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Original Research

Evaluation of Liver Steatosis and Liver Fibrosis in Patients with Type 1 Diabetes Mellitus Using Non-invasive Scores

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Abstract

Objectives: This study aimed to investigate the prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) and clinically significant fibrosis (CSF) in patients with type 1 diabetes mellitus (T1DM), as well as the factors affecting them, using non-invasive tests based on blood and imaging methods.

Methods: Adult T1DM patients who were followed up in the diabetes mellitus outpatient clinic at a tertiary university hospital and who did not have other causes of liver disease were prospectively investigated. MASLD and CSF were evaluated using non-invasive scores based on biochemical tests and FibroScan®. MASLD was defined as a FibroScan® CAP score ≥ 275 dB/m, and CSF was defined as $F \geq 8$ kPa in the absence of any other chronic liver disease or secondary cause of hepatic steatosis in T1DM patients.

Results: The prevalence of MASLD and CSF was 12.9% and 5%, respectively. BMI, fasting blood glucose, and waist and hip circumference were significantly higher in patients with MASLD ($p < 0.05$). The rates of hypertension and dyslipidemia were also higher in patients with MASLD ($p = 0.026$ and $p = 0.012$, respectively). According to Pearson's correlation test, LSM was most strongly correlated with Agile 4 ($p < 0.001$, $r = 0.922$) and Agile 3+ scores ($p < 0.001$, $r = 0.685$). CAP was most strongly correlated with the fatty liver index ($p < 0.001$, $r = 0.514$) and the hepatic steatosis index ($p < 0.001$, $r = 0.404$).

Conclusion: Components of metabolic syndrome are important risk factors for MASLD in patients with T1DM. There is currently no consensus on screening and diagnostic pathways for MASLD in T1DM, and further research is needed in this area.

Keywords: FibroScan®; metabolic dysfunction-associated steatotic liver disease; type 1 diabetes mellitus.

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Type 1 diabetes mellitus (T1DM) is a common, chronic autoimmune disease that typically develops in childhood. Studies show that not only are the incidence and prevalence of T1DM increasing, but the age at which pa-

tients are diagnosed is also decreasing.^[1,2] T1DM is a serious disease that can lead to significant, life-threatening micro- and macrovascular complications in the long term, especially if left uncontrolled.^[3] With the increasing number of

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cases and longer disease duration, steatotic liver disease is being observed more frequently in patients with T1DM.^[4]

Although liver biopsy is the gold standard for diagnosing steatotic liver disease, its invasive nature and the risk of complications have led to increasing use of non-invasive scoring systems based on blood and imaging methods. Information regarding the prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) and associated risk factors in patients with T1DM is limited.

In this study, we aimed to investigate the frequency of MASLD and clinically significant fibrosis (CSF) in patients with T1DM, as well as the factors affecting them, using non-invasive tests based on blood and imaging methods.

Methods

The study was designed as a prospective, cross-sectional cohort study at a single center. One hundred and one adult patients (≥ 18 years old) with T1DM who were followed up in the diabetes mellitus outpatient clinic at Istanbul University Faculty of Medicine and who did not have other causes of liver disease were investigated. MASLD and CSF were evaluated using non-invasive scoring systems based on biochemical tests and FibroScan[®]. Patients with T1DM aged ≥ 18 years were included in the study, and those with other chronic liver diseases or secondary causes of steatotic liver disease were excluded.

Demographic and laboratory characteristics, blood pressure, lipid profile, waist and hip circumference, body mass index (BMI), duration of T1DM, non-invasive fibrosis scoring tests based on biochemical tests, and FibroScan[®] measurements were examined. Hypertension and dyslipidemia were determined according to metabolic syndrome diagnostic criteria.^[5]

In FibroScan[®] measurements, a controlled attenuation parameter (CAP) score ≥ 275 dB/m was considered indicative of liver steatosis ($S1 \geq 275, < 290$ dB/m; $S2 \geq 290, < 302$ dB/m; $S3 \geq 302$ dB/m), and liver stiffness measurement (LSM) ≥ 8.0 kPa was considered indicative of clinically significant fibrosis (CSF) (F2–4). Values ≥ 12 kPa were considered advanced fibrosis (F3–4), and ≥ 15 kPa were considered cirrhosis (F4).

MASLD was defined as a FibroScan[®] CAP score ≥ 275 dB/m in the absence of any other chronic liver disease or secondary cause of hepatic steatosis in patients with T1DM.

The FAST (FibroScan-AST) score, Agile 3+ score, Agile 4 score, Fibrotic NASH Index, Fatty Liver Index, Hepatic Steatosis Index, FIB-4, NAFLD Fibrosis Score, APRI, and HEPAMET Fibrosis Score were evaluated as non-invasive scores based on biochemical tests.^[6–15]

This study was approved by the Ethics Committee of Istanbul University Faculty of Medicine (Approval no=2022/348, assigned on 11/03/2022). All procedures complied with the ethical standards of the Human Testing Committee of our institution and the Helsinki Declaration. Written informed consent was obtained from all patients.

Statistical Analysis

In the descriptive statistics of the data, the mean, standard deviation, and median (IQR 25–75) were used. Categorical variables were expressed as numbers (n) and percentages (%). The independent samples t-test was used to analyze quantitative independent data. The chi-square test was used to analyze independent qualitative data. Pearson's correlation test was used to determine the strength and direction of the relationship between two continuous variables. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off values. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. Multivariate logistic regression analysis was performed to predict the odds ratios of variables. The results were evaluated at a 95% confidence interval and a significance level of $p < 0.05$. Data analysis was performed using SPSS version 22.0.

Results

General Features

The study included 101 patients with T1DM, 66 (65.3%) of whom were female. The mean age of the patients was 34.9 ± 13.5 years (median 32 years, IQR [25–75] [23–44]), and the mean disease duration was 176.8 ± 106.9 (range: 12–561) months (median 156 months, IQR [25–75] [108–246]). The mean BMI of the patients was 24 ± 4.8 kg/m² (median 23.2 kg/m², IQR [25–75] [21–25.8]), mean waist circumference was 86.5 ± 11.6 cm [median 87 cm, IQR (25–75) (78.5–91)], and mean hip circumference was 96.4 ± 9.9 cm (median 96 cm, IQR [25–75] [90–102]). According to BMI characteristics, seven (6.9%) patients were overweight ($25–29.9$ kg/m²), eight (7.9%) patients were obese ($30–39.9$ kg/m²), and one (1%) patient was morbidly obese (≥ 40 kg/m²). Twenty-one (20.8%) patients had hypertension, and 24 (23.8%) had dyslipidemia. Mean systolic blood pressure was 115.8 ± 18.6 mmHg (median 115.5 mmHg, IQR [25–75] [110–124.5]), and mean diastolic blood pressure was 72.8 ± 9.1 mmHg (median 70 mmHg, IQR [25–75] [70–80]).

According to FibroScan[®] features, 13 (12.9%) patients had MASLD (CAP ≥ 275 dB/m), five (5%) patients had CSF (F ≥ 8 kPa), four (4%) patients had advanced fibrosis (F ≥ 12 kPa), and two (2%) patients had cirrhosis (F ≥ 15 kPa).

According to Pearson's correlation test, LSM was most

significantly correlated with the Agile 4 score ($p < 0.001$, $r = 0.922$) and the Agile 3+ score ($p < 0.001$, $r = 0.685$). The CAP score was most significantly correlated with the fatty liver index ($p < 0.001$, $r = 0.514$) and the hepatic steatosis index ($p < 0.001$, $r = 0.404$).

Demographic, laboratory, and non-invasive scores based on blood and imaging characteristics of all patients are shown in Table 1. MASLD and fibrosis risk distribution of patients according to blood-based non-invasive scores in all patients are shown in Table 2.

Characteristics of MASLD Patients and Comparison With Non-MASLD Patients

Thirteen (12.9%) patients had MASLD according to FibroScan® results. Seven (53%) of them were female. The mean age of the patients was 40 ± 15 years (median 40 years, IQR [25–75] [27.5–45.5]), and the mean disease duration was 203 ± 123 months (median 192 months, IQR [25–75] [96–264]). The mean BMI was 27.9 ± 6.7 kg/m² (median 27.3 kg/m², IQR [25–75] [22.6–30.5]), mean waist circumference was 97.4 ± 14 cm (median 95 cm, IQR [25–75] [89–102.5]), and mean hip circumference was 103.4 ± 11.7 cm (median 105 cm, IQR [25–75] [93.5–109]). The degree of steatosis was S3 (CAP ≥ 302 dB/m) in eight (61.5%) patients, S2 (CAP ≥ 290 , < 302 dB/m) in two (15.4%) patients, and S1 (CAP ≥ 275 , < 290 dB/m) in three (23.1%) patients.

BMI and waist and hip circumference were significantly higher in MASLD patients compared to non-MASLD patients ($p = 0.034$, $p < 0.001$, and $p = 0.006$, respectively). The rates of hypertension and dyslipidemia were significantly higher in MASLD patients ($p = 0.026$ and $p = 0.012$).

The AUC of BMI for MASLD detection was 0.733 (95% confidence interval [CI] = 0.573–0.893, $p = 0.007$). At an optimal cut-off of 26 kg/m², BMI had a sensitivity of 62% and a specificity of 82% for MASLD detection. In Kaplan–Meier analysis, it was significantly associated with the development of MASLD in patients with BMI > 26 kg/m² ($p = 0.028$). The AUC of T1DM duration for MASLD detection was 0.585 (95% CI = 0.406–0.765, $p = 0.323$). At an optimal cut-off of 180 months, disease duration had a sensitivity of 54% and a specificity of 63% for MASLD detection. In Kaplan–Meier analysis, it was significantly associated with the development of MASLD in patients with T1DM duration < 180 months ($p = 0.001$). The AUC of waist circumference for MASLD detection was 0.790 (95% CI = 0.658–0.922, $p = 0.001$). At an optimal cut-off of 89.5 cm, independently of gender, waist circumference had a sensitivity of 66% and a specificity of 92% for MASLD detection. In Kaplan–Meier analysis, it was significantly associated with the development of MASLD in patients with waist circumference > 89.5 cm ($p = 0.034$). The

Table 1. Baseline characteristics of all patients (n=101)

Demographic features	
Female, n (%)	66 (65.3)
Age (year) (mean±SD)	34.9±13.5
T1DM duration (month) (mean±SD)	176.8±106.9
Height (cm) (mean±SD)	166±9.2
Weight (kg) (mean±SD)	66.1±14.4
BMI (kg/m ²) (mean±SD)	24±4.8
Over-weight (25 - 29.9 kg/m ²), n (%)	7 (6.9)
Obese (30 - 39.9 kg/m ²), n (%)	8 (7.9)
Morbidly obese (≥ 40 kg/m ²), n (%)	1 (1)
Waist circumference (cm) (mean±SD)	86.5±11.6
Hip circumference (cm) (mean±SD)	96.4±9.9
Systolic Blood Pressure (mmHg) (mean±SD)	115.8±18.6
Diastolic Blood Pressure (mmHg) (mean±SD)	72.8±9.1
Hypertension, n (%)	21 (20.8)
Dyslipidemia, n (%)	24 (23.8)
Biochemical features	
HbA1c (%) (mean±SD)	8.5±1.7
Fasting blood glucose (mg/dl) (mean±SD)	193±73
Total cholesterol (mg/dl) (mean±SD)	168±33
LDL (mg/dl) (mean±SD)	99±28
HDL (mg/dl) (mean±SD)	56±16
Triglyceride (mg/dl) (mean±SD)	97±67
AST (U/L) (mean±SD)	19±18
ALT (U/L) (mean±SD)	19±18
ALP (U/L) (mean±SD)	82±31
GGT (U/L) (mean±SD)	15±13
Total protein (g/dl) (mean±SD)	7±0.6
Albumin (g/dl) (mean±SD)	4.5±0.4
AFP (ng/ml) (mean±SD)	2.2±1
Total Bilirubin (mg/dl) (mean±SD)	0.4±0.2
Platelet (10 ³ /μl) (mean±SD)	278±75
INR (mean±SD)	0.9±0.1
Creatinine (mg/dl) (mean±SD)	0.7±0.5
eGFR (ml/min/1.73 m ²) (mean±SD)	112±22
Uric acid (mg/dl) (mean±SD)	3.5±1.1
Non-invasive scores	
FAST Score (mean±SD)	0.6±0.1
Agile3+ (mean±SD)	0.2±0.2
Agile 4 (mean±SD)	0.03±0.1

Table 1. Continue

Non-invasive scores	
Fibrosis NASH Index (mean±SD)	0.2±0.2
Fatty Liver Index (mean±SD)	21.3±24
Hepatic Steatosis Index (mean±SD)	32.7±5.7
FIB-4 (mean±SD)	0.6±0.4
NAFLD Fibrosis Score (mean±SD)	-2.3±1.5
APRI (mean±SD)	0.2±0.1
Hepamet Fibrosis Score (mean±SD)	0.1±0.1
CAP (dB/m) (mean±SD)	218±45
LSM (kPa) (mean±SD)	5.4±4
MASLD (CAP ≥ 275 dB/m), n (%)	13 (12.9)
S1 (CAP ≥ 275, <290 dB/m)	3 (3)
S2 (CAP ≥ 290, < 302 dB/m)	2 (2)
S3 (CAP ≥ 302 dB/m)	8 (7.9)
Clinically significant fibrosis (F ≥ 8 kPa, F2-4), n (%)	5 (5)
Advanced fibrosis (F ≥ 12, F3-4), n (%)	4 (4)
Cirrhosis (F ≥ 15 kPa, F4), n (%)	2 (2)

Abbreviations: T1DM: Type 1 diabetes mellitus; BMI: Body mass index; LDL: Low density lipoprotein; HDL: High density lipoprotein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; AFP: Alpha-fetoprotein; INR: International normalized ratio; eGFR: Estimated glomerular filtration rate; FIB-4: Fibrosis 4 score; NAFLD: Non-alcoholic fatty liver disease; APRI: AST to platelet ratio index; FAST: Fibroscan-AST; CAP: Controlled attenuation parameter; LSM: Liver stiffness measurement; S: Steatosis; F: Fibrosis.

AUC of hip circumference for MASLD detection was 0.699 (95% CI=0.532–0.866, p=0.021).

HDL cholesterol levels were significantly higher in non-MASLD patients, and uric acid levels were significantly

higher in MASLD patients (p=0.026 and p=0.032), while there was no difference between the groups in LDL cholesterol and triglyceride levels (p>0.05). While HbA1c did not differ between groups (p=0.653), fasting blood glucose was significantly higher in MASLD patients (p=0.011). The AUC of fasting blood glucose for MASLD detection was 0.682 (95% CI=0.515–0.850, p=0.035). At an optimal cut-off of 188.5mg/dL, fasting blood glucose had a sensitivity of 76.9% and a specificity of 56.3% for MASLD detection. In Kaplan–Meier analysis, it was significantly associated with the development of MASLD in patients with fasting blood glucose>188.5mg/dL (p=0.040).

Fatty liver index, hepatic steatosis index, and CAP scores were significantly higher in MASLD patients (p=0.004, p=0.030, and p<0.001, respectively), while there were no differences between the groups in other non-invasive blood-based scores (p>0.05).

Three (23.1%) of the 13 MASLD patients had CSF, and all of them also had advanced fibrosis. Two (66.7%) were cirrhotic.

A comparison of the characteristics of MASLD and non-MASLD patients is shown in Table 3.

According to multivariate logistic regression analysis, waist circumference (OR=7.410; 95% CI=1.499–36.645; p=0.014) and fasting blood glucose (OR=11.699; 95% CI=1.816–75.348; p=0.010) were found to be most significantly associated with MASLD (Table 4).

Discussion

This study investigated liver steatosis and liver fibrosis in adult patients with T1DM using non-invasive blood- and imaging-based tests. MASLD has become a significant global health problem with increasing prevalence worldwide. It

Table 2. MASLD and fibrosis risk distribution of patients according to non-invasive scores in all patients (n=101)

	Median (IQR 25-75)	Low-risk (n, [%])	Intermediate-risk (n, [%])	High-risk (n, [%])
FAST (<0.35, ≥0.35 - <0.67, ≥0.67)	0.024 (0.01 - 0.05)	97 (96)	2 (0.02)	1 (0.01)
Agile 3+ (<0.45, ≥0.45 - ≤0.68, >0.68)	0.14 (0.07 - 0.24)	89 (88)	11 (0.11)	1 (0.01)
Agile 4 (<0.251, ≥0.251 - ≤0.565, >0.565)	0.01 (0 - 0.03)	100 (99)	0	1 (0.01)
Fibrotic NASH index (≤0.1, >0.1 - <0.33, ≥0.33)	0.12 (0.06 - 0.33)	42 (41.5)	34 (33.7)	25 (24.8)
Fatty Liver Index (<30, ≥30 - <60, ≥60)	11.2 (5.62 - 27.58)	78 (77.2)	14 (13.9)	9 (0.09)
Hepatic Steatosis Index (≤36, >36)	32.05 (28.73 - 35.68)	81 (80.2)		20 (19.8)
NAFLD fibrosis (<-1.455, >0.675)	-2.5 [-3.3 - (-1.5)]	77 (76.2)		3 (3)
HEPAMET (<0.12, ≥0.12 - ≤0.47, >0.47)	0.04 (0.04 - 0.1)	88 (87.1)	13 (12.9)	0
FIB-4 (<1.3, ≥1.3 - <2.67, ≥2.67)	0.5 (0.4 - 0.8)	94 (93.1)	7 (6.9)	0
APRI (<0.5, ≥0.5 - <1.5, ≥1.5)	0.14 (0.11 - 0.2)	98 (97)	3 (3)	0

FAST: Fibroscan-AST; NAFLD: Non-alcoholic fatty liver disease; FIB-4: Fibrosis 4 score; APRI: AST to platelet ratio index.

Table 3. Comparison of demographic characteristics, biochemical values, and non-invasive scores of patients without and with MASLD

	No-MASLD (n=88, CAP < 275 dB/m)	MASLD (n=13, CAP ≥ 275 dB/m)	p
Demography			
Age (year)	34.2±13.2	40±15	0.170
Gender, n (%)			
Female	59 (67)	7 (53)	0.351
Male	29 (33)	6 (46.2)	
T1DM duration (month) (mean±SD)	173±104	203±123	0.345
Height (cm) (mean±SD)	166.2±9.1	165±10	0.572
Weight (kg) (mean±SD)	64.7±13.1	75.8±19.6	0.010
BMI (kg/m ²) (mean±SD)	23.3±4.2	27.9±6.7	0.034
Waist circumference (cm) (mean±SD)	84.8±10.4	97.4±14	< 0.001
Hip circumference (cm) (mean±SD)	95.4±9.2	103.4±11.7	0.006
Systolic blood pressure (mmHg) (mean±SD)	114.7±18	122.2±21.7	0.265
Diastolic blood pressure (mmHg) (mean±SD)	73.1±8.6	70.6±12.4	0.440
Hypertension, n (%)	15 (17)	6 (46.2)	0.026
Dyslipidemia, n (%)	17 (19.3)	7 (53.8)	0.012
Biochemistry			
Fasting blood glucose (mg/dl) (mean±SD)	186±67.3	241.3±95.4	0.011
HbA1c (%) (mean±SD)	8.5±1.7	8.7±1.9	0.653
Total cholesterol (mg/dl) (mean±SD)	166±32	179±37	0.190
LDL (mg/dl) (mean±SD)	97±26	107±37	0.262
HDL (mg/dl) (mean±SD)	57±16	47±14	0.026
Triglyceride (mg/dl) (mean±SD)	87±48	161±127	0.060
AST (U/L) (mean±SD)	19±18	21±16	0.663
ALT (U/L) (mean±SD)	19±18	21±16	0.684
ALP (U/L) (mean±SD)	81±29	84±44	0.788
GGT (U/L) (mean±SD)	13±12	20±14	0.085
Total bilirubin (U/L) (mean±SD)	0.4±0.2	0.5±0.3	0.532
Direct bilirubin (U/L) (mean±SD)	0.1±0.1	0.2±0.1	0.673
Total protein (g/dl) (mean±SD)	7±0.6	7.2±0.6	0.202
Albumin (g/dl) (mean±SD)	4.4±0.4	4.5±0.2	0.676
AFP (ng/ml) (mean±SD)	1.9±0.8	2.6±1.4	0.431
Platelet (10 ³ /μl) (mean±SD)	280±72	267±95	0.557
INR (mean±SD)	0.9±0.1	0.9±0.1	0.326
Creatinine (mg/dl) (mean±SD)	0.7±0.5	0.7±0.3	0.957
eGFR (ml/min/1.73 m ²) (mean±SD)	112±22	107±24	0.454
Uric acid (mg/dl) (mean±SD)	3.4±1.1	4.1±1.4	0.032
Scores			
FAST score (mean±SD)	0.1±0.1	0.2±0.2	0.135
Agile 3+ (mean±SD)	0.2±0.2	0.3±0.3	0.120
Agile 4 (mean±SD)	0.02±0.04	0.1±0.2	0.240
Fibrotic NASH index (mean±SD)	0.2±0.2	0.3±0.3	0.195

Table 3. Continue

	No-MASLD (n=88, CAP < 275 dB/m)	MASLD (n=13, CAP ≥ 275 dB/m)	p
Scores			
Fatty liver index (mean±SD)	17.3±19.7	48.7±32	0.004
Hepatic steatosis index (mean±SD)	32±4.9	37.6±8.1	0.030
NAFLD fibrosis score (mean±SD)	-2.4±1.5	-1.9±1.4	0.280
HEPAMET (mean±SD)	0.1±0.1	0.1±0.1	0.125
FIB-4 (mean±SD)	0.6±0.3	0.8±0.6	0.197
APRI (mean±SD)	0.2±0.1	0.3±0.2	0.273
CAP (dB/m) (mean±SD)	205±30	307±25	<0.001
LSM (kPa) (mean±SD)	4.9±1.6	9±9.9	0.157

T1DM: Type 1 diabetes mellitus; BMI: Body mass index; LDL: Low density lipoprotein; HDL: High density lipoprotein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; AFP: Alpha-fetoprotein; INR: International normalized ratio; eGFR: Estimated glomerular filtration rate; FIB-4: Fibrosis 4 score; NAFLD: Non-alcoholic fatty liver disease; APRI: AST to platelet ratio index; FAST: Fibroscan-AST; CAP: Controlled attenuation parameter; LSM: Liver stiffness measurement; MASLD: Metabolic dysfunction-associated liver disease

Table 4. Multivariate logistic regression analysis for risk factors of MASLD in T1DM patients

	p	Odds ratio	95% CI	
			Lower	Upper
Fasting blood glucose (mg/dl)	0.010	11.699	1.816	75.348
Waist circumference (cm)	0.014	7.410	1.499	36.645
Hypertension	0.444	2.199	0.292	16.534
Dyslipidemia	0.124	3.708	0.699	19.678
Body mass index (kg/m ²)	0.611	1.861	0.170	20.352
Type 1 diabetes mellitus duration (months)	0.822	0.821	0.148	4.575

CI: Confidence interval

affects approximately 38% of adults worldwide.^[16] While MASLD has been extensively studied in patients with type 2 diabetes mellitus, and the relationship between the two is well understood, studies and data regarding the burden of MASLD in patients with T1DM are quite limited. Therefore, there is no specific consensus regarding MASLD screening in patients with T1DM. However, with the global rise in metabolic syndrome and related conditions, MASLD is likely becoming increasingly prevalent in this patient group.

The pathophysiology underlying MASLD is not yet fully understood, but obesity and insulin resistance in T1DM are increasing over time,^[17] and these are major risk factors for MASLD. Insulin resistance plays a significant role in the pathogenesis of T2DM; however, its presence has also been demonstrated to a considerable extent in patients with T1DM.^[18] In patients with T1DM, hepatic mitochondrial energy metabolism is impaired. These alterations and progressive mitochondrial dysfunction, together with hepatic

insulin resistance, may contribute to the development of MASLD. An increase in free fatty acids and de novo lipogenesis is observed in the liver. Adiposity distribution also has a significant impact on MASLD development. A study investigating the association between adipose distribution and hepatic steatosis demonstrated a relationship between visceral adipose tissue area and MASLD.^[19]

A recent meta-analysis examined 13,006 T1DM cases and found that 22.24% had MASLD, 13.25% had CSF, and 5.12% had advanced fibrosis.^[20] In our study, according to FibroScan® results, 13 (12.9%) patients had MASLD (CAP≥275dB/m), and three (23.1%) of these patients had CSF, all of whom also had advanced fibrosis. In a study conducted by Serdarova et al.^[21] on 115 adult patients with T1DM, the prevalence of MASLD was found to be 47% based on CAP scores. It should be noted that the CAP cut-off for steatosis was 233dB/m in that study, which may explain the higher prevalence of MASLD compared to our findings. A Belgian study using ultrasonog-

raphy in patients with T1DM reported a MASLD prevalence of 16.2%, and the overall CSF prevalence was 3.8% according to FibroScan® results ($F \geq 8 \text{ kPa}$), while this rate reached 13.2% among MASLD patients.^[22] The prevalence of steatotic liver disease in that study is similar to our findings (12.9%), further supporting the notion that patients with steatosis are more likely to have fibrosis. In our study, the overall CSF prevalence was 5%, while it was 66.7% among MASLD patients. In the study conducted by Fuhri Snethlage et al.^[23] in 453 T1DM patients using vibration-controlled transient elastography ($\text{CAP} \geq 280.0 \text{ dB/m}$ for steatosis, $\text{LSM} \geq 8 \text{ kPa}$ for fibrosis), the prevalence of hepatic steatosis and fibrosis was found to be 9.5% and 3.5%, respectively.

High blood pressure, older age, longer disease duration, and higher BMI were identified as risk factors associated with the development of MASLD in patients with T1DM.^[23] In our study, hypertension, dyslipidemia, and high BMI, particularly $>26 \text{ kg/m}^2$, were found to be significant risk factors for MASLD, whereas no association was found between age and MASLD. Furthermore, based on ROC and survival analyses, MASLD was found to be more common in patients with a disease duration <180 months compared to those with a disease duration >180 months, which is inconsistent with the literature. According to our results, a sensitivity of 54% and a specificity of 63% indicate moderate diagnostic performance. This suggests that predicting MASLD development based solely on disease duration is not sufficiently robust and should be considered alongside other clinical parameters. Nonetheless, the statistically significant association observed suggests that this phenomenon may be particularly relevant in certain subgroups, such as obese young individuals or those exhibiting insulin resistance. This finding, which contradicts the existing literature, was not supported by multivariate analyses (Table 4). We believe that the small number of patients included in the study may have contributed to this discrepancy.

High waist circumference is also a significant risk factor for MASLD in this patient group.^[21] Our study found that waist circumference, especially $>89.5 \text{ cm}$, was a risk factor for the development of MASLD. Prolonged hyperglycemia and poor glucose control are also significant risk factors for MASLD in these patients.^[24] Our study also showed that mean fasting glucose levels were higher in patients with MASLD.

No other study has evaluated MASLD using such detailed non-invasive scores in patients with T1DM. In our study, the scores most strongly associated with MASLD were the Fatty Liver Index and the Hepatic Steatosis Index. However, the blood-based scores used (FAST, Agile, etc.) were originally developed for T2DM/MASLD populations and require

further validation in T1DM patients. The small sample size is the most important limitation of our study. However, MASLD in patients with T1DM remains an extremely understudied topic. We believe that this study, which evaluates the prevalence of MASLD in T1DM patients, the role of non-invasive tests in its diagnosis, and associated risk factors, will contribute significantly to the screening and diagnosis of MASLD in this population, for which no consensus has yet been established. Further studies with larger patient populations are needed to draw more definitive conclusions in this area.

Conclusion

Long-term impaired glucose control, high BMI, increased waist circumference, hypertension, and dyslipidemia are significant risk factors for MASLD in patients with T1DM. Various prevalence rates of MASLD in patients with T1DM have been reported in the literature. As patients are followed for longer periods with newer treatment modalities, MASLD is emerging as a significant health problem that is increasingly encountered. There is currently no consensus on screening and diagnostic pathways for MASLD in T1DM; therefore, further research is needed in this area.

Disclosures

Ethics Committee Approval: This study was approved by the Istanbul University Faculty of Medicine Hospital Ethics Committee (Date: 11.03.2022, Decision no: 2022/348).

Informed Consent: The written informed consent was obtained from the patients.

Conflict of Interest: None declared.

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