabolic organ, the liver plays a crucial role in regulating glucose and lipid metabolism(28). IR is one of the important pathogenic mechanisms of MAFLD(23). There is a strong association between IR and the risk of MAFLD(29). Many traditional metrics that respond to IR, such as TG/HDL-C and HOMA-IR, are complex and expensive to operate, and difficult to use widely in the general population(30). TyG index, calculated from fasting glucose and triglyceride levels is a favorable marker for IR(19). BMI, WC, and WHR are indices for assessing obesity and are associated with the increased risk of IR, and other metabolic diseases(31). The new parameters TyG-BMI, TyG-WC, and TyG-WHR combine the above indices and appear to be more reflective of IR status in MAFLD. Therefore, the parameters above were introduced in our research for a further comprehensive assessment.

We assessed and compared the diagnostic accuracy of the four parameters (TyG index, TyG-WC, TyG-BMI, and TyG-WHR). Consistent with previous research results, all the parameters could identify MAFLD in our study(21, 22). RCS analysis revealed a significant dose-response relationship between the TyG index and MAFLD. The best cut-off value of TyG for the diagnosis of MAFLD was 8.738 (sensitivity: 72.2%, specificity: 75.0%). Additionally, TyG-WC, TyG-BMI, and TyG-WHR showed better discrimination of MAFLD compared with the TyG index. The AUROCs of TyG-related parameters for the diagnosis of MAFLD were larger and the sensitivity was higher. In previous studies, FLI and HSI have been shown to have robust diagnostic power for MAFLD(32, 33). In the present study, the area under the ROC curve of the TyG-WC index for MAFLD diagnosis was larger than that of the FLI and HSI, and the diagnostic performance was better. MAFLD is a typical metabolic disease, and consideration of

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body composition may be critical. Among TyG-related parameters, the AUC of TyG-WC was the largest at 0.873 (sensitivity: 88.7%, specificity: 71.4%). Norbert Stefan et al.(34) found that hepatic steatosis correlated with BMI, but more strongly with visceral fat (measured as WC) because visceral adipose tissue (VAT) is more lipid active than subcutaneous fat on a per unit weight basis. Khamseh et al.(35) findings agreed with our study. The AUROCs of the TyG index, TyG-BMI, and TyG-WC were 0.676, 0.675, and 0.693, respectively, all of which were lower than the AUROCs produced in our study. This difference may be due to the small number of overweight/obese participants in their study.

However, this study has several limitations. Firstly, this is a cross-sectional study, and a causative relationship cannot be established. Secondly, measurement error in self-reported dietary habits and other data is inevitable. Nonetheless, because all participants and researchers in this study were blinded to the results of abdominal ultrasonography and blood tests, the absence of differential reporting bias may simply have weakened our observed associations. Thirdly, although we considered a comprehensive set of confounders, the presence of unmeasured confounders is possible as an observational study.

Conclusions

Our study demonstrated that the TyG index is effective in identifying MAFLD, and the TyG-related parameters improved the identification and prediction of MAFLD. TyG and its related parameters have a certain value in the diagnosis of MAFLD. As an inexpensive and convenient index, TyG and its related parameters, especially TyG-WC may be a useful marker for identifying MAFLD.

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Author Contributions

PXE designed the study. YR, PHW, LLL, XWJ, and YS collected the data. YR analyzed the data. YR, PHW, and LLL contributed to the interpretation of results. YR, PHW, LLL, drafted the manuscript. PXE revised the manuscript. All authors have discussed the results and commented on the manuscript. All authors read and approved the final manuscript.

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Abbreviations

NAFLD: Non-alcoholic fatty liver disease; MAFLD: metabolism-associated fatty liver disease; FLI fatty: liver index; HSI: hepatic steatosis index; BMI: body mass index; ALT: alanine transaminase; AST: aspartate transaminase; IR: insulin resistance; HOMA-IR: Homeostasis model assessment of insulin resistance; TyG: Triglyceride glucose index; TG: triglyceride; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma-glucose; WC: Waist circumference; IQR: interquartile range; RCS: restricted cubic spline; AUC: Area under curve; AUROC: area under receiver operating characteristic; NRI: Net Reclassification Index; IDI: Integrated Discrimination Improvement; UA: uric acid; VAT: visceral adipose tissue

Availability of data and materials

The datasets used can be available from the corresponding author on reason-able

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request.

Ethics approval and consent to participate

The current study was carried out in compliance with the Declaration of Helsinki, and the Ethics Committee of Fujian Medical University approved the study protocol (ethics number 2014096). All subjects provided their informed consent prior to participating in this study.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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Figure legends

Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

Figure 2 ROC curves of TyG and its related parameters and biochemical indexes

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Table 1 Univariate and multivariate logistic analysis of TyG and related parameters and MAFLD

Variables	Crude model		Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value
TyG	6.33 (5.27, 7.60)	<0.001	4.96 (4.09, 6.01)	<0.001	5.15 (4.23, 6.27)	<0.001	4.89 (3.98, 6.00)	<0.001
TyG-WC	1.02 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	<0.001	1.02 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	<0.001
TyG-BMI	1.05 (1.05, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001
TyG-WHR	4.44 (3.89, 5.08)	<0.001	4.18 (3.60, 4.87)	<0.001	4.32 (3.70, 5.04)	<0.001	4.08 (3.48, 4.78)	<0.001

[a]: Adjusted for gender, age, marital status, and educational level;

[b]: Adjusted for gender, age, marital status, educational level, smoking, drinking, and tea drinking;

[c]: Adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension.

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Table 2 Area under curve (AUC) analysis

Variables	AUC（95%*CI*）	AIC	Sensitivity%	Specificity%	optimal cut-off	*P* -value
TC(mmol/L)	0.588 (0.564, 0.613)	3206.9	58.3%	58.6%	5.045	<0.001
GGT(mmol/L)	0.761 (0.742, 0.781)	2982.7	74.8%	65.6%	24.500	<0.001
HDL(mmol/L)	0.711 (0.689, 0.732)	3214.3	69.1%	63.4%	1.285	1.000
TG(mg/dL)	0.784 (0.764, 0.803)	3057.6	68.2%	78.0%	137.618	<0.001
FPG(mg/dL)	0.653 (0.629, 0.677)	3085.7	55.1%	69.7%	95.67	<0.001
WC(cm)	0.846 (0.830, 0.861)	2378.3	80.2%	74.9%	84.500	<0.001
BMI(kg/m²)	0.822 (0.804, 0.839)	2486.4	78.9%	72.5%	23.525	<0.001
FLI	0.872 (0.859, 0.886)	2809.1	87.5%	72.1%	0.419	<0.001
HSI	0.821 (0.803, 0.838)	2554.0	77.1%	73.3%	32.715	<0.001
TyG	0.793 (0.774, 0.812)	2676.8	72.2%	75.0%	8.738	<0.001
TyG-WC	0.873 (0.860, 0.887)	2199.6	88.7%	71.4%	716.743	<0.001
TyG-BMI	0.862 (0.847, 0.876)	2239.1	85.3%	73.3%	203.154	<0.001
TyG-WHR	0.836 (0.820, 0.852)	2448.0	84.6%	67.7%	7.444	<0.001

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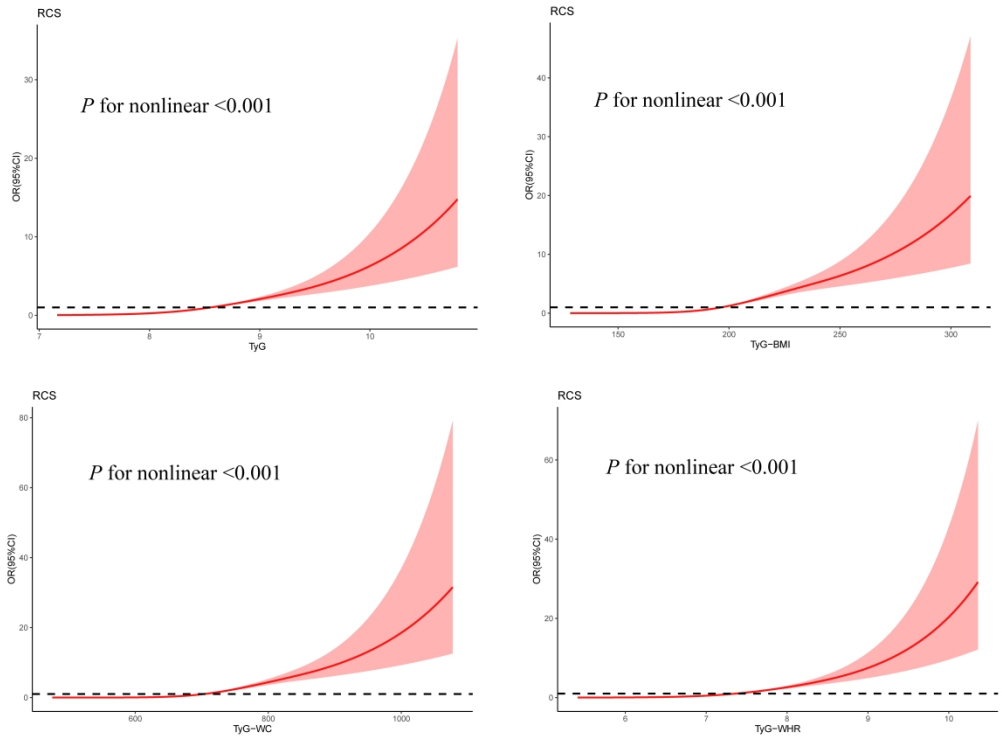

Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

400x294mm (300 x 300 DPI)

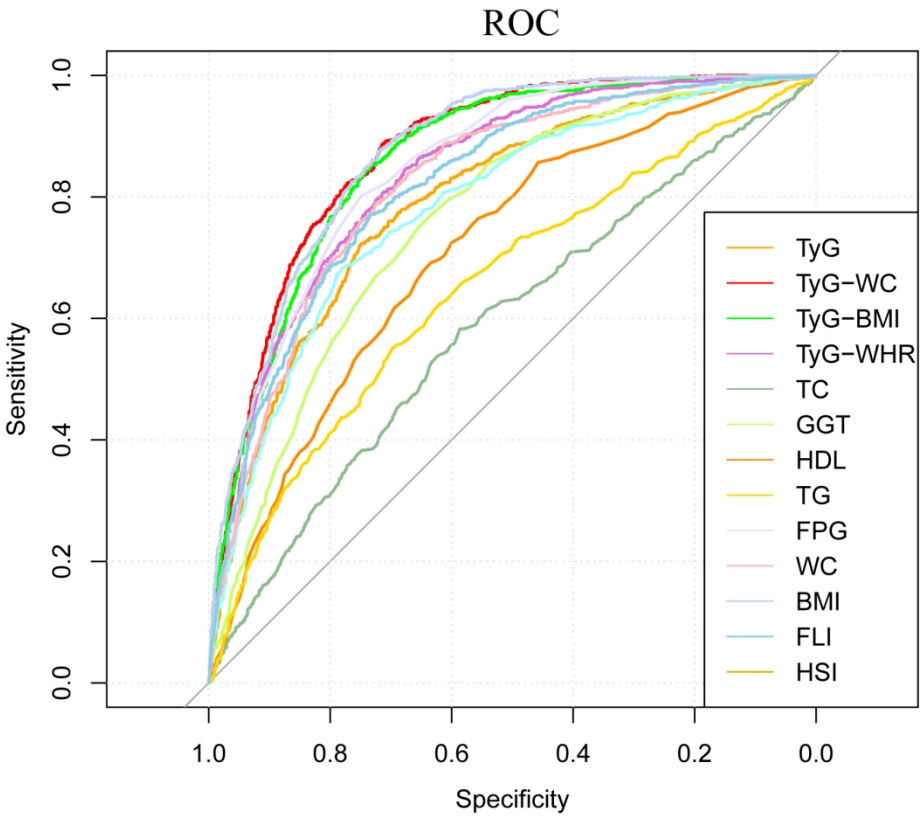

Figure 2 ROC curves of TyG and its related parameters and biochemical indexes

166x141mm (300 x 300 DPI)

Supplementary Table 1 Comparison of general characteristics

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	*P*-value*
Age(years), M (IQR)	45 (33, 52)	43 (31, 51)	48 (38, 54)	<0.001
Gender, n (%)				<0.001
Males	1471 (56.5)	584 (80.4)	887 (47.2)	
Females	1134 (43.5)	142 (19.6)	992 (52.8)	
Marital Status, n (%)				<0.001
Single	378 (14.5)	68 (9.4)	310 (16.5)	
Married	2209 (84.8)	652 (89.8)	1557 (82.9)	
Divorced	9 (0.4)	2 (0.3)	7 (0.4)	
Widowed	9 (0.4)	4 (0.6)	5 (0.3)	
Educational level, n (%)				0.032
Bachelor degree or above	913 (35.1)	228 (31.4)	685 (36.5)	
Junior college	603 (23.2)	172 (23.7)	431 (22.9)	
Senior high school	593 (22.8)	189 (26.0)	404 (21.5)	
Junior high school	319 (12.3)	87 (12.0)	232 (12.3)	
Primary school	140 (5.4)	35 (4.8)	105 (5.6)	
Illiteracy	37 (1.4)	15 (2.1)	22 (1.2)	
Income(yuan/month), n (%)				0.066
<2000	147 (5.6)	35 (4.8)	112 (6.0)	
2000~3000	794 (30.5)	202 (27.8)	592 (31.5)	
≥3000	1664 (63.9)	489 (67.4)	1175 (62.5)	
Smoking status, n (%)				<0.001
Never	1916 (73.6)	448 (61.7)	1468 (78.1)	
Former	113 (4.3)	45 (6.2)	68 (3.6)	
Current	576 (22.1)	233 (32.1)	343 (18.3)	
Drinking status, n (%)				<0.001
Never	1624 (62.3)	389 (53.6)	1235 (65.7)	

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Former	42 (1.6)	15 (2.1)	27 (1.4)	
Current	939 (36.1)	322 (44.4)	617 (32.8)	
Tea drinking status, n (%)				<0.001
Never	1052 (40.4)	205 (28.2)	847 (45.1)	
Former	8 (0.3)	3 (0.4)	5 (0.3)	
Current	1545 (59.3)	518 (71.3)	1027 (54.7)	
History of diabetes, n (%)				<0.001
No	2459 (94.4)	650 (89.5)	1809 (96.3)	
Yes	146 (5.6)	76 (10.5)	70 (3.7)	
History of hypertension, n (%)				<0.001
No	1666 (64.0)	294 (40.5)	1372 (73.0)	
Yes	939 (36.1)	432 (59.5)	507 (27.0)	

Data are presented as median with the interquartile range [M (P25, P75)]. * Comparison of the differences between the groups calculated by Mann-Whitney U test or chi-square test.

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Supplementary Table 2 Evaluation of biochemical indices

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	*P*-value*
BMI(kg/m²), M(IQR)	22.9 (20.8, 25.1)	25.4 (23.9, 27.0)	22.0 (20.3, 23.8)	<0.001
SBP (mmHg), M(IQR)	118 (110, 128)	125 (118, 136)	115 (107, 123)	<0.001
DBP (mmHg), M(*IQR*)	80 (72, 86)	85 (80, 90)	78 (70, 82)	<0.001
TG(mg/dL), M (IQR)	109.7 (79.7, 163.8)	169.0 (118.6, 243.4)	94.7 (73.5, 131.9)	<0.001
FPG(mg/dL), M (IQR)	93.1 (88.4, 99.7)	96.7 (91.1, 106.4)	92.2 (87.7, 97.2)	<0.001
TC(mmol/L), M (IQR)	5.0 (4.5, 5.6)	5.2 (4.7, 5.9)	5.0 (4.4, 5.5)	0.007
GGT(U/L), M (IQR)	23 (16, 36)	34 (24, 52)	20 (15, 29)	<0.001
HDL(mmol/L), M (IQR)	1.3 (1.1, 1.5)	1.2 (1.0, 1.3)	1.4 (1.2, 1.5)	<0.001
WC(cm), M(IQR)	82 (75, 89)	90 (85, 95)	78 (70, 85)	<0.001
WHR, M (IQR)	0.9 (0.8, 0.9)	0.9 (0.9, 0.9)	0.84 (0.8, 0.9)	<0.001
FLI, M (IQR)	0.3 (0.1, 1.1)	1.4 (0.6, 3.4)	0.2 (0.1, 0.5)	<0.001
HSI, M (IQR)	31.6 (28.5, 34.8)	35.5 (32.9, 38.6)	30.2 (27.7, 32.9)	<0.001
TyG, M (IQR)	8.6 (8.2, 9.0)	9.0 (8.7, 9.4)	8.4 (8.1, 8.7)	<0.001
TyG-WC, M (IQR)	703.1 (623.9, 790.6)	814.6 (759.2, 875.4)	660.9 (600.3, 730.5)	<0.001
TyG-BMI, M (IQR)	197.0 (174.2, 222.6)	228.8 (211.0, 248.9)	184.3 (167.4, 205.1)	<0.001
TyG-WHR, M (IQR)	7.4 (6.7, 8.1)	8.2 (7.7, 8.7)	7.1 (6.5, 7.7)	<0.001

Data are presented as median with the interquartile range [M (P25, P75)]. * Comparison of the differences between the groups calculated by Mann-Whitney U test.

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Supplement Table 3 NRI and IDI analyses

Variables	NRI (95%*CI*)	*P*-value	IDI (95%*CI*)	*P*-value
TyG	Reference	<0.001	Reference	<0.001
TC(mmol/L)	-0.437 (-0.479, -0.395)	<0.001	-0.199 (-0.216, -0.182)	<0.001
GGT(mmol/L)	-0.249 (-0.298, -0.195)	<0.001	-0.110 (-0.127, -0.092)	<0.001
HDL(mmol/L)	-0.169 (-0.214, -0.121)	<0.001	-0.119 (-0.136, -0.101)	<0.001
TG(mg/dL)	-0.200 (-0.231, -0.169)	<0.001	-0.053 (-0.059, -0.046)	<0.001
FPG(mg/dL)	-0.661 (-0.695, -0.626)	<0.001	-0.208 (-0.226, -0.191)	<0.001
WC(cm)	0.150 (0.097, 0.202)	<0.001	0.091 (0.067, 0.115)	<0.001
BMI(kg/m²)	0.113 (0.061, 0.167)	<0.001	0.051 (0.027, 0.076)	<0.001
FLI	0.112 (0.060, 0.165)	<0.001	0.033 (0.015, 0.051)	<0.001
HSI	0.059 (-0.005, 0.123)	0.068	0.048 (0.024, 0.072)	<0.001
TyG-WC	0.264 (0.212, 0.316)	<0.001	0.148 (0.129, 0.160)	<0.001
TyG-BMI	0.187 (0.122, 0.258)	<0.001	0.125 (0.107, 0.143)	<0.001
TyG-WHR	0.125 (0.087, 0.167)	<0.001	0.071 (0.059, 0.083)	<0.001

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	77
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8

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		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The Diagnostic Value of Triglyceride-Glucose Index and Related Parameters in Metabolism-associated Fatty Liver Disease in a Chinese Population

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Abstract

Objective To explore the diagnostic value of Triglyceride-Glucose (TyG) and its related parameters in metabolism-associated fatty liver disease (MAFLD).

Design A cross-sectional study of local residents who attended medical checkups at the First Hospital of Nanping City, Fujian Medical University, between 2015 and 2017.

Setting One participation center.

Participants 2605 subjects met the inclusion-exclusion criteria. Subjects were grouped according to whether they had MAFLD or not.

Results The TyG index and its associated parameters are positively associated with the risk of developing MAFLD (P<0.001). Restriction cube spline (RCS) analysis showed a significant dose-response relationship between the TyG index and MAFLD. The risk of developing MAFLD increases significantly with increasing levels of TyG. After adjusting for confounders, this relationship remains (*OR*: 4.89, 95%*CI*: 3.98-6.00). The areas under the receiver operating characteristic curves (AUROC) of the TyG index for MAFLD detection were 0.793 (0.774-0.812). The areas under curve (AUC) of TyG-related parameters were improved, among which TyG-waist circumference (TyG-WC) showed the largest AUC for MAFLD detection (0.873, 95%*CI*: 0.860-0.887). In addition, the best cut-off value of the TyG-WC was 716.743 with a sensitivity and specificity of 88.7% and 71.4%, respectively.

Conclusion The TyG index is effective in identifying MAFLD, and the TyG-related parameters improved the identification and diagnosis of MAFLD, suggesting that TyG-related parameters, especially TyG-WC may be a useful marker for identifying MAFLD.

Keywords: Metabolic-associated Fatty Liver Disease; Triglyceride-Glucose; TyG Related Parameters

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Strengths and limitations of this study

- We combined metabolic-related indices with TyG index to diagnose MFALD with a comprehensive index.
- In this study, the latest diagnostic criteria were used to define MAFLD.
- The strengths of this study are the large sample size and the rigorous screening of subjects. And more comprehensive confounding variables are considered.
- Measurement error in self-reported dietary habits and other data in this study is unavoidable.

Introduction

Non-alcoholic fatty liver disease (NAFLD), with hepatic steatosis as the main pathological manifestation, can progress to cirrhosis and hepatocellular carcinoma(HCC)(1, 2), affecting approximately one-quarter of the adult population worldwide(3). In recent years, there has been increasing recognition of the inherent flaws in the term "non-alcoholic". It overemphasizes the presence or absence of alcohol use disorders and ignores the importance of metabolic risk for NAFLD progression. As such, an international panel of experts renamed NAFLD to metabolism-associated fatty liver disease (MAFLD) in 2020(4). MAFLD is used as a more appropriate disease designation to describe liver diseases associated with metabolic dysfunction(5). Due to its high global prevalence, it poses a serious threat to human health and a huge economic burden to society(6). Steatosis is a reversible condition in its early stages and can be addressed through behavioral changes(7, 8). For example, increasing physical activity and controlling energy intake are particularly effective interventions in the early stages of the disease(9, 10). However, the aggressive form of steatohepatitis can progress to fibrosis and eventually cirrhosis, which is irreversible damage(11). Due to the high prevalence of MAFLD and its progressive nature, the early detection of MAFLD is of

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great significance to enable the provision of early intervention, thus avoiding the progression of MAFLD(12).

Although the gold standard for identifying fatty liver disease (FLD) is still liver biopsy, it is unsuitable for large-scale epidemiological surveys because of its invasiveness, poor acceptability, cost, and sampling variability(12). Thus, it is necessary to develop a simple tool to identify MAFLD. Significant progress has been made in the noninvasive assessment of FLD in recent years, including fatty liver index (FLI) and hepatic steatosis index (HSI)(13). The FLI is a prevalent biomarker panel consisting of body mass index (BMI), waist circumference, triglycerides, and gamma-glutamyl transferase (14). The HSI is a biomarker panel consisting of BMI, diabetes, and the alanine transaminase(ALT)/aspartate transaminase(AST) ratio (15). However, the calculation process of both indices is more complicated and involves more traits and indicators. An ideal non-invasive test should be simple, easily accessible, cost-effective, and efficient, and allow easy visualization to detect and identify people at high risk of MAFLD(16). With such a test, large-scale population-wide screening and preventive programs in large populations would be possible. Prior studies have confirmed that insulin resistance (IR) is an important pathogenic mechanism in MAFLD(17). Homeostasis model assessment of insulin resistance (HOMA-IR) is the gold standard diagnostic method of IR and has an excellent diagnostic effect on MAFLD(18). However, HOMA-IR is costly, time-consuming, and complex, which limits its widespread implementation in large epidemiological investigations(19). TyG, a non-invasive index, calculated from fasting glucose and triglycerides, has been proposed as a reliable marker for IR in clinical practice(20). Since MAFLD is associated with IR and dyslipidemia, the TyG index is also considered a useful predictive marker for MAFLD(21). However, the results from epidemiological studies

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remained controversial(22). The longitudinal association between baseline TyG index and the risk of MAFLD was assessed in a cohort study conducted in Jiangsu, China, which included 2056 subjects(21). The results showed that the TyG index was independently associated with the risk of developing MAFLD (*HR*: 1.784, 95%*CI*: 1.383-2.302, $P< 0.001$)(21). A cross-sectional study in US adults also showed a positive association between the TyG index and the risk of MAFLD/NAFLD, as for MAFLD, TyG-WC presented the highest *OR* (*OR*: 28.435, 95%*CI*: 12.121-66.705)(23). However, the sample sizes of these studies were small, and more large prospective studies are needed to further validate the association between the two. Nanping city is located in the north of Fujian Province. Our previous study reported the prevalence of NAFLD (32.8%) in the population with physical examination in Nanping(24), which is higher than other city of Fujian province(25). The present study aimed to investigate the association of the TyG index and its related parameters with MAFLD in Nanping and to assess their diagnostic efficacy for MAFLD.

Material and Methods

Study subjects and design

This cross-sectional study included 2605 subjects who underwent a physical examination and completed an abdominal ultrasound examination at Nanping First Hospital, Fujian Medical University (Nanping, China) between April 2015 and August 2017. The study protocol conformed to the ethical guidelines of the 1,975 Declaration of Helsinki (6th revision, 2008) and was approved by the Ethics Committee of Fujian Medical University(ethical approval number 2014096). All the participants provided their informed consent before the study started.

The inclusion criteria for participants in the current study were permanent residency in Nanping and age between 18 and 75 years and completed ultrasonography

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examination. The diagnosis of FLD in this study was primarily based on ultrasonographic findings rather than a liver biopsy(26). This is because recent standardized criteria have significantly improved the diagnostic accuracy of ultrasonography so that even minor degrees of steatosis can be detected. Subjects with malignant tumors, incomplete data, or pregnant or lactating women were excluded.

Data collection and measure

Data on MAFLD risk factors were obtained through direct interviews with the help of a structured medical questionnaire. The risk factors included were age, gender, marital status, income, educational level, smoking, drinking, lifestyle, dietary habits, medical history, and family history of MAFLD. All subjects underwent a complete physical examination in the morning after an overnight fast. The clinical variables collected were height (m^2), weight (kg), waist circumference (WC, cm), hip circumference (HC, cm), Waist-to-Hip Ratio (WHR), diastolic blood pressure (DBP, mmHg), and systolic blood pressure (SBP, mmHg), serum triglyceride (TG, mg/dL), total cholesterol (TC, mmol/L), low-density lipoprotein (LDL, mmol/L), and high-density lipoprotein (HDL, mmol/L), fasting plasma glucose (FPG, mg/dL), Gamma-glutamyltransferase (GGT, U/L) alanine transaminase(ALT, U/L), and aspartate aminotransferase (AST, U/L). All these variables were assessed using standard procedures (TG: 1mmol/L=88.5mg/dL; FPG: 1mmol/L=18mg/dL). Body mass index (BMI) was calculated as body weight/$(height)^2$. Food consumption was assessed with the help of a food frequency questionnaire, and total consumption was calculated by multiplying the frequency of food consumption by the amount of food consumed each time. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or the current use of anti-hypertensive medication(27). Diabetes was defined as fasting plasma glucose ≥7.0 mmol/L or the current use of

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hypoglycemic agents(28).

Triglyceride-Glucose Index and Related Parameters

The TyG index and its related parameters were calculated according to the previous studies(20, 26). The specific calculation formulas were as follows：

(1) TyG=ln [fasting triglyceride (mg/dl) × fasting plasma glucose (mg/dl)/2];

(2) TyG-WC=TyG×WC;

(3) TyG-BMI=TyG×BMI;

(4) TyG-WHR=TyG×WHR;

Diagnostic of FLD

Liver ultrasonography is used to diagnose fatty liver. The presence of criteria (i) and any of criteria (ii) through (iv) indicates the presence of fatty liver: (i) Diffuse enhancement of the near-field echoes of the liver and gradual attenuation of the far-field echoes of the liver; (ii) Mild to moderate hepatomegaly with rounded obtuse borders; (iii) unclear structure of intrahepatic ducts; (iv) Reduced hepatic blood flow signal.

Diagnosis of MAFLD

MAFLD is diagnosed by ultrasound showing hepatic steatosis and having one of the following three criteria(3): (1) overweight or obesity (BMI ≥ 23.0kg/m^2 for Asians); (2) type 2 diabetes mellitus (T2DM); and (3) metabolic dysregulation among non-overweight individuals (BMI < 23.0kg/m^2). Metabolic disorder was defined as the presence of at least two of the following metabolic risk abnormalities: (1) WC ≥ 90 cm for Asian men and 80 cm for Asian women; (2) BP ≥ 130/85 mmHg or specific drug treatment; (3) TG ≥ 1.70 mmol/L or specific drug treatment; (4) HDL-c < 1.0

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mmol/L for men and < 1.3 mmol/L for women; (5) prediabetes; (6) HOMA-IR ≥ 2.5; and (7) C-reactive protein (CRP) > 2 mg/L. Non-overweight individuals meeting any two and more of the metabolic disorders are diagnosed as MAFLD.

Statistical Analyses

The baseline characteristics of subjects were analyzed using the Nonparametric Kruskal-Wallis test for non-normal continuous variables and the Chi-Square test for nominal variables. Continuous variables were expressed as median (interquartile range, IQR). Univariate and multivariate logistic regression methods were used to analyze the association of TyG and its related parameters with MAFLD risk. The restricted cubic spline (RCS) was used to explore the dose-response relationship between TyG and its related parameters and the risk of MAFLD. The predictive value of TyG and related parameters were compared using the area under receiver operating characteristic (AUROC). The Net Reclassification Index (NRI) and the Integrated Discrimination Improvement Index (IDI) were used to reflect the overall improvement of the diagnostic model. All analyses were performed in R (version 4.2.1, R Foundation) software or Statistical Product and Service Solutions (SPSS) 26.0 software. All *P* values were based on the two-sided test, and $P<0.05$ was considered statistically significant.

Patient and Public Involvement

Patients and public will not be involved in the development of the research question or in the design of the study. Subjects will receive oral and written information about this study. However, they will not be involved in the recruitment and conduct of the study. After signing informed consent, the participants will be assessed for eligibility and data collection will begin. Eligible subjects will be interviewed face to face by investigators to collect data. In addition, all methods were performed in

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accordance with the relevant guidelines and regulations.

Results

Baseline characteristics

Demographic and lifestyle habits and clinical characteristics were detailed in Table 1 and Table 2. Of the 2605 participants, 747 had FLD, with a FLD prevalence of 28.68%; 726 were MAFLD patients, and the prevalence of MAFLD was 27.9%. The mean age of the participants was 45 years, and 56.5% of the subjects were male. Compared to those without MAFLD, subjects with MAFLD were more likely to be male, older, married, smokers, drinkers, tea drinkers, and have a history of diabetes or hypertension (all $P<0.05$). In addition, the subjects in both groups were different in terms of clinical detection indicators (SBP, DBP, TG, FPG, TC, GGT, HDL, BMI, WC, WHR, FLI, and HSI) (all $P<0.001$).

Association of MAFLD with TyG and its related parameters

The associations between MAFLD and TyG and its related parameters were mainly analyzed using the logistic regression model. In the crude model, TyG and its related parameters were positively correlated with MAFLD risk (Table 3). The positive correlations of TyG and its related parameters with MAFLD remained unchanged after adjusting for gender, age, marital status, and educational level in model 1 (each $P<0.001$). Model 2 further adjusted for variables such as smoking, drinking, and tea drinking based on model 1. The results remained unchanged (each $P<0.001$). Adding adjustments to some disease history indicators in model 3, the results remained similar.

The restricted cubic spline analyses were applied to interpret the dose-response relationships of TyG and its related parameters with MAFLD risk (Figure 1). The *OR*s of MAFLD increased with increasing TyG levels. the *OR*s of MAFLD also rose with the increasing TyG-BMI, TyG-WC, and TyG-WHR.

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Assessment of the accuracy of TyG and its related parameters for the diagnosis of MAFLD

The ROC curve for the ability of TyG and its related parameters and traditional indicators to predict the risk of MAFLD were shown in Figure 2. And the performance of these models was detailed in Table 4. The AUROCs of TyG and its related parameters were greater than that of traditional indicators, including the HSI. The TyG-WC performed the highest AUROC (0.873, 95%*CI*: 0.860-0.887, *P*<0.001), compared with TyG-BMI (0.862, 95%*CI*: 0.847-0.876, *P*<0.001), TyG-WHR (0.836, 95%*CI*: 0.820-0.852, *P*<0.001). Based on the results of NRI, it can be seen that the accuracy of TyG-WC, TyG-BMI and TyG-WHR were improved by 26.4%, 18.7% and 12.5%, respectively, compared with TyG (all P<0.001). Moreover, the IDI values of TyG-WC, TyG-BMI, and TyG-WHR were 0.148, 0.125, and 0.071, respectively, which were all greater than 0, indicating that the diagnostic ability of the TyG-related parameters improved compared with the TyG index alone. Specific results are shown in Supplementary Table 1.

Discussion

In this cross-sectional study, different parameters were tested to predict the presence of MAFLD. The results showed that the TyG index and its associated parameters were independent predictors of MAFLD. Advanced results of ROC curve analysis showed that TyG-BMI, TyG-WC, and TyG-WHR, especially TyG-WC, had better diagnostic values than TyG index alone in diagnosing MAFLD.

Previous studies have shown that factors such as obesity and metabolic disorders contribute to the onset and progression of MAFLD(29). Simple measures such as BMI, WC, and FLI have been independently correlated with MAFLD(30-32). These findings were validated in the present study. BMI, WC, and FLI were better predictors of

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MAFLD than TC, TG, and FPG. The TyG index is a combination of FPG and TG. Some studies have reported that this index can be used as a surrogate marker for IR and effectively identify MAFLD(21), which is further confirmed by our finding. The present study's analysis revealed that the AUC of TyG index for predicting MAFLD was up to 0.793. It has been well-documented that TyG index is a reliable indicator of IR(33). IR induces an imbalance in glucose metabolism, leading to hyperglycemia, which triggers inflammation and oxidative stress(34). It has been proven that oxidative stress and chronic inflammation are associated with the development of MAFLD(35). In addition, previous studies have shown that IR leads to high intrahepatic triglycerides by stimulating hepatic de novo lipogenesis (DNL) and hepatic gluconeogenesis, among others, activated hepatic gluconeogenesis also increases blood glucose levels(36). High intrahepatic triglycerides and fasting blood glucose are the distinguishing features of diagnostic MAFLD pairs. Therefore, it is logical to use the TyG index as a valid predictor of MAFLD.

The TyG index-related parameter is a combination parameter of TyG index with WC, BMI, and WHR. It has been shown that TyG index-related parameters are the best predictors of IR compared with visceral obesity indicators and adipokines(37). This is consistent with the results of the present study. Previous studies have shown that FLI and HSI have strong diagnostic abilities for MAFLD(38). In the present study, the area under the ROC curve of TyG-WC index for diagnosing MAFLD was greater than that of FLI and HSI, and it was more effective in diagnosing MAFLD. The ideal noninvasive test should be simple, easy to use, economical, efficient, and convenient for detecting and identifying people at risk for MAFLD. Although the TyG index and its associated parameters do not differ significantly from the diagnostic performance of the FLI. However, TyG index and its related parameters well balance the above

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requirements. Also, among the TyG-related parameters, TyG-WC had a stronger diagnostic performance than TyG-BMI, TyG-WC, and TyG-WHR. The most probable explanation for the appearance of this phenomenon is that hepatic steatosis correlates with body mass index, but correlates more strongly with visceral fat (as measured by WC) because the lipid activity of visceral adipose tissue (VAT) is higher than that of subcutaneous fat, on a per unit weight basis(39). The findings of Khamseh et al. are consistent with ours(40). The AUROC for TyG index, TyG-BMI, and TyG-WC were 0.676, 0.675, and 0.693, respectively, which were lower than those derived in the present study. This discrepancy may be attributed to the small number of overweight/obese participants in their study. TyG and its related parameters were found to be effective in diagnosing MAFLD in a cross-sectional study utilizing the NHANES database to include 1727 adults, and the diagnostic value was superior to other predictors of MAFLD(41). 28

The strengths of this study are the large sample size and the rigorous screening criteria and the application of the most recent standardized diagnostic criteria for defining MAFLD. However, there are some drawbacks to this study. First, this was a cross-sectional study and causality could not be established. Second, self-reported dietary habits and other data are inevitably subject to measurement error. However, because all participants and researchers in this study were blinded to the results of abdominal ultrasonography and blood tests, the absence of differential reporting bias may simply have weakened the associations we observed. Third, although we considered a full set of confounders, as an observational study, the presence of unmeasured confounders is also possible. In addition, our sample was limited to Chinese adults, and it is unclear whether the findings apply to other populations.

Conclusions

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Our study demonstrated that the TyG index is effective in identifying MAFLD, and the TyG-related parameters improved the identification and diagnosis of MAFLD. As an inexpensive and convenient index, TyG and its related parameters, especially TyG-WC may be a useful marker for identifying MAFLD.

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Author Contributions

PXE designed the study. YR, XWJ, PHW, LLL, and YS collected the data. YR analyzed the data. YR, XWJ, PHW, and LLL contributed to the interpretation of results. YR, XWJ, and PHW drafted the manuscript. PXE, XSH, and HZJ revised the manuscript. All authors have discussed the results and commented on the manuscript. All authors read and approved the final manuscript.

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Abbreviations

NAFLD: Non-alcoholic fatty liver disease; MAFLD: metabolism-associated fatty liver disease; FLI fatty: liver index; HSI: hepatic steatosis index; BMI: body mass index; ALT: alanine transaminase; AST: aspartate transaminase; IR: insulin resistance; HOMA-IR: Homeostasis model assessment of insulin resistance; TyG: Triglyceride glucose index; TG: triglyceride; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma-glucose; WC: Waist circumference; IQR: interquartile range; RCS: restricted cubic spline; AUC: Area under curve; AUROC: area under receiver operating characteristic; NRI: Net Reclassification Index; IDI: Integrated Discrimination Improvement; UA: uric acid; VAT: visceral adipose tissue

Data sharing statement

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Data are stored in Department of Epidemiology and Health Statistics, Fujian Provincial Key Laboratory of Environment Factors and Cancer, School of Public Health, Fujian Medical University, Fujian, China. Data are available upon request from Xian-E Peng; Email address: fmuxe@163.com.

Ethics approval and consent to participate

The current study was carried out in compliance with the Declaration of Helsinki, and the Ethics Committee of Fujian Medical University approved the study protocol (ethics number 2014096). All subjects provided their informed consent prior to participating in this study.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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Figure legends

Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

Figure 2 ROC curves of TyG and its related parameters and biochemical indexes

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Table 1 Comparison of general characteristics

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	*P*-value*
Age(years), M (IQR)	45 (33, 52)	43 (31, 51)	48 (38, 54)	<0.001
Gender, n (%)				<0.001
Males	1471 (56.5)	584 (80.4)	887 (47.2)	
Females	1134 (43.5)	142 (19.6)	992 (52.8)	
Marital Status, n (%)				<0.001
Single	378 (14.5)	68 (9.4)	310 (16.5)	
Married	2209 (84.8)	652 (89.8)	1557 (82.9)	
Divorced	9 (0.4)	2 (0.3)	7 (0.4)	
Widowed	9 (0.4)	4 (0.6)	5 (0.3)	
Educational level, n (%)				0.032
Bachelor degree or above	913 (35.1)	228 (31.4)	685 (36.5)	
Junior college	603 (23.2)	172 (23.7)	431 (22.9)	
Senior high school	593 (22.8)	189 (26.0)	404 (21.5)	
Junior high school	319 (12.3)	87 (12.0)	232 (12.3)	
Primary school	140 (5.4)	35 (4.8)	105 (5.6)	
Illiteracy	37 (1.4)	15 (2.1)	22 (1.2)	
Income(yuan/month), n (%)				0.066
<2000	147 (5.6)	35 (4.8)	112 (6.0)	
2000~3000	794 (30.5)	202 (27.8)	592 (31.5)	
≥3000	1664 (63.9)	489 (67.4)	1175 (62.5)	
Smoking status, n (%)				<0.001
Never	1916 (73.6)	448 (61.7)	1468 (78.1)	
Former	113 (4.3)	45 (6.2)	68 (3.6)	
Current	576 (22.1)	233 (32.1)	343 (18.3)	
Drinking status, n (%)				<0.001

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Never	1624 (62.3)	389 (53.6)	1235 (65.7)	
Former	42 (1.6)	15 (2.1)	27 (1.4)	
Current	939 (36.1)	322 (44.4)	617 (32.8)	
Tea drinking status, n (%)				<0.001
Never	1052 (40.4)	205 (28.2)	847 (45.1)	
Former	8 (0.3)	3 (0.4)	5 (0.3)	
Current	1545 (59.3)	518 (71.3)	1027 (54.7)	
History of diabetes, n (%)				<0.001
No	2459 (94.4)	650 (89.5)	1809 (96.3)	
Yes	146 (5.6)	76 (10.5)	70 (3.7)	
History of hypertension, n (%)				<0.001
No	1666 (64.0)	294 (40.5)	1372 (73.0)	
Yes	939 (36.1)	432 (59.5)	507 (27.0)	

Data are presented as median with the interquartile range [M (P25, P75)]. * Comparison of the differences between the groups calculated by Mann-Whitney U test or chi-square test.

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Table 2 Evaluation of biochemical indices

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	*P*-value*
BMI(kg/m²), M(IQR)	22.9 (20.8, 25.1)	25.4 (23.9, 27.0)	22.0 (20.3, 23.8)	<0.001
SBP (mmHg), M(IQR)	118 (110, 128)	125 (118, 136)	115 (107, 123)	<0.001
DBP (mmHg), M(*IQR*)	80 (72, 86)	85 (80, 90)	78 (70, 82)	<0.001
TG(mg/dL), M (IQR)	109.7 (79.7, 163.8)	169.0 (118.6, 243.4)	94.7 (73.5, 131.9)	<0.001
FPG(mg/dL), M (IQR)	93.1 (88.4, 99.7)	96.7 (91.1, 106.4)	92.2 (87.7, 97.2)	<0.001
TC(mmol/L), M (IQR)	5.0 (4.5, 5.6)	5.2 (4.7, 5.9)	5.0 (4.4, 5.5)	0.007
GGT(U/L), M (IQR)	23 (16, 36)	34 (24, 52)	20 (15, 29)	<0.001
HDL(mmol/L), M (IQR)	1.3 (1.1, 1.5)	1.2 (1.0, 1.3)	1.4 (1.2, 1.5)	<0.001
WC(cm), M(IQR)	82 (75, 89)	90 (85, 95)	78 (70, 85)	<0.001
WHR, M (IQR)	0.9 (0.8, 0.9)	0.9 (0.9, 0.9)	0.84 (0.8, 0.9)	<0.001
FLI, M (IQR)	0.3 (0.1, 1.1)	1.4 (0.6, 3.4)	0.2 (0.1, 0.5)	<0.001
HSI, M (IQR)	31.6 (28.5, 34.8)	35.5 (32.9, 38.6)	30.2 (27.7, 32.9)	<0.001
TyG, M (IQR)	8.6 (8.2, 9.0)	9.0 (8.7, 9.4)	8.4 (8.1, 8.7)	<0.001
TyG-WC, M (IQR)	703.1 (623.9, 790.6)	814.6 (759.2, 875.4)	660.9 (600.3, 730.5)	<0.001
TyG-BMI, M (IQR)	197.0 (174.2, 222.6)	228.8 (211.0, 248.9)	184.3 (167.4, 205.1)	<0.001
TyG-WHR, M (IQR)	7.4 (6.7, 8.1)	8.2 (7.7, 8.7)	7.1 (6.5, 7.7)	<0.001

Data are presented as median with the interquartile range [M (P25, P75)]. * Comparison of the differences between the groups calculated by Mann-Whitney U test. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, serum triglyceride; FPG,

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fasting plasma glucose; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; WC, waist circumference; WHR, waist-to-hip ratio; FLI, fatty liver index; HIS, hepatic steatosis index; TyG, triglyceride-glucose; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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Table 3 Univariate and multivariate logistic analysis of TyG and related parameters and MAFLD

Variables	Crude model		Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value
TyG	6.33 (5.27, 7.60)	<0.001	4.96 (4.09, 6.01)	<0.001	5.15 (4.23, 6.27)	<0.001	4.89 (3.98, 6.00)	<0.001
TyG-WC	1.02 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	<0.001	1.02 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	<0.001
TyG-BMI	1.05 (1.05, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001
TyG-WHR	4.44 (3.89, 5.08)	<0.001	4.18 (3.60, 4.87)	<0.001	4.32 (3.70, 5.04)	<0.001	4.08 (3.48, 4.78)	<0.001

[a]: Adjusted for gender, age, marital status, and educational level;

[b]: Adjusted for gender, age, marital status, educational level, smoking, drinking, and tea drinking;

[c]: Adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension.

TyG, triglyceride-glucose; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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Table 4 Area under curve (AUC) analysis

Variables	AUC（95%*CI*）	AIC	Sensitivity%	Specificity%	optimal cut-off	*P* -value
TC(mmol/L)	0.588 (0.564, 0.613)	3206.9	58.3%	58.6%	5.045	<0.001
GGT(U/L)	0.761 (0.742, 0.781)	2982.7	74.8%	65.6%	24.500	<0.001
HDL(mmol/L)	0.711 (0.689, 0.732)	3214.3	69.1%	63.4%	1.285	1.000
TG(mg/dL)	0.784 (0.764, 0.803)	3057.6	68.2%	78.0%	137.618	<0.001
FPG(mg/dL)	0.653 (0.629, 0.677)	3085.7	55.1%	69.7%	95.67	<0.001
WC(cm)	0.846 (0.830, 0.861)	2378.3	80.2%	74.9%	84.500	<0.001
BMI(kg/m²)	0.822 (0.804, 0.839)	2486.4	78.9%	72.5%	23.525	<0.001
FLI	0.872 (0.859, 0.886)	2809.1	87.5%	72.1%	0.419	<0.001
HSI	0.821 (0.803, 0.838)	2554.0	77.1%	73.3%	32.715	<0.001
TyG	0.793 (0.774, 0.812)	2676.8	72.2%	75.0%	8.738	<0.001
TyG-WC	0.873 (0.860, 0.887)	2199.6	88.7%	71.4%	716.743	<0.001
TyG-BMI	0.862 (0.847, 0.876)	2239.1	85.3%	73.3%	203.154	<0.001
TyG-WHR	0.836 (0.820, 0.852)	2448.0	84.6%	67.7%	7.444	<0.001

AIC, Akaike information criterion; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; TG, serum triglyceride; FPG, fasting plasma glucose; WC, waist circumference; BMI, body mass index; FLI, fatty liver index; HIS, hepatic steatosis index; TyG, triglyceride-glucose; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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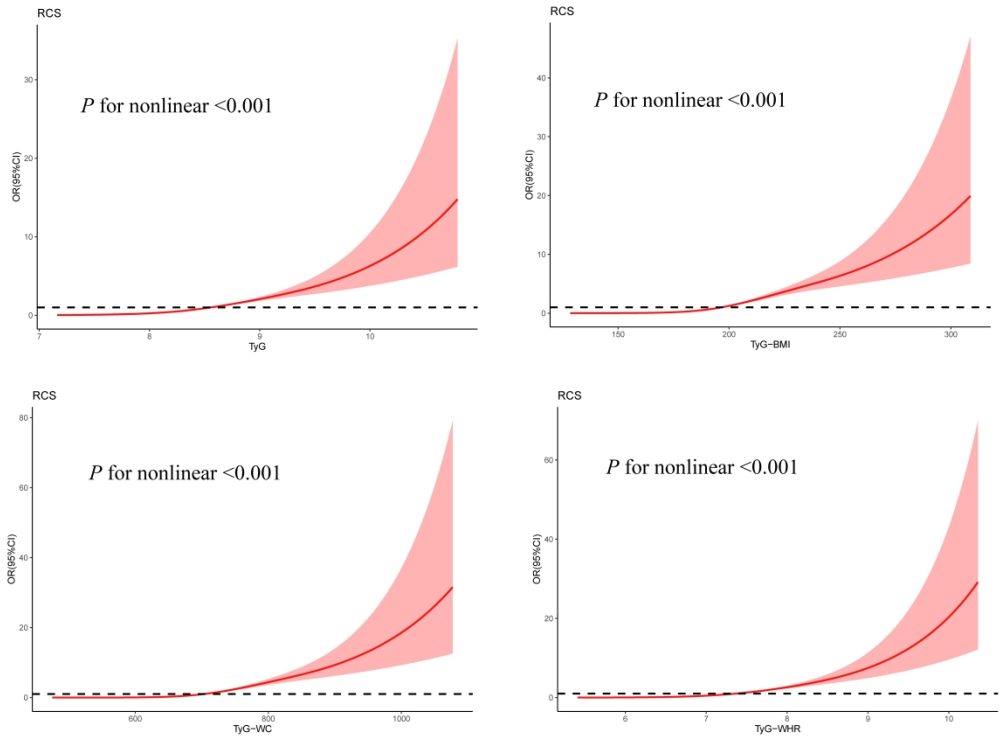
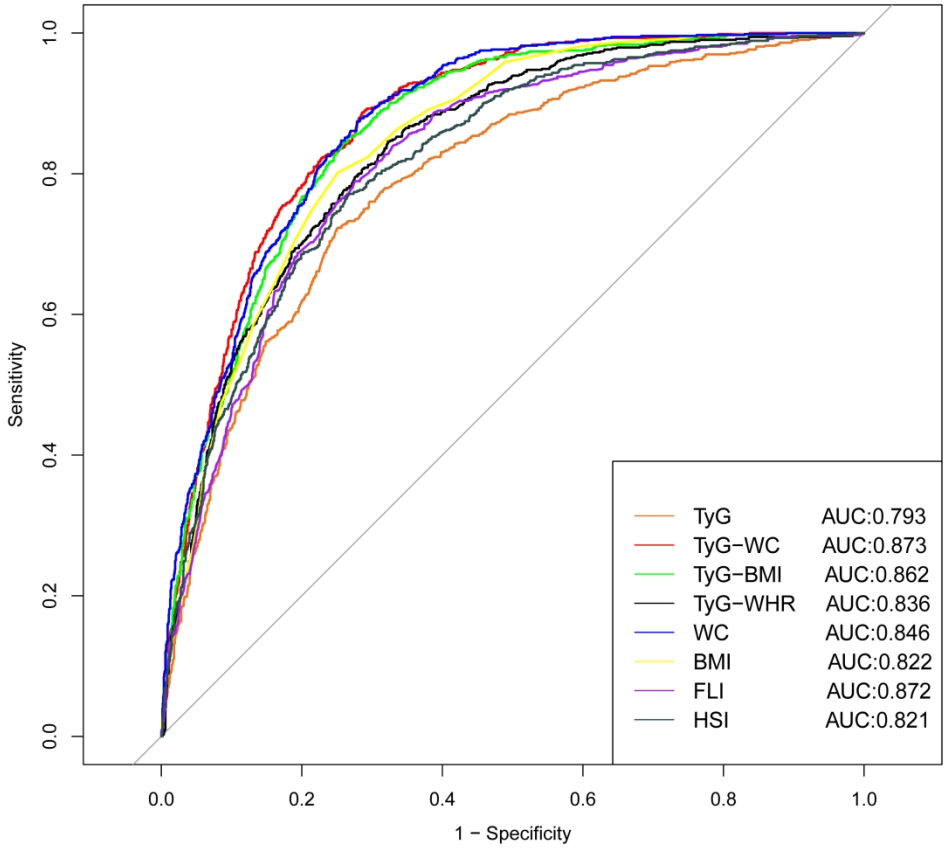


Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

400x294mm (300 x 300 DPI)



ROC curves of TyG and its related parameters and biochemical indexes

223x200mm (300 x 300 DPI)

Supplement Table 1 NRI and IDI analyses

Variables	NRI (95%*CI*)	*P*-value	IDI (95%*CI*)	*P*-value
TyG	Reference	<0.001	Reference	<0.001
TC(mmol/L)	-0.437 (-0.479, -0.395)	<0.001	-0.199 (-0.216, -0.182)	<0.001
GGT(mmol/L)	-0.249 (-0.298, -0.195)	<0.001	-0.110 (-0.127, -0.092)	<0.001
HDL(mmol/L)	-0.169 (-0.214, -0.121)	<0.001	-0.119 (-0.136, -0.101)	<0.001
TG(mg/dL)	-0.200 (-0.231, -0.169)	<0.001	-0.053 (-0.059, -0.046)	<0.001
FPG(mg/dL)	-0.661 (-0.695, -0.626)	<0.001	-0.208 (-0.226, -0.191)	<0.001
WC(cm)	0.150 (0.097, 0.202)	<0.001	0.091 (0.067, 0.115)	<0.001
BMI(kg/m²)	0.113 (0.061, 0.167)	<0.001	0.051 (0.027, 0.076)	<0.001
FLI	0.112 (0.060, 0.165)	<0.001	0.033 (0.015, 0.051)	<0.001
HSI	0.059 (-0.005, 0.123)	0.068	0.048 (0.024, 0.072)	<0.001
TyG-WC	0.264 (0.212, 0.316)	<0.001	0.148 (0.129, 0.160)	<0.001
TyG-BMI	0.187 (0.122, 0.258)	<0.001	0.125 (0.107, 0.143)	<0.001
TyG-WHR	0.125 (0.087, 0.167)	<0.001	0.071 (0.059, 0.083)	<0.001

TyG, triglyceride-glucose; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; TG, serum triglyceride; FPG, fasting plasma glucose; WC, waist circumference; BMI, body mass index; FLI, fatty liver index; HIS, hepatic steatosis index; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	77
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8

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		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The Diagnostic Value of Triglyceride-Glucose Index and Related Parameters in Metabolism-associated Fatty Liver Disease in a Chinese Population: A cross-sectional study

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The Diagnostic Value of Triglyceride-Glucose Index and Related Parameters in Metabolism-associated Fatty Liver Disease in a Chinese Population: A cross-sectional study

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Abstract

Objective Our study aimed to explore the diagnostic value of Triglyceride-Glucose (TyG) and its related parameters in metabolism-associated fatty liver disease (MAFLD).

Design A cross-sectional study of residents who attended medical checkups at the First Hospital of Nanping City, Fujian Medical University, between 2015 and 2017.

Setting One participation center.

Participants 2605 subjects met the inclusion-exclusion criteria and were grouped according to whether they had MAFLD.

Results The TyG index and its associated parameters are positively associated with the risk of developing MAFLD (P<0.001). Restriction cube spline (RCS) analysis showed a significant dose-response relationship between the TyG index and MAFLD. The risk of developing MAFLD increases significantly with a higher TyG index. After adjusting for confounders, this relationship remains (*OR*: 4.89, 95%*CI*: 3.98-6.00). The areas under the receiver operating characteristic curves (AUROC) of the TyG index for MAFLD detection were 0.793 (0.774-0.812). The areas under the curve (AUC) of TyG-related parameters were improved, among which TyG-waist circumference (TyG-WC) showed the largest AUC for MAFLD detection (0.873, 95%*CI*: 0.860-0.887). In addition, the best cut-off value of the TyG-WC was 716.743, with a sensitivity and specificity of 88.7% and 71.4%, respectively.

Conclusion The TyG index effectively identifies MAFLD, and the TyG-related parameters improved the identification and diagnosis of MAFLD, suggesting that TyG-related parameters, especially TyG-WC, may be a useful marker for diagnosing MAFLD.

Keywords: Metabolic-associated Fatty Liver Disease; Triglyceride-Glucose; TyG Related Parameters.

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Strengths and limitations of this study

- We combined metabolic-related indices with the TyG index to diagnose MFALD with a comprehensive index.
- This study used the latest diagnostic criteria to define MAFLD.
- The strengths of this study are the large sample size and the rigorous screening of subjects.
- A more comprehensive range of confounding variables was considered compared to previous studies.
- Measurement error in self-reported dietary habits and other data in this study is unavoidable.

Introduction

Non-alcoholic fatty liver disease (NAFLD), with hepatic steatosis as the main pathological manifestation, can progress to cirrhosis and hepatocellular carcinoma(HCC)(1,2), affecting approximately one-quarter of the adult population worldwide(3). In recent years, there has been increasing recognition of the inherent flaws in the term "non-alcoholic". It overemphasizes the presence or absence of alcohol use disorders and ignores the importance of metabolic risk for NAFLD progression. As such, an international panel of experts renamed NAFLD to metabolism-associated fatty liver disease (MAFLD) in 2020(4). MAFLD is a more appropriate disease designation for liver diseases associated with metabolic dysfunction(5). Due to its high global prevalence, it poses a serious threat to human health and a huge economic burden to society(6). Steatosis is a reversible condition in its early stages and can be addressed through behavioral changes(7,8). For example, increasing physical activity and controlling energy intake are particularly effective interventions in the early stages of the disease(9,10). However, the aggressive form of steatohepatitis can progress to

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fibrosis and eventually cirrhosis, which is irreversible damage(11). Due to the high prevalence of MAFLD and its progressive nature, the early detection of MAFLD is of great significance to enable the provision of early intervention, thus avoiding the progression of MAFLD(12).

Although the gold standard for identifying fatty liver disease (FLD) is still liver biopsy, it is unsuitable for large-scale epidemiological surveys because of its invasiveness, poor acceptability, cost, and sampling variability(12). Thus, it is necessary to develop a simple tool to identify MAFLD. Significant progress has been made in the noninvasive assessment of FLD in recent years, including fatty liver index (FLI) and hepatic steatosis index (HSI)(13). The FLI is a prevalent biomarker panel consisting of body mass index (BMI), waist circumference, triglycerides, and gamma-glutamyl transferase(14). The HSI is a biomarker panel consisting of BMI, diabetes, and the alanine transaminase(ALT)/aspartate transaminase(AST) ratio(15). However, the calculation process of both indices is more complicated and involves more traits and indicators. An ideal noninvasive test should be simple, easily accessible, cost-effective, and efficient and allow easy visualization to detect and identify people at high risk of MAFLD(16). With such a test, large-scale population-wide screening and preventive programs in large populations would be possible. Prior studies have confirmed that insulin resistance (IR) is an important pathogenic mechanism in MAFLD(17). Homeostasis model assessment of insulin resistance (HOMA-IR) is the gold standard diagnostic method of IR and has an excellent diagnostic effect on MAFLD(18). However, HOMA-IR is costly, time-consuming, and complex, which limits its widespread implementation in large epidemiological investigations(19). TyG, a noninvasive index calculated from fasting glucose and triglycerides, has been proposed as a reliable marker for IR in clinical practice(20). Since MAFLD is

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associated with IR and dyslipidemia, the TyG index is also considered a useful predictive marker for MAFLD(21). However, the results from epidemiological studies remain controversial(22). The longitudinal association between baseline TyG index and the risk of MAFLD was assessed in a cohort study conducted in Jiangsu, China, which included 2056 subjects(21). The results showed that the TyG index was independently associated with the risk of developing MAFLD (*HR*: 1.784, 95%*CI*: 1.383-2.302, *P*< 0.001)(21). A cross-sectional study in US adults also showed a positive association between the TyG index and the risk of MAFLD/NAFLD; as for MAFLD, TyG-WC presented the highest *OR* (*OR*: 28.435, 95%*CI*: 12.121-66.705)(23). However, the sample sizes of these studies were small, and more large prospective studies are needed to validate the association between the two further. Nanping City is located in the north of Fujian Province. Our previous study reported the prevalence of NAFLD (32.8%) in the population with physical examination in Nanping(24), which is higher than in other cities in Fujian province(25). The present study aimed to investigate the association of the TyG index and its related parameters with MAFLD in Nanping and to assess their diagnostic efficacy for MAFLD.

Material and Methods

Study subjects and design

This cross-sectional study included 2605 subjects who underwent a physical examination and completed an abdominal ultrasound examination at Nanping First Hospital, Fujian Medical University (Nanping, China) between April 2015 and August 2017. The study protocol conformed to the ethical guidelines of the 1,975 Declaration of Helsinki (6th revision, 2008) and was approved by the Ethics Committee of Fujian Medical University(ethical approval number 2014096). All the participants provided their informed consent before the study started.

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The inclusion criteria for participants in the current study were permanent residency in Nanping, aged between 18 and 75 years, and completed ultrasonography examination. The diagnosis of FLD in this study was primarily based on ultrasonographic findings rather than a liver biopsy(26) because recent standardized criteria have significantly improved the diagnostic accuracy of ultrasonography so that even minor degrees of steatosis can be detected. Subjects with malignant tumors, incomplete data, or pregnant or lactating women were excluded.

Data collection and measure

Data on MAFLD risk factors were obtained through direct interviews with the help of a structured medical questionnaire. The risk factors included were age, gender, marital status, income, educational level, smoking, drinking, lifestyle, dietary habits, medical history, and family history of MAFLD. After an overnight fast, all subjects underwent a physical examination in the morning. The clinical variables collected were height (m^2), weight (kg), waist circumference (WC, cm), hip circumference (HC, cm), Waist-to-Hip Ratio (WHR), diastolic blood pressure (DBP, mmHg), and systolic blood pressure (SBP, mmHg), serum triglyceride (TG, mg/dL), total cholesterol (TC, mmol/L), low-density lipoprotein (LDL, mmol/L), and high-density lipoprotein (HDL, mmol/L), fasting plasma glucose (FPG, mg/dL), Gamma-glutamyltransferase (GGT, U/L) alanine transaminase(ALT, U/L), and aspartate aminotransferase (AST, U/L). All these variables were assessed using standard procedures (TG: 1mmol/L=88.5mg/dL; FPG: 1mmol/L=18mg/dL). Body mass index (BMI) was calculated as body weight/$(height)^2$. Food consumption was assessed with the help of a food frequency questionnaire, and total consumption was calculated by multiplying the frequency of food consumption by the amount of food consumed each time. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90

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mmHg or the current use of anti-hypertensive medication(27). Diabetes was defined as fasting plasma glucose ≥7.0 mmol/L or the current use of hypoglycemic agents(28).

Triglyceride-Glucose Index and Related Parameters

The TyG index and its related parameters were calculated according to the previous studies(20,26). The specific calculation formulas were as follows:

(1) TyG=ln [fasting triglyceride (mg/dl) × fasting plasma glucose (mg/dl)/2];

(2) TyG-WC=TyG×WC;

(3) TyG-BMI=TyG×BMI;

(4) TyG-WHR=TyG×WHR;

Diagnostic of FLD

Liver ultrasonography is used to diagnose fatty liver. The presence of criteria (i) and any of criteria (ii) through (iv) indicates the presence of fatty liver: (i) Diffuse enhancement of the near-field echoes of the liver and gradual attenuation of the far-field echoes of the liver; (ii) Mild to moderate hepatomegaly with rounded obtuse borders; (iii) unclear structure of intrahepatic ducts; (iv) Reduced hepatic blood flow signal.

Diagnosis of MAFLD

MAFLD is diagnosed by ultrasound showing hepatic steatosis and having one of the following three criteria(3): (1) overweight or obesity (BMI ≥ 23.0kg/m^2 for Asians); (2) type 2 diabetes mellitus (T2DM); and (3) metabolic dysregulation among non-overweight individuals (BMI < 23.0kg/m^2). The metabolic disorder was defined as the presence of at least two of the following metabolic risk abnormalities: (1) WC ≥ 90 cm for Asian men and 80 cm for Asian women; (2) BP ≥ 130/85 mmHg or specific drug treatment; (3) TG ≥ 1.70 mmol/L or specific drug treatment; (4) HDL-c < 1.0 mmol/L for men and < 1.3 mmol/L for women; (5) prediabetes; (6) HOMA-IR ≥ 2.5; and (7) C-

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reactive protein (CRP) > 2 mg/L. Non-overweight individuals meeting any two or more metabolic disorders are diagnosed as MAFLD.

Statistical Analyses

The baseline characteristics of subjects were analyzed using the Nonparametric Kruskal-Wallis test for non-normal continuous variables and the Chi-Square test for nominal variables. Continuous variables were expressed as median (interquartile range, IQR). Univariate and multivariate logistic regression methods were used to analyze the association of TyG and related parameters with MAFLD risk. The restricted cubic spline (RCS) was used to explore the dose-response relationship between TyG and its related parameters and the risk of MAFLD. The predictive value of TyG and related parameters were compared using the area under receiver operating characteristic (AUROC). The Net Reclassification Index (NRI) and the Integrated Discrimination Improvement Index (IDI) were used to reflect the overall improvement of the diagnostic model. All analyses were performed in R (version 4.2.1, R Foundation) software or Statistical Product and Service Solutions (SPSS) 26.0 software. All *P* values were based on the two-sided test, and $P<0.05$ was considered statistically significant.

Patient and Public Involvement

Patients or the public were not involved in our research's design, conduct, reporting, or dissemination plans.

Results

Baseline characteristics

Demographic and lifestyle habits and clinical characteristics are detailed in Table 1 and Table 2. Of the 2605 participants, 747 had FLD, with an FLD prevalence of 28.68%; 726 were MAFLD patients, and the prevalence of MAFLD was 27.9%. The mean age of the participants was 45 years, and 56.5% of the subjects were male.

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Compared to those without MAFLD, subjects with MAFLD were more likely to be male, older, married, smokers, drinkers, tea drinkers, and have a history of diabetes or hypertension (all $P<0.05$). In addition, the subjects in both groups were different in terms of clinical detection indicators (SBP, DBP, TG, FPG, TC, GGT, HDL, BMI, WC, WHR, FLI, and HSI) (all $P<0.001$).

Association of MAFLD with TyG and its related parameters

The associations between MAFLD and TyG and its related parameters were mainly analyzed using the logistic regression model. In the crude model, TyG and its related parameters were positively correlated with MAFLD risk (Table 3). The positive correlations of TyG and its related parameters with MAFLD remained unchanged after adjusting for gender, age, marital status, and educational level in model 1 (each $P<0.001$). Model 2 further adjusted for variables such as smoking, drinking, and tea drinking based on model 1. The results remained unchanged (each $P<0.001$). The results remained similar after adjusting some disease history indicators in model 3.

The restricted cubic spline analyses were applied to interpret the dose-response relationships of TyG and its related parameters with MAFLD risk (Figure 1). The *OR*s of MAFLD increased with increasing TyG levels. The *OR*s of MAFLD also rose with the increasing TyG-BMI, TyG-WC, and TyG-WHR.

Assessment of the accuracy of TyG and its related parameters for the diagnosis of MAFLD

The ROC curve for the ability of TyG and its related parameters and traditional indicators to predict the risk of MAFLD is shown in Figure 2. The performance of these models is detailed in Supplement Table 1. The AUROCs of TyG and related parameters were greater than traditional indicators, including the HSI. The TyG-WC performed the highest AUROC (0.873, 95%*CI*: 0.860-0.887, $P<0.001$), compared with TyG-BMI

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(0.862, 95%*CI*: 0.847-0.876, *P*<0.001), TyG-WHR (0.836, 95%*CI*: 0.820-0.852, *P*<0.001). Based on the results of NRI, it can be seen that the accuracy of TyG-WC, TyG-BMI, and TyG-WHR were improved by 26.4%, 18.7%, and 12.5%, respectively, compared with TyG (all P<0.001). Moreover, the IDI values of TyG-WC, TyG-BMI, and TyG-WHR were 0.148, 0.125, and 0.071, respectively, which were all greater than 0, indicating that the diagnostic ability of the TyG-related parameters improved compared with the TyG index alone. The related results are shown in Supplementary Table 2.

Discussion

In this cross-sectional study, different parameters were tested to predict the presence of MAFLD. The results showed that the TyG index and its associated parameters were independent predictors of MAFLD. Advanced results of ROC curve analysis showed that TyG-BMI, TyG-WC, and TyG-WHR, especially TyG-WC, had better diagnostic values than the TyG index alone in diagnosing MAFLD.

Previous studies have shown that factors such as obesity and metabolic disorders contribute to the onset and progression of MAFLD(29). Simple measures such as BMI, WC, and FLI have been independently correlated with MAFLD(30-32). These findings were validated in the present study. BMI, WC, and FLI were better predictors of MAFLD than TC, TG, and FPG. The TyG index is a combination of FPG and TG. Some studies have reported that this index can be used as a surrogate marker for IR and effectively identify MAFLD(21), further confirmed by our findings. The present study's analysis revealed that the AUC of the TyG index for predicting MAFLD was up to 0.793. It has been well-documented that the TyG index is a reliable indicator of IR(33). IR induces an imbalance in glucose metabolism, leading to hyperglycemia, which triggers inflammation and oxidative stress(34). It has been proven that oxidative stress

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and chronic inflammation are associated with the development of MAFLD(35). In addition, previous studies have shown that IR leads to high intrahepatic triglycerides by stimulating hepatic de novo lipogenesis (DNL) and hepatic gluconeogenesis, among others. Activated hepatic gluconeogenesis also increases blood glucose levels(36). High intrahepatic triglycerides and fasting blood glucose are the distinguishing features of diagnostic MAFLD pairs. Therefore, using the TyG index as a valid diagnostic indicator of MAFLD is logical.

The TyG index-related parameter combines the TyG index with WC, BMI, and WHR. It has been shown that TyG index-related parameters are the best predictors of IR compared with visceral obesity indicators and adipokines(37), consistent with the results of the present study. Previous studies have shown that FLI and HSI have strong diagnostic abilities for MAFLD(38). In the present study, the area under the ROC curve of the TyG-WC index for diagnosing MAFLD was greater than that of FLI and HSI, and it was more effective in diagnosing MAFLD. The ideal noninvasive test should be simple, easy to use, economical, efficient, and convenient for detecting and identifying people at risk for MAFLD. Although the TyG index and its associated parameters do not differ significantly from the diagnostic performance of the FLI, the TyG index and its related parameters provide a better balance of the above requirements. Also, among the TyG-related parameters, TyG-WC had a stronger diagnostic performance than TyG-BMI, TyG-WC, and TyG-WHR. The most probable explanation for the appearance of this phenomenon is that hepatic steatosis correlates with body mass index but correlates more strongly with visceral fat (as measured by WC) because the lipid activity of visceral adipose tissue (VAT) is higher than that of subcutaneous fat, on a per unit weight basis(39). The findings of Khamseh et al. are consistent with ours(40). The AUROC for the TyG index, TyG-BMI, and TyG-WC were 0.676, 0.675, and 0.693,

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respectively, lower than those derived in the present study. This discrepancy may be attributed to the small number of overweight/obese participants in their study. TyG and its related parameters were found to be effective in diagnosing MAFLD in a cross-sectional study utilizing the NHANES database to include 1727 adults, and the diagnostic value was superior to other predictors of MAFLD(41).

The strengths of this study are the large sample size, rigorous screening criteria, and application of the most recent standardized diagnostic criteria for defining MAFLD. However, there are some limitations to this study. First, this was a cross-sectional study, and causality could not be established. Second, self-reported dietary habits and other data are inevitably subject to measurement error. However, because all participants and researchers in this study were blinded to the results of abdominal ultrasonography and blood tests, the absence of differential reporting bias may have weakened our observed associations. Third, unmeasured confounders are also possible in an observational study, even if we consider all potential confounders. In addition, our sample was limited to Chinese adults, and it is unclear whether the findings apply to other populations.

Conclusions

Our study demonstrated that the TyG index effectively identifies MAFLD, and the TyG-related parameters improved the identification and diagnosis of MAFLD. As an inexpensive and convenient index, TyG and its related parameters, especially TyG-WC, maybe a useful marker for identifying MAFLD.

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Author Contributions

PXE designed the study. YR, XWJ, PHW, LLL, and YS collected the data. YR analyzed the data. YR, XWJ, PHW, and LLL contributed to interpreting the results. YR, XWJ, and PHW drafted the manuscript. PXE, XSH, and HZJ revised the manuscript. All authors have discussed the results and commented on the manuscript. All authors read and approved the final manuscript.

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Abbreviations

NAFLD: Non-alcoholic fatty liver disease; MAFLD: metabolism-associated fatty liver disease; FLI fatty: liver index; HSI: hepatic steatosis index; BMI: body mass index; ALT: alanine transaminase; AST: aspartate transaminase; IR: insulin resistance; HOMA-IR: Homeostasis model assessment of insulin resistance; TyG: Triglyceride glucose index; TG: triglyceride; TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma-glucose; WC: Waist circumference; IQR: interquartile range; RCS: restricted cubic spline; AUC: Area under curve; AUROC: area under receiver operating characteristic; NRI: Net Reclassification Index; IDI: Integrated Discrimination Improvement; UA: uric acid; VAT: visceral adipose tissue

Data sharing statement

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Data are stored in the Department of Epidemiology and Health Statistics, Fujian Provincial Key Laboratory of Environment Factors and Cancer, School of Public Health, Fujian Medical University, Fujian, China. Data are available upon request from Xian-E Peng; Email address: fmuxe@163.com.

Ethics approval and consent to participate

The current study complied with the Declaration of Helsinki, and the Ethics Committee of Fujian Medical University approved the study protocol (ethics number 2014096). All subjects provided their informed consent before participating in this study.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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Figure legends

Figure 1. Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension.

Figure 2. ROC curves of TyG and its related parameters and biochemical indexes.

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Table 1. Comparison of general characteristics.

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	*P*-value*
Age(years), M (IQR)	45 (33, 52)	43 (31, 51)	48 (38, 54)	<0.001
Gender, n (%)				<0.001
Males	1471 (56.5)	584 (80.4)	887 (47.2)	
Females	1134 (43.5)	142 (19.6)	992 (52.8)	
Marital Status, n (%)				<0.001
Single	378 (14.5)	68 (9.4)	310 (16.5)	
Married	2209 (84.8)	652 (89.8)	1557 (82.9)	
Divorced	9 (0.4)	2 (0.3)	7 (0.4)	
Widowed	9 (0.4)	4 (0.6)	5 (0.3)	
Educational level, n (%)				0.032
Bachelor's degree or above	913 (35.1)	228 (31.4)	685 (36.5)	
Junior college	603 (23.2)	172 (23.7)	431 (22.9)	
Senior high school	593 (22.8)	189 (26.0)	404 (21.5)	
Junior high school	319 (12.3)	87 (12.0)	232 (12.3)	
Primary school	140 (5.4)	35 (4.8)	105 (5.6)	
Illiteracy	37 (1.4)	15 (2.1)	22 (1.2)	
Income(yuan/month), n (%)				0.066
<2000	147 (5.6)	35 (4.8)	112 (6.0)	
2000~3000	794 (30.5)	202 (27.8)	592 (31.5)	
≥3000	1664 (63.9)	489 (67.4)	1175 (62.5)	
Smoking status, n (%)				<0.001
Never	1916 (73.6)	448 (61.7)	1468 (78.1)	
Former	113 (4.3)	45 (6.2)	68 (3.6)	
Current	576 (22.1)	233 (32.1)	343 (18.3)	
Drinking status, n (%)				<0.001

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Never	1624 (62.3)	389 (53.6)	1235 (65.7)	
Former	42 (1.6)	15 (2.1)	27 (1.4)	
Current	939 (36.1)	322 (44.4)	617 (32.8)	
Tea drinking status, n (%)				<0.001
Never	1052 (40.4)	205 (28.2)	847 (45.1)	
Former	8 (0.3)	3 (0.4)	5 (0.3)	
Current	1545 (59.3)	518 (71.3)	1027 (54.7)	
History of diabetes, n (%)				<0.001
No	2459 (94.4)	650 (89.5)	1809 (96.3)	
Yes	146 (5.6)	76 (10.5)	70 (3.7)	
History of hypertension, n (%)				<0.001
No	1666 (64.0)	294 (40.5)	1372 (73.0)	
Yes	939 (36.1)	432 (59.5)	507 (27.0)	

Data are presented as median with the interquartile range [M (P25, P75)]. * Comparison of the differences between the groups calculated by Mann-Whitney U or chi-square tests.

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Table 2. Evaluation of biochemical indices.

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	*P*-value*
BMI(kg/m²), M(IQR)	22.9 (20.8, 25.1)	25.4 (23.9, 27.0)	22.0 (20.3, 23.8)	<0.001
SBP (mmHg), M(IQR)	118 (110, 128)	125 (118, 136)	115 (107, 123)	<0.001
DBP (mmHg), M(*IQR*)	80 (72, 86)	85 (80, 90)	78 (70, 82)	<0.001
TG(mg/dL), M (IQR)	109.7 (79.7, 163.8)	169.0 (118.6, 243.4)	94.7 (73.5, 131.9)	<0.001
FPG(mg/dL), M (IQR)	93.1 (88.4, 99.7)	96.7 (91.1, 106.4)	92.2 (87.7, 97.2)	<0.001
TC(mmol/L), M (IQR)	5.0 (4.5, 5.6)	5.2 (4.7, 5.9)	5.0 (4.4, 5.5)	0.007
GGT(U/L), M (IQR)	23 (16, 36)	34 (24, 52)	20 (15, 29)	<0.001
HDL(mmol/L), M (IQR)	1.3 (1.1, 1.5)	1.2 (1.0, 1.3)	1.4 (1.2, 1.5)	<0.001
WC(cm), M(IQR)	82 (75, 89)	90 (85, 95)	78 (70, 85)	<0.001
WHR, M (IQR)	0.9 (0.8, 0.9)	0.9 (0.9, 0.9)	0.84 (0.8, 0.9)	<0.001
FLI, M (IQR)	0.3 (0.1, 1.1)	1.4 (0.6, 3.4)	0.2 (0.1, 0.5)	<0.001
HSI, M (IQR)	31.6 (28.5, 34.8)	35.5 (32.9, 38.6)	30.2 (27.7, 32.9)	<0.001
TyG, M (IQR)	8.6 (8.2, 9.0)	9.0 (8.7, 9.4)	8.4 (8.1, 8.7)	<0.001
TyG-WC, M (IQR)	703.1 (623.9, 790.6)	814.6 (759.2, 875.4)	660.9 (600.3, 730.5)	<0.001
TyG-BMI, M (IQR)	197.0 (174.2, 222.6)	228.8 (211.0, 248.9)	184.3 (167.4, 205.1)	<0.001
TyG-WHR, M (IQR)	7.4 (6.7, 8.1)	8.2 (7.7, 8.7)	7.1 (6.5, 7.7)	<0.001

Data are presented as median with the interquartile range [M (P25, P75)]. * Comparison of the differences between the groups calculated by the Mann-Whitney U test. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, serum triglyceride; FPG, fasting

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plasma glucose; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; WC, waist circumference; WHR, waist-to-hip ratio; FLI, fatty liver index; HIS, hepatic steatosis index; TyG, triglyceride-glucose; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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Table 3. Univariate and multivariate logistic analysis of TyG and related parameters and MAFLD.

Variables	Crude model		Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value	*OR* (95%*CI*)	*P*-value
TyG	6.33 (5.27, 7.60)	<0.001	4.96 (4.09, 6.01)	<0.001	5.15 (4.23, 6.27)	<0.001	4.89 (3.98, 6.00)	<0.001
TyG-WC	1.02 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	<0.001	1.02 (1.01, 1.02)	<0.001	1.01 (1.01, 1.02)	<0.001
TyG-BMI	1.05 (1.05, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001	1.05 (1.04, 1.05)	<0.001
TyG-WHR	4.44 (3.89, 5.08)	<0.001	4.18 (3.60, 4.87)	<0.001	4.32 (3.70, 5.04)	<0.001	4.08 (3.48, 4.78)	<0.001

[a]: Adjusted for gender, age, marital status, and educational level;

[b]: Adjusted for gender, age, marital status, educational level, smoking, drinking, and tea drinking;

[c]: Adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension.

TyG, triglyceride-glucose; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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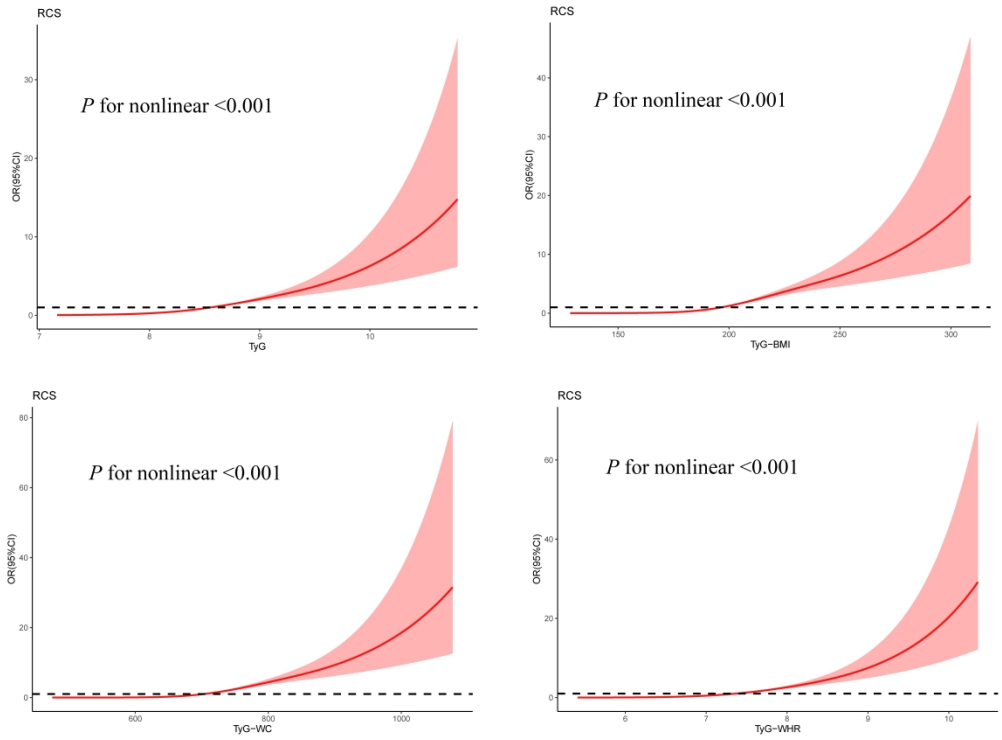
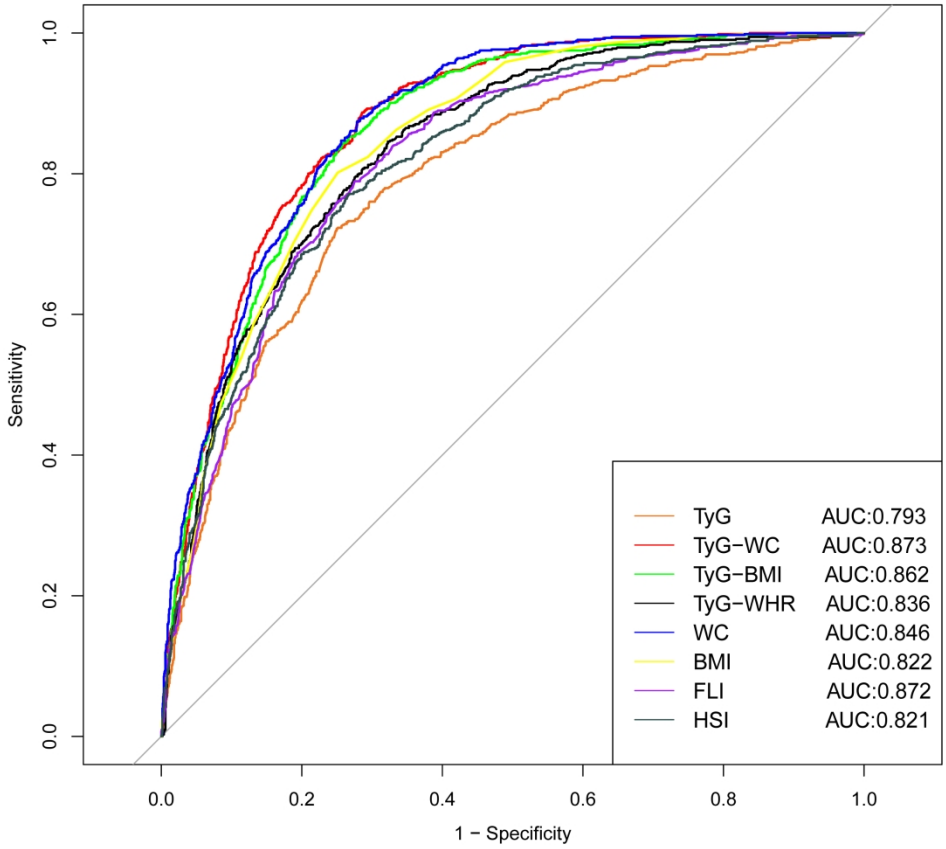


Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

400x294mm (300 x 300 DPI)



ROC curves of TyG and its related parameters and biochemical indexes

223x200mm (300 x 300 DPI)

Supplement Table 1. Area under curve (AUC) analysis.

Variables	AUC（95%*CI*）	AIC	Sensitivity%	Specificity%	optimal cut-off	*P* -value
TC(mmol/L)	0.588 (0.564, 0.613)	3206.9	58.3%	58.6%	5.045	<0.001
GGT(U/L)	0.761 (0.742, 0.781)	2982.7	74.8%	65.6%	24.500	<0.001
HDL(mmol/L)	0.711 (0.689, 0.732)	3214.3	69.1%	63.4%	1.285	1.000
TG(mg/dL)	0.784 (0.764, 0.803)	3057.6	68.2%	78.0%	137.618	<0.001
FPG(mg/dL)	0.653 (0.629, 0.677)	3085.7	55.1%	69.7%	95.67	<0.001
WC(cm)	0.846 (0.830, 0.861)	2378.3	80.2%	74.9%	84.500	<0.001
BMI(kg/m²)	0.822 (0.804, 0.839)	2486.4	78.9%	72.5%	23.525	<0.001
FLI	0.872 (0.859, 0.886)	2809.1	87.5%	72.1%	0.419	<0.001
HSI	0.821 (0.803, 0.838)	2554.0	77.1%	73.3%	32.715	<0.001
TyG	0.793 (0.774, 0.812)	2676.8	72.2%	75.0%	8.738	<0.001
TyG-WC	0.873 (0.860, 0.887)	2199.6	88.7%	71.4%	716.743	<0.001
TyG-BMI	0.862 (0.847, 0.876)	2239.1	85.3%	73.3%	203.154	<0.001
TyG-WHR	0.836 (0.820, 0.852)	2448.0	84.6%	67.7%	7.444	<0.001

AIC, Akaike information criterion; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; TG, serum triglyceride; FPG, fasting plasma glucose; WC, waist circumference; BMI, body mass index; FLI, fatty liver index; HIS, hepatic steatosis index; TyG, triglyceride-glucose; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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Supplement Table 2 NRI and IDI analyses

Variables	NRI (95%*CI*)	*P*-value	IDI (95%*CI*)	*P*-value
TyG	Reference	<0.001	Reference	<0.001
TC(mmol/L)	-0.437 (-0.479, -0.395)	<0.001	-0.199 (-0.216, -0.182)	<0.001
GGT(mmol/L)	-0.249 (-0.298, -0.195)	<0.001	-0.110 (-0.127, -0.092)	<0.001
HDL(mmol/L)	-0.169 (-0.214, -0.121)	<0.001	-0.119 (-0.136, -0.101)	<0.001
TG(mg/dL)	-0.200 (-0.231, -0.169)	<0.001	-0.053 (-0.059, -0.046)	<0.001
FPG(mg/dL)	-0.661 (-0.695, -0.626)	<0.001	-0.208 (-0.226, -0.191)	<0.001
WC(cm)	0.150 (0.097, 0.202)	<0.001	0.091 (0.067, 0.115)	<0.001
BMI(kg/m²)	0.113 (0.061, 0.167)	<0.001	0.051 (0.027, 0.076)	<0.001
FLI	0.112 (0.060, 0.165)	<0.001	0.033 (0.015, 0.051)	<0.001
HSI	0.059 (-0.005, 0.123)	0.068	0.048 (0.024, 0.072)	<0.001
TyG-WC	0.264 (0.212, 0.316)	<0.001	0.148 (0.129, 0.160)	<0.001
TyG-BMI	0.187 (0.122, 0.258)	<0.001	0.125 (0.107, 0.143)	<0.001
TyG-WHR	0.125 (0.087, 0.167)	<0.001	0.071 (0.059, 0.083)	<0.001

TyG, triglyceride-glucose; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; TG, serum triglyceride; FPG, fasting plasma glucose; WC, waist circumference; BMI, body mass index; FLI, fatty liver index; HIS, hepatic steatosis index; TyG-WC, triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-hip ratio.

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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	11
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	77
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	8
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8

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		(*b*) Report category boundaries when continuous variables were categorized	8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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