Cardiometabolic risk in non-diabetic metabolic dysfunction-associated steatotic liver disease (MAFLD) patients: insights from the triglyceride-glucose, plasma atherogenic, and cardiometabolic index

Sedat Ciftel[1], Serpil Çiftel[2]*, Ahmed R. Baykan[1], Serkan Cerrah[1], Enver Çiftel[3], Filiz Mercantepe[4]

[1]Department of Gastroenterology, Erzurum Training and Research Hospital, Erzurum, Turkey
[2]Department of Endocrinology and Metabolism, Erzurum Training and Research Hospital, Erzurum, Turkey
[3]Department of Endocrinology and Metabolism, Sivas Numune Hospital, Sivas, Turkey
[4]Department of Endocrinology and Metabolism, Rize Recep Tayyip Erdoğan University, Rize, Turkey

***Corresponding author:**
Asst. Prof. Serpil Çiftel
Erzurum Training and Research Hospital
Turkey
E-mail: serpilim2008@hotmail.com

Submitted: 11 June 2024; **Accepted:** 7 July 2024
Online publication: 25 July 2024

Arch Med Sci 2025; 21 (2): 401–408
DOI: https://doi.org/10.5114/aoms/190867

Abstract

Introduction: The objective of our study was to examine the correlation between hepatosteatosis and the triglyceride-glucose index (TyG), plasma atherogenic index (PAI), and cardiometabolic index (CMI) in nondiabetic patients. We also aimed to assess the usefulness of these indices in evaluating cardiometabolic risk in metabolic dysfunction-associated steatotic liver disease (MAFLD).

Material and methods: This retrospective cross-sectional study included 695 individuals who did not have diabetes, with an average age of 39.8 ±11.3 years. A total of 595 individuals, comprising 359 women and 236 men, were diagnosed with MAFLD. The control group consisted of 100 individuals who did not have MAFLD. All the subjects underwent transabdominal ultrasonography, anthropometric measurements, and blood analyses. The groups were assessed based on the TyG index, PAI, and CMI.

Results: TyG, PAI, and CMI were greater in patients with MAFLD than those without MAFLD. The TyG index, with a cutoff point of 8.47, excluded significant simple steatosis with a sensitivity of 65.3% and a specificity of 66.0%. The PAI and CMI cutoff values were 0.39 and 1.40, with sensitivities of 66.6% and 70.1% and specificities of 67.0% and 70.1%, respectively. The TyG index was independently associated with MAFLD (OR = 2.21, 95% CI: 1.339–3.665).

Conclusions: The presence of MAFLD patients with a normal BMI and waist circumference indicates that these variables alone do not provide enough evidence for the diagnosis of MAFLD. Hence, it is advisable to incorporate the TyG index, the PAI, and the CMI into regular clinical practice to obtain a more precise and thorough evaluation of MAFLD and cardiometabolic risk.

Key words: metabolic dysfunction-associated steatotic liver disease, cardiometabolic risk, cardiometabolic index, triglyceride-glucose index, plasma atherogenic index.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is a condition characterized by fatty liver without significant alcohol consumption [1, 2]. Although the prevalence of this condition may differ among societies, it is increasingly becoming a global issue, impacting approximately one out of every 3–4 individuals worldwide and showing a steady rise [3–5]. Its prevalence is approximately 70% in the diabetic population and 38% in the general population [6, 7]. Additionally, the current population-based prevalence of NAFLD is approximately 30–40% in males and 15–20% in females [8]. NAFLD can often be asymptomatic, but it can also be a progressive disease process that can lead to serious liver diseases such as steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma [9, 10]. The development of NAFLD involves various mechanisms, including insulin resistance, oxidative stress, disruption of lipid metabolism, and inflammation [11]. In recent years, increasing evidence has shown that fatty liver disease is a multisystem disease that not only increases liver-related morbidity and mortality but also has adverse effects on extrahepatic organs [4]. Metabolic syndrome (MS) is closely related to obesity, dyslipidemia, hypertension (HT), and type 2 diabetes mellitus (DM) [4, 12]. Also the risk of atherosclerotic cardiovascular disease, which is the main cause of death, is increased in these patients [13].

NAFLD can have profound effects on metabolic health. For this reason, a new term, "metabolic dysfunction-associated steatotic liver disease (MAFLD)", rather than NAFLD, was first proposed by a multisociety consensus in 2020 to refer to fatty liver disease that occurs due to metabolic disorders [14]. For the diagnosis of MAFLD, the presence of at least one of five cardiometabolic risk factors is required in patients with liver steatosis who do not exceed the daily alcohol intake limit (> 20–30 g/day for females and males, respectively).

The diagnostic criteria for MAFLD in adults [14, 15] are as follows:

1. Boddy mass index (BMI) ≥ 25 kg/m^2 or waist circumference (WC) > 94 cm (male), 80 cm (female), or ethnicity-adjusted equivalent;
2. Fasting plasma glucose (FPG) ≥ 100 mg/dl, glycosylated hemoglobin (HbA_{1c}) ≥ 5.7% or type 2 DM;
3. Blood pressure ≥ 130/85 mm Hg or specific antihypertensive drug treatment;
4. Plasma triglyceride (TG) ≥ 150 mg/dl or lipid-lowering treatment;
5. Plasma high-density lipoprotein (HDL)-cholesterol ≤ 40 mg/dl (male), ≤ 50 mg/dl or lipid-lowering treatment.

MAFLD is a more comprehensive variant of NAFLD and is linked to metabolic dysfunction. This revised definition may enhance the ability to evaluate and handle patients by offering a more comprehensive outlook on clinical practice. When diagnosing and treating MAFLD, it is crucial to consider metabolic risk factors. This technique enables a more precise evaluation and control of patients' cardiometabolic risks.

The triglyceride-glucose index (TyG index) has become increasingly accepted as an indicator of insulin resistance in the healthy nondiabetic population. The TyG index is calculated from triglyceride and fasting glucose levels. It offers a more convenient and cost-effective alternative to other methods used in insulin resistance assessments. A high TyG index plays a predictive role for diseases such as diabetes mellitus [16], coronary artery disease [17, 18], and atherosclerosis [19]. It is a strong determinant of cardiovascular mortality in diabetic and prediabetic patients [20]. Since dyslipidemia is a significant risk factor for both hepatosteatosis and cardiovascular diseases, we need cost-effective alternatives in clinical practice to effectively predict diseases such as hepatosteatosis that pose metabolic risks, especially cardiovascular events. The plasma atherogenic index (PAI), a new quantitative index used to evaluate lipid levels, is a strong marker of dyslipidemia [21]. The cardiometabolic index (CMI) is a recently developed index based on TG/HDL-C and waist-height ratio (WHtR) values that can be easily obtained during health checks. Multiple key metabolic indicators that comprise the CMI also contribute to the development of fatty liver disease [22]. For this reason, the relationships between the TyG index and MAFLD, along with the PAI and CMI, which are other indicators of cardiovascular mortality, have emerged as essential research topics. Therefore, investigating whether the TyG index is associated with the severity of hepatosteatosis is critical for developing new approaches for the management of these patients. Although previous studies have investigated the effects of insulin resistance and related biomarkers on diabetic fatty liver, studies explicitly investigating the TyG index are limited in nondiabetic patients.

The objective of this study was to analyze the TyG index, PAI, and CMI in nondiabetic patients with MAFLD and to estimate the significance of these indices in diagnosing MAFLD and evaluating cardiometabolic risk. The objective in this context is to incorporate these indices into regular clinical practice to enable early detection of MAFLD and enhance the management of cardiometabolic risks.

Materials and methods

Participants and study design

Six hundred ninety-five nondiabetic individuals aged ≥ 18 years participated in this single-center

retrospective study. Our study population consisted of 595 patients with MAFLD (359 females, 236 males). Of these, 271 patients had grade 1 hepatosteatosis (HS), 214 had grade 2 HS, and 110 had grade 3 HS. The control group included 100 subjects of the same age (38.47 ±12) without HS. All the volunteers had undergone transabdominal ultrasonography (US) scanning, in which the liver's echogenicity was increased compared to that of the renal cortex [23]. US was performed by a single experienced radiologist. The degree of hepatosteatosis was classified into three grades based on echogenicity and the visibility of intrahepatic structures. The patients were categorized into three groups according to their HS grade. The diagnosis of MAFLD was established using the 2020 International Consensus criteria [14]. The study excluded individuals with a known history of DM, cardiovascular disease, other chronic liver diseases, those who consumed more than 20–30 g of alcohol per day, pregnant and breastfeeding women, and patients under 18 years of age and over 65 years of age. DM was defined as an FPG > 125 mg/dl, an HbA_{1c} > 6.5%, a previous diagnosis of diabetes, or the use of any antidiabetic medication. No separate oral glucose tolerance test (OGTT) was conducted to diagnose DM.

Peripheral venous blood samples were taken after 8 h of overnight fasting to assess the serum levels of glucose, TG, HDL, low-density lipoprotein (LDL) cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and γ-glutamyl transferase (GGT). BMI was defined as weight (kg)/height (m^2) [24]. WC was measured from the midpoint between the lowest rib and the anterior-superior iliac crests with a nonelastic flexible tape measure by the same trained health personnel.

The following formulas were used for calculating lipid-related indices: The TyG index was calculated using TyG = Ln (TG (mg/dl) × FPG (mg/dl)/2 [20, 25]. The PAI was calculated as follows: PAI = log(TG/HDL-C) [25]. The CMI was calculated as follows: CMI = TG/HDL-C × WHtR (WHtR = waist circumference/height) [26].

Statistical analysis

Statistical analysis was performed using the IBM Statistics (SPSS) software, version 22 (IBM Corp., Armonk, NY). The distribution of the variables was assessed using the Kolmogorov-Smirnov test. The independent *t* test and one-way ANOVA were used to compare normally distributed data. The Mann-Whitney *U* and Kruskal-Wallis tests were used to compare groups with nonnormally distributed parameters. The Dunn-Bonferroni post hoc correction was used for pairwise comparisons. The normally distributed data between groups are presented as the mean ± standard deviation. The nonnormally distributed data are presented as medians and quartiles. Comparisons between categorical variables were made using the χ^2 test. Correlation analysis and logistic regression analysis were performed to evaluate the relationships between categorical and continuous independent variables and dependent variables. Receiver operating characteristic (ROC) curve analysis was performed to determine whether continuous variables can be used in diagnosis and to determine cutoff values. A binary logistic regression analysis was conducted to investigate the effects of common variables in a mixed model for patients with and without hepatosteatosis. The level of statistical significance was set at $p < 0.05$.

Results

Table I shows the initial characteristics and laboratory measurements of the subjects. The BMI and WC of the patient group with HS were greater than those of the group without HS. There was no statistically significant difference in the BMIs of individuals with grade 1, 2, or 3 hepatosteatosis. The TyG index, PAI, and CMI of the group without HS were significantly lower than those of the group with HS ($p < 0.001$). In addition, as the HS grade increased, the values of these three parameters increased significantly. The ALT/AST ratio and triglyceride level were found to be significantly lower in the non-HS group ($p < 0.001$).

Table II presents the results of the ROC analysis conducted to investigate the contributions of the TyG, PAI, and CMI indices in differentiating hepatosteatosis and to establish the threshold values. The analytical results indicated that TyG (AUC ± SE; 95% CI: 0.729 ±0.028; 0.674–0.785), PAI (AUC ± SE; 95% CI: 0.748 ±0.027; 0.694–0.801), and CMI (AUC ± SE; 95% CI: 0.779 ±0.027; 0.726–0.831) have the potential to be utilized for the identification of hepatosteatosis. The TyG index, using a cutoff point of 8.47, effectively ruled out the presence of severe simple steatosis, with a sensitivity of 65.3% and a specificity of 66.0%. The PAI, with a cutoff point of 0.39, effectively ruled out the presence of severe simple steatosis, with a sensitivity of 66.6% and a specificity of 67.0%. CMI, with a threshold of 1.40, effectively ruled out cases of significant steatosis, with a sensitivity of 70.1% and specificity of 70.1%.

In Table III, a binary logistic regression analysis was performed to examine the impact of common factors in a mixed model, which included TyG index, the ALT/AST ratio, and WC. The analysis yielded a specificity of 40.4 and a sensitivity of 96.7. The analytical results indicate that in the TyG index model (B ± SE; 1.186 ±0.271, OR = 3.273, $p < 0.001$), age (B ± SE; –0.007 ±0.012, OR = 0.993, $p = 0.575$),

Table I. Baseline characteristics and laboratory parameters of participants

Parameter	No HS (*n* = 100)	Grade 1 HS (*n* = 271)	Grade 2 HS (*n* = 214)	Grade 3 HS (*n* = 110)	*P*-value (*n* = 695)
Age [years]	38.47 ±12	38.87 ±11.3	41.01 ±10.9	41.28 ±11.0	0.057
Gender, *n* (%)					
Female	81 (81)	200 (73.8)	111 (51.9)	48 (43.6)	< 0.001
Male	19 (19)	71 (26.2)	103 (48.1)	62 (56.4)	
BMI [kg/m^2]	25.3 (20.5–40.4)	31.2 (17.9–52.7)	33.9 (18.1–57)	32.1 (18.3–56.1)	< 0.001* 0–1 ≤ 0.001 0–3 ≤ 0.001 0–2 ≤ 0.001
WC [cm]	86 (7–126)	98 (65–136)	108 (67–140)	109 (64–149)	0.001* 0–3 = 0.001 0–2 ≤ 0.001 0–1 = 0.001 1–3 = 0.001 1–2 ≤ 0.001
WHtR	0.52 (0.42–0.75)	0.60 (0.38–0.83)	0.64 (0.38–0.90)	0.64 (0.39–0.91)	< 0.001* 0–3 ≤ 0.001 0–2 ≤ 0.001 0–1 ≤ 0.001 1–3 = 0.036 1–2 = 0.001
Glucose [mg/dl]	87 (65–154)	88 (57–160)	93 (57–141)	93 (57–141)	< 0.001* 1–3 = 0.041 1–2 = 0.001 0–3 = 0.007 0–2 ≤ 0.001
Triglyceride [mg/dl]	86 (31–240)	116 (43–433)	133 (33–500)	177 (50–680)	< 0.001* 0–3 ≤ 0.001 0–2 ≤ 0.001 0–1 ≤ 0.001 1–3 ≤ 0.001 1–2 = 0.044 2–3 = 0.004
HDL [mg/dl]	48 (29–78)	42 (23–77)	40 (21–94)	39 (22–77)	< 0.001* 0–3 ≤ 0.001 0–2 ≤ 0.001 0–1 ≤ 0.001 1–3 = 0.001
LDL [mg/dl]	110 (40–196)	121 (53–245)	129 (43–258)	128 (49–226)	0.002* 0–2 = 0.001
ALT [U/l]	25 (10–200)	22 (9–229)	31 (9–194)	31 (8–310)	< 0.001* 1–3 = 0.007 1–2 ≤ 0.001 0–3 ≤ 0.001 0–2 ≤ 0.001
AST [U/l]	25 (10–190)	19 (8–130)	23 (5–200)	24 (5–184)	< 0.001* 1–3 = 0.001 1–2 ≤ 0.001 0–1 ≤ 0.001
ALT/AST	1.00 (0.58–2.70)	1.31 (0.46–3.67)	1.53 (0.47–4)	1.47 (0.45–4)	< 0.001* 0–1 ≤ 0.001 0–2 = 0.001 0–3 = 0.001 1–2 = 0.001
GGT [U/l]	30 (10–230)	20 (3–197)	28 (9–255)	30 (9–271)	0.001* 1–3 = 0.000 1–2 = 0.000 1–0 = 0.000

Table I. Cont.

Parameter	No HS (*n* = 100)	Grade 1 HS (*n* = 271)	Grade 2 HS (*n* = 214)	Grade 3 HS (*n* = 110)	*P*-value (*n* = 695)
TyG index	8.24 ±0.52	8.62 ±0.48	8.77 ±0.56	8.99 ±0.56	< 0.001* 0–1 ≤ 0.001 0–2 ≤ 0.001 0–3 ≤ 0.001 1–2 = 0.010 1–3 ≤ 0.001 2–3 = 0.003
AIP	0.27 ±0.24	0.46 ±0.23	0.52 ±0.27	0.65 ±0.27	< 0.001* 0–1 = 0.030 0–2 = 0.031 0–3 = 0.035 1–2 = 0.023 1–3 = 0.028 2–3 = 0.030
CMI	0.89 (0.29–5.90)	1.58 (0.42–8.89)	2.01 (0.24–8.50)	2.87 (0.53–16.9)	0.000* 0–1 ≤ 0.001 0–2 ≤ 0.001 0–3 ≤ 0.001 1–2 = 0.004 1–3 ≤ 0.001 2–3 = 0.008

HS – hepatosteatosis, BMI – body mass index, WC – waist circumference, WHtR – waist-height ratio, ALT – alanine aminotransferase, AST – aspartate aminotransferase, GGT – γ-glutamyl transferase, HDL-C – high-density lipoprotein cholesterol, LDL-C – low-density lipoprotein cholesterol, TyG – triglyceride-glucose index, AIP – atherogenic index of plasma, CMI – cardiometabolic index.

Table II. Analysis of ROC curve results of TyG, AIP, and CMI for MAFLD

Variables	AUC ± SE (95% CI)	*P*-value	Cut-off value	Sensitivity (%)	Specificity (%)
TyG	0.729 ±0.028 (0.674–0.785)	< 0.001*	8.47	65.3	66.0
AIP	0.748 ±0.027 (0.694–0.801)	< 0.001*	0.39	66.6	67.0
CMI	0.779 ±0.027 (0.726–0.831)	< 0.001*	1.40	70.1	70.1

AUC – area under the ROC curve, CI 95% – confidence interval, MAFLD – metabolic dysfunction-associated steatotic liver disease, TyG – triglyceride-glucose index, AIP – atherogenic index of plasma, CMI – cardiometabolic index.

Table III. Logistic regression analysis of participants in terms of hepatosteatosis presence in a mixed model

Parameters	B ± S.E	OR	95% CI Lower-upper	*P*-value
TyG	1.186 ±0.271	3.27	1.925–5.564	< 0.001*
BMI	0.149 ±0.037	1.16	1.079–1.247	< 0.001*
Age	–0.007 ±0.012	1.160	0.971–1.017	0.575
ALT/AST ratio	1.798 ±0.314	6.037	3.261–11.17	< 0.001*
WHtR	0.319±2.457	1.375	0.011–169.7	0.897
Gender (female)	–0.967 ±0.328	0.380	0.200–0.722	0.003*

R^2 = 0.182, correct percentage for specificity (28.3%) and sensitivity (98%).

the ALT/AST ratio (B ± SE; 1.798 ±0.314, OR = 6.037, $p < 0.001$), and the WHtR (B ± SE; 0.319 ±2.45, OR = 1.375, $p = 0.897$) are significant factors. The sex distribution was analyzed using logistic regression. The estimated coefficient (B) was –0.967, with a standard error (SE) of 0.328. The odds ratio (OR) was calculated to be 0.380. The body mass index (BMI) was calculated as B ± SE; 0.149 ±0.012, with an odds ratio (OR) of 1.160 and a *p*-value < 0.001.

Spearman correlation analyses were performed to compare TyG with other metabolic markers. Table IV shows that there was a moderate association between the TyG index and other parameters that were not included in the calculation.

Discussion

In this study, we investigated the impact of the presence and degree of hepatosteatosis on the TyG index, PAI, and CMI in individuals with-

Table IV. Spearman's correlation analysis of metabolic parameters

Parameter		TyG
WHtR	*r*	0.250
	P-value	< 0.001*
ALT/AST	*r*	0.199
	P-value	< 0.001*
Liver diameter	*r*	0.289
	P-value	< 0.001*
WHtR	*r*	0.250
	P-value	< 0.001*
BMI	*r*	0.174
	P-value	< 0.001*
HS grade	*r*	0.359
	P-value	< 0.001*

TyG – triglyceride-glucose index, WHtR – waist-height ratio, ALT – alanine aminotransferase, AST – aspartate aminotransferase, BMI – body mass index, HS – hepatosteatosis.

out diabetes. The findings showed that patients with hepatosteatosis had significantly greater TyG index, PAI, and CMI values than those without hepatosteatosis. Furthermore, in patients with MAFLD, these index levels progressively increased as the degree of hepatosteatosis increased, even though the BMI remained the same. These findings clearly demonstrate the relationship between hepatosteatosis and cardiometabolic risk factors in the absence of diabetes mellitus. The impact of hepatosteatosis on cardiometabolic risk factors can be explained through a series of biological mechanisms. First, hepatosteatosis can lead to insulin resistance, adversely affecting triglyceride and glucose metabolism. This condition results in an elevated TyG index. The literature has previously reported a strong association between the TyG index and cardiometabolic risk factors, such as insulin resistance and metabolic syndrome [19]. A previous cohort study, comparable to our own, revealed that the TyG index could serve as an independent predictor of cardiovascular disease (CVD) in nondiabetic patients [27].

Our study revealed that this relationship is also valid in nondiabetic individuals and that hepatosteatosis can be an essential indicator of cardiometabolic risk. Second, fat accumulation in the liver and the resulting inflammation can lead to changes in the atherogenic lipoprotein profile, contributing to an elevated PAI. Given the effects of hepatosteatosis on metabolic dysfunction and lipid metabolism, the PAI is expected to be elevated in these patients [28]. A recent study was undertaken to assess new indices for predicting MAFLD. This study revealed that the AIP can be used as a predictive marker for MAFLD in nondiabetic patients, which is consistent with our own findings [29]. Our study confirms this expectation, showing that the PAI is significantly greater in patients with MAFLD. Third, the progression of hepatosteatosis, with increased oxidative stress and inflammation [30], can adversely affect overall cardiometabolic health, leading to an elevated CMI, a valuable new index for assessing visceral obesity [22, 25, 26]. A recently published study revealed a link between systemic immune-inflammatory indices (SIIs) and the presence and severity of NAFLD [31]. Another study demonstrated a positive association between the pan-immune-inflammation value (PIV) rather than the systemic immune-inflammation index and NAFLD or hepatic fibrosis [32]. These three metabolic indices are essential markers that should be evaluated together to reflect metabolic health. Abdominal obesity, increased BMI, and the presence of DM are known to be the most important triggers of MAFLD [25]. In our patients with hepatosteatosis, risk factors other than diabetes were present, but there was no difference in BMI among the different grades of hepatosteatosis. The presence of MAFLD patients with a normal BMI and normal WC, TG, HDL, LDL, ALT, and AST levels indicates that these factors alone are insufficient for diagnosing MAFLD. Therefore, measuring the TyG index, PAI, and CMI, which encompass multiple factors, is a more accurate and practical approach.

Our study revealed that grade 3 hepatosteatosis was more prevalent among males. One possible explanation for this finding is that women are more resistant to NAFLD than males are during the premenopausal phase. Estrogen signaling in the female liver enhances metabolic flexibility, preventing hepatic, metabolic, and inflammatory alterations even in situations of imbalanced nutrition [33]. The liver-protective action of estrogens may be attributed to a decrease in sex hormone-binding globulin (SHBG) levels, which limits the progression of NAFLD to hepatocytes in men, women with polycystic ovary syndrome, and postmenopausal women [34]. Following menopause, the occurrence of NAFLD becomes similar across males and females. The menopausal status of the female participants in our study was not known. Nevertheless, our study included persons aged 18–65, with a high likelihood that the majority of female participants were in their reproductive years.

Fatty liver diseases, such as MAFLD, discussed in this study, currently present significant challenges in terms of both diagnosis and treatment [31, 35–37]. This condition, frequently overlooked in clinical practice, has emerged as a growing health concern. The identification of MAFLD enables the implementation of more focused treatment strategies that are tailored to individuals' metabolic risk profiles. Aside from invasive procedures such as biopsies, the absence of sensitive noninvasive diagnostics hinders the early detection and treatment of the disease, hence complicating the diagnosis

and treatment process [6, 10, 38]. The contemporary literature concurs that the existing screening approaches based on liver enzymes have certain shortcomings, which can result in overlooked diagnoses and delays in treatment [39]. Scientific evidence supports our work by demonstrating that the likelihood of developing MAFLD is elevated even when ALT levels fall within the normal range. Hence, there is an urgent need for cost-effective and easily deployable new diagnostic approaches to enhance the precision of MAFLD diagnosis and facilitate early intervention. Currently, there are limited diagnostic tools and treatment alternatives available for this particular condition. Ongoing efforts are being made to discover a straightforward and easily applicable diagnostic procedure as well as an effective pharmacotherapeutic drug. Hence, incorporating this subject into our investigation is crucial for broadening the scope of our research and emphasizing the existing difficulties in the management of MAFLD.

Although this study revealed the relationship between hepatosteatosis and cardiometabolic risk indices in nondiabetic patients, it has several limitations. The ultrasound method used to detect hepatosteatosis is known to be less reliable when the fat content is less than 20% [40]. Despite concerns about underestimating the prevalence of MAFLD, the low cost, patient comfort, ease of use, and accessibility of ultrasound, along with the sampling errors and postprocedural complications associated with the gold standard liver biopsy [41], were the main reasons for preferring ultrasound. The imbalance in the number of patients and controls and the sex distribution is another limiting factor of our study. Due to the limited sample size and the retrospective cross-sectional nature of the study, a causal relationship cannot be established. Future studies can examine these relationships more profoundly using larger sample groups and longitudinal designs. Additionally, similar studies in different patient populations can enhance the generalizability of the findings.

In conclusion, the use of the PAI, CMI, and TyG indices in routine clinical evaluations can aid in the early detection of patients with hepatosteatosis and the more effective management of cardiometabolic risks. Considering that the levels of these indices increase with the degree of hepatosteatosis, periodic evaluation of these indices can be recommended to monitor the progression of hepatosteatosis. Particularly in nondiabetic individuals, using these indices can enhance the sensitivity of cardiometabolic risk assessment and expand the opportunities for early intervention.

Funding

No external funding.

Ethical approval

The study was approved by the Erzurum Health Science University Local Ethics Committee (Decision KAEK 2022/15-152, 03.10.2022). The study was performed in accordance with the Declaration of Helsinki. Since this was a retrospective study, an informed consent form was not needed.

Conflict of interest

The authors declare no conflict of interest.

References

1. Kwanten WJ. Diet and non-alcoholic fatty liver disease: a short narrative review. Acta Gastroenterol Belg 2023; 86: 306-10.
2. Rafaqat S, Gluscevic S, Mercantepe F, Rafaqat S, Klisic A. Interleukins: pathogenesis in non-alcoholic fatty liver disease. Metabolites 2024; 14: 153.
3. Perdomo CM, Frühbeck G, Escalada J. Impact of nutritional changes on nonalcoholic fatty liver disease. Nutrients 2019; 11: 677.
4. Mitrovic B, Gluvic ZM, Obradovic M, et al. Nonalcoholic fatty liver disease, metabolic syndrome, and type 2 diabetes mellitus: where do we stand today? Arch Med Sci 2023; 19: 884-94.
5. Pojsakorn D, Kanokphong S, Priyata D, et al. Disparities in metabolic dysfunction-associated steatotic liver disease and cardiometabolic conditions in low and lower middle-income countries: systematic analysis from the global burden of disease study 2019. Metabolism 2024; 2004; 158: 155958.
6. Lomonaco R, Leiva EG, Bril F, et al. Advanced liver fibrosis is common in patients with type 2 diabetes followed in the outpatient setting: The need for systematic screening, Diabetes Care 2021; 44: 399-406.
7. Harrison SA, Gawrieh S, Roberts K, et al. Prospective evaluation of the prevalence of nonalcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. J Hepatol 2021; 75: 284-91.
8. Williams CD, Stengel J, Asike MI, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study, Gastroenterology 2011; 140: 124-31.
9. Klisic A, Isakovic A, Kocic G, et al. Relationship between oxidative stress, inflammation and dyslipidemia with fatty liver index in patients with type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes 2018; 126: 371-8.
10. Meneses D, Olveira A, Corripio R, et al. Performance of noninvasive liver fibrosis scores in the morbid obese patient, same scores but different thresholds. Obes Surg 2020; 30: 2538-46.
11. Tian F, Guo Y, Zhou L, et al. Comparison of glimepiride and linagliptin in the treatment of nonalcoholic hepatic disease with type 2 diabetes mellitus. Arch Med Sci 2024; 20: 1407-15.
12. Borges-Canha M, Neves JS, Mendonça F, et al. The impact of bariatric surgery on hepatic function and predictors of liver steatosis and fibrosis. Obes Surg 2020; 30: 2935-41.
13. Barton Duell P, Welty FK, Miller M, et al. Nonalcoholic fatty liver disease and cardiovascular risk: a scientific

statement from the American Heart Association. Arterioscler Thromb Vasc Biol 2022; 42: E168-85.
14. Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. J Hepatol 2020; 73: 202-9.
15. Zhou XD, Targher G, Byrne CD, et al. An international multidisciplinary consensus statement on MAFLD and the risk of CVD. Hepatol Int 2023; 17: 773-91.
16. Li X, Sun M, Yang Y, et al. Predictive effect of triglyceride glucose-related parameters, obesity indices, and lipid ratios for diabetes in a Chinese population: a prospective cohort study. Front Endocrinol (Lausanne) 2022; 13: 862919.
17. Cho YK, Lee J, Kim HS, et al. Triglyceride glucose-waist circumference better predicts coronary calcium progression compared with other indices of insulin resistance: a longitudinal observational study. J Clin Med 2021; 10: 92.
18. Dang K, Wang X, Hu J, et al. The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003–2018, Cardiovasc Diabetol 2024; 23: 8.
19. Irace C, Carallo C, Scavelli FB, et al. Markers of insulin resistance and carotid atherosclerosis. A comparison of the homeostasis model assessment and triglyceride glucose index. Int J Clin Pract 2013; 67: 665-72.
20. Zhang Q, Xiao S, Jiao X, Shen Y. The triglyceride-glucose index is a predictor for cardiovascular and all-cause mortality in CVD patients with diabetes or prediabetes: evidence from NHANES 2001–2018. Cardiovasc Diabetol 2023; 22: 279.
21. Fernández-Macías JC, Ochoa-Martínez AC, Varela-Silva JA, Pérez-Maldonado IN. Atherogenic index of plasma: novel predictive biomarker for cardiovascular illnesses. Arch Med Res 2019; 50: 285-94.
22. Duan S, Yang D, Xia H, Ren Z, Chen J, Yao S. Cardiometabolic index: a new predictor for metabolic associated fatty liver disease in Chinese adults. Front Endocrinol (Lausanne) 2022; 13: 1004855.
23. Wong VWS, Chan WK, Chitturi S, et al. Asia–Pacific Working Party on Nonalcoholic Fatty Liver Disease guidelines 2017 – Part 1: Definition, risk factors and assessment. J Gastroenterol Hepatol 2018; 33: 70-85.
24. Mercantepe F, Baydur Sahin S, Cumhur Cure M, Karadag Z. Relationship between serum endocan levels and other predictors of endothelial dysfunction in obese women. Angiology 2023; 74: 948-57.
25. Hosseini SA, Alipour M, Sarvandian S, Haghighat N, Bazyar H, Aghakhani L. Assessment of the appropriate cut-off points for anthropometric indices and their relationship with cardio-metabolic indices to predict the risk of metabolic associated fatty liver disease. BMC Endocr Disord 2024; 24: 79.
26. Xi WF, Yang AM. Association between cardiometabolic index and controlled attenuation parameter in U.S. adults with NAFLD: findings from NHANES (2017–2020). Lipids Health Dis 2024; 23: 40.
27. Wu Z, Xie L, Guo D, et al. Triglyceride-glucose index in the prediction of adverse cardiovascular events in patients without diabetes mellitus after coronary artery bypass grafting: a multicenter retrospective cohort study. Cardiovasc Diabetol 2023; 22: 230.
28. Li Y, Men X, Liu Y, et al. Association with the plasma atherogenic index with hepatic steatosis and fibrosis in the US population. Medicine (United States) 2024; 103: E37152.
29. Li XM, Liu SL, He YJ, Shu JC. Using new indices to predict metabolism dysfunction-associated fatty liver disease (MAFLD): analysis of the national health and nutrition examination survey database. BMC Gastroenterol 2024; 24: 109.
30. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. Arch Med Sci 2017; 13: 851-63.
31. Arefhosseini S, Aghajani T, Tutunchi H, Ebrahimi-Mameghani M. Association of systemic inflammatory indices with anthropometric measures, metabolic factors, and liver function in nonalcoholic fatty liver disease. Sci Rep 2024; 14: 12829.
32. Jiang R, Hua Y, Hu X, Hong Z. The pan immune inflammatory value in relation to nonalcoholic fatty liver disease and hepatic fibrosis. Clin Res Hepatol Gastroenterol 2024; 48: 102393.
33. Della Torre S. Beyond the X factor: relevance of sex hormones in nafld pathophysiology. Cells 2021; 10: 2502.
34. Wang X, Xie J, Pang J, et al. Serum SHBG is associated with the development and regression of nonalcoholic fatty liver disease: a prospective study. J Clin Endocrinol Metab 2020; 105: 791-804.
35. Abe RAM, Masroor A, Khorochkov A, et al. The role of vitamins in non-alcoholic fatty liver disease: a systematic review. Cureus 2021; 13: e16855.
36. Xie C, Halegoua-Demarzio D. Role of probiotics in nonalcoholic fatty liver disease: does gut microbiota matter? Nutrients 2019; 11: 2837.
37. Borges-Canha M, Neves JS, Silva MM, et al. Waist-to-hip ratio and inflammatory parameters are associated with risk of non-alcoholic fatty liver disease in patients with morbid obesity. Biomedicines 2022; 10: 2416.
38. De Carli MAL, De Carli LA, Correa MB, Junqueira G, Tovo CV, Coral GP. Performance of noninvasive scores for the diagnosis of advanced liver fibrosis in morbidly obese with nonalcoholic fatty liver disease. Eur J Gastroenterol Hepatol 2020; 32: 420-5.
39. Huang CX, Zhou XD, Pan CQ, Zheng MH. Screening for metabolic dysfunction-associated fatty liver disease: time to discard the emperor's clothes of normal liver enzymes. World J Gastroenterol 2024; 30: 2839-42.
40. Dasarathy S, Dasarathy J, Khiyami A, Joseph R, Lopez R, Mccullough AJ, C.C. Foundation, U. States, M. Health, M. Health, U. States, C.C. Foundation, U. States, Validity of real time ultrasound in the diagnosis of hepatic steatosis: a prospective study. J Hepatol 2018; 51: 1061-7.
41. Sumida Y, Nakajima A, Itoh Y. Limitations of liver biopsy and noninvasive diagnostic tests for the diagnosis of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. World J Gastroenterol 2014; 20: 475-85.