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# The Role of the Triglyceride–Glucose Index and Its Derivatives in Predicting the Risk of Metabolic Dysfunction–Associated Steatotic Liver Disease and Hepatic Fibrosis

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**Research Article**

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# The Role of the Triglyceride–Glucose Index and Its Derivatives in Predicting the Risk of Metabolic Dysfunction–Associated Steatotic Liver Disease and Hepatic Fibrosis

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## Abstract

**Background:** Metabolic dysfunction–associated steatotic liver disease (MASLD) has emerged as a major global health burden due to its increasing prevalence and its substantial contribution to liver-related morbidity and mortality. In primary care settings, simple, non-invasive, and cost-effective diagnostic biomarkers are needed to facilitate early detection.

**Methods**: This retrospective cross-sectional study included 408 adults attending a family medicine outpatient clinic between January 2023 and December 2024. Following the exclusion of secondary causes, MASLD was diagnosed in accordance with current diagnostic criteria and imaging findings. Liver fibrosis risk was evaluated using the Fibrosis-4 (FIB-4) index. The triglyceride–glucose (TyG) index and its composite derivatives—TyG × body mass index (TyG-BMI), TyG × waist circumference (TyG-WC), and TyG × waist-to-height ratio (TyG-WHtR)—were calculated. Multivariable logistic regression and receiver operating characteristic (ROC) analyses were performed.

**Results**: MASLD was present in 50.5% of participants. All TyG-related indices demonstrated significant dose–response associations with MASLD ($p < 0.001$). In fully adjusted analyses, participants in the highest quartile of TyG-WC had a 14.46-fold higher odds of MASLD

compared with the lowest quartile (95% CI: 6.85–30.56; $p < 0.001$). ROC analysis showed that TyG-WC had the highest discriminative performance (AUC: 0.761), followed by TyG-WHtR (AUC: 0.752) and TyG-BMI (AUC: 0.750). Subgroup analyses revealed stronger diagnostic performance in younger individuals and those without hypertension or diabetes. **Conclusions**: TyG and its anthropometric derivatives, particularly TyG-WC, are independently associated with MASLD and show moderate diagnostic accuracy. These easily accessible indices may serve as practical screening tools for MASLD in primary care settings.

**Keywords:** MASLD; liver fibrosis; triglyceride–glucose index; insulin resistance; non-invasive diagnostics; primary care; ROC analysis

## Background

Metabolic dysfunction–associated steatotic liver disease (MASLD) is one of the most common causes of chronic liver disease worldwide and was previously known as non-alcoholic fatty liver disease (NAFLD) [1]. MASLD is defined by the presence of hepatic steatosis in addition to at least one cardiometabolic risk factor [2,3]. These risk factors include obesity, insulin resistance, hypertension, and hypertriglyceridemia; for instance, a meta-analysis reported a MASLD prevalence of 75.27% among obese individuals [4,5]. Although the majority of patients with MASLD are obese, the prevalence among lean individuals has also been increasing [6]. In a study including approximately 21,000 participants using data from the National Health and Nutrition Examination Surveys (NHANES) between 1999 and 2018, the prevalence of MASLD was found to be 27.7% [7]. In our country, the prevalence of NAFLD was reported by Değertekin et al. to be 43.5% between 2007–2010, 47.6% between 2011–2013, and 53.1% between 2014–2016, representing an overall increase of 22% [8]. The marked rise in NAFLD prevalence indicates a substantial public health burden. The clinical course of MASLD is highly heterogeneous, ranging from simple steatosis to advanced fibrosis and cirrhosis [9].

Hepatic fibrosis is one of the most important risk factors for liver-related mortality in patients with fatty liver disease [10]. Liver biopsy is the gold standard for assessing hepatic fibrosis; however, it is an invasive procedure associated with several disadvantages, including bleeding risk, high cost, and interobserver variability [11]. Given the global prevalence of MASLD, there is a clear need for non-invasive tests (NITs) before resorting to high-risk procedures such as liver biopsy [12]. Accordingly, the 2018 practice guidance of the American Association for the Study of Liver Diseases (AASLD) recommends the use of the NAFLD Fibrosis Score (NFS), the Fibrosis-4 (FIB-4) index, vibration-controlled transient elastography (VCTE), and magnetic resonance elastography (MRE) [13]. However, advanced imaging modalities such as VCTE and MRE are not available in many healthcare centers. The FIB-4 index, which consists of four parameters—age, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and platelet count—is widely used as a simple, inexpensive, and reliable tool for assessing the risk of hepatic fibrosis [14,15].

The combination of serum biomarkers and other indicators is commonly used in disease screening due to its accessibility and low cost. Parameters associated with the triglyceride–glucose (TyG) index—including triglyceride–glucose body mass index (TyG-BMI), triglyceride–glucose waist-to-height ratio (TyG-WHtR), and triglyceride–glucose waist circumference (TyG-WC)—are considered reliable and simple markers of insulin resistance and have significant value in metabolic diseases [16,17]. Reflecting the underlying mechanisms of insulin resistance, the TyG index can accurately assess its severity and is closely associated with metabolic disturbances in pathways such as fatty acid and glucose metabolism [18].

In this study, we aimed to evaluate the association between the triglyceride–glucose (TyG) index and its derivatives—triglyceride–glucose waist circumference (TyG-WC), triglyceride–glucose waist-to-height ratio (TyG-WHtR), and triglyceride–glucose body mass index (TyG-BMI)—and the risk of MASLD and hepatic fibrosis. For this purpose, routine laboratory

parameters and anthropometric measurements of adult patients presenting to a family medicine outpatient clinic were analyzed. Additionally, the predictive performance of these indices for MASLD and hepatic fibrosis risk was assessed.

## Materials and Methods

This study included all individuals aged 18 years and older who presented to the Family Medicine outpatient clinic of Recep Tayyip Erdogan University Rize Training and Research Hospital between 02 January 2023 and 31 December 2024, whose biochemical test results were available and whose hepatic steatosis status had been evaluated by ultrasonography (USG), computed tomography (CT), or magnetic resonance imaging (MRI).

The sample size was calculated using G*Power [19]. In the logistic regression analysis module, assuming an effect size of 2 (odds ratio [OR] = 2 for the association between the TyG index and the presence of MASLD), H0 = 0.5, a type I error rate of 5%, a statistical power of 80%, and $\pi = 0.25$, the required sample size was calculated as 374 [20]. Considering the possibility of missing data, approximately 10% more participants were added, and a total of 408 individuals meeting the inclusion criteria were randomly selected (Figure 1).

For all participants included in the study, demographic characteristics, lifestyle habits, clinical diagnoses, anthropometric measurements, and laboratory findings were recorded. The diagnosis of MASLD was established according to current clinical and biochemical criteria (Figure 3).

Participants were divided into two groups based on the presence of MASLD: MASLD and non-MASLD. In addition, the Fibrosis-4 (FIB-4) index was used to assess the risk of hepatic fibrosis, and risk levels were classified according to age-specific cutoff values.

The sociodemographic variables analyzed included age, sex, smoking status, and alcohol consumption.

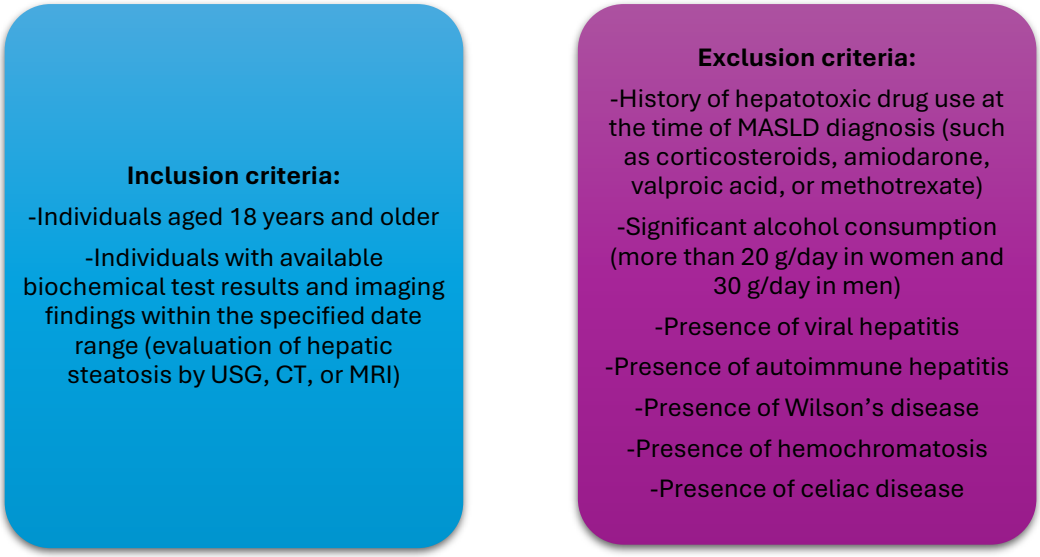



**Figure 1:** Inclusion and Exclusion criterias

**Anthropometric and Biochemical Measurements**

Anthropometric measurements (height, weight, waist circumference, body mass index [BMI], and blood pressure) were obtained from records documented by healthcare personnel at the time of the outpatient clinic visit. Body mass index (BMI, kg/m²) was calculated using body weight in kilograms divided by the square of height in meters [21]. Waist circumference was measured at a standard anatomical landmark, and the waist-to-height ratio (WHtR) was calculated by dividing waist circumference by height. Overweight/obesity and increased waist circumference risk were defined according to internationally accepted cutoff values.

Within the scope of biochemical analyses, fasting plasma glucose, HbA1c, aspartate aminotransferase (AST), alanine aminotransferase (ALT), platelet count, triglycerides, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and non-HDL cholesterol levels were evaluated by the same laboratory.

**Definition and Calculation of the Triglyceride–Glucose (TyG) Index and Its Derivatives**

The triglyceride–glucose (TyG) index was calculated using the standard formula (Figure 2).

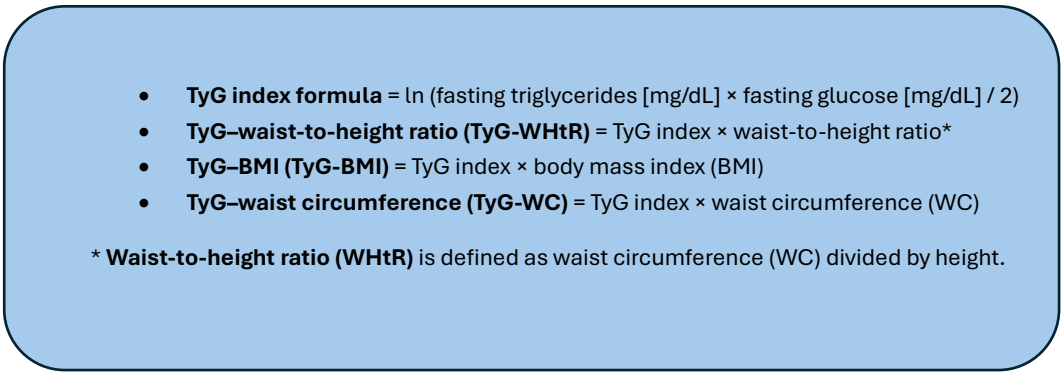



**Figure 2**: Standard formulas of Triglyceride–Glucose Index and Its Derivatives

**Assessment of MASLD Diagnosis**

Within the hospital data management system, recorded imaging reports (USG,CT,MRI) of patients with available biochemical results were reviewed. Based on these imaging studies, the presence of hepatic steatosis was evaluated (Figure 3).

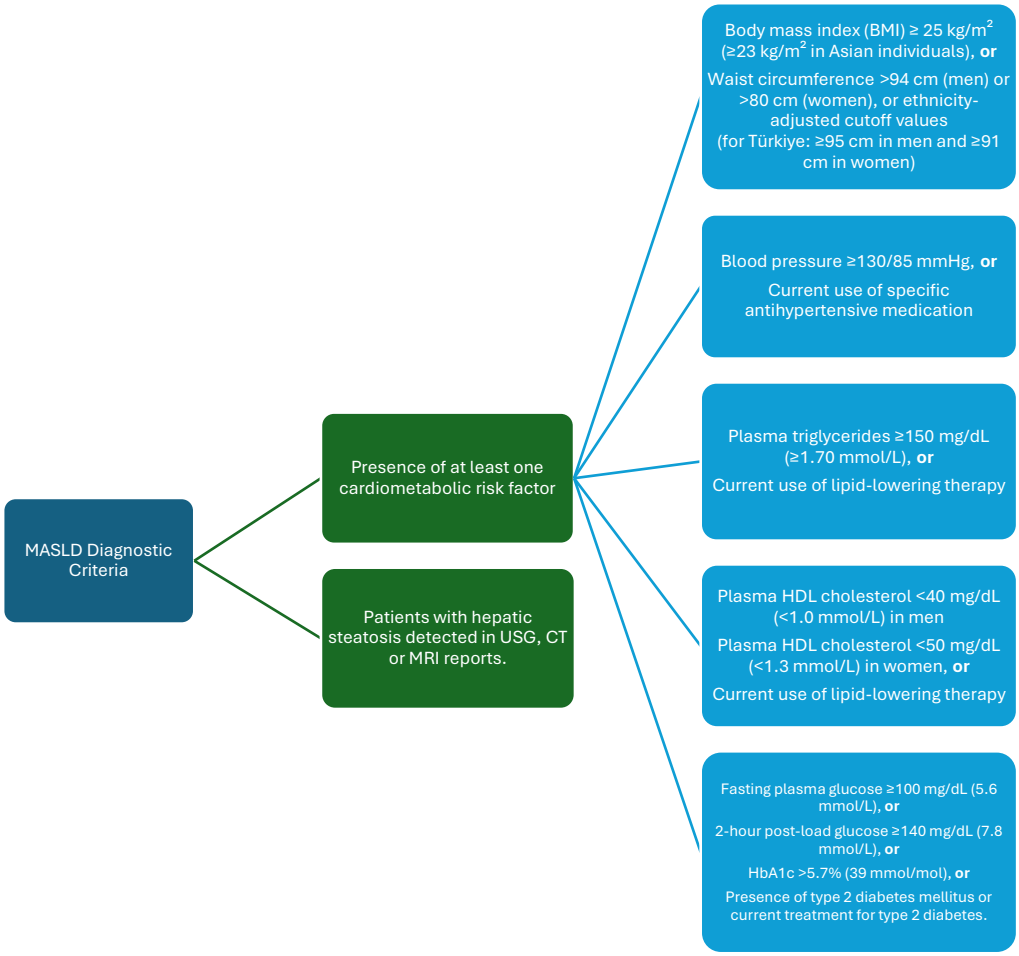



**Figure 3:** Flowchart of MASLD diagnostic criteria

## Assessment of Fibrosis Risk

The Fibrosis-4 (FIB-4) score was used to determine the risk of hepatic fibrosis and was calculated using the following formula:

$$\left(\text{Age} \times \text{AST [U/L]}\right) / \left(\text{Platelet count} \times \sqrt{\text{ALT [U/L]}}\right)$$

Age-specific cutoff values were used as follows:

- FIB-4 Level 1: <1.3 for individuals <64 years; <2.0 for individuals ≥65 years
- FIB-4 Level 2: 1.3–2.67 for individuals <64 years; 2.0–2.67 for individuals ≥65 years
- FIB-4 Level 3: >2.67 for individuals <64 years; >2.67 for individuals ≥65 years

In the analyses, FIB-4 Level 1 was compared with FIB-4 Levels 2–3.

**Statistical Analysis**

The distribution of the data was evaluated using the Kolmogorov–Smirnov test, histograms, and skewness and kurtosis values. Continuous variables were presented as mean ± standard deviation when normally distributed, and as median (interquartile range) when not normally distributed. Categorical variables were expressed as numbers and percentages.

Comparisons between the MASLD and non-MASLD groups were performed using the Student's *t*-test or the Mann–Whitney *U* test for continuous variables, and the chi-square test or Fisher's exact test (when appropriate) for categorical variables. Linear trends in ordinal categorical variables were evaluated using the linear-by-linear association test.

Receiver operating characteristic (ROC) analysis was used to evaluate the predictive performance of FIB-4, TyG, and TyG-related composite indices for MASLD risk. The area under the curve (AUC) was reported together with the 95% confidence interval (CI), and optimal cutoff values were determined using the Youden index.

Multivariable logistic regression analyses were performed to evaluate factors associated with MASLD. TyG and TyG-related indices were categorized into quartiles, with the lowest quartile used as the reference group. Separate logistic regression models were constructed for each TyG-related index.

A three-stage modeling approach was used:

Model 1: Adjusted for age and sex.

Model 2: Adjusted for age, sex, HDL cholesterol, AST, and ALT.

Model 3: Additionally adjusted for age, sex, alcohol consumption, smoking status, hypertension, diabetes mellitus, and HDL cholesterol.

The results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). In all statistical analyses, a two-sided p value $<0.05$ was considered statistically significant. All

analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

**Results**

A total of 408 individuals were included in the study, of whom 206 were diagnosed with MASLD. The sex distribution was similar between the MASLD and non-MASLD groups ($p = 0.925$). However, the proportion of participants in the older age groups was significantly higher in the MASLD group ($p = 0.001$).

The prevalence of hypertension and diabetes mellitus was significantly higher in the MASLD group compared with the non-MASLD group (54.9% vs. 40.1%, $p = 0.003$; 25.7% vs. 10.4%, $p = 0.001$, respectively). The proportion of individuals who were overweight or obese was markedly higher in the MASLD group (96.6% vs. 64.4%, $p < 0.001$). Similarly, an increased waist circumference risk was more frequently observed in the MASLD group (81.6% vs. 44.1%, $p < 0.001$).

The MASLD group had significantly higher mean body mass index and waist-to-height ratio values (BMI: $32.5 \pm 5.0$ vs. $27.9 \pm 6.1$; WHtR: $0.63 \pm 0.08$ vs. $0.56 \pm 0.09$; both $p < 0.001$). In terms of metabolic parameters, glucose, HbA1c, AST, and HDL levels differed significantly between the groups (all $p < 0.01$).

When the quartiles of the TyG index and TyG-related composite indices were examined, the proportion of individuals in the higher quartiles was significantly greater in the MASLD group, demonstrating a clear linear trend (all $p < 0.001$) (Table 1).

Table 1. Comparison of sociodemographic, clinical, and metabolic characteristics between participants with and without MASLD (n=408)

| Variables | Non-MASLD | MASLD | Total | *p* |
|---|---|---|---|---|
| | Mean ± SD[1]/ Median (IQR)[2]/ n (%)[3] | Mean ± SD/ Median (IQR)/ n (%) | Mean ± SD/ Median (IQR)/ n (%) | |
| **Sex** | | | | |
| Female | 145(71.8) | 147 (71.4) | 292 (71.6) | 0.925 |
| Male | 57 (28.2) | 59 (28.6) | 116 (28.4) | |
| **Age** | | | | |
| =<44 | 75 (37.1) | 28 (13.6) | 103 (25.2) | **0.001** |
| >44-57 | 43 (21.3) | 56 (27.2) | 99 (24.3) | |
| >57-67 | 44 (21.8) | 64 (31.0) | 108 (26.5) | |
| >67 | 40 (19.8) | 58 (28.2) | 98 (24.0) | |
| **Smoking status** | | | | |
| Current smoker | 179 (88.6) | 175 (85.0) | 354 (86.8) | 0.539 |
| Non smoker | 18 (8.9) | 25 (12.1) | 43 (10.5) | |
| Former smoker | 5 (2.5) | 6 (2.9) | 11 (2.7) | |
| Alcohol use* | 4 (2.0) | 1 (0.5) | 5 (1.2) | 0.212 |
| Hypertension diagnosis* | 81 (40.1) | 113 (54.9) | 194 (47.5) | **0.003** |
| Diabetes mellitus diagnosis* | 21 (10.4) | 53 (25.7) | 74 (18.1) | **0.001** |
| Cholesterol-lowering medication* | 24 (11.9) | 35 (17.0) | 59 (14.5) | 0.137 |
| Overweight or obesity* | 130 (64.4) | 199 (96.6) | 329 (80.6) | **0.001** |
| Increased waist circumference risk* | 89 (44.1) | 168 (81.6) | 257 (63.0) | **0.001** |
| BMI | 27.9±6.1 | 32.5±5.0 | 30.2±6.0 | **0.001** |
| WHtR | 0.56±0.09 | 0.63±0.08 | 0.6±0.1 | **0.001** |
| AST | 20.0 (9.0) | 23.0 (11.0) | 21.0 (10.0) | **0.001** |
| ALT | 26.0 (11.0) | 23.0 (20.0) | 19.0 (16.0) | **0.001** |
| Glucose | 92.5 (16.0) | 99.0 (21.0) | 95.0 (19.0) | **0.001** |
| HbA1c | 5.7 (0.5) | 6.0 (0.7) | 5.9 (0.7) | **0.001** |
| Non-HDL cholesterol | 157.3±49.6 | 166.4±48.1 | 161.9±49.0 | 0.061 |
| HDL cholesterol | 57.0±12.9 | 53.2±12.6 | 55.1±12.9 | **0.003** |
| FIB-4 risk category | | | | |
| Level 2-3 | 48 (23.8) | 63 (30.6) | 111 (27.2) | 0.122 Chi-square test |
| Level 1 | 154 (76.2) | 143(69.4) | 297 (72.8) | |
| TyG Index Quartiles | | | | |
| Q1-<8.35 | 74 (36.7) | 28 (13.6) | 102 (25.0) | **0.001** Linear by linear association |
| Q2- 8.35-8.68 | 52 (25.7) | 50 (24.3) | 102 (25.0) | |
| Q3- >8.68-9.11 | 42 (20.8) | 60 (29.1) | 102 (25.0) | |
| Q4- >9.11 | 34 (16.8) | 68 (33.0) | 102 (25.0) | |
| TyG × BMI Quartiles | | | | |
| Q1-<219.1 | 85 (42.1) | 17 (8.3) | 102 (25.0) | **0.001** |
| Q2- 219.1-260.5 | 51 (25.2) | 51 (24.7) | 102 (25.0) | Linear by linear association |
| Q3- >260.5-303.7 | 41 (20.3) | 61 (29.6) | 102 (25.0) | |
| Q4- >303.7 | 25 (12.4) | 77 (37.4) | 102 (25.0) | |
| TyG × Waist Circumference Quartiles | | | | |
| Q1 <733 | 86 (42.6) | 16 (7.8) | 102 (25.0) | **0.001** |
| Q2 733-844 | 51 (25.2) | 51 (24.8) | 102 (25.0) | Linear by linear association |
| Q3 >844-944.2 | 43 (21.3) | 59 (28.6) | 102 (25.0) | |
| Q4 >944.2 | 22 (10.9) | 80 (38.8) | 102 (25.0) | |
| TyG × WHtR Quartiles | | | | |
| Q1 =<4.5 | 85 (42.1) | 17 (8.3) | 102 (25.0) | **0.001** |
| Q2 >4.50-5.16 | 49 (24.2) | 53 (25.7) | 102 (25.0) | Linear by linear association |
| Q3 >5.16-5.87 | 46 (22.8) | 56 (27.2) | 102 (25.0) | |
| Q4 >5.87 | 22 (10.9) | 80 (38.8) | 102 (25.0) | |

*TyG index:* Triglyceride–Glucose Index, *TyG × BMI:* Triglyceride–Glucose Index × Body Mass Index, *TyG × WC:* Triglyceride–Glucose Index × Waist Circumference, *TyG × WHtR:* Triglyceride–Glucose Index × Waist-to-Height Ratio, *BMI*: Body Mass Index, *HbA1c:* Glycated Hemoglobin, *AST:* Aspartate Aminotransferase, *ALT:* Alanine Aminotransferase, *HDL:* High-Density Lipoprotein, *Non-HDL:* Non-High-Density Lipoprotein Cholesterol, *Fib 4:* Fibrosis-4 Index, *MASLD:* Metabolic Dysfunction–Associated Steatotic Liver Disease, *SD:* Standard deviation, *IQR:* Interquartile range

Categorical variables were compared using Chi-square test; continuous variables were compared using

[1]Student's t-test

[2]Mann–Whitney U test

[3]Chi-square

Trend analyses were performed using linear-by-linear association test.

*Column percentages are presented for the single category of the variable.

**Fibrosis Risk Analysis**

Participants were stratified into two age groups (<65 years and ≥65 years) and compared according to FIB-4 risk categories. In both age groups, the prevalence of increased waist circumference was higher in the FIB-4 Level 2–3 group compared with the Level 1 group, although this difference did not reach statistical significance ($p>0.05$).

Among participants younger than 65 years, the waist-to-height ratio, AST, ALT, and HbA1c levels were significantly higher in the FIB-4 Level 2–3 group than in the Level 1 group ($p=0.039$, $p<0.001$, $p=0.004$, and $p<0.001$, respectively). However, no significant differences were observed between the groups with respect to body mass index, fasting glucose, lipid parameters, or TyG-related composite indices.

In participants aged 65 years and older, AST levels were significantly higher in the FIB-4 Level 2–3 group ($p<0.001$). In contrast, non-HDL cholesterol levels were significantly higher in the FIB-4 Level 1 group ($p=0.010$). The TyG index was also significantly higher in the FIB-4 Level 2–3 group ($p=0.048$). No statistically significant differences were observed between the groups for other metabolic or anthropometric parameters (Table 2).

Table 2. Metabolic and biochemical parameters according to FIB-4 risk categories stratified by age (<65 and ≥65 years).

| Variables | <65 years | | | ≥65 years | | |
|---|---|---|---|---|---|---|
| | **FIB-4 Level 1 Mean±SD[1] Median (IQR)[2] n (%)[3]** | **FIB-4 Level 2–3 Mean±SD[1] Median (IQR)[2] n (%)[3]** | ***p*** | **FIB-4 Level 1 Mean±SD[1] Median (IQR)[2] n (%)[3]** | **FIB-4 Level 2–3 Mean±SD[1] Median (IQR)[2] n (%)[3]** | ***p*** |
| Waist circumference | | | | | | |
| Normal | 86 (72.8) | 2 (27.2) | 0.893 | 26 (78.8) | 7 (21.2) | 0.643 |
| Increased risk | 118 (71.5) | 47 (28.5) | | 67 (72.8) | 25 (27.2) | |
| BMI | 29.4±6.2 | 30.5±5.5 | 0.160 | 31.8±5.6 | 30.5±6.0 | 0.266 |
| WHtR | 0.57±0.10 | 0.60±1.0 | **0.039** | 0.62±0.08 | 0.63±0.08 | 0.629 |
| AST | 20.0 (8.0) | 26.0 (15.0) | **0.001** | 19.0 (7.5) | 25.0 (13.0) | **0.001** |
| ALT | 18.5 (15.8) | 26.0 (21.0) | **0.004** | 17.0 (12.0) | 19.0 (18.3) | 0.543 |
| Glucose | 92.0 (17.0) | 96.0 (14.0) | 0.070 | 99.0 (19.0) | 106.0 (28.5) | 0.134 |
| HbA1c | 5.7 (0.5) | 6.0 (0.5) | **0.001** | 6.3 (0.6) | 6.0 (0.5) | 0.400 |
| Non-HDL cholesterol | 158.4±47.9 | 163.8±47.9 | 0.395 | 173.3±50.8 | 146.4±48.4 | **0.010** |
| HDL cholesterol | 54.6±12.6 | 57.7±13.2 | 0.074 | 55.1±14.1 | 51.9±9.8 | 0.229 |
| TyG index | 8.7±0.6 | 8.7±0.4 | 0.780 | 8.9±0.5 | 8.7±0.5 | **0.048** |
| TyG*BMI | 256.6±67.0 | 265.8±54.2 | 0.273 | 284.0±56.7 | 266.5±60.5 | 0.141 |
| TyG*WC | 819.6±168.9 | 842.9±155.0 | 0.289 | 891.1±127.6 | 884.5±134.5 | 0.803 |
| TyG*WHtR | 5.0±1.1 | 5.2±1.0 | 0.098 | 5.6±0.9 | 5.5±0.9 | 0.746 |

*TyG index*: Triglyceride–Glucose Index, *TyG × BMI*: Triglyceride–Glucose Index × Body Mass Index, *TyG × WC:* Triglyceride–Glucose Index × Waist Circumference, *TyG × WHtR*: Triglyceride–Glucose Index × Waist-to-Height Ratio, *BMI*: Body Mass Index, *HbA1c:* Glycated Hemoglobin, *AST*: Aspartate Aminotransferase, *ALT*: Alanine Aminotransferase, *WHtR:* Waist-to-Height Ratio, *HDL:* High-Density Lipoprotein, *Non-HDL:* Non-High-Density Lipoprotein Cholesterol, *FIB-4*: Fibrosis-4 Index. Values are presented as mean ± standard deviation (*SD*), median (interquartile range, *IQR*), or number (percentage) as appropriate.

[1]Student's t-test,

[2]Mann–Whitney U test, or

[3]Chi-square test as appropriate.

## ROC Analysis

The predictive performance of the FIB-4 index, TyG index, and TyG-related composite indices for identifying MASLD risk was evaluated using receiver operating characteristic (ROC) analysis (Table 3). The discriminative ability of the FIB-4 index was limited, with an area under the curve (AUC) of 0.617 (95% CI: 0.562–0.671).

The TyG index demonstrated a higher discriminative performance compared with FIB-4, with an AUC of 0.667 (95% CI: 0.615–0.719). Among the TyG-related composite indices, TyG × waist circumference showed the highest discriminative power, with an AUC of 0.761 (95% CI: 0.715–0.807), a sensitivity of 79%, and a specificity of 62%. This was followed by TyG ×

waist-to-height ratio (AUC: 0.752) and TyG × body mass index (AUC: 0.750) (Table 3; Figure 1).

Table 3. Receiver Operating Characteristic (ROC) Analysis of FIB-4 and TyG-Related Indices for Predicting MASLD

| Index | Cut-off | Sensitivity | Specificity | AUC | 95% CI for AU |
|---|---|---|---|---|---|
| FIB 4 | 0.90 | 0.70 | 0.55 | 0.617 | 0.562-0.671 |
| TyG index | 8.571 | 0.70 | 0.53 | 0.667 | 0.615-0.719 |
| TyG*BMI | 243 | 0.80 | 0.55 | 0.750 | 0.703-0.797 |
| TyG*WHtR | 4.88 | 0.80 | 0.57 | 0.752 | 0.705-0.799 |
| TyG*WC | 805 | 0.79 | 0.62 | 0.761 | 0.715-0.807 |

*TyG index:* Triglyceride–Glucose Index, *TyG × BMI:* Triglyceride–Glucose Index × Body Mass Index, *TyG × WC:* Triglyceride–Glucose Index × Waist Circumference, *TyG × WHtR:* Triglyceride–Glucose Index × Waist-to-Height Ratio, *Fib 4:* Fibrosis-4 Index

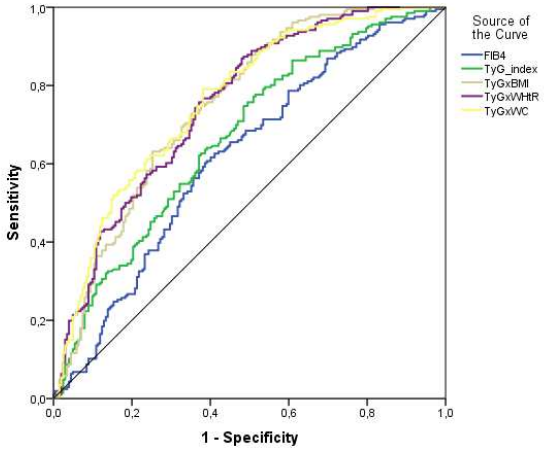



**Figure 1.** Receiver operating characteristic (ROC) curve of FIB-4 and TyG-related indices for predicting MASLD. Optimal cut-off values were determined using the Youden index.

In the logistic regression analysis adjusted for age and sex, a clear dose–response relationship was observed between the quartiles of the TyG index and TyG-related composite indices and the presence of MASLD (Table 4). Using the lowest quartile (Q1) as the reference group, the odds of MASLD increased by 2.11-, 2.86-, and 4.25-fold in the Q2, Q3, and Q4 quartiles of the TyG index, respectively (all $p \leq 0.015$).

Among the TyG-related indices, the product of TyG and waist circumference (TyG × WC) showed the strongest association with MASLD. Individuals in the highest quartile (Q4) had approximately a 15-fold higher risk of MASLD compared with those in Q1 (OR: 15.28; 95%

CI: 7.36–31.69; $p < 0.001$). Similarly, a marked increase in MASLD risk was observed in the upper quartiles of the TyG × BMI and TyG × WHtR indices (OR: 12.12 and OR: 13.98, respectively; both $p < 0.001$).

Overall, a progressively increasing and statistically significant risk pattern across quartiles was observed for all TyG-related indices (Table 4).

Table 4. Multivariable logistic regression analysis for MASLD adjusted for age and sex-Model 1

| Variable | Quartile | B | Wald | Adjusted OR(%95 CI) | *p* |
|---|---|---|---|---|---|
| TyG index | Q1 | | | *Ref* | |
| | Q2 | 0.748 | 5.938 | 2.11 (1.02-4.34) | **0.015** |
| | Q3 | 1.049 | 11.337 | 2.86 (1.55-5.26) | **0.001** |
| | Q4 | 1.446 | 21.079 | 4.25 (2.29-7.88) | **0.001** |
| TyG*WC | Q1 | | | *Ref* | |
| | Q2 | 1.467 | 17.980 | 4.34 (2.20-8.54) | **0.001** |
| | Q3 | 1.794 | 26.900 | 6.02 (3.05-11.85) | **0.001** |
| | Q4 | 2.726 | 53.625 | 15.28 (7.36-31.69) | **0.001** |
| TyG*BMI | Q1 | | | *Ref* | |
| | Q2 | 1.421 | 17.573 | 4.14 (2.13-8.04) | **0.001** |
| | Q3 | 1.798 | 27.785 | 6.04 (3.09-11.78) | **0.001** |
| | Q4 | 2.495 | 48.185 | 12.12 (5.99-24.52) | **0.001** |
| TyG*WHtR | Q1 | | | *Ref* | |
| | Q2 | 1.490 | 19.053 | 4.44 (2.27-8.67) | **0.001** |
| | Q3 | 1.595 | 21.665 | 4.93 (2.52-9.65) | **0.001** |
| | Q4 | 2.638 | 50.205 | 13.98 (6.74-29.01) | **0.001** |

*TyG index*: Triglyceride–Glucose Index, *TyG × BMI*: Triglyceride–Glucose Index × Body Mass Index, *TyG × WC*: Triglyceride–Glucose Index × Waist Circumference, *TyG × WHtR*: Triglyceride–Glucose Index × Waist-to-Height Ratio

Q1 was used as the reference category. Separate logistic regression models were constructed for each TyG-related index.

In Model 2, which additionally included HDL cholesterol, AST, and ALT levels, these associations were largely preserved. Individuals in the highest quartile of the TyG index had a threefold higher likelihood of MASLD compared with the reference group (OR: 3.00; 95% CI: 1.55–5.79).

The TyG × waist circumference index remained the strongest predictor in Model 2; individuals in the highest quartile had a 13.5-fold higher risk of MASLD compared with those in the lowest quartile (OR: 13.52; 95% CI: 6.46–28.31). Similarly, the TyG × BMI and TyG × WHtR indices showed a significant and increasing trend in MASLD risk across the higher quartiles (all $p <$

0.001). These findings indicate that TyG-related anthropometric indices are strongly associated with MASLD independently of classical biochemical markers (Table 5).

Table 5. Multivariable logistic regression analysis for MASLD adjusted for age, sex, HDL cholesterol, AST, and ALT -Model 2

| Variable | **Quartile** | **B** | **Wald** | **Adjusted OR(%95 CI)** | ***p*** |
|---|---|---|---|---|---|
| TyG index | Q1 | | | *Ref* | |
| | Q2 | 0.656 | 4.428 | 1.93 (1.05-3.55) | **0.035** |
| | Q3 | 0.880 | 7.552 | 2.41 (1.29-4.51) | **0.006** |
| | Q4 | 1.098 | 10.691 | 3.00 (1.55-5.79) | **0.001** |
| TyG*WC | Q1 | | | *Ref* | |
| | Q2 | 1.416 | 16.512 | 4.12 (2.08-8.16) | **0.001** |
| | Q3 | 1.696 | 23.508 | 5.45 (2.75-10.82) | **0.001** |
| | Q4 | 2.604 | 47.692 | 13.52 (6.46-28.31) | **0.001** |
| TyG*BMI | Q1 | | | *Ref* | |
| | Q2 | 1.377 | 16.069 | 3.96 (2.02-7.77) | **0.001** |
| | Q3 | 1.738 | 25.347 | 5.69 (2.89-11.18) | **0.001** |
| | Q4 | 2.402 | 43.630 | 11.05 (5.42-22.53) | **0.001** |
| TyG*WHtR | Q1 | | | *Ref* | |
| | Q2 | 1.396 | 16.275 | 4.04 (2.05-7.96) | **0.001** |
| | Q3 | 1.489 | 18.394 | 4.43 (2.25-8.76) | **0.001** |
| | Q4 | 2.538 | 45.621 | 12.65 (6.06-26.42) | **0.001** |

*TyG index*: Triglyceride–Glucose Index, *TyG × BMI*: Triglyceride–Glucose Index × Body Mass Index, *TyG × WC*: Triglyceride–Glucose Index × Waist Circumference, *TyG × WHtR*: Triglyceride–Glucose Index × Waist-to-Height Ratio

Q1 was used as the reference category.

In age- and sex-adjusted analyses (Model 1), TyG and all TyG-related composite indices demonstrated a clear dose–response association with MASLD. These associations remained largely unchanged after further adjustment for HDL cholesterol, AST, and ALT (Model 2).

In the fully adjusted Model 3, which additionally accounted for alcohol consumption, smoking status, hypertension, diabetes, HDL cholesterol and all composite indices continued to be independently associated with MASLD (Table 6). Compared with the lowest quartile, individuals in the highest TyG quartile had an approximately threefold increased odds of MASLD (OR: 2.94; 95% CI: 1.52–5.65).

Among the composite indices, TyG×waist circumference showed the strongest association with MASLD. Participants in the highest quartile of TyG×waist circumference had a more than 14-fold higher odds of MASLD compared with those in the lowest quartile (OR: 14.46; 95% CI: 6.85–30.56; $p<0.001$). Similarly, TyG×BMI and TyG×waist-to-height ratio were also strongly

associated with MASLD in a graded manner, with significantly increased odds observed across increasing quartiles (all p<0.001).

These findings indicate that TyG-related anthropometric indices are robust and independent predictors of MASLD, even after extensive adjustment for potential confounders and metabolic biomarkers (Tablo 6).

Table 6. Multivariable logistic regression analysis for MASLD with further adjustment for sociodemographic, lifestyle, clinical, and biochemical variables-Model 3

| Variable | **Quartile** | **B** | **Wald** | **Adjusted OR(%95 CI)** | ***p*** |
|---|---|---|---|---|---|
| TyG index | Q1 | | | *Ref* | |
| | Q2 | 0.460 | 4.212 | 1.90 (1.03-3.49) | **0.040** |
| | Q3 | 0.903 | 8.081 | 2.47 (1.32-4.60) | **0.004** |
| | Q4 | 1.077 | 10.374 | 2.94 (1.52-5.65) | **0.001** |
| TyG*WC | Q1 | | | *Ref* | |
| | Q2 | 1.417 | 16.313 | 4.13 (2.07-8.21) | **0.001** |
| | Q3 | 1.727 | 24.137 | 5.63 (2.82-11.21) | **0.001** |
| | Q4 | 2.672 | 49.020 | 14.46 (6.85-30.56) | **0.001** |
| TyG*BMI | Q1 | | | *Ref* | |
| | Q2 | 1.383 | 16.028 | 3.99 (2.03-7.84) | **0.001** |
| | Q3 | 1.749 | 25.420 | 5.75 (2.91-11.34) | **0.001** |
| | Q4 | 2.423 | 43.763 | 11.28 (5.50-23.11) | **0.001** |
| TyG*WHtR | Q1 | | | *Ref* | |
| | Q2 | 1.464 | 17.347 | 4.33 (2.17-8.62) | **0.001** |
| | Q3 | 1.579 | 20.018 | 4.85 (2.43-9.68) | **0.001** |
| | Q4 | 2.669 | 47.676 | 14.43 (6.76-30.77) | **0.001** |

*TyG index:* Triglyceride–Glucose Index, *TyG × BMI*: Triglyceride–Glucose Index × Body Mass Index, *TyG × WC*: Triglyceride–Glucose Index × Waist Circumference, *TyG × WHtR*: Triglyceride–Glucose Index × Waist-to-Height Ratio

Further adjusted for age, sex, alcohol consumption, smoking status, hypertension, diabetes, HDL

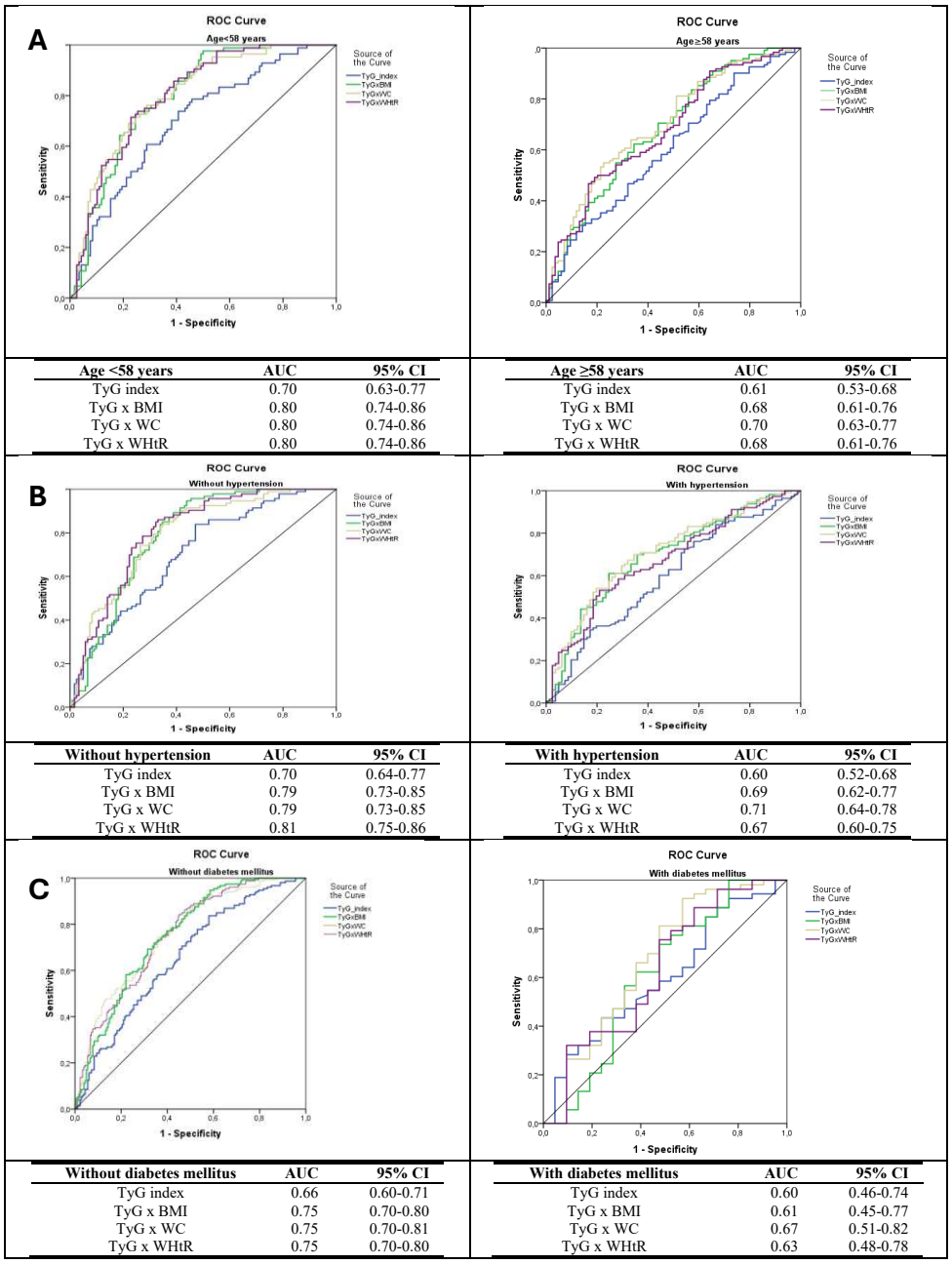
ROC analyses were further conducted across subgroups stratified by age, hypertension, and diabetes mellitus status (Figure 2). Among individuals younger than 58 years, TyG-related composite indices demonstrated markedly higher discriminative performance compared with the TyG index alone. In this subgroup, TyG × body mass index, TyG × waist circumference, and TyG × waist-to-height ratio all showed strong predictive ability, with area under the curve (AUC) values of approximately 0.80.

In contrast, among individuals aged 58 years and older, the discriminative performance of all indices declined. Nevertheless, the TyG × waist circumference index remained the best-

performing parameter within this age group, yielding the highest AUC value (0.70) among the evaluated indices.

When stratified by hypertension status, TyG-related composite indices exhibited better predictive performance in individuals without hypertension. In this subgroup, TyG × waist-to-height ratio demonstrated the highest discriminative capacity, with an AUC of 0.81. Although the overall discriminative ability of the indices was reduced in individuals with hypertension, the TyG × waist circumference index still showed relatively higher predictive performance compared with the other indices.

Similarly, subgroup analyses according to diabetes mellitus status revealed that TyG and particularly TyG-related composite indices showed moderate predictive performance in individuals without diabetes (AUC approximately 0.75). However, in individuals with diabetes, the discriminative ability of all indices was limited, accompanied by relatively wider confidence intervals. Overall, these findings suggest that TyG-related composite indices may provide greater discriminatory ability for MASLD in metabolically healthier subgroups.




| Age <58 years | AUC | 95% CI |
|---|---|---|
| TyG index | 0.70 | 0.63-0.77 |
| TyG x BMI | 0.80 | 0.74-0.86 |
| TyG x WC | 0.80 | 0.74-0.86 |
| TyG x WHtR | 0.80 | 0.74-0.86 |

| Age ≥58 years | AUC | 95% CI |
|---|---|---|
| TyG index | 0.61 | 0.53-0.68 |
| TyG x BMI | 0.68 | 0.61-0.76 |
| TyG x WC | 0.70 | 0.63-0.77 |
| TyG x WHtR | 0.68 | 0.61-0.76 |

| Without hypertension | AUC | 95% CI |
|---|---|---|
| TyG index | 0.70 | 0.64-0.77 |
| TyG x BMI | 0.79 | 0.73-0.85 |
| TyG x WC | 0.79 | 0.73-0.85 |
| TyG x WHtR | 0.81 | 0.75-0.86 |

| With hypertension | AUC | 95% CI |
|---|---|---|
| TyG index | 0.60 | 0.52-0.68 |
| TyG x BMI | 0.69 | 0.62-0.77 |
| TyG x WC | 0.71 | 0.64-0.78 |
| TyG x WHtR | 0.67 | 0.60-0.75 |

| Without diabetes mellitus | AUC | 95% CI |
|---|---|---|
| TyG index | 0.66 | 0.60-0.71 |
| TyG x BMI | 0.75 | 0.70-0.80 |
| TyG x WC | 0.75 | 0.70-0.81 |
| TyG x WHtR | 0.75 | 0.70-0.80 |

| With diabetes mellitus | AUC | 95% CI |
|---|---|---|
| TyG index | 0.60 | 0.46-0.74 |
| TyG x BMI | 0.61 | 0.45-0.77 |
| TyG x WC | 0.67 | 0.51-0.82 |
| TyG x WHtR | 0.63 | 0.48-0.78 |

**Figure 2.** ROC curves and the area under the ROC curve (AUC) values of TyG index, TyG-WHtR, TyG-BMI, and TyG-WC for MASDL. (A)Subgroup analyses based on median age. (B)Subgroup analyses based on hypertension. (C)Subgroup analyses based on diabetes.

## Discussion

In the present study, we evaluated the association between the triglyceride–glucose (TyG) index and TyG-related anthropometric composite indices with the presence of metabolic dysfunction–associated steatotic liver disease (MASLD) and the risk of hepatic fibrosis among adult individuals attending a family medicine outpatient clinic. Our findings demonstrated that the TyG index and particularly TyG-derived indices combined with waist circumference, waist-to-height ratio, and body mass index were strongly and independently associated with MASLD. Moreover, these composite indices showed a clear dose–response relationship across quartiles. Importantly, the diagnostic performance of TyG-related indices for identifying MASLD was higher than that of the TyG index alone and the FIB-4 index.

In our study, the prevalence of MASLD was 50.5%, which is higher than the prevalence reported in the NHANES data (27–30%). However, this finding appears to be consistent with the increasing trend reported by Değertekin et al. in Türkiye [7,8]. This relatively high prevalence may be explained by the characteristics of the study population, which consisted of individuals presenting to a primary care setting where metabolic risk factors are commonly encountered. Furthermore, the higher frequency of advanced age, hypertension, diabetes mellitus, obesity, and central obesity observed in the MASLD group supports the close relationship between MASLD and the metabolic syndrome spectrum.

The relationship between the TyG index and MASLD has been demonstrated in several cohort studies and meta-analyses[22]. However, recent studies have suggested that combining the TyG index with anthropometric parameters may improve the prediction of hepatic steatosis[18,23]. In a recent meta-analysis by Boushehri et al., the TyG-BMI index showed greater predictive ability for MASLD compared with the TyG index alone[1]. Consistent with these findings, our results also demonstrated that TyG × BMI, TyG × WHtR, and particularly TyG × waist circumference were more strongly associated with MASLD.

Similarly, in a cohort study conducted by Priego-Parra et al., which evaluated the diagnostic performance of sixteen biomarkers for MASLD, the TyG-WC index was identified as the best predictor of MASLD[24]. In line with our results, Demirci et al. reported that TyG-WC demonstrated higher diagnostic accuracy compared with conventional markers in both women and men in the Turkish population, with area under the curve (AUC) values of 0.82 ($p < 0.001$) and 0.86 ($p < 0.001$), respectively[25].

A notable finding of this study was that the TyG × waist circumference index demonstrated the highest odds ratios across all models. The approximately 14–15-fold increase in MASLD risk observed in the highest quartile suggests that the combined assessment of visceral adiposity and insulin resistance may be particularly important for identifying hepatic steatosis. Although waist circumference alone is not sufficient to fully characterize visceral adiposity, it represents one of the most practical anthropometric measures reflecting visceral fat accumulation and has been directly associated with hepatic lipid deposition and inflammation [26]. This finding further supports the central role of central obesity in the pathogenesis of MASLD.

Insulin resistance plays a fundamental role in the development of hepatic steatosis through increased hepatic de novo lipogenesis, enhanced free fatty acid flux to the liver, and activation of inflammatory cytokines. The TyG index, which is considered a practical surrogate marker of insulin resistance, may indirectly reflect these underlying pathophysiological processes [27].

In the analyses evaluating fibrosis risk, the association between TyG-related indices and FIB-4 levels was found to vary according to age groups. In particular, the discriminative performance of TyG-related composite indices was higher among individuals younger than 65 years, suggesting that metabolic disturbances may be more closely associated with fibrotic processes during earlier stages of the disease. In contrast, among older individuals, the discriminative ability of metabolic indices may be relatively reduced due to the influence of age on the FIB-4 score.

Previous studies have also reported that the performance of the FIB-4 index may vary according to age. Sung et al. reported that the effectiveness of FIB-4 in predicting liver fibrosis may differ in older populations [28]. Additionally, another study emphasized that increasing age may elevate FIB-4 scores independently, which may potentially reduce the discriminatory ability of the index [29].

In the ROC analyses, the AUC values of TyG-related composite indices ranged between 0.75 and 0.76, indicating moderate to good diagnostic performance. Notably, the TyG × waist circumference index achieved the highest AUC value, with 79% sensitivity and 62% specificity, suggesting that this index may serve as a practical screening tool in primary care settings. Similarly, Forouzesh et al. reported that TyG-related composite indices demonstrated moderate to good diagnostic performance in predicting MASLD[27]. These findings suggest that TyG-based indices may provide consistent risk stratification across different populations. In contrast, the relatively limited performance of the FIB-4 index in predicting MASLD appears to be consistent with the fact that this score was primarily developed to identify advanced liver fibrosis rather than hepatic steatosis.

In the subgroup analyses, TyG-related indices demonstrated higher discriminative ability among individuals without diabetes and hypertension. This finding suggests that these indices may serve as early warning markers before the development of advanced metabolic diseases. In other words, TyG-based indices may be more sensitive in detecting early metabolic alterations prior to the establishment of overt metabolic comorbidities. Consistent with our findings, Forouzesh et al. also reported that the TyG index had higher predictive value particularly among individuals without metabolic comorbidities[27].

## Limitations of the Study

This study has several limitations that should be acknowledged. First, its retrospective and cross-sectional design precludes causal inference between TyG-related indices and the risk of MASLD or hepatic fibrosis. Therefore, the observed associations should be interpreted as correlational rather than causal.

Second, the diagnosis of MASLD was based on imaging modalities, including ultrasonography, computed tomography, or magnetic resonance imaging, rather than histopathological confirmation. Although liver biopsy remains the gold standard for fibrosis staging, it is not feasible in large-scale screening settings. In this study, fibrosis risk was assessed using the FIB-4 index instead of elastography or histological evaluation. While FIB-4 is a practical and widely accepted noninvasive test in primary care settings, it may be influenced by age and transaminase levels, particularly in older individuals, which could potentially affect subgroup analyses.

Third, this single-center study included individuals presenting to a family medicine outpatient clinic. Consequently, the generalizability of the findings to populations with different demographic or metabolic characteristics, or to other healthcare settings, may be limited.

Finally, although comprehensive multivariable adjustments were performed, residual confounding cannot be completely excluded. Important variables such as dietary patterns, detailed measurements of physical activity, genetic predisposition, and insulin resistance assessed using gold-standard methods were not available in the dataset.

## Strengths of the Study

This study provides real-world data from a primary care setting, where early detection of MASLD is of critical importance. By focusing on routinely obtainable biochemical and anthropometric parameters, the findings enhance the clinical applicability of the results.

Second, multiple TyG-related composite indices (TyG × BMI, TyG × WC, and TyG × WHtR) were simultaneously evaluated and compared within the same population. This comprehensive

approach enabled the identification of the strongest predictor, with TyG × waist circumference consistently demonstrating the strongest association with MASLD across all adjusted models. Third, the use of stepwise multivariable modeling with incremental adjustment for sociodemographic, clinical, and biochemical variables strengthens the validity of the observed independent associations. Moreover, the persistence of graded dose–response relationships across quartiles further supports the robustness of the findings.

Fourth, subgroup analyses stratified by age, hypertension, and diabetes status provided additional insights into the performance of TyG-related indices across different metabolic contexts. The higher discriminative performance observed among younger and metabolically healthier individuals suggests potential value for early risk stratification.

Finally, the relatively adequate sample size determined through power analysis, along with the balanced distribution of quartiles, enhances the statistical reliability of the results.

**Conclusion**

In this study, TyG and all TyG-related composite indices demonstrated a clear dose–response relationship with MASLD. The findings indicate that the combined evaluation of a biochemical marker reflecting insulin resistance and anthropometric measurements indicating central obesity may be useful in identifying the risk of MASLD. Both TyG and its derivatives showed moderate-to-good diagnostic performance in ROC analyses and exhibited a dose–response relationship.

Furthermore, subgroup analyses revealed that these indices demonstrated higher discriminative ability, particularly among younger individuals and those without pronounced metabolic comorbidities. This finding suggests that these indices may serve as valuable early risk markers. Considering the progressive nature of MASLD, this observation provides an important clinical implication for early detection and intervention in primary care settings.

In conclusion, the simplicity, accessibility, and routine availability of TyG and its derivatives in clinical practice suggest that they may serve as potential screening tools for the early detection of MASLD risk. In primary care settings where access to advanced imaging modalities may be limited, the TyG × waist circumference index may be used as a simple, low-cost, and easily applicable risk stratification tool. However, these findings should be further validated by prospective, multicenter studies and supported by histopathological methods.

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