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

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3 **The Application of Triglyceride-Glucose Index and Related**
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6 **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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3 comprehensive index.

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5 In this study, the latest diagnostic criteria were used for the diagnosis of MAFLD.

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7 Measurement error in self-reported dietary habits and other data in this study is
8
9 unavoidable.

10 11 12 **Introduction**

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15 Non-alcoholic fatty liver disease (NAFLD), with hepatic steatosis as the main
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17 pathological manifestation, can progress to cirrhosis and hepatocellular
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19 carcinoma(HCC)(1, 2), affecting approximately one-quarter of the adult population
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21 worldwide(3). In recent years, there has been increasing recognition of the inherent
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23 flaws in the term "non-alcoholic". It overemphasizes the presence or absence of alcohol
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25 use disorders and ignores the importance of metabolic risk for NAFLD progression. As
26
27 such, an international panel of experts renamed NAFLD to metabolism-associated fatty
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29 liver disease (MAFLD) in 2020(4). MAFLD is used as a more appropriate disease
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31 designation to describe liver diseases associated with metabolic dysfunction(5). Due to
32
33 its high global prevalence, it poses a serious threat to human health and a huge economic
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35 burden to society(6). Steatosis is a reversible condition in its early stages and can be
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37 addressed through behavioral changes(7, 8). For example, increasing physical activity
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39 and controlling energy intake are particularly effective interventions in the early stages
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41 of the disease(9, 10). However, the aggressive form of steatohepatitis can progress to
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43 fibrosis and eventually cirrhosis, which is irreversible damage(11). Due to the high
44
45 prevalence of MAFLD and its progressive nature, the early detection of MAFLD is of
46
47 great significance to enable the provision of early intervention, thus avoiding the
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49 progression of MAFLD(12).

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52 Although the gold standard for identifying fatty liver disease (FLD) is still liver
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54 biopsy, it is unsuitable for large-scale epidemiological surveys because of its
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3 invasiveness, poor acceptability, cost, and sampling variability(12). Thus, it is
4 necessary to develop a simple tool to identify MAFLD. Significant progress has been
5 made in the noninvasive assessment of FLD in recent years, including fatty liver index
6 (FLI) and hepatic steatosis index (HSI)(13). The FLI is a prevalent biomarker panel
7 consisting of body mass index (BMI), waist circumference, triglycerides, and gamma-
8 glutamyl transferase ($FLI = e^{0.953 \cdot \ln(TG) + 0.139 \cdot BMI + 0.718 \cdot \ln(GGT) + 0.053 \cdot WC - 15.745} /$
9 $(1 + e^{0.953 \cdot \ln(TG) + 0.139 \cdot BMI + 0.718 \cdot \ln(GGT) + 0.053 \cdot WC - 15.745}) \times 100$)(14). The HSI is a biomarker
10 panel consisting of BMI, diabetes, and the alanine transaminase(ALT)/aspartate
11 transaminase(AST) ratio ($HSI = 8 \cdot ALT/AST + BMI (+2 \text{ if type 2 diabetes, } +2 \text{ if}$
12 $\text{female})$)(15). However, the calculation process of both indices is more complicated and
13 involves more traits and indicators. An ideal non-invasive test should be simple, easily
14 accessible, cost-effective, and efficient, and allow easy visualization to detect and
15 identify people at high risk of MAFLD(16). With such a test, large-scale population-
16 wide screening and preventive programs in large populations would be possible. Prior
17 studies have confirmed that insulin resistance (IR) is an important pathogenic
18 mechanism in MAFLD(17). Homeostasis model assessment of insulin resistance
19 (HOMA-IR) is the gold standard diagnostic method of IR and has an excellent
20 diagnostic effect on MAFLD(18). However, HOMA-IR is costly, time-consuming, and
21 complex, which limits its widespread implementation in large epidemiological
22 investigations(19). TyG, a non-invasive index, calculated from fasting glucose and
23 triglycerides, has been proposed as a reliable marker for IR in clinical practice(20).
24 Since MAFLD is associated with IR and dyslipidemia, the TyG index is also considered
25 a useful predictive marker for MAFLD(21). However, the results from epidemiological
26 studies remained controversial(22). The longitudinal association between baseline TyG
27 index and the risk of MAFLD was assessed in a cohort study conducted in Jiangsu,
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3 China, which included 2056 subjects(21). The results showed that the TyG index was
4 independently associated with the risk of developing MAFLD (*HR*: 1.784, 95%*CI*:
5 1.383-2.302, *P*< 0.001)(21). A cross-sectional study in US adults also showed a positive
6 association between the TyG index and the risk of MAFLD/NAFLD, as for MAFLD,
7 TyG-WC presented the highest *OR* (*OR*: 28.435, 95%*CI*: 12.121-66.705)(23). However,
8 the sample sizes of these studies were small, and more large prospective studies are
9 needed to further validate the association between the two.
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19 The present study aimed to investigate the association of the TyG index and its
20 related parameters with MAFLD in a Chinese population and to assess their predictive
21 efficacy for MAFLD.
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26 **Material and Methods**

27 **Study subjects and design**

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30 This cross-sectional study included 2605 subjects who underwent a physical
31 examination and completed an abdominal ultrasound examination at Nanping First
32 Hospital, Fujian Medical University (Nanping, China) between April 2015 and August
33 2017. The study protocol conformed to the ethical guidelines of the 1,975 Declaration
34 of Helsinki (6th revision, 2008) and was approved by the Ethics Committee of Fujian
35 Medical University(ethical approval number 2014096). All the participants provided
36 their informed consent before the study started.
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47 The inclusion criteria for participants in the current study were permanent
48 residency in Nanping and age between 18 and 75 years and completed ultrasonography
49 examination. The diagnosis of fatty liver disease (FLD) in this cohort was primarily
50 based on ultrasonographic findings rather than a liver biopsy(24). This is because recent
51 standardized criteria have significantly improved the diagnostic accuracy of
52 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) $TyG = (\ln[\text{triglyceride}(\text{mg/dL}) \times \text{glucose}(\text{mg/dL})/2])$;
- (2) $TyG-WC = TyG \times WC$;

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3 (3) $TyG-BMI = TyG \times BMI$;
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5 (4) $TyG-WHR = TyG \times WHR$;
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8 **Diagnosis of MAFLD**

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10 MAFLD is diagnosed by ultrasound showing hepatic steatosis and having one of
11 the following three criteria(3): (1) overweight or obesity ($BMI \geq 23.0\text{kg/m}^2$); (2) type
12 2 diabetes mellitus (T2DM); and (3) metabolic dysregulation among non-overweight
13 individuals ($BMI < 23.0\text{kg/m}^2$). Metabolic disorders include abnormalities in WC,
14 blood pressure (BP), TG, HDL, prediabetes, HOMA-IR, and C-reactive protein (CRP).
15 Non-overweight individuals meeting any two and more of the metabolic disorders are
16 diagnosed as MAFLD.
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26 **Statistical Analyses**

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28 The baseline characteristics of subjects were analyzed using the Nonparametric
29 Kruskal-Wallis test for non-normal continuous variables and the Chi-Square test for
30 nominal variables. Continuous variables were expressed as median (interquartile range,
31 IQR). Univariate and multivariate logistic regression methods were used to analyze the
32 association of TyG and its related parameters with MAFLD risk. The restricted cubic
33 spline (RCS) was used to explore the dose-response relationship between TyG and its
34 related parameters and the risk of MAFLD. The predictive value of TyG and related
35 parameters were compared using the area under receiver operating characteristic
36 (AUROC).
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49 All analyses were performed in R (version 4.2.1, R Foundation) software or
50 Statistical Product and Service Solutions (SPSS) 26.0 software. All *P* values were based
51 on the two-sided test, and $P < 0.05$ was considered statistically significant.
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56 **Results**

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58 **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 *ORs* of MAFLD increased with increasing TyG levels. the *ORs* 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

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

16
17 We assessed and compared the diagnostic accuracy of the four parameters (TyG
18 index, TyG-WC, TyG-BMI, and TyG-WHR). Consistent with previous research results,
19 all the parameters could identify MAFLD in our study(21, 22). RCS analysis revealed
20 a significant dose-response relationship between the TyG index and MAFLD. The best
21 cut-off value of TyG for the diagnosis of MAFLD was 8.738 (sensitivity: 72.2%,
22 specificity: 75.0%). Additionally, TyG-WC, TyG-BMI, and TyG-WHR showed better
23 discrimination of MAFLD compared with the TyG index. The AUROCs of TyG-related
24 parameters for the diagnosis of MAFLD were larger and the sensitivity was higher. In
25 previous studies, FLI and HSI have been shown to have robust diagnostic power for
26 MAFLD(32, 33). In the present study, the area under the ROC curve of the TyG-WC
27 index for MAFLD diagnosis was larger than that of the FLI and HSI, and the diagnostic
28 performance was better. MAFLD is a typical metabolic disease, and consideration of
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3 body composition may be critical. Among TyG-related parameters, the AUC of TyG-
4 WC was the largest at 0.873 (sensitivity: 88.7%, specificity: 71.4%). Norbert Stefan et
5 al.(34) found that hepatic steatosis correlated with BMI, but more strongly with visceral
6 fat (measured as WC) because visceral adipose tissue (VAT) is more lipid active than
7 subcutaneous fat on a per unit weight basis. Khamseh et al.(35) findings agreed with
8 our study. The AUROCs of the TyG index, TyG-BMI, and TyG-WC were 0.676, 0.675,
9 and 0.693, respectively, all of which were lower than the AUROCs produced in our
10 study. This difference may be due to the small number of overweight/obese participants
11 in their study.
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24 However, this study has several limitations. Firstly, this is a cross-sectional study,
25 and a causative relationship cannot be established. Secondly, measurement error in self-
26 reported dietary habits and other data is inevitable. Nonetheless, because all participants
27 and researchers in this study were blinded to the results of abdominal ultrasonography
28 and blood tests, the absence of differential reporting bias may simply have weakened
29 our observed associations. Thirdly, although we considered a comprehensive set of
30 confounders, the presence of unmeasured confounders is possible as an observational
31 study.
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42 **Conclusions**

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45 Our study demonstrated that the TyG index is effective in identifying MAFLD,
46 and the TyG-related parameters improved the identification and prediction of MAFLD.
47 TyG and its related parameters have a certain value in the diagnosis of MAFLD. As an
48 inexpensive and convenient index, TyG and its related parameters, especially TyG-WC
49 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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3 request.
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6 **Ethics approval and consent to participate**
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8 The current study was carried out in compliance with the Declaration of Helsinki, and
9
10 the Ethics Committee of Fujian Medical University approved the study protocol (ethics
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12 number 2014096). All subjects provided their informed consent prior to participating
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14 in this study.
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17 **Competing interests**
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19 The authors declare that they have no competing interests.
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22 **Consent for publication**
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24 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	
	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -value	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -value	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -value	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -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.

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/m ²)	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

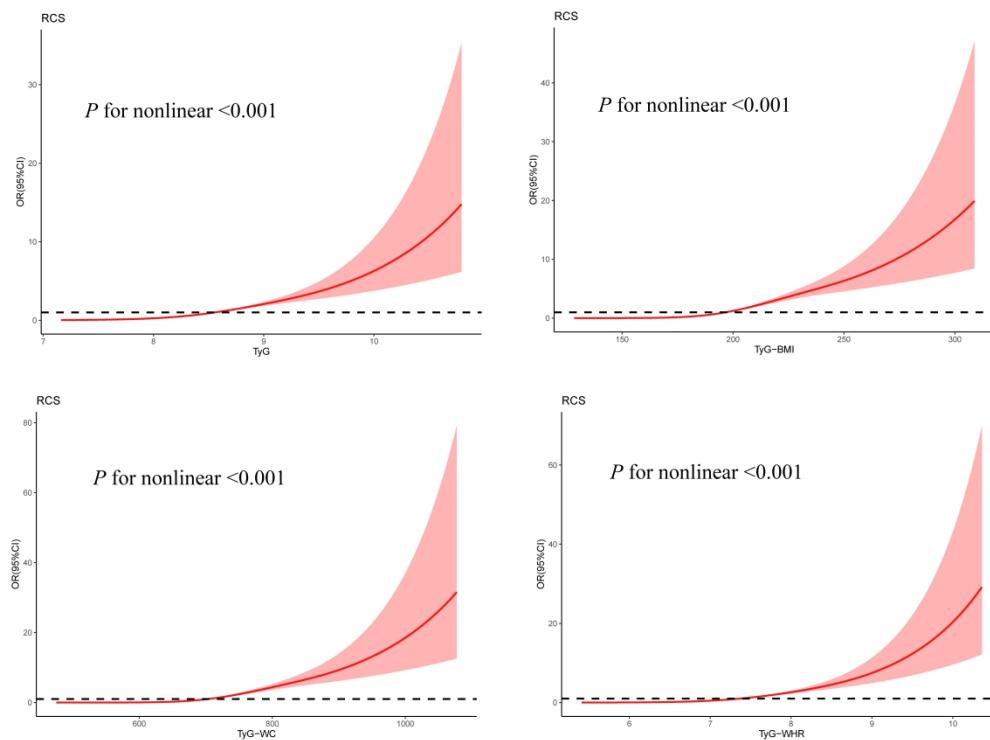


Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

400x294mm (300 x 300 DPI)

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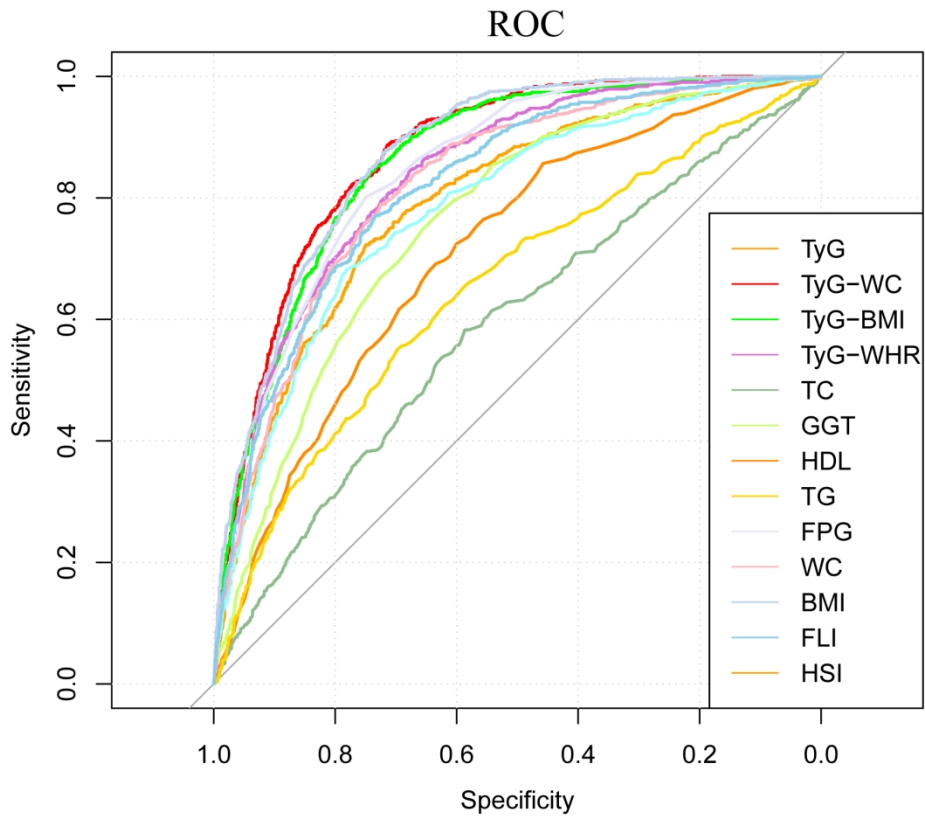


Figure 2 ROC curves of TyG and its related parameters and biochemical indexes

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)	

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/m ²), 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.

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/m ²)	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

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

		(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.

BMJ Open

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

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Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLOGY, Hepatology < INTERNAL MEDICINE, Lipid disorders < DIABETES & ENDOCRINOLOGY

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3 **1 The Diagnostic Value of Triglyceride-Glucose Index and Related**
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6 **2 Parameters in Metabolism-associated Fatty Liver Disease in a Chinese**
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9 **3 Population**

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58 24 Word count: 2825

25 Abstract

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

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

30 **Setting** One participation center.

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

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

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

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

50 **Strengths and limitations of this study**

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

58 **Introduction**

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

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3 75 great significance to enable the provision of early intervention, thus avoiding the
4
5 76 progression of MAFLD(12).
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8 77 Although the gold standard for identifying fatty liver disease (FLD) is still liver
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10 78 biopsy, it is unsuitable for large-scale epidemiological surveys because of its
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12 79 invasiveness, poor acceptability, cost, and sampling variability(12). Thus, it is
13
14 80 necessary to develop a simple tool to identify MAFLD. Significant progress has been
15
16 81 made in the noninvasive assessment of FLD in recent years, including fatty liver index
17
18 82 (FLI) and hepatic steatosis index (HSI)(13). The FLI is a prevalent biomarker panel
19
20 83 consisting of body mass index (BMI), waist circumference, triglycerides, and gamma-
21
22 84 glutamyl transferase (14). The HSI is a biomarker panel consisting of BMI, diabetes,
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24 85 and the alanine transaminase(ALT)/aspartate transaminase(AST) ratio (15). However,
25
26 86 the calculation process of both indices is more complicated and involves more traits
27
28 87 and indicators. An ideal non-invasive test should be simple, easily accessible, cost-
29
30 88 effective, and efficient, and allow easy visualization to detect and identify people at
31
32 89 high risk of MAFLD(16). With such a test, large-scale population-wide screening and
33
34 90 preventive programs in large populations would be possible. Prior studies have
35
36 91 confirmed that insulin resistance (IR) is an important pathogenic mechanism in
37
38 92 MAFLD(17). Homeostasis model assessment of insulin resistance (HOMA-IR) is the
39
40 93 gold standard diagnostic method of IR and has an excellent diagnostic effect on
41
42 94 MAFLD(18). However, HOMA-IR is costly, time-consuming, and complex, which
43
44 95 limits its widespread implementation in large epidemiological investigations(19). TyG,
45
46 96 a non-invasive index, calculated from fasting glucose and triglycerides, has been
47
48 97 proposed as a reliable marker for IR in clinical practice(20). Since MAFLD is
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50 98 associated with IR and dyslipidemia, the TyG index is also considered a useful
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52 99 predictive marker for MAFLD(21). However, the results from epidemiological studies
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3 100 remained controversial(22). The longitudinal association between baseline TyG index
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5 101 and the risk of MAFLD was assessed in a cohort study conducted in Jiangsu, China,
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7 102 which included 2056 subjects(21). The results showed that the TyG index was
8
9 103 independently associated with the risk of developing MAFLD (*HR*: 1.784, 95%*CI*:
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11 104 1.383-2.302, *P*< 0.001)(21). A cross-sectional study in US adults also showed a positive
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13 105 association between the TyG index and the risk of MAFLD/NAFLD, as for MAFLD,
14
15 106 TyG-WC presented the highest *OR* (*OR*: 28.435, 95%*CI*: 12.121-66.705)(23). However,
16
17 107 the sample sizes of these studies were small, and more large prospective studies are
18
19 108 needed to further validate the association between the two. Nanping city is located in
20
21 109 the north of Fujian Province. Our previous study reported the prevalence of NAFLD
22
23 110 (32.8%) in the population with physical examination in Nanping(24), which is higher
24
25 111 than other city of Fujian province(25). The present study aimed to investigate the
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27 112 association of the TyG index and its related parameters with MAFLD in Nanping and
28
29 113 to assess their diagnostic efficacy for MAFLD.

114 **Material and Methods**

115 **Study subjects and design**

116 This cross-sectional study included 2605 subjects who underwent a physical
117 examination and completed an abdominal ultrasound examination at Nanping First
118 Hospital, Fujian Medical University (Nanping, China) between April 2015 and August
119 2017. The study protocol conformed to the ethical guidelines of the 1,975 Declaration
120 of Helsinki (6th revision, 2008) and was approved by the Ethics Committee of Fujian
121 Medical University(ethical approval number 2014096). All the participants provided
122 their informed consent before the study started.

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

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3 125 examination. The diagnosis of FLD in this study was primarily based on
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5 126 ultrasonographic findings rather than a liver biopsy(26). This is because recent
6
7 127 standardized criteria have significantly improved the diagnostic accuracy of
8
9 128 ultrasonography so that even minor degrees of steatosis can be detected. Subjects with
10
11 129 malignant tumors, incomplete data, or pregnant or lactating women were excluded.

130 **Data collection and measure**

131 Data on MAFLD risk factors were obtained through direct interviews with the help
132 of a structured medical questionnaire. The risk factors included were age, gender,
133 marital status, income, educational level, smoking, drinking, lifestyle, dietary habits,
134 medical history, and family history of MAFLD. All subjects underwent a complete
135 physical examination in the morning after an overnight fast. The clinical variables
136 collected were height (m²), weight (kg), waist circumference (WC, cm), hip
137 circumference (HC, cm), Waist-to-Hip Ratio (WHR), diastolic blood pressure (DBP,
138 mmHg), and systolic blood pressure (SBP, mmHg), serum triglyceride (TG, mg/dL),
139 total cholesterol (TC, mmol/L), low-density lipoprotein (LDL, mmol/L), and high-
140 density lipoprotein (HDL, mmol/L), fasting plasma glucose (FPG, mg/dL), Gamma-
141 glutamyltransferase (GGT, U/L) alanine transaminase(ALT, U/L), and aspartate
142 aminotransferase (AST, U/L). All these variables were assessed using standard
143 procedures (TG: 1mmol/L=88.5mg/dL; FPG: 1mmol/L=18mg/dL). Body mass index
144 (BMI) was calculated as body weight/(height)². Food consumption was assessed with
145 the help of a food frequency questionnaire, and total consumption was calculated by
146 multiplying the frequency of food consumption by the amount of food consumed each
147 time. Hypertension was defined as systolic blood pressure \geq 140 mmHg and/or diastolic
148 blood pressure \geq 90 mmHg, or the current use of anti-hypertensive medication(27).
149 Diabetes was defined as fasting plasma glucose \geq 7.0 mmol/L or the current use of

150 hypoglycemic agents(28).

151 **Triglyceride-Glucose Index and Related Parameters**

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

154 (1) $TyG = \ln [\text{fasting triglyceride (mg/dl)} \times \text{fasting plasma glucose (mg/dl)} / 2]$;

155 (2) $TyG-WC = TyG \times WC$;

156 (3) $TyG-BMI = TyG \times BMI$;

157 (4) $TyG-WHR = TyG \times WHR$;

158 **Diagnostic of FLD**

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

165 **Diagnosis of MAFLD**

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

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4 173 mmol/L for men and < 1.3 mmol/L for women; (5) prediabetes; (6) HOMA-IR ≥ 2.5 ;
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7 174 and (7) C-reactive protein (CRP) > 2 mg/L. Non-overweight individuals meeting any
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9 175 two and more of the metabolic disorders are diagnosed as MAFLD.

11 176 **Statistical Analyses**

13 177 The baseline characteristics of subjects were analyzed using the Nonparametric
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15
16 178 Kruskal-Wallis test for non-normal continuous variables and the Chi-Square test for
17
18 179 nominal variables. Continuous variables were expressed as median (interquartile range,
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20 180 IQR). Univariate and multivariate logistic regression methods were used to analyze the
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23 181 association of TyG and its related parameters with MAFLD risk. The restricted cubic
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25 182 spline (RCS) was used to explore the dose-response relationship between TyG and its
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27 183 related parameters and the risk of MAFLD. The predictive value of TyG and related
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29 184 parameters were compared using the area under receiver operating characteristic
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32 185 (AUROC). The Net Reclassification Index (NRI) and the Integrated Discrimination
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34 186 Improvement Index (IDI) were used to reflect the overall improvement of the diagnostic
35
36 187 model. All analyses were performed in R (version 4.2.1, R Foundation) software or
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39 188 Statistical Product and Service Solutions (SPSS) 26.0 software. All *P* values were based
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41 189 on the two-sided test, and $P < 0.05$ was considered statistically significant.

43 190 **Patient and Public Involvement**

45 191 Patients and public will not be involved in the development of the research
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48 192 question or in the design of the study. Subjects will receive oral and written information
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50 193 about this study. However, they will not be involved in the recruitment and conduct of
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52
53 194 the study. After signing informed consent, the participants will be assessed for
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55 195 eligibility and data collection will begin. Eligible subjects will be interviewed face to
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57 196 face by investigators to collect data. In addition, all methods were performed in

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3 197 accordance with the relevant guidelines and regulations.
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5 198 **Results**

6 199 **Baseline characteristics**

10 200 Demographic and lifestyle habits and clinical characteristics were detailed in
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12 201 Table 1 and Table 2. Of the 2605 participants, 747 had FLD, with a FLD prevalence of
13
14 202 28.68%; 726 were MAFLD patients, and the prevalence of MAFLD was 27.9%. The
15
16 203 mean age of the participants was 45 years, and 56.5% of the subjects were male.
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18 204 Compared to those without MAFLD, subjects with MAFLD were more likely to be
19
20 205 male, older, married, smokers, drinkers, tea drinkers, and have a history of diabetes or
21
22 206 hypertension (all $P<0.05$). In addition, the subjects in both groups were different in
23
24 207 terms of clinical detection indicators (SBP, DBP, TG, FPG, TC, GGT, HDL, BMI, WC,
25
26 208 WHR, FLI, and HSI) (all $P<0.001$).
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30 209 **Association of MAFLD with TyG and its related parameters**

31 210 The associations between MAFLD and TyG and its related parameters were
32
33 211 mainly analyzed using the logistic regression model. In the crude model, TyG and its
34
35 212 related parameters were positively correlated with MAFLD risk (Table 3). The positive
36
37 213 correlations of TyG and its related parameters with MAFLD remained unchanged after
38
39 214 adjusting for gender, age, marital status, and educational level in model 1 (each
40
41 215 $P<0.001$). Model 2 further adjusted for variables such as smoking, drinking, and tea
42
43 216 drinking based on model 1. The results remained unchanged (each $P<0.001$). Adding
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45 217 adjustments to some disease history indicators in model 3, the results remained similar.
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50 218 The restricted cubic spline analyses were applied to interpret the dose-response
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52 219 relationships of TyG and its related parameters with MAFLD risk (Figure 1). The *ORs*
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54 220 of MAFLD increased with increasing TyG levels. the *ORs* of MAFLD also rose with
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56 221 the increasing TyG-BMI, TyG-WC, and TyG-WHR.
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3 222 **Assessment of the accuracy of TyG and its related parameters for the diagnosis of**
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5 223 **MAFLD**

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7 224 The ROC curve for the ability of TyG and its related parameters and traditional
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9 225 indicators to predict the risk of MAFLD were shown in Figure 2. And the performance
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11 226 of these models was detailed in Table 4. The AUROCs of TyG and its related
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13 227 parameters were greater than that of traditional indicators, including the HSI. The TyG-
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15 228 WC performed the highest AUROC (0.873, 95%CI: 0.860-0.887, $P<0.001$), compared
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17 229 with TyG-BMI (0.862, 95%CI: 0.847-0.876, $P<0.001$), TyG-WHR (0.836, 95%CI:
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19 230 0.820-0.852, $P<0.001$). Based on the results of NRI, it can be seen that the accuracy of
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21 231 TyG-WC, TyG-BMI and TyG-WHR were improved by 26.4%, 18.7% and 12.5%,
22
23 232 respectively, compared with TyG (all $P<0.001$). Moreover, the IDI values of TyG-WC,
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25 233 TyG-BMI, and TyG-WHR were 0.148, 0.125, and 0.071, respectively, which were all
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27 234 greater than 0, indicating that the diagnostic ability of the TyG-related parameters
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29 235 improved compared with the TyG index alone. Specific results are shown in
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31 236 Supplementary Table 1.

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37 237 **Discussion**

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39 238 In this cross-sectional study, different parameters were tested to predict the
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41 239 presence of MAFLD. The results showed that the TyG index and its associated
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43 240 parameters were independent predictors of MAFLD. Advanced results of ROC curve
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45 241 analysis showed that TyG-BMI, TyG-WC, and TyG-WHR, especially TyG-WC, had
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47 242 better diagnostic values than TyG index alone in diagnosing MAFLD.

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49 243 Previous studies have shown that factors such as obesity and metabolic disorders
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51 244 contribute to the onset and progression of MAFLD(29). Simple measures such as BMI,
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53 245 WC, and FLI have been independently correlated with MAFLD(30-32). These findings
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55 246 were validated in the present study. BMI, WC, and FLI were better predictors of
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3 247 MAFLD than TC, TG, and FPG. The TyG index is a combination of FPG and TG.
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5 248 Some studies have reported that this index can be used as a surrogate marker for IR and
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7 249 effectively identify MAFLD(21), which is further confirmed by our finding. The
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9 250 present study's analysis revealed that the AUC of TyG index for predicting MAFLD
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11 251 was up to 0.793. It has been well-documented that TyG index is a reliable indicator of
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13 252 IR(33). IR induces an imbalance in glucose metabolism, leading to hyperglycemia,
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15 253 which triggers inflammation and oxidative stress(34). It has been proven that oxidative
16
17 254 stress and chronic inflammation are associated with the development of MAFLD(35).
18
19 255 In addition, previous studies have shown that IR leads to high intrahepatic triglycerides
20
21 256 by stimulating hepatic de novo lipogenesis (DNL) and hepatic gluconeogenesis, among
22
23 257 others, activated hepatic gluconeogenesis also increases blood glucose levels(36). High
24
25 258 intrahepatic triglycerides and fasting blood glucose are the distinguishing features of
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27 259 diagnostic MAFLD pairs. Therefore, it is logical to use the TyG index as a valid
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29 260 predictor of MAFLD.
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35 261 The TyG index-related parameter is a combination parameter of TyG index with
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37 262 WC, BMI, and WHR. It has been shown that TyG index-related parameters are the best
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39 263 predictors of IR compared with visceral obesity indicators and adipokines(37). This is
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41 264 consistent with the results of the present study. Previous studies have shown that FLI
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43 265 and HSI have strong diagnostic abilities for MAFLD(38). In the present study, the area
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45 266 under the ROC curve of TyG-WC index for diagnosing MAFLD was greater than that
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47 267 of FLI and HSI, and it was more effective in diagnosing MAFLD. The ideal
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49 268 noninvasive test should be simple, easy to use, economical, efficient, and convenient
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51 269 for detecting and identifying people at risk for MAFLD. Although the TyG index and
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53 270 its associated parameters do not differ significantly from the diagnostic performance of
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55 271 the FLI. However, TyG index and its related parameters well balance the above
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3 272 requirements. Also, among the TyG-related parameters, TyG-WC had a stronger
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5 273 diagnostic performance than TyG-BMI, TyG-WC, and TyG-WHR. The most probable
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7 274 explanation for the appearance of this phenomenon is that hepatic steatosis correlates
8
9 275 with body mass index, but correlates more strongly with visceral fat (as measured by
10
11 276 WC) because the lipid activity of visceral adipose tissue (VAT) is higher than that of
12
13 277 subcutaneous fat, on a per unit weight basis(39). The findings of Khamseh et al. are
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15 278 consistent with ours(40). The AUROC for TyG index, TyG-BMI, and TyG-WC were
16
17 279 0.676, 0.675, and 0.693, respectively, which were lower than those derived in the
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19 280 present study. This discrepancy may be attributed to the small number of
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21 281 overweight/obese participants in their study. TyG and its related parameters were found
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23 282 to be effective in diagnosing MAFLD in a cross-sectional study utilizing the NHANES
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25 283 database to include 1727 adults, and the diagnostic value was superior to other
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27 284 predictors of MAFLD(41). 28

28 285 The strengths of this study are the large sample size and the rigorous screening
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30 286 criteria and the application of the most recent standardized diagnostic criteria for
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32 287 defining MAFLD. However, there are some drawbacks to this study. First, this was a
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34 288 cross-sectional study and causality could not be established. Second, self-reported
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36 289 dietary habits and other data are inevitably subject to measurement error. However,
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38 290 because all participants and researchers in this study were blinded to the results of
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40 291 abdominal ultrasonography and blood tests, the absence of differential reporting bias
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42 292 may simply have weakened the associations we observed. Third, although we
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44 293 considered a full set of confounders, as an observational study, the presence of
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46 294 unmeasured confounders is also possible. In addition, our sample was limited to
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48 295 Chinese adults, and it is unclear whether the findings apply to other populations.

296 **Conclusions**

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3 297 Our study demonstrated that the TyG index is effective in identifying MAFLD,
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5 298 and the TyG-related parameters improved the identification and diagnosis of MAFLD.
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8 299 As an inexpensive and convenient index, TyG and its related parameters, especially
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10 300 TyG-WC may be a useful marker for identifying MAFLD.
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For peer review only

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4

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6
7 303 all staffs for recruiting subjects and their technical assistance.
8
9

10 304 **Author Contributions**
11

12 305 PXE designed the study. YR, XWJ, PHW, LLL, and YS collected the data. YR
13
14 306 analyzed the data. YR, XWJ, PHW, and LLL contributed to the interpretation of results.
15
16 307 YR, XWJ, and PHW drafted the manuscript. PXE, XSH, and HZJ revised the
17
18 308 manuscript. All authors have discussed the results and commented on the manuscript.
19
20 309 All authors read and approved the final manuscript.
21
22

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30
31

32 314 **Abbreviations**
33

34 315 NAFLD: Non-alcoholic fatty liver disease; MAFLD: metabolism-associated fatty liver
35
36 316 disease; FLI fatty: liver index; HSI: hepatic steatosis index; BMI: body mass index;
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38 317 ALT: alanine transaminase; AST: aspartate transaminase; IR: insulin resistance;
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40 318 HOMA-IR: Homeostasis model assessment of insulin resistance; TyG: Triglyceride
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42 319 glucose index; TG: triglyceride; TC: total cholesterol; LDL-C: low-density lipoprotein
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44 320 cholesterol; HDL-C: high-density lipoprotein cholesterol; FPG: fasting plasma-glucose;
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46 321 WC: Waist circumference; IQR: interquartile range; RCS: restricted cubic spline; AUC:
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48 322 Area under curve; AUROC: area under receiver operating characteristic; NRI: Net
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50 323 Reclassification Index; IDI: Integrated Discrimination Improvement; UA: uric acid;
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52 324 VAT: visceral adipose tissue
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58 325 **Data sharing statement**
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3 326 Data are stored in Department of Epidemiology and Health Statistics, Fujian Provincial
4
5 327 Key Laboratory of Environment Factors and Cancer, School of Public Health, Fujian
6
7
8 328 Medical University, Fujian, China. Data are available upon request from Xian-E Peng;
9
10 329 Email address: fmuxe@163.com.

12 330 **Ethics approval and consent to participate**

14 331 The current study was carried out in compliance with the Declaration of Helsinki, and
15
16 332 the Ethics Committee of Fujian Medical University approved the study protocol (ethics
17
18 333 number 2014096). All subjects provided their informed consent prior to participating
19
20
21 334 in this study.

24 335 **Competing interests**

26 336 The authors declare that they have no competing interests.

28 337 **Consent for publication**

30 338 Not applicable.

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3 455 **Figure legends**
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5 456 **Figure 1** Restrictive cubic spline modeling of the association between NAFLD and
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8 457 TyG and its related parameters. Red area, 95% confidence interval. Each model was
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10 458 adjusted for gender, age, marital status, educational level, smoking, drinking, tea
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12 459 drinking, history of diabetes, and history of hypertension
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14 460 **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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5	Never	1624 (62.3)	389 (53.6)	1235 (65.7)	
6	Former	42 (1.6)	15 (2.1)	27 (1.4)	
7	Current	939 (36.1)	322 (44.4)	617 (32.8)	
8	Tea drinking status, n (%)				<0.001
9	Never	1052 (40.4)	205 (28.2)	847 (45.1)	
10	Former	8 (0.3)	3 (0.4)	5 (0.3)	
11	Current	1545 (59.3)	518 (71.3)	1027 (54.7)	
12	History of diabetes, n (%)				<0.001
13	No	2459 (94.4)	650 (89.5)	1809 (96.3)	
14	Yes	146 (5.6)	76 (10.5)	70 (3.7)	
15	History of hypertension, n (%)				<0.001
16	No	1666 (64.0)	294 (40.5)	1372 (73.0)	
17	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.

Table 2 Evaluation of biochemical indices

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	P-value*
BMI(kg/m ²), 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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5 fasting plasma glucose; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; WC, waist
6 circumference; WHR, waist-to-hip ratio; FLI, fatty liver index; HIS, hepatic steatosis index; TyG, triglyceride-glucose; TyG-WC,
7 triglyceride-glucose-waist circumference; TyG-BMI, triglyceride-glucose-body mass index; TyG-WHR, triglyceride-glucose- waist-to-
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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	
	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -value	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -value	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -value	<i>OR</i> (95% <i>CI</i>)	<i>P</i> -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.

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/m ²)	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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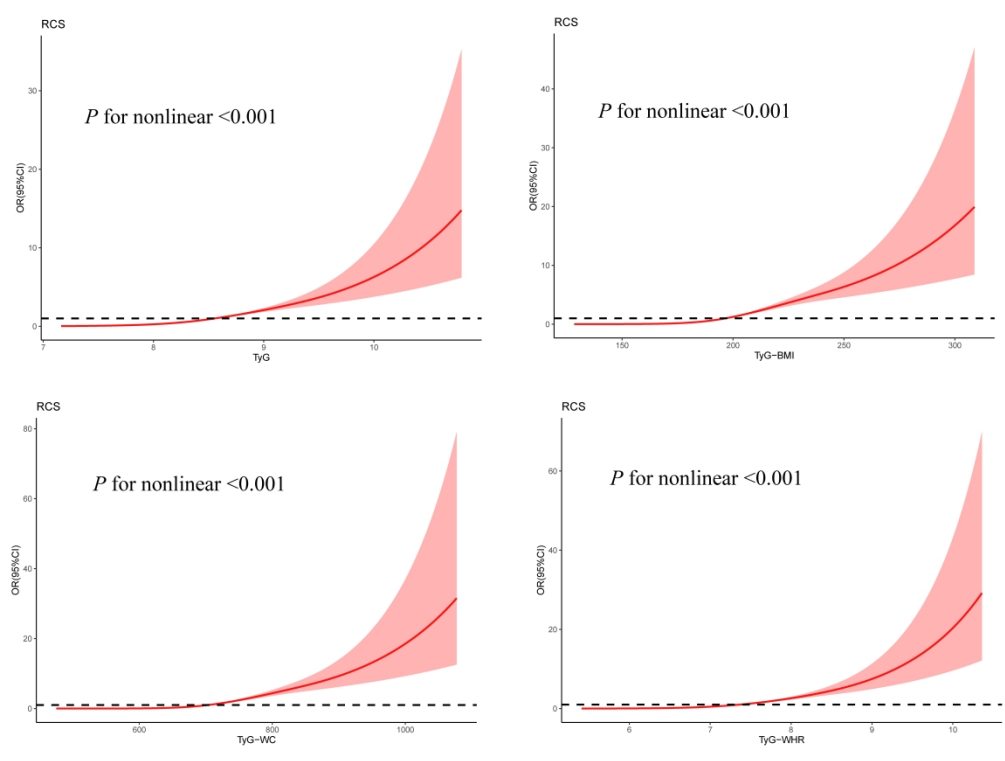
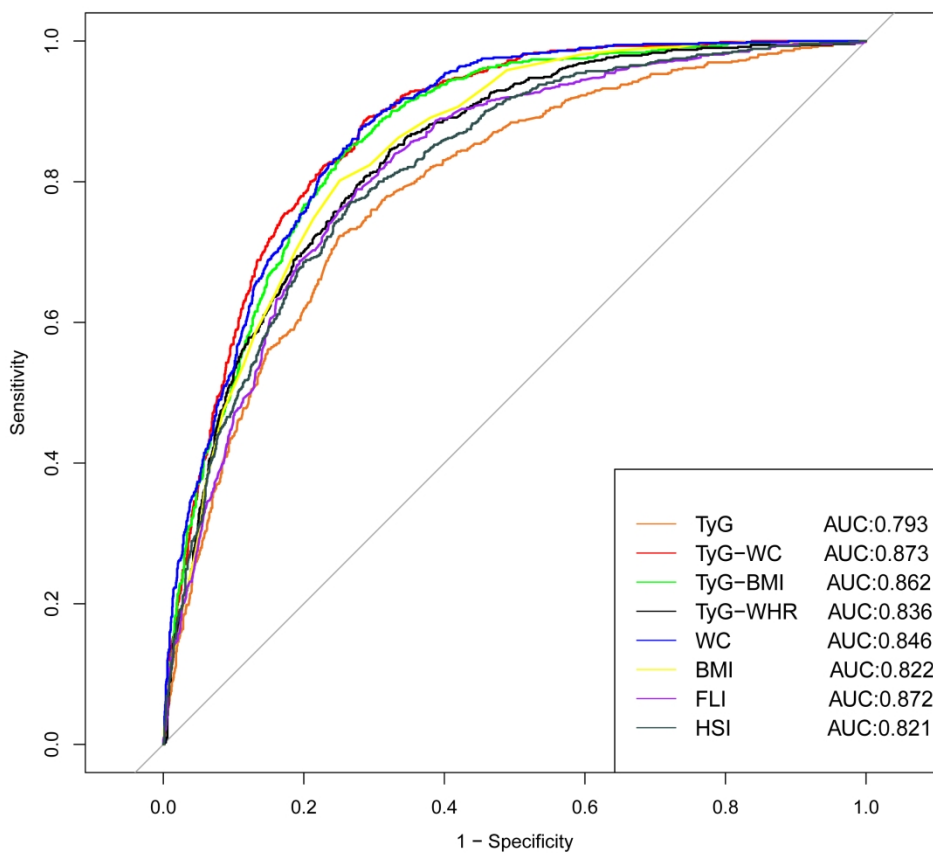


Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

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/m ²)	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.

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

		(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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3 **The Diagnostic Value of Triglyceride-Glucose Index and Related**
4 **Parameters in Metabolism-associated Fatty Liver Disease in a Chinese**
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6 **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.

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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3 fibrosis and eventually cirrhosis, which is irreversible damage(11). Due to the high
4 prevalence of MAFLD and its progressive nature, the early detection of MAFLD is of
5 great significance to enable the provision of early intervention, thus avoiding the
6 progression of MAFLD(12).
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12 Although the gold standard for identifying fatty liver disease (FLD) is still liver
13 biopsy, it is unsuitable for large-scale epidemiological surveys because of its
14 invasiveness, poor acceptability, cost, and sampling variability(12). Thus, it is
15 necessary to develop a simple tool to identify MAFLD. Significant progress has been
16 made in the noninvasive assessment of FLD in recent years, including fatty liver index
17 (FLI) and hepatic steatosis index (HSI)(13). The FLI is a prevalent biomarker panel
18 consisting of body mass index (BMI), waist circumference, triglycerides, and gamma-
19 glutamyl transferase(14). The HSI is a biomarker panel consisting of BMI, diabetes,
20 and the alanine transaminase(ALT)/aspartate transaminase(AST) ratio(15). However,
21 the calculation process of both indices is more complicated and involves more traits
22 and indicators. An ideal noninvasive test should be simple, easily accessible, cost-
23 effective, and efficient and allow easy visualization to detect and identify people at high
24 risk of MAFLD(16). With such a test, large-scale population-wide screening and
25 preventive programs in large populations would be possible. Prior studies have
26 confirmed that insulin resistance (IR) is an important pathogenic mechanism in
27 MAFLD(17). Homeostasis model assessment of insulin resistance (HOMA-IR) is the
28 gold standard diagnostic method of IR and has an excellent diagnostic effect on
29 MAFLD(18). However, HOMA-IR is costly, time-consuming, and complex, which
30 limits its widespread implementation in large epidemiological investigations(19). TyG,
31 a noninvasive index calculated from fasting glucose and triglycerides, has been
32 proposed as a reliable marker for IR in clinical practice(20). Since MAFLD is
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3 associated with IR and dyslipidemia, the TyG index is also considered a useful
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5 predictive marker for MAFLD(21). However, the results from epidemiological studies
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7 remain controversial(22). The longitudinal association between baseline TyG index and
8
9 the risk of MAFLD was assessed in a cohort study conducted in Jiangsu, China, which
10
11 included 2056 subjects(21). The results showed that the TyG index was independently
12
13 associated with the risk of developing MAFLD ($HR: 1.784, 95\%CI: 1.383-2.302, P <$
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15 0.001)(21). A cross-sectional study in US adults also showed a positive association
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17 between the TyG index and the risk of MAFLD/NAFLD; as for MAFLD, TyG-WC
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19 presented the highest OR ($OR: 28.435, 95\%CI: 12.121-66.705$)(23). However, the
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21 sample sizes of these studies were small, and more large prospective studies are needed
22
23 to validate the association between the two further. Nanping City is located in the north
24
25 of Fujian Province. Our previous study reported the prevalence of NAFLD (32.8%) in
26
27 the population with physical examination in Nanping(24), which is higher than in other
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29 cities in Fujian province(25). The present study aimed to investigate the association of
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31 the TyG index and its related parameters with MAFLD in Nanping and to assess their
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33 diagnostic efficacy for MAFLD.
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39 **Material and Methods**

40 **Study subjects and design**

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43 This cross-sectional study included 2605 subjects who underwent a physical
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45 examination and completed an abdominal ultrasound examination at Nanping First
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47 Hospital, Fujian Medical University (Nanping, China) between April 2015 and August
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49 2017. The study protocol conformed to the ethical guidelines of the 1,975 Declaration
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51 of Helsinki (6th revision, 2008) and was approved by the Ethics Committee of Fujian
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53 Medical University(ethical approval number 2014096). All the participants provided
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55 their informed consent before the study started.
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3 The inclusion criteria for participants in the current study were permanent
4 residency in Nanping, aged between 18 and 75 years, and completed ultrasonography
5 examination. The diagnosis of FLD in this study was primarily based on
6 ultrasonographic findings rather than a liver biopsy(26) because recent standardized
7 criteria have significantly improved the diagnostic accuracy of ultrasonography so that
8 even minor degrees of steatosis can be detected. Subjects with malignant tumors,
9 incomplete data, or pregnant or lactating women were excluded.

19 **Data collection and measure**

21 Data on MAFLD risk factors were obtained through direct interviews with the help
22 of a structured medical questionnaire. The risk factors included were age, gender,
23 marital status, income, educational level, smoking, drinking, lifestyle, dietary habits,
24 medical history, and family history of MAFLD. After an overnight fast, all subjects
25 underwent a physical examination in the morning. The clinical variables collected were
26 height (m²), weight (kg), waist circumference (WC, cm), hip circumference (HC, cm),
27 Waist-to-Hip Ratio (WHR), diastolic blood pressure (DBP, mmHg), and systolic blood
28 pressure (SBP, mmHg), serum triglyceride (TG, mg/dL), total cholesterol (TC,
29 mmol/L), low-density lipoprotein (LDL, mmol/L), and high-density lipoprotein (HDL,
30 mmol/L), fasting plasma glucose (FPG, mg/dL), Gamma-glutamyltransferase (GGT,
31 U/L) alanine transaminase(ALT, U/L), and aspartate aminotransferase (AST, U/L). All
32 these variables were assessed using standard procedures (TG: 1mmol/L=88.5mg/dL;
33 FPG: 1mmol/L=18mg/dL). Body mass index (BMI) was calculated as body
34 weight/(height)². Food consumption was assessed with the help of a food frequency
35 questionnaire, and total consumption was calculated by multiplying the frequency of
36 food consumption by the amount of food consumed each time. Hypertension was
37 defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90
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3 mmHg or the current use of anti-hypertensive medication(27). Diabetes was defined as
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5 fasting plasma glucose ≥ 7.0 mmol/L or the current use of hypoglycemic agents(28).
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8 **Triglyceride-Glucose Index and Related Parameters**

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10 The TyG index and its related parameters were calculated according to the
11
12 previous studies(20,26). The specific calculation formulas were as follows:
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14
15 (1) $TyG = \ln [\text{fasting triglyceride (mg/dl)} \times \text{fasting plasma glucose (mg/dl)} / 2]$;

16
17 (2) $TyG-WC = TyG \times WC$;

18
19 (3) $TyG-BMI = TyG \times BMI$;

20
21 (4) $TyG-WHR = TyG \times WHR$;

22 **Diagnostic of FLD**

23
24 Liver ultrasonography is used to diagnose fatty liver. The presence of criteria (i)
25
26 and any of criteria (ii) through (iv) indicates the presence of fatty liver: (i) Diffuse
27
28 enhancement of the near-field echoes of the liver and gradual attenuation of the far-
29
30 field echoes of the liver; (ii) Mild to moderate hepatomegaly with rounded obtuse
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32 borders; (iii) unclear structure of intrahepatic ducts; (iv) Reduced hepatic blood flow
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34 signal.
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40 **Diagnosis of MAFLD**

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42 MAFLD is diagnosed by ultrasound showing hepatic steatosis and having one of
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44 the following three criteria(3): (1) overweight or obesity ($BMI \geq 23.0 \text{ kg/m}^2$ for Asians);
45
46 (2) type 2 diabetes mellitus (T2DM); and (3) metabolic dysregulation among non-
47
48 overweight individuals ($BMI < 23.0 \text{ kg/m}^2$). The metabolic disorder was defined as the
49
50 presence of at least two of the following metabolic risk abnormalities: (1) $WC \geq 90$ cm
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52 for Asian men and 80 cm for Asian women; (2) $BP \geq 130/85$ mmHg or specific drug
53
54 treatment; (3) $TG \geq 1.70$ mmol/L or specific drug treatment; (4) $HDL-c < 1.0$ mmol/L
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56 for men and < 1.3 mmol/L for women; (5) prediabetes; (6) $HOMA-IR \geq 2.5$; and (7) C-
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3 reactive protein (CRP) > 2 mg/L. Non-overweight individuals meeting any two or more
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5 metabolic disorders are diagnosed as MAFLD.
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7 8 **Statistical Analyses**

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10 The baseline characteristics of subjects were analyzed using the Nonparametric
11
12 Kruskal-Wallis test for non-normal continuous variables and the Chi-Square test for
13
14 nominal variables. Continuous variables were expressed as median (interquartile range,
15
16 IQR). Univariate and multivariate logistic regression methods were used to analyze the
17
18 association of TyG and related parameters with MAFLD risk. The restricted cubic
19
20 spline (RCS) was used to explore the dose-response relationship between TyG and its
21
22 related parameters and the risk of MAFLD. The predictive value of TyG and related
23
24 parameters were compared using the area under receiver operating characteristic
25
26 (AUROC). The Net Reclassification Index (NRI) and the Integrated Discrimination
27
28 Improvement Index (IDI) were used to reflect the overall improvement of the diagnostic
29
30 model. All analyses were performed in R (version 4.2.1, R Foundation) software or
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32 Statistical Product and Service Solutions (SPSS) 26.0 software. All *P* values were based
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34 on the two-sided test, and *P*<0.05 was considered statistically significant.
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40 **Patient and Public Involvement**

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42 Patients or the public were not involved in our research's design, conduct, reporting, or
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44 dissemination plans.
45

46 **Results**

47 **Baseline characteristics**

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49 Demographic and lifestyle habits and clinical characteristics are detailed in Table
50
51 1 and Table 2. Of the 2605 participants, 747 had FLD, with an FLD prevalence of
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53 28.68%; 726 were MAFLD patients, and the prevalence of MAFLD was 27.9%. The
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55 mean age of the participants was 45 years, and 56.5% of the subjects were male.
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3 Compared to those without MAFLD, subjects with MAFLD were more likely to be
4 male, older, married, smokers, drinkers, tea drinkers, and have a history of diabetes or
5 hypertension (all $P<0.05$). In addition, the subjects in both groups were different in
6 terms of clinical detection indicators (SBP, DBP, TG, FPG, TC, GGT, HDL, BMI, WC,
7 WHR, FLI, and HSI) (all $P<0.001$).
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9

14 **Association of MAFLD with TyG and its related parameters**

16
17 The associations between MAFLD and TyG and its related parameters were
18 mainly analyzed using the logistic regression model. In the crude model, TyG and its
19 related parameters were positively correlated with MAFLD risk (Table 3). The positive
20 correlations of TyG and its related parameters with MAFLD remained unchanged after
21 adjusting for gender, age, marital status, and educational level in model 1 (each
22 $P<0.001$). Model 2 further adjusted for variables such as smoking, drinking, and tea
23 drinking based on model 1. The results remained unchanged (each $P<0.001$). The
24 results remained similar after adjusting some disease history indicators in model 3.
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35 The restricted cubic spline analyses were applied to interpret the dose-response
36 relationships of TyG and its related parameters with MAFLD risk (Figure 1). The *ORs*
37 of MAFLD increased with increasing TyG levels. The *ORs* of MAFLD also rose with
38 the increasing TyG-BMI, TyG-WC, and TyG-WHR.
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44 **Assessment of the accuracy of TyG and its related parameters for the diagnosis of** 45 **MAFLD**

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47
48 The ROC curve for the ability of TyG and its related parameters and traditional
49 indicators to predict the risk of MAFLD is shown in Figure 2. The performance of these
50 models is detailed in Supplement Table 1. The AUROCs of TyG and related parameters
51 were greater than traditional indicators, including the HSI. The TyG-WC performed the
52 highest AUROC (0.873, 95%*CI*: 0.860-0.887, $P<0.001$), compared with TyG-BMI
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3 (0.862, 95%CI: 0.847-0.876, $P<0.001$), TyG-WHR (0.836, 95%CI: 0.820-0.852,
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5 $P<0.001$). Based on the results of NRI, it can be seen that the accuracy of TyG-WC,
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7 TyG-BMI, and TyG-WHR were improved by 26.4%, 18.7%, and 12.5%, respectively,
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9 compared with TyG (all $P<0.001$). Moreover, the IDI values of TyG-WC, TyG-BMI,
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11 and TyG-WHR were 0.148, 0.125, and 0.071, respectively, which were all greater than
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13 0, indicating that the diagnostic ability of the TyG-related parameters improved
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15 compared with the TyG index alone. The related results are shown in Supplementary
16
17 Table 2.
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22 Discussion

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24 In this cross-sectional study, different parameters were tested to predict the
25
26 presence of MAFLD. The results showed that the TyG index and its associated
27
28 parameters were independent predictors of MAFLD. Advanced results of ROC curve
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30 analysis showed that TyG-BMI, TyG-WC, and TyG-WHR, especially TyG-WC, had
31
32 better diagnostic values than the TyG index alone in diagnosing MAFLD.
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36 Previous studies have shown that factors such as obesity and metabolic disorders
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38 contribute to the onset and progression of MAFLD(29). Simple measures such as BMI,
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40 WC, and FLI have been independently correlated with MAFLD(30-32). These findings
41
42 were validated in the present study. BMI, WC, and FLI were better predictors of
43
44 MAFLD than TC, TG, and FPG. The TyG index is a combination of FPG and TG.
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46 Some studies have reported that this index can be used as a surrogate marker for IR and
47
48 effectively identify MAFLD(21), further confirmed by our findings. The present study's
49
50 analysis revealed that the AUC of the TyG index for predicting MAFLD was up to
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52 0.793. It has been well-documented that the TyG index is a reliable indicator of IR(33).
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54 IR induces an imbalance in glucose metabolism, leading to hyperglycemia, which
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56 triggers inflammation and oxidative stress(34). It has been proven that oxidative stress
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3 and chronic inflammation are associated with the development of MAFLD(35). In
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5 addition, previous studies have shown that IR leads to high intrahepatic triglycerides
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7 by stimulating hepatic de novo lipogenesis (DNL) and hepatic gluconeogenesis, among
8
9 others. Activated hepatic gluconeogenesis also increases blood glucose levels(36).
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11 High intrahepatic triglycerides and fasting blood glucose are the distinguishing features
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13 of diagnostic MAFLD pairs. Therefore, using the TyG index as a valid diagnostic
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15 indicator of MAFLD is logical.
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18
19 The TyG index-related parameter combines the TyG index with WC, BMI, and
20
21 WHR. It has been shown that TyG index-related parameters are the best predictors of
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23 IR compared with visceral obesity indicators and adipokines(37), consistent with the
24
25 results of the present study. Previous studies have shown that FLI and HSI have strong
26
27 diagnostic abilities for MAFLD(38). In the present study, the area under the ROC curve
28
29 of the TyG-WC index for diagnosing MAFLD was greater than that of FLI and HSI,
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31 and it was more effective in diagnosing MAFLD. The ideal noninvasive test should be
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33 simple, easy to use, economical, efficient, and convenient for detecting and identifying
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35 people at risk for MAFLD. Although the TyG index and its associated parameters do
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37 not differ significantly from the diagnostic performance of the FLI, the TyG index and
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39 its related parameters provide a better balance of the above requirements. Also, among
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41 the TyG-related parameters, TyG-WC had a stronger diagnostic performance than
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43 TyG-BMI, TyG-WC, and TyG-WHR. The most probable explanation for the
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45 appearance of this phenomenon is that hepatic steatosis correlates with body mass index
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47 but correlates more strongly with visceral fat (as measured by WC) because the lipid
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49 activity of visceral adipose tissue (VAT) is higher than that of subcutaneous fat, on a
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51 per unit weight basis(39). The findings of Khamseh et al. are consistent with ours(40).
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53 The AUROC for the TyG index, TyG-BMI, and TyG-WC were 0.676, 0.675, and 0.693,
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3 respectively, lower than those derived in the present study. This discrepancy may be
4 attributed to the small number of overweight/obese participants in their study. TyG and
5 its related parameters were found to be effective in diagnosing MAFLD in a cross-
6 sectional study utilizing the NHANES database to include 1727 adults, and the
7 diagnostic value was superior to other predictors of MAFLD(41).
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15 The strengths of this study are the large sample size, rigorous screening criteria,
16 and application of the most recent standardized diagnostic criteria for defining MAFLD.
17 However, there are some limitations to this study. First, this was a cross-sectional study,
18 and causality could not be established. Second, self-reported dietary habits and other
19 data are inevitably subject to measurement error. However, because all participants and
20 researchers in this study were blinded to the results of abdominal ultrasonography and
21 blood tests, the absence of differential reporting bias may have weakened our observed
22 associations. Third, unmeasured confounders are also possible in an observational study,
23 even if we consider all potential confounders. In addition, our sample was limited to
24 Chinese adults, and it is unclear whether the findings apply to other populations.
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37 **Conclusions**

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40 Our study demonstrated that the TyG index effectively identifies MAFLD, and the
41 TyG-related parameters improved the identification and diagnosis of MAFLD. As an
42 inexpensive and convenient index, TyG and its related parameters, especially TyG-WC,
43 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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3 Data are stored in the Department of Epidemiology and Health Statistics, Fujian
4 Provincial Key Laboratory of Environment Factors and Cancer, School of Public
5 Health, Fujian Medical University, Fujian, China. Data are available upon request from
6
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8 Xian-E Peng; Email address: fmuxe@163.com.
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11 **Ethics approval and consent to participate**

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

21
22 The authors declare that they have no competing interests.
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25 **Consent for publication**

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27 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

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.

Table 2. Evaluation of biochemical indices.

Variables	Overall (n=2605)	With MAFLD (n=726)	Without MAFLD (n=1879)	P-value*
BMI(kg/m ²), 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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5 plasma glucose; TC, total cholesterol; GGT, Gamma-glutamyltransferase; HDL, high-density lipoprotein; WC, waist circumference; WHR, waist-
6 to-hip ratio; FLI, fatty liver index; HIS, hepatic steatosis index; TyG, triglyceride-glucose; TyG-WC, triglyceride-glucose-waist circumference;
7 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	
	<i>OR (95%CI)</i>	<i>P-value</i>	<i>OR (95%CI)</i>	<i>P-value</i>	<i>OR (95%CI)</i>	<i>P-value</i>	<i>OR (95%CI)</i>	<i>P-value</i>
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.

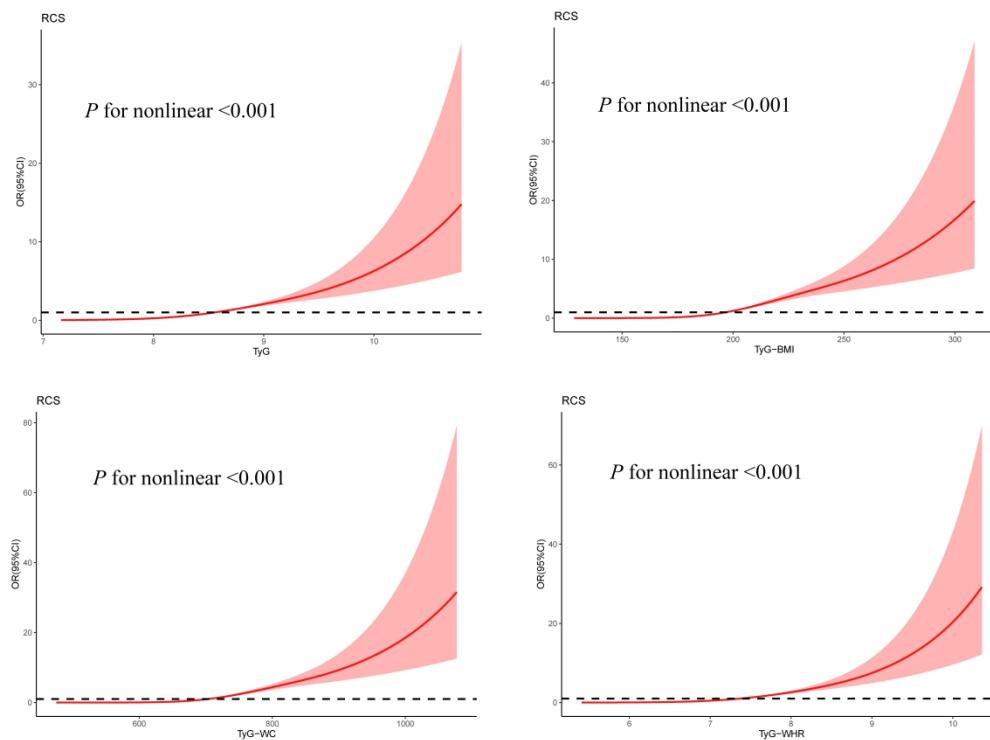
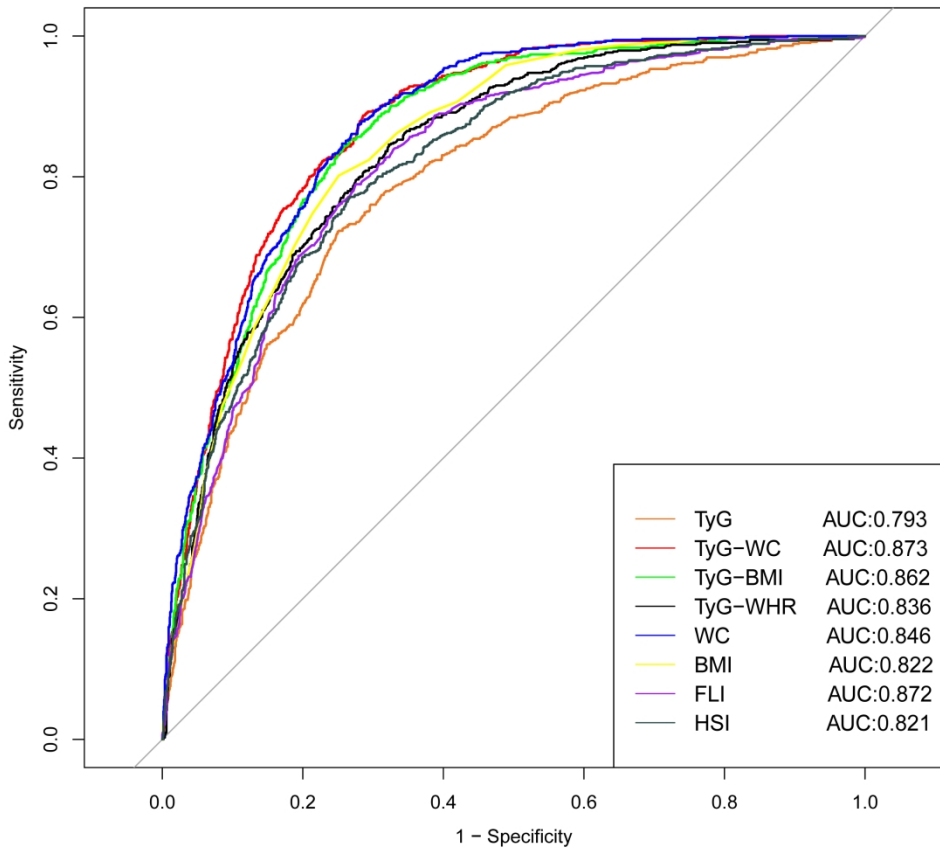


Figure 1 Restrictive cubic spline modeling of the association between NAFLD and TyG and its related parameters. Red area, 95% confidence interval. Each model was adjusted for gender, age, marital status, educational level, smoking, drinking, tea drinking, history of diabetes, and history of hypertension

400x294mm (300 x 300 DPI)

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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/m ²)	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.

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/m ²)	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.

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

		(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.