Non-invasive Screening of Metabolic Associated Fatty Liver Disease and Affecting Factors in Primary Care

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ABSTRACT

Objective: To identify the presence of MAFLD (metabolic associated fatty liver disease) with some non-invasive screening methods and the factors affecting in patients with metabolic dysfunction.

Study Design: A cross-sectional study.

Place and Duration of the Study: University of Health Sciences, Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Turkiye, from March to June 2021.

Methodology: This study included 233 participants with metabolic disease over the age of 18 who applied to family medicine clinics. The participants' sociodemographic data, chronic disease status, biochemical parameters, waist circumference, weight, height, body mass index, and presence of steatosis by ultrasonography were recorded. The risk of developing hepatic fibrosis and steatosis was calculated with the non-alcoholic fatty liver disease liver fat score (NAFLD-LFS), hepatic steatosis index (HSI), fatty liver index (FLI), fibrosis-4 index (FIB-4), NAFLD fibrosis score (NAFLD-FS), and aspartate aminotransaminase to platelet ratio index (APRI). The conclusions were evaluated with SPSS.

Results: According to the diagnostic criteria, MAFLD was detected in 58.4% of the participants. Statistically significant difference was found between FLI, HSI, NAFLD-LFS and MAFLD ($p<0.001$). According to the steatosis index risk groups of the participants, 64.4% - 89.7% were found to be high-risk. Steatosis was confirmed by ultrasonography in 63.6% - 77.8% of those at high-risk for index steatosis. The statistically significant difference was found between hypertension, diabetes mellitus, hyperlipidemia, metabolic syndrome, obesity, and MAFLD ($p=0.039$, $p<0.001$, $p<0.001$, $p<0.001$, and $p=0.011$, respectively).

Conclusion: Using non-invasive screening methods for steatosis can be clinically useful in detecting patients at risk for steatosis, and these methods are applicable in predicting MAFLD.

Key Words: *NAFLD, Fatty liver ındex, Hepatic steatosis index, MAFLD, Steatosis*.

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INTRODUCTION

The prevalence of fatty liver disease (Non-Alcoholic Fatty Liver Disease, NAFLD) is increasing, its incidence is estimated at 25% worldwide.[1] Even if fat is present in more than 5% of the liver weight in NAFLD, there is no inflammation or cell damage. However, in NASH (Non-Alcoholic Steatohepatitis), fat is together with inflammation and cell damage. Additionally, fibrosis can be present in NASH.[2] Although NAFLD is unlikely to progress to cirrhosis, cirrhosis may develop in NASH in the following years. Due to its insulin resistance status in its pathogenesis, NAFLD is associated with metabolic syndrome and obesity. It also plays a role in exacerbating the pathophysiology of atherosclerosis, type 2 diabetes mellitus (DM), cardiovascular diseases, and chronic kidney disease.[3]

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This disease group was evaluated in the form of NAFLD and NASH since its first definition. It has a close relationship with metabolic dysfunction and heterogeneous pathogenesis. Because of the inaccuracies in terminology, the NAFLD definition should be reconsidered as a new comprehensive term. In 2020, experts from 22 countries proposed to change the definition of NAFLD to "metabolic associated fatty liver disease (MAFLD)" with a consensus. The diagnosis of MAFLD better reflects metabolic diseases as a new definition that is both simple and comprehensive, independent of other liver diseases and to better explains the complex aetiology and heterogeneous pathogenesis of the fatty liver disease. In the MAFLD diagnostic criteria, any imaging method, non-invasive scores, or liver fattening with at least a biopsy indicated MAFLD if patients are overweight or have DM. However, at least two metabolic risks were sought for patients with normal weight.[4-6]

Although there are many non-invasive imaging methods for diagnosis, the gold standard is a liver biopsy. The first imaging method performed in suspected high-risk patients is liver ultrasonography. The non-invasive screening method used in hepatic fibrosis examination is ultrasound elastography. Diet and exercise form the basis of treatment.[7]

The NAFLD liver fat score (NAFLD-LFS), fatty liver index (FLI), and hepatic steatosis index (HSI) were used to predict the risk of steatosis from non-invasive screening methods; the fibrosis-4 index (FIB-4), NAFLD fibrosis score (NAFLD-FS), and aspartate transaminase to platelet ratio index (APRI) were used to predict the risk of advanced fibrosis.[8]

The main purpose of primary healthcare services is to control risk factors on time, to prevent the development of disease by explaining lifestyle changes to patients, and to detect diseases that develop later on early and non-invasively. The frequency of metabolic disorders in society is increasing everyday. As metabolic disorder frequency, obesity, insulin resistance, prediabetes, DM, and hypertension increased, new approaches were needed to identify and direct patients at risk for hepatic steatosis and fibrosis. In this context, MAFLD terminology entered the literature, and the usability of some non-invasive scoring methods for screening purposes has been investigated. The aim of this study was to determine the effectiveness of non-invasive screening methods in predicting the risk of fibrosis and steatosis in patients with metabolic diseases and determine the relationship between the presence of MAFLD and the factors affecting it.

METHODOLOGY

This cross-sectional study took place between March to June 2021 in the University of Health Sciences, Kartal Dr. Lutfi Kirdar City Hospital Family Medicine Clinics. Two hundred and thirty-three participants were included in the study by calculating the sample size according to the 95% confidence interval, 20% incidence, 5% margin of error, and 10% wastage in the unknown population. A total of 233 participants over 18 years old were in this study with the following metabolic diseases associated with liver fattening: hypertension, DM, prediabetes, hyperlipidemia, and obesity. Those with known liver disease (medicine, viral, genetic causes, *etc.*) and daily alcohol use over 20 grams for women and 30 grams for men were excluded from this study. In the MAFLD diagnostic criteria, any imaging modality, non-invasive scores, or fatty liver with at least one biopsy indicated MAFLD if patients were overweight, obese, or had DM. However, at least two metabolic risks have been sought in patients with normal weight.[4-6] These criteria were examined for all of the patients, those who met the MAFLD diagnostic criteria were considered to have MAFLD, and those who did not meet the MAFLD diagnostic criteria were considered to have no MAFLD.

The participants' sociodemographic and health-related data included the following information: sex, age, employment status, marital status and education level, chronic disease status, medications used, alcohol use, and smoking (package/year) status. The following parameters were in the examinations: height, weight, waist circumference values, and biochemical tests (fasting blood glucose, HbA1C, insulin, creatinine, urea, alanine aminotransferase, aspartate transaminase, gama glutamyl transferase, albumin, triglyceride, high-density lipoprotein (HDL), low-density lipoprotein) of the patients were calculated. The body mass index (BMI) value was calculated with the formula weight (Kg) / height (m^2). According to BMI values, 18.5-24.9 Kg/m^2 normal weight; BMI 25-29.9 Kg/m^2 overweight; BMI ≥30 Kg/m^2 classified as obese. The presence of metabolic syndrome was determined according to NCEP-ATP-III (National Cholesterol Education Program Adult Treatment Panel III) diagnostic criteria including increased waist circumference, high blood pressure or receiving treatment for hypertension, high fasting blood glucose and triglycerides, and low level of HDL[9]. The presence of qualitative steatosis was evaluated by Mindray DP-8500 standard 2D abdominal ultrasonography. Three steatosis indices (FLI, HSI, NAFLD-LFS) and three fibrosis indices (FIB-4, NAFLD-FS, APRI) were calculated using the formulations shown in Figure 1.[10,11] FLI was evaluated as <30 low steatosis risk, 30-60 medium risk, and >60 high steatosis risk.[12] HSI <30 was evaluated low risk, 30-36 medium risk, and >36 high risk of steatosis.[13]

FLI	• ($\log_e$(Triglyceride) × $e^{0.953}$+ BMI × 0.139+ 0.718 × $\log_e$ (GGT) + Waist circumference × 0.053 - 15.745) / (1 + $e^{0.953}$ × $\log_e$ (Triglyceride) + 0.139 × BMI + 0.718 × $\log_e$ (GGT) + Waist circumference × 0.053 - 15.745) ×100
HSI	• 8 × ALT/AST ratio + BMI (+2 if female, +2 if DM)
NAFLD-LFS	• - 2.89 + metabolic syndrome (no = 0, yes = 1) ×1.18 + type 2 diabetes (no = 0, yes = 2) × 0.45 +fasting serum insulin in mU/L×0.15+ AST in U/L×0.04 − 0.94 × (AST/ALT)
FIB-4	• (Age×AST)/(Platelet count × $(ALT)^{1/2}$)
NAFLD-FS	• -1.675 + (Age × 0.037) + BMI (kg/m^2) × 0.094 + (1.13 × IFG/diabetes (no = 0, yes = 1) + AST/ALT ratio ×0.99 - 0.013 × Platelet (*10^9/L) - albumin (g/dl) × 0.66
APRI	• (AST) / (AST Upper Limit of Normal) / (Platelets in 10^9/L)

Figure 1: Formulas used for steatosis/fibrosis indices.

The participants in this study were evaluated as NAFLD-LFS <-0.640 low risk, -0.640 to 0.16 mild-moderate risk, >0.16 high steatosis risk.[14] FIB-4, values <1.45 were considered as low fibrosis risk, and values >3.25 were considered as high risk of fibrosis.[15] In terms of NAFLD-FS, the risk of advanced fibrosis was classified as >0.676 high-risk, -1.455-0.676 intermediate-risk, and <-1,455 low-risk. Those with an APRI score <0.5 at low risk of fibrosis, and those with an APRI score of >1.5 were considered to have a high risk of fibrosis.[11] In order to demonstrate the power of the indices used in steatosis screening to determine the risk of steatosis; diagnostic performance statistics such as sensitivity, specificity, positive predictive value, and negative predictive value were used.

Study data were analysed using SPSS version 21.0. The Kolmogorov-Smirnov test was used to evaluate the suitability of the data for normal distribution. Categorical variables were expressed as counts and percentages. Of the continuous variables, those with a normal distribution were expressed as mean and standard deviation (SD), and those not with normal distribution were expressed as median and 25^{th} - 75^{th} percentiles. Normally distributed data according to the Kolmogorov-Smirnov test were evaluated with the independent sample Student's t-test. Data that did not fit the normal distribution according to the Kolmogorov-Smirnov test were evaluated with

the Mann Whitney U-test. The chi-square test was used to evaluate categorical data. For all statistical analyses, a value of p smaller than 0.05 was considered statistically significant.

RESULTS

A total of 233 participants (male/female: 138/95) with metabolic dysfunction were included in the analysis. Most of the participants were male (59.2%). The mean age was 55.4 ± 10.8 years. It was observed that 56 (24.0%) of the participants were smokers, and 12 (5.2%) were non-smokers.

When the laboratory parameters of the participants are examined, the median value of fasting blood glucose is 113.0 (25^{th} - 75^{th} percentile, 98.5-150.5) mg/dL, for HbA1C 6.1% (5.7-7.4), for insulin 12.7 (9.4-18.5) mIU/L, for HDL 48.0 (40.0-61.0) mg/dL, for triglyceride 151.0 (114.5-208.0) mg/dL, for AST 22.0 (16.0-33.0) U/L, for ALT 23.0 (16.0-47.0) U/L, for GGT 24.0 (15.0-45.0) U/L and for the platelet count 275 (232-315) 10^3/uL was found. The mean value of LDL was 120 ± 43.1 mg/dL, and the mean albumin value was 4.5 ± 0.3 g/dL.

According to their metabolic status, 152 (65.2%) had DM, 48 (20.6%) had prediabetes, 115 (49.4%) had hypertension, 180 (77.3%) had hyperlipidemia, and 168 (72.1%) had metabolic syndrome, and 125 (53.6%) had obesity.

Considering the BMI groups, 24 (10.3%) participants were normal weight, 81 (34.8%) were overweight, 77 (33.0%) were mildly obese, 33 (14.2%) were moderately obese, and 18 (7.7%) were morbidly obese.

According to the ultrasonography data, steatosis was present in 136 (58.4%) patients, stage 1 steatosis was present in 60 (25.8%) patients, stage 2 steatosis was present in 63 (27.0%) patients, and stage 3 steatosis was present in 13 (5.6%) patients. Steatosis was not present in 97 (41.6%) participants, and liver parenchymal echogenicity was normal. Eight (5.9%) participants with steatosis according to the ultrasonography were in the group of normal weight, 44 (32.4%) were in the group of overweight, and 84 (61.8%) were in the group of obese. There was statistically significant difference between the participants' presence of steatosis and obesity groups (p=0.014).

The median FLI of participants was 73.0 (50.0–88.5), the mean HSI was 43.7±6.5, and the median NAFLD-LFS was 0.75 (-0.25-2.17). Among the fibrosis indices, the median FIB-4 was 0.92 (0.71–1.17), the mean NAFLD-FS was -1.52±1.3, and the median APRI was 0.25 (0.18–0.40). According to FLI, 150 (64.4%) participants had a high risk of hepatic steatosis, and 21 (9.0%) had a low risk for hepatic steatosis. According to the HSI, 209 (89.7%) participants had a high risk of hepatic steatosis, and 4 (1.7%) had a low risk of hepatic steatosis. According to the NAFLD-LFS, 153 (65.7%) participants had a high risk for hepatic steatosis, and 44 (18.9%) had a low risk of hepatic steatosis. According to FIB-4, 1 (0.4%) of the participants had a high risk for fibrosis, whereas 203 (87.1%) had a low risk. According to the NAFLD-FS, 11 (4.7%) participants had a high risk of fibrosis, and 125 (53.6%) had a low risk of fibrosis. According to the APRI, 1 (0.4%) of the participants had a high risk of fibrosis, and 195 (83.7%) had a low risk of fibrosis.

There was a significant difference among FLI risk groups and the presence of obesity and metabolic syndrome (p<0.001). There was a significant difference among HSI risk groups and the presence of DM, obesity, hyperlipidemia, and metabolic syndrome (p<0.001, p<0.001, p=0.017, and p<0.001, respectively). There was a significant difference between NAFLD-LFS risk groups and the presence of DM, obesity, hyperlipidemia, prediabetes, and metabolic syndrome (p<0.001, p<0.001, p<0.001, p<0.001, p=0.034, and p<0.001, respectively).

In NAFLD-FS risk groups and metabolic diseases, a significant difference was present between the presence for DM, prediabetes, hypertension, obesity, and metabolic syndrome (p<0.001, p=0.015, p=0.039, p=0.006, and p=0.005, respectively). In APRI risk groups and metabolic diseases, there was a significant difference between hypertension and metabolic syndrome presence (p=0.001 and p=0.032).

Considering the presence of DM, obesity, overweight status, and metabolic syndrome, 136 (58.4%) of the participants with steatosis had MAFLD.

The relationship between the presence of MAFLD and the factors affecting it is in Table I. According to the steatosis/fibrosis score risk groups, statistically significant difference was present between APRI, FLI, HSI, NAFLD-LFS, and MAFLD (p=0.002, p<0.001, p<0.001, and p<0.001, respectively). Of the participants with MAFLD, 112 (82.4%) were at high-risk compared to FLI, 133 (97.8%) were at high-risk according to HSI, and 119 (87.5%) were at high-risk according to NAFLD-LFS. Nevertheless, there was no statistically significant difference among FIB-4 and NAFLD-FS with MAFLD (p=0.456, p=0.873). Considering the fibrosis risk groups in patients with MAFLD, 7 (5.1%) was at high risk compared to NAFLD-FS, 1 (0.7%) was at high risk compared to APRI, and there was no high-risk participant according to FIB-4.

In this study, the cut-off point for FLI was determined as 62. According to the results of the diagnostic performance analysis using the 95% confidence interval for the cut-off point of FLI 62, the sensitivity was 0.824, the specificity was 0.619, the positive predictive value was 0.752, and the negative predictive value was 0.714. The cut-off point for HSI was determined as 41.5. According to this value, the sensitivity was 0.779, the specificity was 0.608, the positive predictive value was 0.736, and the negative predictive value was 0.663. The cut-off point for NAFLD-LFS was determined as 0.38. According to this value, the sensitivity was 0.846, the specificity was 0.763, the positive predictive value was 0.833, and the negative predictive value was 0.779.

DISCUSSION

The metabolic associated fatty liver disease brings more patients under one over-arching category by better revealing the relationship between fatty liver disease and metabolic disease. In this context, the use of non-invasive screening methods to identify patients at risk for steatosis is becoming widespread.

Table I: The relationship between the presence of MAFLD and the factors affecting.

Parameters	Not MAFLD (n=97)	MAFLD (n=136)	p-value
Age (years)	58.7±10.4	53.1±10.5	<0.001**
Gender [F-M n(%)]	34(35.1)-63(64.9)	61(44.9)-75(55.1)	0.086*
Smoking, n(%)	22 (22.7)	34 (25.0)	0.264*
Alcohol use, n(%)	4 (4.1)	8 (5.9)	0.059*
Diabetes Mellitus, n(%)	46 (47.4)	106 (77.9)	<0.001*
Prediabetes, n(%)	23 (23.7)	25 (18.4)	0.204*
Hypertension, n(%)	55 (56.7)	60 (44.1)	0.039*
Hyperlipidemia, n(%)	64 (66.0)	116 (85.3)	<0.001*
Obesity, n(%)	43 (44.3)	82 (60.3)	0.011*
Metabolic syndrome, n(%)	50 (51.5)	118 (86.8)	<0.001*
BMI (Kg/m^2)	29.9±4.8	32.5±5.4	<0.001**
Waist circumference (cm)	95.8±10.6	100.0 (94.0-110.0)	<0.001***
Fasting blood glucose (mg/dL)	103.0 (94.0-122.0)	125.0 (105.3-166.0)	<0.001***
HbA1c (%)	5.8 (5.5-6.4)	6.6 (5.9-8.2)	<0.001***
AST (U/L)	17.0 (15.0-22.0)	28.0 (18.0-41.0)	<0.001***
ALT (U/L)	16.0 (13.0-22.5)	38.5 (21.0-57.0)	<0.001***
GGT (U/L)	16.0 (12.0-25.0)	35.5 (20.0-53.6)	<0.001***
LDL (mg/dL)	120.5±50.7	119.6±36.8	0.883**
Triglyceride (mg/dL)	125.0 (92.5-161.5)	177.0 (131.3-229.8)	<0.001***
FIB-4	0.9 (0.6-1.1)	0.9 (0.7-1.2)	0.171***
NAFLD Fibrosis Score	-1.5±1.3	-1.6 (-2.5- -0.4)	0.764***
APRI	0.2 (0.2-0.3)	0.3 (0.2-0.5)	<0.001***
FLI	52.9±25.9	78.2±17.2	<0.001**
HSI	40.4±5.8	45.6 (41.7-49.1)	<0.001***
NAFLD Liver Fat Score	-0.4±1.3	1.8 (0.6-2.9)	<0.001***

** Chi-Square test; ** Student's t-test; *** Mann-Whitney U-test. MAFLD: Metabolic associated fatty liver disease, NAFLD: Non-alcoholic Fatty liver disease, BMI: Body mass index, AST: Aspartate aminotransaminase, ALT: Alanine aminotransferase, GGT: Gama glutamyl transferase, LDL: Low-density lipoprotein, FIB-4: Fibrosis-4 index, APRI: AST to platelet ratio index, FLI: Fatty liver ındex, HSI: Hepatic steatosis index.*

Fedchuk *et al*. investigating the performance and limitations of steatosis biomarkers in patients with NAFLD, found the median FLI as 80, the median HSI as 42.8, and the median NAFLD-LFS as 0.8.[10] In the study by Onnerhag *et al*. investigated non-invasive index to predict metabolic complications in fatty liver disease, and reported the median FIB-4 in NAFLD patients was 1.3, the median NAFLD-FS was -1.57, and the median APRI was 0.5, which were similar to this study.[11] Yamamura *et al*. also found that the median FIB-4 was 0.99, the median NAFLD-FS was -1.78, and the median APRI was 0.3. Although there was statistically significant difference between MAFLD with APRI and NAFLD-FS, similar to this study, there was no statistically significant difference with FIB-4.[16]

Ciardullo *et al*. included 2770 individuals with DM in their study. Among the steatosis scores, 64.7% of the participants were high-risk according to the FLI, and 85.7% were high-risk according to the HSI. Of the fibrosis scores, 6.7% were high--risk compared to FIB-4, 33.3% were high-risk compared to NAFLD-FS, and 0.7% were high-risk compared to APRI.[8] In a study by Koehler *et al*. investigating FLI in NAFLD, 8.5% of NAFLD patients were low-risk, and 60.4% were high-risk. There was a statistically significant difference between NAFLD and FLI.[12] According to the steatosis risk groups in this study, most patients with MAFLD were found to be at high-risk for steatosis compared with HSI, NAFLD-LFS, and FLI. However, according to NAFLD-FS, APRI, and FIB-4, very few of them were found to be at high-risk of fibrosis. Similar to other studies, a statistically significant difference was present between his FLI, HSI, NAFLD-LFS, and APRI risk groups and MAFLD.

According to this study, with 60.4% sensitivity and 82.3% specificity for the 60 cut-off points determined in the study of Koehler *et al*. it is insufficient to distinguish the ones with steatosis, but it is sufficient to distinguish the ones without steatosis.[12] In the study by Lee *et al*., it is found sufficient to distinguish the ones with steatosis as in this study with 92% sensitivity for the 30 cut-off points of HSI. With 92.4% specificity for 36 cut-off points, it is found sufficient in distinguishing the ones without steatosis[13]. In the study of Kotronen *et al*., 84% sensitivity and 69% specificity for the -0.64 cut-off points taken for NAFLD-LFS is sufficient to distinguish those with steatosis, similar to the result in this study, but it is insufficient to distinguish those without steatosis.[14]

Degertekin *et al*. investigating the changing prevalence of NAFLD in Turkey in the last decade, comparing individuals with and without NAFLD with 113.239 participants, and the prevalence of NAFLD in Turkey was found to be 48.3%. Additionally, the study showed that the prevalence of NAFLD, which was 43.5% in 2007, increased to 53.1% in 2016.[17] In the study by Yılmaz *et al*., the prevalence of MAFLD was 45.5%.[18] Yamamura *et al*. when MAFLD and NAFLD were compared, MAFLD rate of the participants was found to be 79.6%.[16] Han *et al*. confirmed FLI as a marker in MAFLD patients. The incidence of MAFLD was 32.6% in their participants.[19]

Younossi *et al*. investigated the global prevalence for NAFLD. In their study, DM was in 43.6% of patients, hypertension in 39.3%, hyperlipidemia in 69.1%, and metabolic syndrome in 42.5% in NAFLD patients.[1] In a study by Wong *et al*. investigating the effect of the new definition of MAFLD on the epidemiology of the disease, DM, hypertension, and insulin resistance rates were higher in those with MAFLD than in those without MAFLD, and a statistically significant difference was present between them and MAFLD.[20] In a study comparing the diagnostic criteria of MAFLD and NAFLD by Lin *et al*., the frequency of DM was 30.1%, and the frequency of hypertension was 36.1% in MAFLD patients with a statistically significant difference.[21] In a study by Yilmaz *et al*., the diagnosis for MAFLD was made in 60.2% of diabetic patients, 71.3% of obese patients, 69.3% of patients with metabolic syndrome, and 60.8% of hypertensive patients, and a statistically significant difference was present between them.[18] In a study by Li *et al*., DM (31.1%) and insulin resistance (40.2%) were more frequent in NAFLD patients, and there was a statistically significant difference between them and those without NAFLD.[22] In the study by Degertekin *et al*., the frequency of dyslipidemia, DM, and hypertension was higher in individuals with NAFLD than in those without NAFLD. Moreover, a statistically significant difference was present between NAFLD and dyslipidemia, DM, and hypertension.[17]

In a study by Wong *et al*., the mean BMI of participants with NAFLD was 25.6 Kg/m^2, with a statistically significant difference.[20] Masroor *et al*. compared HbA1C, which is a marker in NAFLD, with anthropometric parameters in a study of 450 people in case and control groups. In the NAFLD group, 30% overweight and 58% obese individuals were present, and a statistically significant difference was present between the obese group and NAFLD, similar to this study.[23] In parallel with the increasing prevalence for obesity, the frequency of NAFLD is increasing and becoming a socioeconomic problem for countries.

In a study by Degertekin *et al*., the mean BMI of patients with NAFLD was 29.3 Kg/m^2, and a statistically significant difference was present between NAFLD and BMI.[17] Jimenez *et al*. found a significant difference between the presence for steatosis in the USG and obesity groups, similar to this study.[24] Generally, the risk of NAFLD increases with the degree of obesity. Therefore, BMI alone is considered a NAFLD risk factor.

The clinical and biochemical features of MAFLD subtypes were compared in the study by Huang *et al.* A new study designed by dividing MAFLD, which is a new definition, into subgroups can be done.[25]

CONCLUSION

Scores used to predict the risk of steatosis/fibrosis determined the patients' risk of steatosis with high precision. Hence, non-invasive screening methods are applicable in primary care for predicting MAFLD. It may be appropriate to conduct larger-scale studies involving different patient groups to clarify the role of non-invasive screening methods in predicting MAFLD.

ETHICAL APPROVAL:

Approval for the study was obtained from the ethics committee of University of Health Sciences, Kartal Dr. Lutfi Kirdar City Hospital (Approval No. 2021/514/196/19).

PATIENTS' CONSENT:

Written informed consent was obtained from the participants.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

ICB, NH, CO, HC, EES: This study has made significant contribution to the concept and design of the study, the collection of data for business analysis and interpretation of data, preparation of the working draft has been supporting the final approval of the version to be published.

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