# Comparison of triglyceride-glucose index and anthropometric obesity indices in predicting severe grades of hepatic steatosis in nonalcoholic fatty liver disease among non-diabetic obese individuals

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### Abstract

**Background and Aim:** The triglyceride glucose index (TyG) has been proposed as a promising indicator of both insulin resistance (IR) and non-alcoholic fatty liver disease (NAFLD). However, the efficacy of the TyG index in predicting NAFLD has not been adequately studied, particularly in obese individuals.

**Materials and Methods:** We analyzed 190 morbidly obese individuals. The TyG index, anthropometric obesity indices, homeostatic model assessment (HOMA-IR), and biochemical parameters were compared. NAFLD was diagnosed by hepatic ultrasonography and classified into four grades (0, 1, 2, and 3). Individuals in grades 2 and 3 are considered to have severe steatosis, while those in grades 0 and 1 do not.

**Results:** The area under the curve (AUC) values of the TyG index, body mass index, neck circumferences, waist-to-hip ratio, and HOMA-IR did not differ significantly in predicting severe steatosis (0.640, 0.742, 0.725, 0.620, and 0.624 respectively). However, the AUC values of waist circumference and alanine aminotransferase provided better predictions than the TyG index (0.782, 0.744, and 0.640 respectively).

**Conclusion:** The TyG index is highly effective in predicting both the presence and severity of NAFLD. However, it did not outperform simple obesity indices in predicting NAFLD and its severity in obese patients.

**Keywords:** Anthropometric obesity indices; insülin resistance; non-alcoholic fatty liver disease; obesity; triglyceride glucose index.

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# Introduction

Non-alcoholic fatty liver disease (NAFLD) is a rapidly growing pathology, paralleling the increasing global prevalence of obesity and type 2 diabetes mellitus.<sup>[1]</sup> Although the pathophysiology of NAFLD is not fully understood, insulin resistance (IR) has been identified as a significant factor in both the initiation and progression of the disease.<sup>[2]</sup> The term NAFLD has been widely used since its formal introduction in 1980. <sup>[3]</sup> However, the nomenclature of NAFLD has been debated in recent years. In 2020, the definition of NAFLD was altered from a negative, exclusionary diagnosis to a positive condition linked to metabolic dysfunction, introducing the term "metabolic dysfunction-associated fatty liver disease" (MAFLD).<sup>[4]</sup> Owing to ongoing debates, the name was changed again in a multi-society Delphi consensus statement in 2023 to "metabolic dysfunction-associated steatotic liver disease" (MASLD).<sup>[5]</sup>

In recent years, the triglyceride glucose index (TyG), derived from fasting plasma glucose (FPG) and triglycerides (TG), has gained popularity as an alternative measurement for IR. Several studies have demonstrated that the TyG index correlates highly with both the Homeostatic Model Assessment (HOMA-IR) and the hyperinsulinemic-euglycemic clamp tests in assessing IR.<sup>[6,7]</sup> Further studies have shown its effectiveness in predicting NAFLD in both adults and adolescents.<sup>[8-11]</sup> Given the link between obesity, IR, and NAFLD, modified TyG indices combining the TyG index with anthropometric obesity indices (such as body mass index (BMI), waist circumference (WC), and waist-to-hip ratio (WHR) have been developed. Numerous studies have indicated that these modified TyG indices are superior to the TyG index alone in predicting IR and NAFLD.<sup>[12-17]</sup> Additionally, evidence suggests that large neck circumferences (NC) are associated with an increased risk of IR and NAFLD,<sup>[18,19]</sup> although TyG-NC has not yet been studied among modified TyG indices. This study examined and compared the TyG index, modified TyG indices (including TyG-NC), and anthropometric obesity indices as predictors of NAFLD in non-diabetic obese patients. In this regard, our study is the first to directly compare the TyG index with anthropometric obesity indices in this specific patient group.

# **Materials And Methods**

This was a prospective study conducted between July 2021 and August 2022 at the endocrinology clinic of Harran University, School of Medicine. The local ethical committee authorized the study protocol in accordance with the Helsinki Declaration (approval No: 45391, 09 July 2021). Prior to data collection, each participant provided written informed consent.

# **Study Participants**

During our clinical routine, a prospective study was conducted on patients who consecutively and prospectively visited our obesity clinic due to their overweight status. Consequently, 190 non-diabetic patients with a body BMI  $\geq$ 30 kg/m<sup>2</sup> were included in the study. We excluded diabetic patients to eliminate any potential effects of diabetic dyslipidemia, such as elevated triglycerides, and the influence of medications used to treat diabetes on the TyG index and hepatosteatosis. None of the patients had a history of alcohol consumption. Subjects were also excluded if they: (1) had viral hepatitis, cirrhosis, or any other liver disease; (2) had a history of hypo- or hyperthyroidism; (3) were on lipid-lowering, antidiabetic, antihypertensive, or steroid replacement therapy; (4) were pregnant.

## **Physical Examinations and Laboratory Measurements**

We utilized standardized methods for anthropometric measurements. Patients' height and weight were measured with an accuracy of 0.1 cm and 0.1 kg, respectively, while they were wearing light clothing and without shoes. BMI was calculated by dividing the weight in kilograms by the square of height in meters (kg/m<sup>2</sup>). A plastic tape with an accuracy of 0.1 cm was used to measure WC, NC, and hip circumference (HC). The WHR was calculated as WC (cm) divided by HC (cm). All blood samples were drawn from the antecubital vein after an overnight fast. Laboratory investigations included fasting plasma glucose (FPG), fasting insulin, thyroid-stimulating hormone (TSH), alanine aminotransferase (ALT), hemoglobin A1c (A1C), and triglycerides (TG).

# Definitions

Obesity is defined as a BMI  $\geq$ 30 kg/m<sup>2</sup>. The abdominal ultrasound examination was conducted by a single-blinded experienced observer using the same EPIQ 7 diagnostic ultrasound system (Philips Healthcare, Andover, MA, USA) for all patients. Hepatic fat accumulation was classified into four grades (0, 1, 2, 3) based on the degree of liver echogenicity compared to the right kidney and the visualization of intrahepatic vessels and diaphragm.<sup>[20]</sup> Grades 1 to 3 were considered indicative of NAFLD, whereas grade 0 was considered normal. The HOMA-IR, TyG index, and modified TyG indices were calculated as follows:

HOMA–IR=(Fasting Insulin [ $\mu$ U/mL]×Fasting Plasma Glucose [mg/ dL]/405).<sup>[10]</sup>

TyG index=Ln [TG (mg/dL)×FPG (mg/dL)/2].<sup>[6]</sup> TyG-NC=TyG×NC, TyG-BMI=TyG×BMI, TyG-WC=TyG×WC, TyG-WHR=TyG×WHR.<sup>[12]</sup>

#### **Statistical Analysis**

Statistical analyses were conducted using SPSS (version 20.0, SPSS Inc., Chicago, IL, USA) and MedCalc Statistical Software version 20.116 (MedCalc Software, Ostend, Belgium). Depending on the distribution of the data, we calculated either the mean±standard devia-

tion or the median and interquartile range. Continuous variables were analyzed using independent samples t-tests or Mann-Whitney U tests based on their distribution. Categorical variables were compared using the Chi-square test. For comparisons among three or more groups with normally distributed data, an analysis of variance (ANOVA) was performed. In post-hoc analyses, Tukey's test was applied if homogeneity of variance was assumed; otherwise, the Brown Forsythe test was preferred, and the Tamhane T2 test was used for post-hoc analysis. The Kruskal-Wallis test was used when normality tests failed, and pairwise comparisons were made for subgroup analysis.

Since our study cohort had a low percentage of patients without steatosis, we conducted further analysis in two subgroups: those without severe steatosis (grades 0 and 1) and those with severe steatosis (grades 2 and 3). Receiver operating characteristic (ROC) curve analysis was used to predict severe steatosis, and areas under the curve (AUC) were determined and compared using the DeLong method. We constructed a two-sided 95% confidence interval (CI) to determine the relative risk around a point estimate. Finally, logistic regression analysis was employed to examine the TyG index, BMI, WC, and NC values in predicting severe steatosis. The variables were divided into four quartiles (Q1-Q4). As a reference group, Q1 was chosen, and odds ratios and 95% CIs were calculated by comparing all other groups to Q1. In this study, a p-value of <0.05 was considered statistically significant.

## Results

The study included 190 patients: 118 (62.1%) females and 72 (37.9%) males (p=0.001). The prevalence of NAFLD was 88.1% in females and 90.3% in males (p=0.648). Values of WC, NC, WHR, ALT, HOMA-IR, and TyG index were significantly higher in males than in females (TyG, p=0.001; p<0.001 for all other parameters). The baseline characteristics of participants according to their sex are summarized in Table 1. The results of an analysis of variance demonstrated that with increasing grades of hepatic steatosis, age, BMI, WC, NC, WHR, and ALT values increased significantly (p<0.001 for all). A significant positive correlation was also observed between the TyG index (p=0.004), HOMA-IR (p=0.001), and A1C (p=0.001) values and the grades of hepatic steatosis. The results further revealed that males had significantly higher grades of hepatic steatosis compared to females (p<0.001) (Table 2).

Table 3 summarizes the clinical and biochemical characteristics of patients with or without severe steatosis. It was found that 112 patients (58.9%) had severe steatosis, while 78 patients (41.1%) did not. The mean and/or median values of BMI, WC, NC, and ALT were significantly higher in the severe steatosis group (p<0.001 for all). The TyG index, HOMA-IR, WHR, and A1C values were also significantly increased in patients with severe steatosis (p=0.001, p=0.004, p=0.005, and p=0.002, respectively). Additionally, a higher prevalence of severe steatosis was observed in males than in females, and in older patients compared to younger ones (p=0.004 and p=0.023, respectively).

An analysis of the ROC curves and comparisons of the AUCs for each variable for predicting severe steatosis are presented in Table 4. Severe steatosis was significantly predicted by all variables (TyG index, p=0.001; HOMA-IR, p=0.003; WHR, p=0.003; other predictors in all subjects, p<0.001). Among the cut-off values for the prediction of severe steatosis, the TyG index was 8.76, WC was 119 cm, NC was 41 cm, WHR was 0.894, BMI was 37.4 kg/m<sup>2</sup>, HOMA-IR was 4.45, and ALT was 39 U/L. The highest AUC values for the detection of severe steatosis were found in TyG-WC and WC (0.795 and 0.782,

| Table 1. Baseline characteristics of subjects by sex |                    |                    |                  |                     |  |
|--|--------------------|--------------------|------------------|---------------------|--|
| Variables  | Total (n=180)      | Females (n=118)    | Males (n=72)     | р                   |  |
| Age (years)  | 38 (29–49)         | 40 (28–50)         | 35 (29–45)       | 0.142 <sup>b</sup>  |  |
| Sex (%)  |                    | 62.1               | 37.9             | 0.001 <sup>b</sup>  |  |
| BMI (kg/m <sup>2</sup> )                             | 40.0 (35.4–44.8)   | 40.0 (35.0–45.1)   | 39.9 (35.6–43.5) | 0.924 <sup>b</sup>  |  |
| WC (cm)  | 119.0(108.7–129.0) | 112.5(105.0-121.0) | 127.5 (118–134)  | <0.001 <sup>b</sup> |  |
| NC (cm)  | 40.0 (37.0–43.0)   | 38.0 (36.0–40.0)   | 43.0 (41.0–45.0) | <0.001 <sup>b</sup> |  |
| WHR  | 0.94 (0.87-1.03)   | 0.89 (0.84–0.94)   | 1.04 (1.02–1.06) | <0.001 <sup>b</sup> |  |
| FPG (mg/dL)  | 97 (92–104)        | 97 (92–105)        | 96 (91–101)      | 0.192 <sup>⊳</sup>  |  |
| HbA1c (%)  | 5.70 (5.30-6.02)   | 5.70 (5.20-6.00)   | 5.70 (5.60-6.10) | 0.033 <sup>b</sup>  |  |
| ALT (IU/L)   | 29 (22–42)         | 24 (21–32)         | 42 (33–58)       | <0.001 <sup>b</sup> |  |
| HOMA-IR  | 4.83 (3.67–6.60)   | 4.34(3.35-5.59)    | 6.07(4.32-7.59)  | <0.001 <sup>b</sup> |  |
| TyG index  | 8.92±0.51          | 8.82±0.51          | 9.08±0.47        | 0.001ª              |  |
| NAFLD, n (%)   | 169 (88.9)         | 104 (88.1)         | 65 (90.3)        | 0.648°              |  |

Data are expressed as the mean and standard deviation or the number (%) of patients or median (first and third quartile) values. P<0.05 was considered significant. Significant p values are highlighted in bold. <sup>a</sup>: Independent samples t-test; <sup>b</sup>: Mann-Whitney U test; <sup>c</sup>: Chi-square test. BMI: Body mass index; WC: Waist circumference; NC: Neck circumference; WHR: Waist-to-hip ratio; FPG: Fasting plasma glucose; HbA1c: Glycosylated hemoglobin; ALT: Alanine aminotransferase; HOMA-IR: Homeostatic model assessment of insulin resistance; TyG index: Triglyceride-glucose index; NAFLD: Non-alcoholic fatty liver disease.

| Table 2. Comparison of clinical and laboratory findings based on grade of hepatic steatosis |                                    |                                 |                               |                         |                     |  |
|---|------------------------------------|---------------------------------|-------------------------------|-------------------------|---------------------|--|
| Parameter   | Grade 0<br>n=21 (11.1%)            | Grade 1<br>n=57 (30%)           | Grade 2<br>n=82 (43.2%)       | Grade 3<br>n=30 (15.8%) | р                   |  |
| Age (years)   | 28.2±6.2 <sup>a**b***c***</sup>    | 40.1±12.7                       | 40.3±12.1                     | 41.8±11.2               | <0.001 <sup>£</sup> |  |
| Sex (F/M)   | 14/7°**                            | 44/13 <sup>e***f**</sup>        | 52/30                         | 8/22                    | <0.001#             |  |
| BMI (kg/m <sup>2</sup> )  | 32.94±2.10 <sup>a***b***c***</sup> | 38.95±5.49 <sup>d*e***</sup>    | 41.85±5.83                    | 44.59±7.58              | <0.001 <sup>£</sup> |  |
| WC (cm)   | 104.4±6.46 <sup>a**b***c***</sup>  | 114.1±10.9 <sup>d**e***</sup>   | 121.4±11.0 <sup>+***</sup>    | 131.4±13.1              | <0.001 <sup>£</sup> |  |
| NC (cm)   | 37.28±2.90 <sup>b**c***</sup>      | 38.45±3.16 <sup>d**e***</sup>   | 40.40±3.91 <sup>f***</sup>    | 43.83±3.47              | <0.001 <sup>£</sup> |  |
| WHR   | 0.93±0.08 <sup>c*</sup>            | 0.92±0.09e***                   | 0.95±0.10 <sup>f*</sup>       | 1.00±0.06               | <0.001 <sup>£</sup> |  |
| HOMA-IR   | 4.04 (3.19–5.02)°***               | 4.14(3.47–6.03) <sup>e**</sup>  | 5.10 (3.66–6.55) <sup>+</sup> | 6.34 (4.90-7.63)        | 0.001 <sup>×</sup>  |  |
| TyG index   | 8.66±0.64 <sup>c*</sup>            | 8.80±0.55e*                     | 8.99±0.43                     | 9.14±0.43               | 0.004 <sup>£</sup>  |  |
| FPG (mg/dL)   | 94 (91–99)                         | 97 (91–104)                     | 97 (92–106)                   | 97 (92–104)             | 0.399 <sup>×</sup>  |  |
| ALT (IU/L)  | 24 (18–30) <sup>b**c***</sup>      | 24 (21–34) <sup>d**e***</sup>   | 31 (23–44) <sup>r***</sup>    | 42 (39–58)              | <0.001 <sup>×</sup> |  |
| HbA1c (%)   | 5.60 (5.20-5.70) <sup>b*c***</sup> | 5.70 (5.25-5.90) <sup>e**</sup> | 5.70 (5.40–6.10) <sup>+</sup> | 5.90 (5.70-6.30)        | 0.001 <sup>×</sup>  |  |

Data are expressed as the mean and standard deviation or the number (%) of patients or median (first and third quartile) values. P<0.05 was considered significant. Significant p values are highlighted in bold. The definition of post hoc analysis: a: Between grade 0 and 1; b: Between grade 0 and 2; c: between grade 0 and 3; d: Between grade 1 and 2; c: between grade 1 and 3; f: Between grade 2 and 3; f: P value between 0.05-0.01, \*\*: P value between 0.01-0.001; \*\*\*: P<0.001; \*: Kruskal-Wallis test; c: One-way ANOVA; #: Chi-square test. BMI: Body mass index; WC: Waist circumference; NC: Neck circumference; WHR: Waist-to-hip ratio; HOMA-IR: Homeostatic model assessment of insulin resistance; TyG index: Triglyceride-glucose index; FPG: Fasting plasma glucose; ALT: Alanine aminotransferase; HbA1c: Glycosylated hemoglobin.

respectively). Based on the AUC comparisons, WC and ALT values were statistically superior to the TyG index in predicting severe steatosis (p=0.006 and p=0.049, respectively).

Pairwise comparisons with other indexes were conducted to determine the performance of NC and the proposed modified TyG index (TyG-NC) in predicting severe steatosis (Table 5). Although WC (0.782) had a higher AUC value than NC (0.725), this difference was not statistically significant (p=0.073). However, when modified with the TyG index, TyG-WC was found to be superior to TyG-NC in predicting severe steatosis (p=0.033).

Finally, we divided the variables into quartiles and applied logistic regression analysis to measure the odds ratio of anthropometric obesity indices and the TyG index in predicting severe steatosis. WC mea-

sures had the highest odds ratios (95% CIs), 2.91 (1.25-6.79), 8.48 (3.28-21.90), and 23.91 (7.67-74.52) for subjects in the second, third, and fourth quartiles, respectively, when compared with the first quartile. In Table 6, we summarize the odds ratios (95% CIs) according to the quartiles for each of the parameters.

# Discussion

In this study, we found that the TyG index and modified TyG indices such as TyG-BMI, TyG-WC, TyG-WHR, and TyG-NC were significantly associated with the presence and severity of NAFLD. The TyG-NC was evaluated for the first time as a novel modified TyG index. In terms of predicting NAFLD and its severity, modified TyG indices performed better than the TyG index alone. Further, TyG-WC signifi-

| Table 3. Clinical and biochemical characteristics of patients with and without severe fatty liver |                            |                          |                     |  |  |
|---|----------------------------|--------------------------|---------------------|--|--|
| Parameters  | No severe steatosis (n=78) | Severe steatosis (n=112) | р                   |  |  |
| Age (years)   | 33.5 (27.0–45.0)           | 39 (30–51)               | 0.023 <sup>⊳</sup>  |  |  |
| Sex (F/M)   | 58/20                      | 60/52                    | 0.004°              |  |  |
| BMI (kg/m <sup>2</sup> )  | 36.0 (33.0–40.6)           | 41.5 (38.0–46.0)         | <0.001 <sup>b</sup> |  |  |
| WC (cm)   | 109.5 (102.0–119.0)        | 124.0(114.2–132.0)       | <0.001 <sup>b</sup> |  |  |
| NC (cm)   | 38.14±3.11                 | 41.32±4.07               | <0.001ª             |  |  |
| WHR   | 0.90 (0.85–1.02)           | 0.97 (0.89–1.04)         | 0.005 <sup>⊾</sup>  |  |  |
| HOMA-IR   | 4.07 (3.43–5.89)           | 5.39 (3.97-6.91)         | 0.004 <sup>b</sup>  |  |  |
| TyG index   | 8.76±0.57                  | 9.03±0.44                | 0.001ª              |  |  |
| ALT (IU/L)  | 24.0 (19.0–32.0)           | 36.0 (25.0–50.5)         | <0.001 <sup>b</sup> |  |  |
| FPG (mg/dL)   | 95 (91–103)                | 97 (92–105)              | 0.207 <sup>b</sup>  |  |  |
| HbA1C (%)   | 5.65 (5.20-5.80)           | 5.80 (5.50-6.20)         | 0.002 <sup>b</sup>  |  |  |
| TyG–BMI   | 310.4 (289.1–361.9)        | 376.0 (342.1–414.8)      | <0.001 <sup>b</sup> |  |  |
| TyG-WC  | 979.1±121.9                | 1121.8±129.5             | <0.001ª             |  |  |
| TyG-NC  | 334.9±39.6                 | 373.6±44.5               | <0.001ª             |  |  |
| TyG-WHR   | 8.12±1.09                  | 8.73±1.08                | <0.001ª             |  |  |

Table 3. Clinical and biochemical characteristics of patients with and without severe fatty liver

Data are expressed as the mean and standard deviation or the number (%) of patients or median (first and third quartile) values. P<0.05 was considered significant. Significant p values are highlighted in bold. <sup>a</sup>: Independent samples t-test; <sup>b</sup>: Mann-Whitney U test; <sup>c</sup>: Chi-square test. BMI: Body mass index; WC: Waist circumference; NC: Neck circumference; WHR: Waist-to-hip ratio; HOMA-IR: Homeostatic model assessment of insulin resistance; TyG index: Triglyceride-glucose index; ALT: Alanine aminotransferase; FPG: Fasting plasma glucose; HbA1c: Glycosylated hemoglobin.

| Table 4. ROC curve analysis and pairwise compariso | n of the AUCs for each variable for predicting severe steatosis |
|--|---|
|--|---|

| Parameter                | Cut-Off        | Sensitivity | Specificity  | AUC   | 95% CI      | р      |
|--------------------------|----------------|-------------|--------------|-------|-------------|--------|
| TyG-WC                   | >1071.6        | 69.64       | 78.21        | 0.795 | 0.730–0.850 | <0.001 |
| WC (cm)                  | >119.0         | 65.18       | 79.49        | 0.782 | 0.716–0.838 | <0.001 |
| TyG-BMI                  | >326.5         | 88.39       | 58.97        | 0.775 | 0.709–0.832 | <0.001 |
| ALT (IU/L)               | >39.0          | 43.75       | 92.31        | 0.744 | 0.676-0.805 | <0.001 |
| BMI (kg/m <sup>2</sup> ) | >37.4          | 79.46       | 61.54        | 0.742 | 0.673-0.802 | <0.001 |
| TyG-NC                   | >345.8         | 72.32       | 66.67        | 0.740 | 0.672-0.801 | <0.001 |
| NC (cm)                  | >41.0          | 49.11       | 87.18        | 0.725 | 0.656-0.787 | <0.001 |
| TyG-WHR                  | >8.31          | 66.96       | 58.97        | 0.656 | 0.583–0.723 | <0.001 |
| TyG index                | >8.76          | 77.68       | 55.13        | 0.640 | 0.568-0.709 | 0.001  |
| HOMA-IR                  | >4.45          | 68.75       | 61.54        | 0.624 | 0.551-0.693 | 0.003  |
| WHR                      | >0.894         | 75.89       | 47.44        | 0.620 | 0.547–0.689 | 0.003  |
| Pairwise comparison      | Difference AUC |             | 95% CI       |       | р           |        |
| WC vs. TyG               | 0.141          |             | 0.039–0.243  |       | 0.006       |        |
| NC vs. TyG               | 0.084          |             | -0.015–0.185 |       | 0.098       |        |
| WHR vs. TyG              | 0.020          |             | -0.082–0.123 |       | 0.697       |        |
| BMI vs. TyG              | 0.101          |             | -0.011-0.214 |       | 0.077       |        |
| HOMA-IR vs. TyG          | 0.016          |             | -0.080-0.114 |       | 0.338       |        |
| ALT vs. TyG              | 0.104          |             | 0.000-0.208  |       | 0.049       |        |
| TyG-WC vs. TyG           | 0.154          |             | 0.078-0.230  |       | <0.001      |        |
| TyG-NC vs. TyG           | 0.099          |             | 0.031-0.168  |       | 0.004       |        |
| TyG-BMI vs. TyG          | 0.135          |             | 0.043-0.226  |       | 0.003       |        |
| TyG-WHR vs. TyG          | 0.015          |             | -0.059–0.089 |       | 0.692       |        |

P<0.05 was considered significant. Significant p values are highlighted in bold. ROC: Receiver operating characteristic; AUC: area under the curve; CI: Confidence interval; WC: Waist circumference; ALT: Alanine aminotransferase; BMI: Body mass index; NC: Neck circumference; WHR: Waist-to-hip ratio; TyG index: Triglyceride-glucose index; HOMA-IR: Homeostatic model assessment of insulin resistance.

**Table 5.** Pairwise comparison of AUCs of the proposed modified TyG index (TyG-NC) with other indices in predicting severe steatosis

| Pairwise comparison | Difference<br>AUC | 95% CI       | р     |
|---------------------|-------------------|--------------|-------|
| WC vs. NC           | 0.056             | 0.039–0.243  | 0.073 |
| TyG-WC vs. TyG-NC   | 0.054             | -0.015–0.185 | 0.033 |
| BMI vs. NC          | 0.016             | -0.082-0.123 | 0.689 |
| TyG-BMI vs. TyG-NC  | 0.034             | -0.011–0.214 | 0.333 |
| WHR vs. NC          | 0.105             | -0.080-0.114 | 0.020 |
| TyG-WHR vs. TyG-NC  | 0.084             | 0.000-0.208  | 0.020 |

P<0.05 was considered significant. Significant p values are highlighted in bold. AUC: area under the curve; TyG index: Triglyceride-glucose index; WC: Waist circumference; NC: Neck circumference; CI: Confidence interval; BMI: Body mass index; WHR: Waist-to-hip ratio.

cantly outperformed the other parameters in predicting severe steatosis with the largest AUC of 0.795. Considering that both the TyG index and obesity were associated with IR, it was not surprising that the combination of these two variables provided stronger predictions. In predicting severe hepatosteatosis, NC was found to be the third most effective anthropometric obesity index after WC and BMI. Additionally, the TyG-NC index was found to be the third most effective modified TyG index, following TyG-WC and TyG-BMI. On the other hand, we found that the TyG index was not superior to simple anthropometric obesity indices for predicting NAFLD and its severity in this specific group of patients.

The TyG index was initially introduced as a surrogate for the identification of IR.<sup>[7,8]</sup> Similarly, we found a significant positive correlation between HOMA-IR and the TyG index in the Pearson correlation analysis (r=0.342, p<0.001) (data not shown). Additionally, several subsequent studies have demonstrated that the TyG index is a reliable, practical, and cost-effective method for identifying individuals at risk of NAFLD.<sup>[9–12]</sup> In the presence of IR, there is an increase in de novo lipogenesis in the liver and ineffective suppression of lipolysis in the adipose tissue. Thus, the high level of circulating fatty acids can disrupt insulin signaling pathways and lead to hepatic IR and steatosis.<sup>[21]</sup> Moreover, IR causes adipose tissue dysfunction and triggers the release of inflammatory cytokines and adipokines from adipose tissue.<sup>[22]</sup> In support of these data, a study involving 263 patients with biopsy-proven NAFLD showed that patients with IR experienced more severe steatosis than those without IR.<sup>[23]</sup>

A growing number of studies have investigated the role of the TyG index in predicting NAFLD. However, the majority were retrospective and conducted on general populations.<sup>[24,25]</sup> There are only a few studies examining the TyG index for predicting NAFLD in patients with obesity. In two retrospective studies examining liver biopsy samples from obese patients undergoing bariatric surgery, the TyG index has been found to be strongly associated with NAFLD. In these studies, patients with diabetes were also included, and the frequency of NAFLD was found to be 67% and 90%, respectively.<sup>[26,27]</sup> In our study, patients with diabetes were excluded, and the results showed that 88.9% of patients had NAFLD. This is in line with previous studies that report the prevalence of NAFLD ranging from 65% to 95% in obese individuals, which varies depending on the degree of obesity. <sup>[26-29]</sup> The number of female patients (n=118) in our study was higher than the number of males (n=72) (p=0.001). In our opinion, this is due

**Table 6.** Odds ratios for severe liver steatosis in quartiles of

 TyG index and anthropometric obesity indices

| BMI (kg/m²) <0.0                                 | 01 |
|--|----|
| 1 <sup>st</sup> Q Ret                            |    |
| 2 <sup>nd</sup> Q 0.867 2.379 1.058–5.350 0.03   | 6  |
| 3 <sup>rd</sup> Q 1.889 6.613 2.583-16.935 <0.0  | 01 |
| 4 <sup>th</sup> Q 2.066 7.893 3.116–19.997 <0.0  | 01 |
| WC (cm) <0.0                                     | 01 |
| 1 <sup>st</sup> Q Ref                            |    |
| 2 <sup>nd</sup> Q 1.070 2.917 1.253-6.792 0.01   | 3  |
| 3 <sup>rd</sup> Q 2.138 8.485 3.287-21.901 <0.0  | 01 |
| 4 <sup>th</sup> Q 3.175 23.917 7.675–74.528 <0.0 | 01 |
| NC (cm) <0.0                                     | 01 |
| 1 <sup>st</sup> Q Ref                            |    |
| 2 <sup>nd</sup> Q 0.457 1.579 0.738–3.377 0.23   | 9  |
| 3 <sup>rd</sup> Q 1.150 3.158 1.335-7.472 0.00   | 9  |
| 4 <sup>th</sup> Q 2.885 17.895 4.814–66.513 <0.0 | 01 |
| TyG index 0.00                                   | 2  |
| 1 <sup>st</sup> Q Ref                            |    |
| 2 <sup>nd</sup> Q 1.085 2.961 1.284-6.828 0.01   | 1  |
| 3 <sup>rd</sup> Q 1.619 5.048 2.095–12.163 <0.0  | 01 |
| 4 <sup>th</sup> Q 1.290 3.633 1.544–8.548 0.00   | 3  |

OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; WC: Waist circumference; NC: Neck circumference: TyG index: Triglyceride-glucose index.

to the fact that females complain about their excess weight more often and therefore apply to obesity clinics more frequently. Even though their mean BMI was not different, males had significantly higher measurements of WC, NC, and WHR than females. This may be explained by differences in fat distribution between males and females, specifically apple-shaped (abdominal pattern) obesity in males versus pearshaped (gluteal–femoral pattern) obesity in females.<sup>[30]</sup> Furthermore, males exhibited more severe steatosis and had higher TyG index, HO-MA-IR, and ALT values than females. The abdominal pattern of obesity and the higher IR levels in male patients may explain the higher grades of hepatic steatosis and higher ALT values.<sup>[30,31]</sup>

In recent years, modified TyG indices have been studied more extensively and are reported to provide better predictions for IR and related conditions.<sup>[12-16]</sup> Lim et al.<sup>[12]</sup> examined TyG-WC, TyG-BMI, and TyG-WHtR (waist-to-height ratio) for predicting IR and concluded that TyG-BMI had better predictive power than other combined indices and the TyG index alone. In another study by Er et al.,<sup>[13]</sup> TyG-BMI and TyG-WC were found to provide better AUCs for the prediction of IR compared with lipid parameters, lipid ratios, adipokines, visceral obesity indicators, and the TyG index alone. Several further studies have demonstrated that modified TyG indices (TyG-BMI, TyG-WC, and TyG-WHR) are superior at predicting NAFLD than the TyG index alone.<sup>[14-16]</sup> Similarly, in our study, TyG-WC and WC were found to be the two variables with the highest AUC in predicting severe steatosis (0.795 and 0.782, respectively). Our study findings were also supported by a cross-sectional study of 12,757 Korean adults, which found that the TyG-WC index showed a stronger association with NAFLD severity than other modified TyG indices (AUC=0.848 (0.840-0.855).[17]

Our study differs from other existing studies in the following ways: first, all of our participants had a BMI  $>30 \text{ kg/m}^2$ ; second, diabetic patients were excluded; and thirdly, considering the low percentage of patients without steatosis, we conducted further analyses between patients with and without severe steatosis.

To date, despite some evidence of the effectiveness of the TyG index in predicting NAFLD, there are no studies that specifically compare the TyG index with anthropometric obesity indices in obese individuals. For this reason, we specifically compared the TyG index with simple obesity indices, ALT, and HOMA-IR levels. When the TyG index was compared with BMI, WHR, NC, and HOMA-IR, the AUC values did not differ significantly. However, the AUC values of WC and ALT provided better predictions of severe steatosis than the TyG index (0.782, 0.744, and 0.640, respectively). As a final step, odds ratios and 95% CIs were calculated for each parameter and compared to quartile 1. It was found that WC measurements provided the highest odds ratio for predicting severe steatosis, followed by NC, BMI, and TyG index, respectively.

# **Study Limitations**

The limitation of our study is that it was a single-center study with a relatively small sample size. To confirm our findings, multicenter, prospective studies with a large number of patients are needed. As another limitation of the study, abdominal ultrasound was used instead of liver biopsy for the diagnosis of NAFLD. However, liver biopsy is unrealistic to use for screening NAFLD in the general population. Currently, abdominal ultrasound is considered the most cost-effective and feasible screening method for steatosis in the general population.<sup>[22]</sup> Furthermore, hepatic elastography using Fibroscan appears to be more effective than ultrasonography in detecting hepatic steatosis and fibrosis.<sup>[32,33]</sup> However, we could not apply it since it was not available in our center.

# Conclusion

In conclusion, the TyG index and modified TyG indices are highly effective in predicting the severity of NAFLD. Despite this, we found that the TyG index alone was not superior to simple anthropometric obesity indices as a predictor of NAFLD severity in non-diabetic obese individuals.

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