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Cutoff Value of Metabolic Score for Visceral Fat in Patients with Nonalcoholic Fatty Liver Disease

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ABSTRACT

Objectives: This study aimed to determine the cutoff values of a novel adiposity index and the metabolic score for visceral fat (METS-VF) for nonalcoholic fatty liver disease (NAFLD) and its related factors.

Methods: A total of 1603 individuals participated in our checkup program and were retrospectively evaluated between June 2020 and January 2022. Patients who were less than 18 years of age and those with malignancies, hepatitis, HIV, insulin-dependent diabetes mellitus (DM), corticosteroid, parenteral nutrition, or alcohol use were excluded from the study. As a result, 1034 (64.5%) subjects were included in the study. Anthropometric and biochemical values in patient files were used to calculate indexes. Ultrasonography was used for the diagnosis of hepatic steatosis.

Results: Among the 1034 participants, 611 (59.1%) were females. The mean age was 48.7±12.9 years. Metabolic syndrome, DM, and hypertension were identified in 331 (50.5%), 96 (14.7%), and 179 (27.3%) patients with NAFLD, respectively, and in 47 (12.4%), 11 (12.4%), 34 (9.0%) patients without NAFLD ($p<0.001$, $p<0.001$, $p<0.001$, respectively). METS-VF cutoff value was 6.43 regardless of gender (sensitivity:85.1%, specificity:66.9%, AUC=0.836, $p<0.001$). When the genders were examined separately, the cutoff value was 6.41 for females (sensitivity: 78.2%, specificity: 82.8%, AUC=0.872, $p<0.001$) and the cutoff value was 6.91 for males (sensitivity: 79.6%, specificity: 67.9%, AUC=0.813, $p<0.001$).

Conclusion: The cutoff values of METS-VF in patients with NAFLD were found to be 6.41 in females and 6.91 in males.

Keywords: Adiposity, fatty liver, nonalcoholic fatty liver disease

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INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD), considered the hepatic manifestation of metabolic disorders, is observed in one out of every four adults, and its prevalence has been increasing every day.[1] NAFLD occurs following insulin resistance-induced hepatic lipogenesis. It starts with simple steatosis and is associated with increased morbidity and mortality as progression to nonalcoholic steatohepatitis and cirrhosis.[2] Although the histopathological examination is the definitive method for determining NAFLD, ultrasound is generally used for its diagnosis because it is noninvasive and cost-effective.[3] As a device and a radiologist are required for ultrasound, there is a need for more accessible methods that can predict NAFLD.

The distribution of adipose tissue in the human body varies depending on factors such as age, gender, ethnicity, nutritional characteristics, physical activity, hormones, and medications used.[4] When obesity is measured using body mass index (BMI), metabolically toxic

visseral fat and metabolically inactive subcutaneous fat are both included without distinction. Therefore, BMI may not always correlate with metabolic disorders.[5]

Magnetic resonance imaging, the gold standard method of measuring visceral adipose tissue (VAT), is expensive and difficult to access, and therefore it is not frequently used in clinical practice.[6] It is important to develop new practical formulas for measuring body fat distribution in clinical practice because visceral obesity, which is defined as abnormal fat accumulation in visceral tissues, is linked to many metabolic disorders.[4]

Several new insulin resistance and adiposity-related indexes are being evaluated for their use in predicting metabolic diseases.[6–10] These include triglyceride glucose (TyG) index and triglyceride/HDL cholesterol ratio (TG/HDL) that are measured from laboratory parameters and visceral adiposity index (VAI), metabolic score for insulin resistance (METS-IR), and metabolic score for visceral fat (METS-VF), which also include anthropometric measurements as well as laboratory findings.

It is important to detect NAFLD, which may progress to advanced hepatic diseases or metabolic disorders in the future, as health centers that do not have easy access to imaging methods, such as family health centers, calculate indexes by simple biochemical and anthropometric measurements.[1,11–13] Although many studies have used indexes such as waist circumference (WC), BMI, and VAI to predict NAFLD, to the best of our knowledge, no studies have been conducted using METS-VF.

This study aimed to determine the cutoff value of METS-VF for NAFLD and its related factors.

METHOD

This study was performed with individuals who participated in a checkup program conducted by a tertiary university hospital between June 2020 and January 2022. The files of 1603 patients were retrospectively evaluated. Patients who did not have the required data, those with age less than 18 years, those with malignancies, hepatitis, HIV, insulin-dependent diabetes mellitus (DM), use of corticosteroids, and use of parenteral nutrition, and those consuming alcohol (>20 g/day for women and >30 g/day for men) were excluded from the study. After consideration of exclusion criteria, 1034 (64.5%) subjects were included in the study.

Patients' height, weight, waist and hip circumferences, blood pressure values, smoking status, alcohol consumption, chronic diseases, medications, complete blood count, fasting glucose, fasting insulin, lipid values, HbA1c, and abdominal ultrasonography results were evaluated retrospectively from the patient files. NAFLD was determined by detecting Grade 1 or higher stage fatty liver disease by abdominal ultrasonography, which was performed by the same two radiologists on the day of blood tests taken. IDF-2006 guidelines for metabolic syndrome (MetS) were followed for the diagnosis of MetS.[14] Indexes related to obesity and insulin resistance are summarized in Table 1.[6–10,15]

IBM SPSS Statistics 25.0 software (IBM Corp., Released 2017, IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY, USA) was used for statistical analysis. Normality was tested with the Kolmogorov–Smirnov test. For descriptive results, variables indicated by count were expressed in frequency and percentages. Continuous variables with a normal distribution were expressed as mean and standard devia-

Table 1. Indexes related to obesity and insulin resistance

Index	Formula
BMI	Weight (kg)/height (m^2)
WHR	Waist circumference (cm)/hip circumference (cm)
HOMA-IR	Fasting glucose (mg/dL) × fasting insulin (μIU/mL)/405
VAI (women)	(WC/[36.58 + (1.89 × BMI)]) × (TG (mmol/L)/0.81) × (1.52/HDL-C (mmol/L))
VAI (men)	(WC/[39.68 + (1.88 × BMI)]) × (TG (mmol/L)/1.03) × (1.31/HDL-C(mmol/L))
METS-VF	4.466 + 0.011[(ln(METS-IR))3] + 3.239[(ln(WHtR))3] + 0.319 (sex) + 0.594(ln (age)), where sex was a binary response variable (male = 1, female = 0)
METS-IR	ln((2 × fasting glucose (mg/dL)) + TG (mg/dL)) × BMI)/(ln(HDL-C (mg/dL))
TyG	ln[TG (mg/dL) × fasting glucose (mg/dL)/2]
TG/HDL	TG (mg/dL)/HDL-C (mg/dL)

BMI: Body mass index; HOMA-IR: Homeostasis model assessment of insulin resistance; METS-IR: Metabolic score for insulin resistance; METS-VF: Metabolic score for visceral fat; TG/HDL: Triglyceride/HDL cholesterol ratio; TyG: Triglyceride glucose; WHR: Waist/hip ratio; WHtR: Waist/height ratio; VAI: Visceral adiposity index.

tion. Those without a normal distribution were expressed as median (min–max). The Chi-squared test was used to compare categorical data. Comparison between the continuous variables in the studied groups was achieved using Student's t-test, One-way ANOVA test, the Mann–Whitney U-test, or the Kruskal–Wallis tests as appropriate. The predictive performance and cutoff values of the indexes were determined using receiver operating characteristic (ROC) curve analysis. A value of p<0.05 was considered statistically significant.

RESULTS

Among the 1034 participants, 611 (59.1%) were females. The mean age of the subjects was 48.7±12.9 years. The prevalence of NAFLD was 656 (63.4%). Demographic, anthropometric, clinical, and biochemical features of patients with or without NAFLD are summarized in Table 2.

The participants were categorized into four quartiles according to METS-VF: the first quartile was 3.1–6.2, the second quartile was 6.2–6.8, the third quartile was 6.8–7.2, and the fourth quartile was 7.2–8.1. Demographic, anthropometric, clinical, and biochemical features of patients according to METS-VF index quartiles are summarized in Table 3.

METS-VF and BMI had the highest relation with NAFLD (AUC=0.836, p<0.001 and AUC=0.832, p<0.001, respectively). Moreover, METS-IR (AUC=0.836, p<0.001), WC (AUC=0.811, p<0.001), VAI (AUC=0.781, p<0.001), and TyG indexes (AUC=0.715, p<0.001) were also related with NAFLD. The ROC curve of indexes related to obesity and insulin resistance for NAFLD is shown in Figure 1.

The cutoff value of 6.43 of METS-VF was found to have a sensitivity of 85.1% and a specificity of 66.9% (AUC=0.836, p<0.001). The ROC curve of the METS-VF index for NAFLD is shown in Figure 2a. The METS-VF cutoff value of 6.41 for females had a sensitivity of 78.2% and a specificity of 82.8% (AUC=0.872, p<0.001). The METS-VF cutoff value of 6.91 for

Table 2. Demographic, anthropometric, clinical, and biochemical features of patients with or without NAFLD

	Without NAFLD (n=378)	With NAFLD (n=656)	p
Gender			
Female	244 (64.5)	367 (55.9)	0.007*
Male	134 (35.5)	289 (44.1)	
Age (years)	42.7±12.7	52.1±11.9	<0.001†
Comorbidity			
MetS	47 (12.4)	331 (50.5)	<0.001*
DM	11 (12.4)	96 (14.7)	<0.001*
HT	34 (9.0)	179 (27.3)	<0.001*
Smoking (pack-years)	5.0 (0.0–100.0)	10.0 (0.0–105.0)	<0.001‡
SBP (mmHg)	119.0 (90.0–165.0)	120.0 (90.0–220.0)	<0.001‡
DBP (mmHg)	75.0 (58.0–102.0)	80.0 (60.0–110.0)	<0.001‡
WC (cm)	82.0 (60.0–118.0)	98.0 (60.0–165.0)	<0.001‡
WHR	0.8 (0.4–1.1)	0.9 (0.6–1.1)	<0.001‡
BMI (kg/m2)	23.9±3.3	29.1±4.2	<0.001†
HbA1c (%)	5.4 (4.4–10.6)	5.6 (0.2–12.2)	<0.001‡
HOMA-IR	1.6 (0.4–5.8)	2.3 (0.4–16.9)	<0.001‡
TG/HDL	1.4 (0.2–16.6)	2.6 (0.3–35.7)	<0.001‡
TyG	8.3 (6.4–10.4)	8.8 (7.1–11.5)	<0.001‡
VAI	2.4 (0.4–23.0)	4.3 (0.5–63.7)	<0.001‡
METS-IR	33.9±6.9	44.1±8.7	<0.001†
METS-VF	6.1 (3.2–7.8)	7.0 (4.3–8.1)	<0.001‡

BMI: Body mass index; DBP: Diastolic blood pressure; DM: Diabetes mellitus; HT: Hypertension; HOMA-IR: Homeostatic model assessment for insulin resistance; MetS: Metabolic syndrome; METS-IR: Metabolic score for insulin resistance; METS-VF: Metabolic score for visceral fat; NAFLD: Nonalcoholic fatty liver disease; SBP: Systolic blood pressure; TG/HDL: Triglyceride to HDL cholesterol ratio; TyG: Triglyceride to glucose ratio; VAI: Visceral adiposity index; WC: Waist circumference; WHR: Waist hip ratio.

*Chi-squared test, †Student's t-test, ‡Mann–Whitney U-test.

Table 3. Demographic, anthropometric, clinical, and biochemical features of patients according to METS-VF index quartiles

	METS-VF				p
	Q1	Q2	Q3	Q4	
Gender					
Female	222 (86.1)	173 (66.8)	127 (49.2)	89 (34.4)	<0.001*
Male	36 (13.9)	86 (33.2)	131 (50.8)	170 (65.6)	
Age (years)	40.2±11.7	46.7±11.5	50.9±11.4	56.8±11.3	<0.001†
Comorbidity					
MetS	9 (3.5)	61 (23.5)	120 (46.5)	188 (72.6)	<0.001*
DM	10 (3.9)	15 (5.8)	31 (12.1)	51 (19.7)	<0.001*
HT	19 (7.4)	37 (14.3)	55 (21.3)	102 (39.6)	<0.001*
Smoking (pack-years)	5.0 (0.0–65.0)	6.0 (0.0–75.0)	10.0 (0.0–100.0)	15.0 (0.0–105.0)	<0.001‡
SBP (mmHg)	110.0 (90.0–157.0)	120.0 (90.0–160.0)	120.0 (90.0–160.0)	130.0 (90.0–220.0)	<0.001‡
DBP (mmHg)	70.0 (58.0–100.0)	80.0 (60.0–110.0)	80.0 (60.0–102.0)	80.0 (60.0–110.0)	<0.001‡
WC (cm)	76.0 (60.0–95.0)	88.0 (73.0–108.0)	98.0 (84.0–130.0)	110.0 (92.0–165.0)	<0.001‡
WHR	0.8 (0.4–0.9)	0.9 (0.6–1.1)	0.9 (0.6–1.1)	0.9 (0.7–1.1)	<0.001‡
BMI (kg/m^2)	22.1±2.4	25.9±2.1	28.6±2.6	32.1±3.8	<0.001†
HbA1c (%)	5.3 (0.2–11.0)	5.4 (4.4–7.5)	5.6 (4.4–12.2)	5.7 (4.6–12.2)	<0.001‡
HOMA-IR	1.5 (0.40–4.6)	1.8 (0.5–5.2)	2.2 (0.9–8.1)	3.2 (0.9–16.9)	<0.001‡
TG/HDL	1.2 (0.2–10.9)	1.9 (0.3–13.7)	2.7 (0.3–35.7)	3.1 (0.7–28.8)	<0.001‡
TyG	8.2 (6.4–9.9)	8.6 (7.2–10.3)	8.8 (7.1–10.8)	8.9 (7.8–11.5)	<0.001‡
VAI	2.1 (0.4–20.3)	3.4 (0.5–25.8)	4.4 (0.6–63.7)	5.2 (1.0–54.4)	<0.001‡
METS-IR	30.2±4.8	37.6±4.8	43.1±5.2	50.4±7.9	<0.001†

BMI: Body mass index; DBP: Diastolic blood pressure; DM: Diabetes mellitus; HT: Hypertension; HOMA-IR: Homeostatic model assessment for insulin resistance; MetS: Metabolic syndrome; METS-IR: Metabolic score for insulin resistance; METS-VF: Metabolic score for visceral fat; SBP: Systolic blood pressure; TG/HDL: Triglyceride to HDL ratio; TyG: Triglyceride to glucose ratio; VAI: Visceral adiposity index; WC: Waist circumference; WHR: Waist/hip ratio.

*Chi-squared test , †One-way ANOVA test, ‡Kruskal–Wallis test.

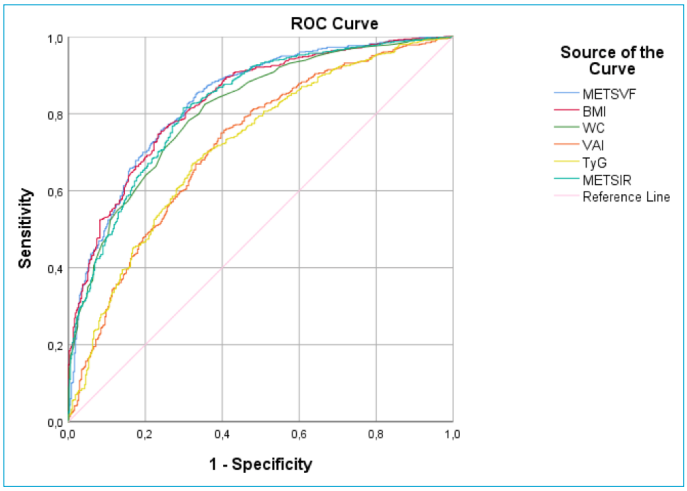

Figure 1. ROC curve of indexes related to obesity and insulin resistance for NAFLD.

BMI: Body mass index; METS-IR: Metabolic score for insulin resistance; METS-VF: Metabolic score for visceral fat; NAFLD: Non-alcoholic fatty liver disease; ROC: Receiver operating characteristic; TyG: Triglycerides–glucose index; VAI: Visceral adiposity index; WC: Waist circumference.

males had a sensitivity of 79.6% and a specificity of 67.9% (AUC=0.813, p<0.001). The ROC curves of the METS-VF index of females and males for NAFLD are shown in Figure 2b and Figure 2c, respectively.

DISCUSSION

In this study, the cutoff value of METS-VF for NAFLD and its related factors were evaluated. The METS-VF cutoff value was 6.43 regardless of gender. The cutoff value was 6.41 for females and 6.91 for males. Moreover, the frequencies of DM, HT, MET, HOMA-IR, TG/HDL, TyG, VAI, METS-IR, and METS-VF were found to be increasing.

Owing to its increasing prevalence, detecting NAFLD through a noninvasive, simple, and cost-effective method is important for preventing advanced hepatic disease.[6] METS-VF has been considered one of the most accurate indicators for the detection of visceral obesity and is also a good predictor of DM, hypertension (HT), and cardiometabolic risk factors that are related to the occurrence

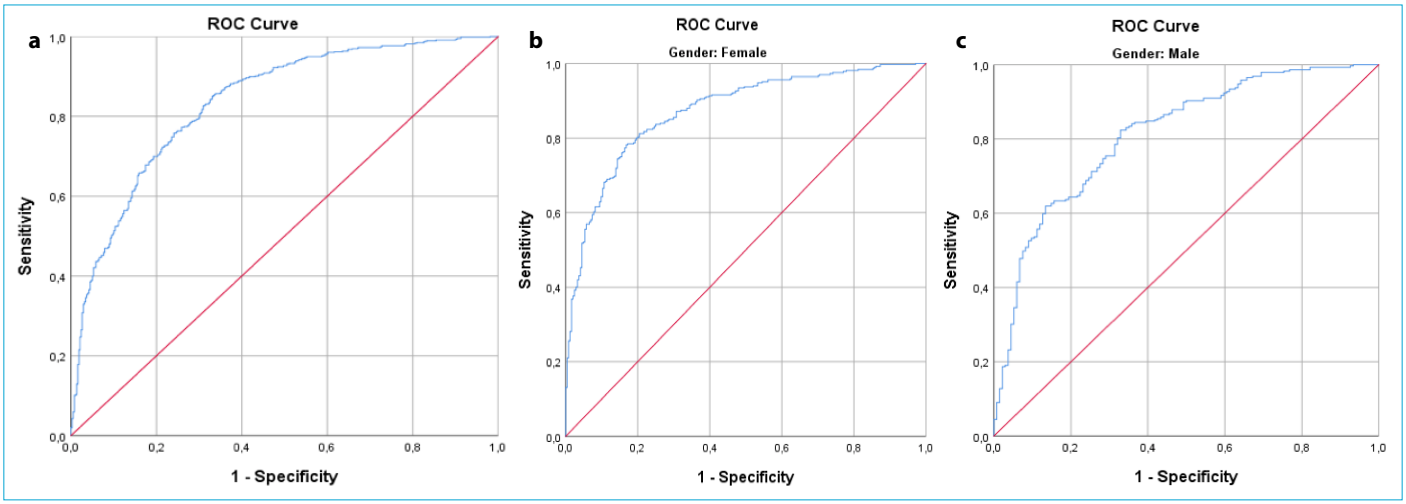

Figure 2. ROC curve of METS-VF index **(a)** for NAFLD, **(b)** of females for NAFLD, **(c)** of males for NAFLD.
METS-VF: Metabolic score for visceral fat; NAFLD: Nonalcoholic fatty liver disease; ROC: Receiver operating characteristic.

of NAFLD. METS-VF also incorporates easy-to-measure parameters, including sex, age, BMI, fasting glucose, TG, and HDL-C. METS-VF was developed by Bello-Chavolla et al. as a novel surrogate to estimate VAT in 366 Mexican individuals with BMI > 18.5 kg/m^2.[6] METS-VF was found to be a better predictor for the incidence of DM and HT compared with other VAT indexes. Kapoor et al. found that METS-VF correlates well with VAT values as estimated by DXA in 350 Indian individuals with BMI ≥ 35 kg/m^2.[5] A METS-VF value of 7.3 was found to have a good prediction of elevated VAT in obese individuals. In this study, a METS-VF cutoff value in NAFLD was 6.43. This difference could be a result of our population's lower BMI or variations in body fat distribution of different ethnic groups.

VAT distribution varies between genders due to the effects of sex hormones on adipose tissue function and metabolism.[16] Men tend to accumulate more visceral fat, resulting in increased cardiometabolic risk. The fat distribution of women, who have more subcutaneous fat, shifts to the visceral area after menopause. Similar to men, this shift is accompanied by a parallel increase in cardiometabolic risk. For this reason, cutoff values of METS-VF were also calculated according to gender in this study, and the cutoff value was found to be 6.91 for males and 6.41 for females.

A study conducted with 10297 nonhypertensive adults in China showed that METS-VF predicted the incidence of HT better than METS-IR, VAI, WC, and BMI indexes.[17] Similarly, higher HT prevalence is observed with increasing quartiles of METS-VF in the current study. Moreover, the frequencies of MetS and DM are found to be increasing in this study.

Vassilatoua et al. investigated the diagnostic performance of VAI for NAFLD in 145 premenopausal women with polycystic ovary syndrome and 145 age- and BMI-matched healthy control women.[12] Although VAI was found to be a statistically significant predictor for NAFLD, it was reported to have lower diagnostic performance than LAP, fatty liver index, and hepatic steatosis indexes. In this study, VAI was found to be associated with NAFLD with lower performance compared with METS-VF, BMI, METS-IR, and WC. However, VAI was higher in patients with NAFLD than in those without NAFLD. Almeida et al. reported that anthropometric clinical indicators of visceral adiposity such as WC, BMI, and LAP showed a high predictive capacity for NAFLD, similar to the findings of our study.[13]

The strength of our study is that, to our knowledge, this is the first study to investigate the relationship between METS-VF and NAFLD. On the other hand, our study has some limitations. First, the diagnosis of NAFLD was made using ultrasonography rather than the gold standard liver biopsy. Additional research is required to assess the sensitivity and specificity of the METS-VF index in comparison with hepatic histopathological imaging. Second, the study does not include patients with advanced stage NAFLD because it was conducted among checkup patients.

CONCLUSION

The inability to perform radiological imaging methods in family health centers, which are the main centers of preventive medicine, can hinder the early diagnosis of NAFLD. In this study, the cutoff value for METS-VF, which is an indicator of visceral adiposity, was determined as 6.43. Considering that METS-VF values above 6.43 may be associated with NAFLD may provide us with an early diagnosis, especially when radiological imaging is not available. Nevertheless, future study on this issue is necessary.

Disclosures

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