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# Liver fibrosis and liver stiffness in patients with obesity and type 1 diabetes

Ebaa Al-Ozairi MD[1] | Mohammad Irshad PhD[1] | Jumana AlKandari MSc[1,2] | Anant Mashankar MD[3] | Dherar Alroudhan MD[1,2] | Carel W. le Roux MD[1,4,5]

[1]DAFNE Unit, Clinical Care Research and Clinical Trials Unit, Dasman Diabetes Institute, Kuwait City, Kuwait

[2]Amiri Hospital, Ministry of Health, Kuwait City, Kuwait

[3]Diagnostic Imaging Centre, Dasman Diabetes Institute, Kuwait City, Kuwait

[4]Diabetes Complications Research Centre, University College Dublin, Dublin, Ireland

[5]Diabetes Research Centre, Ulster University, Belfast, UK

**Correspondence**
Ebaa Al-Ozairi, MD, DAFNE Unit, Clinical Care Research and Clinical Trials Unit, Dasman Diabetes Institute, Kuwait City, Kuwait and Carel W. le Roux, MD, Diabetes Research Center, Ulster University, Belfast, UK.
Email: ebaa.alozairi@dasmaninstitute.org and carel.leroux@ucd.ie

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## Abstract

**Aim:** To compare hepatic stiffness and fat fraction in patients with obesity and type 1 diabetes (T1D) with type 2 diabetes (T2D) with a similar body mass index (BMI).

**Methods:** In this prospective cross-sectional study, 90 participants with T1D (BMI 30.5 ± 4.5 kg/m$^2$; diabetes duration 20.5 ± 9.8 years; HbA1c 8.2% ± 1.4%) and 69 with T2D (BMI: 30.8 ± 4.6 kg/m$^2$; diabetes duration: 11.7 ± 7.8 years; HbA1c: 7.3% ± 1.4%) were included. Liver fat fraction and stiffness were examined by magnetic resonance imaging and elastography, respectively. Logistic regressions were used to evaluate associations with biomedical variables.

**Results:** The mean liver stiffness score in patients with obesity and T1D was 2.2 ± 0.5 kPa, while in T2D it was 2.6 ± 0.8 kPa ($P < .001$). The liver fat fraction in patients with obesity and T1D was 3.7% ± 6.3%, and in T2D it was 10.6% ± 7.9% ($P < .001$). Metabolic dysfunction-associated steatotic liver disease (MASLD) was present in 13.3% of patients with T1D and in 69.6% of patients with T2D, whereas fibrosis was suggested in 7.8% of patients with T1D and in 27.5% of patients with T2D. Liver stiffness was four times higher in patients with T2D compared with those with T1D (odds ratio = 5.4, 95% confidence interval: 2.1-13.6, $P < .001$). Aspartate transaminase (AST), alanine transaminase, gamma-glutamyl transferase (GGT), triglycerides and the android-to-gynoid ratio were associated with elevated fat fraction in both cohorts. AST and GGT were associated with elevated liver stiffness in both cohorts.

**Conclusions:** Patients with obesity and T1D had lower liver fat and liver stiffness compared with those patients with T2D, despite similar levels of BMI, a longer duration of diabetes and worse glycaemic control.

KEYWORDS
liver fat fraction, liver stiffness, MASLD, MRE, type 1 diabetes

## 1 | INTRODUCTION

Type 2 diabetes (T2D) has been associated with an increased risk of metabolic dysfunction-associated steatotic liver disease (MASLD),[1] previously known as non-alcoholic fatty liver disease (or NAFLD),[2] which can cause liver fibrosis and cirrhosis and end-stage liver disease.[3,4] The aetiology of MASLD is multifactorial, and the 'multiple hit' theory recognizes various components in its pathophysiology, such as hyperglycaemia, insulin resistance, obesity and gut microbiota, as well as environmental and genetic factors.[5] The pathophysiological changes in adipose tissue, the intestinal barrier or the immune system may also trigger and promote the progression of MASLD.[6]

The prevalence of MASLD has been increasing along with obesity, affecting an estimated 25% of the global population, with the highest prevalence observed in the Middle East region, especially in those with T2D.[7,8] The incidence rate is thought to be lower in type 1 diabetes (T1D), although altered glucose and lipid metabolism in inadequately controlled T1D or T2D could theoretically contribute to the development of MASLD. MASLD appears to be increasing in patients with T1D because of the increase in metabolic risk factors such as obesity.[9,10] However, it is unknown whether the prevalence of MASLD is higher in T2D than in T1D when the degree of obesity is similar.

The prevalence of MASLD in patients with T1D correlated with the degree of obesity.[11] Insulin deficiency in T1D may contribute to elevate fatty acid release from adipose tissue, leading to fat accumulation in the liver.[12] Frequent non-severe hypoglycaemia episodes in patients with T1D are also associated with subsequent weight gain.[13] Moreover, fluctuations in blood glucose levels in patients with T1D contribute to metabolic imbalances, potentially influencing the accumulation of fat in the liver, which appears to increase the risk of MASLD.[12]

Not all cases of MASLD exhibit elevated levels of alanine transaminase (ALT), aspartate transaminase (AST) and gamma-glutamyl transferase (GGT) enzymes, and elevated levels of ALT do not consistently predict the degree of inflammation and cirrhosis.[14] Calculation of the MASLD fibrosis score and the fibrosis-4 (FIB-4) index based on serum biomarkers still have suboptimal accuracy and precision.[15] Histological examinations of liver biopsies remain the gold standard for ascertaining the degree of inflammation, cirrhosis and fibrosis.[16] However, liver biopsy is associated with potentially serious complications.[17] Alternative non-invasive methods, such as ultrasound and magnetic resonance imaging (MRI) techniques, are increasingly used in clinical practice. Magnetic resonance elastography (MRE) measures liver stiffness (LS), and it is a more sensitive and specific technique with regard to inflammation, fibrosis and cirrhosis.[18] Another MRI-based technique, proton-density fat fraction (PDFF) scanning, provides steatosis stages.[19] To the best of our knowledge, no other studies have examined LS by MRE in patients with T1D. We aimed to compare liver stiffness (LS) and fat fraction (FF) by MRE in patients with T1D and T2D with a similar body mass index (BMI).

## 2 | METHODS

### 2.1 | Study design and participants

This cross-sectional study was conducted at a specialist diabetes institute, after receiving ethical approval from the Institutional Review Board, and it followed the guidelines set out in the Declaration of Helsinki. All participants were of Arab ethnicity, residing in Kuwait and receiving clinical care at the Dasman Diabetes Institute in Kuwait. Demographic and biomedical variables of people with T1D and T2D were collected from their electronic health records. The inclusion criteria were age 18 years or older and a documented diagnosis of T1D or T2D (as per the American Diabetes Association 2022 definition/criteria). All T1D participants were on insulin treatment, whereas T2D participants were on oral glycaemic drugs.

### 2.2 | Demographic and biomedical data

Ninety participants with T1D and 69 with T2D were recruited sequentially from routine clinics. The participants were matched on a group level for BMI to ensure that obesity was not a confounder for liver fat. Age, body mass, height, BMI (kg/m$^2$), waist circumference, HbA1c, ALT, AST, GGT, FIB-4 index, total cholesterol, HDL-C, LDL-C and triglycerides were measured.

### 2.3 | Imaging techniques

The radiologists conducting the PDFF and LS measurements were blinded to clinical and biochemical data. All MRI examinations were conducted using the same equipment from GE Healthcare (Signa Artist). Patients were instructed to fast for a minimum of 4 hours before the MRI scan to minimize potential physiological confounding factors. A torso phased-array coil was positioned over the abdomen as the patient lay supine during imaging. Two MRI techniques were used. For MASLD diagnosis, hepatic PDFF or FF was estimated using chemical shift-encoded MRI (Double Dixon technique). Liver fibrosis and LS were estimated using MRE. Significant metabolic dysfunction-associated fibrosis (MAF) was defined as MRE stiffness of 2.97 kPa or higher.[20,21] MASLD was defined as FF of 5% or higher.[22]

### 2.4 | Dual-energy x-ray absorptiometry

Dual-energy x-ray absorptiometry (DXA) (Lunar iDXA; GE Healthcare) systems include different types of hardware (filters, collimators, detectors) and analysis software (iDXA enCORE). DXA is based on the variable absorption of x-ray by different body components at high (70 keV) and low energy (40 keV) x-ray photons. These energies generate the image and dataset. The DXA software uses an analysis algorithm to process the generated dataset and estimate the body fat in

the form of regional and whole-body components. We used DXA to estimate fat mass, percentage body fat, android fat and gynoid fat through a whole-body scan. Android fat distribution is defined as having more fat around the midsection or waist (belly button). Gynoid fat distribution refers to the area of the hips that is located at the top of the thighs. The central fat distribution pattern was assessed by the android-to-gynoid fat ratio (AG ratio).

### 2.5 | Statistical analyses

This study included the maximum possible number of patients with T1D and T2D, matched by BMI and sex. In a post hoc power calculation, 60 participants per group were sufficient to detect differences in LS, and 24 participants per group were sufficient to detect differences in FF, and these numbers of participants achieved 90% power to identify statistically significant differences between these groups at $\alpha = .05$.

An independent *t*-test was employed to compare the mean values of variables between T1D and T2D. The chi-squared test was used to compare categorical variables. The outcomes are expressed as mean difference (MD), mean ± standard deviation, or as frequency with percentage. Multiple linear regression analysis was employed to investigate the association of liver FF and LS with biomedical variables. The models were 1: unadjusted; and 2: adjusted for sex, age, diabetes duration and BMI. The biomedical variables were compared between the MASLD (yes and no groups) or MAF (yes and no groups) using Mann–Whitney *U* tests. Data were analysed using SPSS software version 29.0 (Chicago, IL). A two-sided *P* value of .05 or less was considered statistically significant.

## 3 | RESULTS

In total, 90 patients with T1D and 69 patients with T2D were screened for liver MRI. The baseline characteristics of patients with T1D and those with T2D are provided in Table 1. For T1D, 50 patients (55.6%) were male, with a mean age of 35.3 years and mean diabetes duration of 20.5 years. For T2D, 40 patients (58.0%) were male, with a mean age of 60.4 years and mean diabetes duration of 11.7 years. Patients with T1D were younger and had a longer duration of diabetes compared with those with T2D ($P < .001$). However, there were no differences between T1D and T2D for mean BMI (30.5 ± 4.5 vs. 30.8 ± 4.6 kg/m$^2$, $P = .73$), while patients with T2D had a slightly larger waist circumference than patients with T1D (MD 7.6 cm, $P < .001$). Patients with T1D had significantly lower triglyceride levels and higher LDL-C, HDL-C and total cholesterol levels compared with those with T2D (all $P < .015$). Diabetes regulation, as measured by HbA1c, was slightly better in the T2D group compared with the T1D group (−0.9%, $P < .001$). A significant difference was found between the T1D and T2D groups for ALT ($P = .037$), but not for AST ($P = .72$) or GGT ($P = .86$). The T2D group had a higher FIB-4 index compared with the T1D group (0.9 ± 0.4 vs. 0.5 ± 0.3, $P < .001$). The DXA scan showed that the T2D group had more android fat and a higher AG ratio than the T1D group ($P = .001$ and $P < .001$, respectively). However, there were no significant differences in total tissue fat, gynoid fat, lean mass and total mass between the T1D and T2D groups.

LS was higher in T2D than in T1D (2.6 ± 0.8 vs. 2.2 ± 0.5 kPa, $P < .001$). The liver FF in T2D was also higher than in T1D (10.6% ± 7.9% vs. 3.7% ± 6.3%, $P < .001$). In logistic regression, adjusted for sex, BMI and diabetes duration, LS was five times higher in T2D compared with T1D (odds ratio [OR] = 5.4, 95% confidence interval [CI]: 2.1-13.3, $P < .001$). However, FF was slightly higher in T2D compared with T1D (OR = 1.2, 95% CI: 1.1-1.3, $P < .001$) (Table S1). MASLD (as assessed by MRI-PDFF > 5%) was present in 13.3% of T1D patients and in 69.6% of T2D ($P < .001$). MAF (as assessed by MRE > 2.97 kPa) was present in 7.8% of T1D patients and in 27.5% of T2D patients ($P < .001$). No severe MAF was reported in either the T1D group or the T2D group. A detailed description of biomedical variables in T1D and T2D with and without MASLD and fibrosis is presented in Tables S2 and S3.

Among the T2D participants, 23 used sodium-glucose co-transporter-2 inhibitors (SGLT2i), while six used both SGLT2i and glucagon-like peptide-1 receptor agonists (GLP1-RA); meanwhile, among the T1D participants, three used a GLP1-RA and four used both GLP1-RA and SGLT2i. In post hoc tests, there were no significant differences in liver FF and LS between the therapeutic and non-therapeutic groups for T1D or T2D (Table S4).

Regression analysis is presented in Tables 2 and 3. In model 1 (unadjusted), the FF in T1D was positively associated with ALT, AST, GGT, triglycerides, HbA1c, android fat, total mass, lean tissue, bone mineral content (BMC) and the AG ratio, and was negatively associated with HDL-C. In model 2 (adjusted for sex, diabetes duration and BMI), the FF remained associated with ALT, AST, GGT, triglycerides and HbA1c, total mass, the AG ratio and HDL-C. The FF score in T2D was positively associated with ALT, AST, GGT, triglycerides, android fat and the AG ratio. In model 2, the FF score remained associated with ALT, AST, GGT, triglycerides, android fat and the AG ratio.

In model 1 (unadjusted), the LS in T1D was positively associated with AST, GGT, triglycerides and the FiB-4 index, and was negatively associated with HDL-C. In model 2, the LS score remained associated with AST, GGT, triglycerides and HDL-C. The LS score in T2D was positively associated with ALT, AST, GGT and the FiB-4 index and, in model 2, remained associated with these variables.

## 4 | DISCUSSION

FF (%) and LS (kPa) were lower in patients with T1D compared with those with T2D when BMI was similar, even although glycaemia and the duration of diabetes were worse in patients with T1D. In logistic regression, T1D had lower odds of LS compared with T2D, and this association persisted even after adjustment for BMI, sex and diabetes duration. The majority of participants with T1D and T2D (92.2% and 72.5%, respectively) had no fibrosis. However, there was a higher

**TABLE 1** Baseline characteristics of patients with type 1 diabetes and type 2 diabetes in the current study.

| Variable | Type 1 diabetes ($N = 90$) Mean (SD) or *n* (%) | Type 2 diabetes ($N = 69$) Mean (SD) or *n* (%) | *P* value |
|---|---|---|---|
| Age (y) | 35.3 (9.4) | 60.4 (8.4) | < .001 |
| Male | 50 (55.6) | 40 (58.0) | .761 |
| Female | 40 (44.4) | 29 (42.0) | |
| Diabetes duration (y) | 20.5 (9.8) | 11.7 (7.8) | < .001 |
| BMI (kg/m$^2$) | 30.5 (4.5) | 30.8 (4.6) | .732 |
| BMI range (kg/m$^2$) | 25.0-47.7 | 25.0-44.3 | |
| Waist circumference (cm) | 96.1 (13.8) | 103.7 (11.1) | < .001 |
| Systolic BP (mmHg) | 124.7 (12.4) | 124.1 (14.0) | .758 |
| Diastolic BP (mmHg) | 74.4 (8.3) | 71.7 (9.9) | .060 |
| AST (u/L) | 25.2 (17.0) | 20.8 (7.6) | .047 |
| ALT (u/L) | 29.9 (19.8) | 35.9 (14.6) | .037 |
| GGT (u/L) | 34.6 (43.4) | 36.1 (24.3) | .799 |
| FIB-4 index | 0.5 (0.3) | 0.9 (0.4) | < .001 |
| Triglycerides (mmol/L) | 1.0 (0.9) | 1.5 (0.8) | .003 |
| LDL-cholesterol (mmol/L) | 2.6 (1.0) | 2.2 (1.0) | .014 |
| HDL-cholesterol (mmol/L) | 1.5 (0.4) | 1.3 (0.4) | .001 |
| Total cholesterol (mmol/L) | 4.6 (1.1) | 4.1 (1.1) | .015 |
| HbA1c (%) | 8.2 (1.4) | 7.3 (1.4) | < .001 |
| Total tissue fat (%) | 39.5 (8.5) | 40.3 (6.5) | .510 |
| Android tissue fat (%) | 41.3 (10.2) | 46.4 (8.7) | .001 |
| Gynoid tissue fat (%) | 42.3 (9.7) | 39.5 (8.3) | .056 |
| Total mass (kg) | 81.8 (12.9) | 81.9 (14.6) | .985 |
| Total lean mass (g) | 48 030.5 (10 015.1) | 47 207.0 (8625.3) | .587 |
| BMC (g) | 2390.6 (432.5) | 2498.1 (457.9) | .133 |
| AG ratio | 1.0 (0.2) | 1.2 (0.3) | < .001 |
| FF (%) | 3.7 (6.3) | 10.6 (7.9) | < .001 |
| MASLD | | | |
| Yes | 12 (13.3) | 48 (69.6) | < .001 |
| No | 78 (86.7) | 21 (30.4) | |
| Liver stiffness (kPa) | 2.2 (0.5) | 2.6 (0.8) | < .001 |
| MAF | | | |
| Yes | 7 (7.8) | 19 (27.5) | < .001 |
| No | 83 (92.2) | 50 (72.5) | |

Abbreviations: AG, android-to-gynoid fat; ALT, alanine transaminase; AST, aspartate transaminase; BMC, bone mineral content; BMI, body mass index; BP, blood pressure; FF, fat fraction; FIB-4 index, fibrosis-4 index; GGT, gamma-glutamyl transferase; MAF, metabolic dysfunction-associated fibrosis; MASLD, metabolical dysfunction-associated steatotic liver disease; SD, standard deviation.

prevalence of MASLD in patients with T2D compared with those with T1D.

The comparatively low incidence of MASLD in T1D may be attributed to the suppression of lipolysis by exogenous insulin therapy.[23] T1D is associated with insufficient insulin secretion caused by β-cell dysfunction or loss, while T2D involves insulin resistance. Insulin normally inhibits lipolysis in adipose tissue and, without sufficient insulin, lipolysis is increased and raises the levels of free fatty acids in the blood. Insulin resistance increased hepatic de novo lipogenesis, converting carbohydrates into fatty acids. In both cases, fatty acids are taken up by the liver, and these mechanisms collectively contribute to increased liver fat and triglycerides, often progressing to MASLD.[24] Insulin treatment in T1D may restrict the serum free fatty acid flux to the liver and reduce triglyceride synthesis.[25] Lipolysis appears to be suppressed by insulin in T1D patients compared with age- and BMI-matched healthy subjects,

**TABLE 2** Associations of liver stiffness (pKa) with biomedical variables in patients with type 1 diabetes and type 2 diabetes.

| | Type 1 diabetes | | | | Type 2 diabetes | | | |
|---|---|---|---|---|---|---|---|---|
| | Model 1 | | Model 2 | | Model 1 | | Model 2 | |
| Variable | β (95% CI) | *P* | β (95% CI) | *P* | β (95% CI) | *P* | β (95% CI) | *P* |
| ALT (u/L) | 0.01 (0.001, 0.01) | .03 | 0.005 (−0.0004, 0.01) | .07 | 0.02 (0.01, 0.03) | .002 | 0.02 (0.01, 0.04) | .001 |
| AST (u/L) | 0.01 (0.001, 0.01) | .02 | 0.009 (−0.0003, 0.01) | .05 | 0.05 (0.03, 0.08) | < .001 | 0.06 (0.03, 0.08) | < .001 |
| GGT (u/L) | 0.004 (0.002, 0.01) | < .001 | 0.004 (0.002, 0.007) | < .001 | 0.02 (0.01, 0.03) | < .001 | 0.02 (0.01, 0.03) | < .001 |
| FIB-4 index | 0.23 (−0.11, 0.57) | .18 | 0.005 (−0.44, 0.45) | .98 | 0.92 (0.41, 1.43) | .001 | 1.24 (0.68, 1.80) | < .001 |
| Triglycerides (mmol/L) | 0.23 (0.13, 0.33) | < .001 | 0.22 (0.12, 0.32) | < .001 | 0.06 (−0.19, 0.31) | .63 | 0.05 (−0.21, 0.31) | .68 |
| LDL-cholesterol (mmol/L) | −0.02 (−0.11, 0.06) | .60 | −0.003 (−0.08, 0.08) | .94 | 0.18 (−0.02, 0.38) | .08 | 0.15 (−0.07, 0.38) | .18 |
| HDL-cholesterol (mmol/L) | −0.41 (−0.64, −0.18) | .001 | −0.48 (−0.73, −0.23) | < .001 | 0.03 (−0.50, 0.56) | .91 | −0.04 (−0.72, 0.65) | .91 |
| Total cholesterol (mmol/L) | 0.01 (−0.09, 0.10) | .91 | 0.03 (−0.06, 0.12) | .53 | 0.17 (−0.01, 0.36) | .07 | 0.16 (−0.06, 0.37) | .15 |
| HbA1c (%) | 0.03 (−0.05, 0.10) | .50 | 0.04 (−0.04, 0.11) | .31 | −0.06 (−0.21, 0.08) | .36 | −0.07 (−0.22, 0.07) | .31 |
| Total tissue fat (%) | −0.002 (−0.0003, 0.021) | .75 | 0.003 (−0.02, 0.02) | .76 | 0.02 (−0.01, 0.05) | .18 | −0.016 (−0.09, 0.05) | .65 |
| Android tissue fat (%) | 0.01 (−0.003, 0.02) | .18 | 0.009 (−0.004, 0.02) | .17 | 0.02 (−0.004, 0.04) | .10 | 0.012 (−0.02, 0.04) | .39 |
| Gynoid tissue fat (%) | −0.01 (−0.02, 0.004) | .20 | −0.009 (−0.03, 0.01) | .32 | 0.01 (−0.02, 0.03) | .60 | −0.037 (−0.08, 0.01) | .11 |
| Total mass (kg) | 0.01 (-0.0003, 0.02) | .06 | 0.003 (−0.01, 0.02) | .66 | 0.01 (−0.01, 0.02) | .29 | 0.006 (−0.03, 0.04) | .74 |
| Total lean mass (g) | 0.00001 (−0.000002, 0.00002) | .09 | 0.000001 (−0.00001, 0.00002) | .90 | 0.000002 (−0.00002, 0.00003) | .83 | 0.00001 (−0.00004, 0.00006) | .64 |
| BMC (g) | 0.0001 (−0.00014, 0.0003) | .40 | 0.00004 (−0.0003, 0.0004) | .80 | 0.0002 (−0.0003, 0.0006) | .40 | 0.001 (−0.00004, 0.001) | .07 |
| AG ratio | 0.81 (0.35, 1.27) | .001 | 0.60 (−0.27, 1.47) | .17 | 0.19 (−0.42, 0.81) | .53 | 0.46 (−0.26, 1.18) | .21 |
| Liver fat fraction (%) | 0.014 (−0.002, 0.03) | .09 | 0.01 (−0.005, 0.03) | .16 | 0.023 (−0.002, 0.05) | .07 | 0.02 (−0.01, 0.04) | .17 |

*Note*: Model 1: unadjusted. Model 2: adjusted for sex, age, BMI and diabetes duration.
Abbreviations: AG, android-to-gynoid fat; ALT, alanine transaminase; AST, aspartate transaminase; BMC, bone mineral content; BMI, body mass index; CI, confidence interval; FIB-4 index, fibrosis-4 index; GGT, gamma-glutamyl transferase.

suggesting that insulin therapy may play a protective role in preventing the development of MASLD.[26] Therefore, despite having longer disease durations and poorer glycaemic control, T1D patients exhibited less accumulation of liver fat and slower progression towards liver fibrosis.[12] Even patients with T2D who not being treated with insulin may have increased fat synthesis, contributing to liver fat accumulation and progression to liver fibrosis.[27] Cusi et al. also found that patients with T2D had a higher liver fat content compared with patients with T1D.[25] However, among patients with T2D, those undergoing insulin therapy had lower liver fat content than those who were not receiving insulin.[25] The results suggest that insulin therapy may help in reducing liver fat accumulation in patients with T1D and that this mechanism could be extended to patients with T2D.

The mean LS in patients with T1D was almost equal to the values reported for healthy adults (2.1 kPa).[28] By contrast, patients with T2D in Kuwait had similar LS to those reported in a Korean T2D population (2.7 kPa).[29] A meta-analysis encompassing 29 different studies revealed that elevated LS in patients with T2D was four times higher than in patients with T1D.[30] Liver fat content was also lower in patients with T1D compared with patients with T2D.[25]

In the current study, various biomedical variables showed an association with FF and LS. Some associations were common in both the T1D and T2D groups. AST, ALT, GGT, triglycerides and the AG ratio were associated with elevated FF in both the T1D and T2D groups. AST and GGT were associated with elevated LS in both the T1D and T2D groups. Increased AST is a known and independent predictor of hepatic fibrosis and MASLD in T2D.[31,32] An elevated FIB-4 index was associated with LS in both T1D (univariate analysis) and T2D (univariate and multivariate analysis). FIB-4 index is considered a useful tool for screening patients with T1D or T2D who may be at risk of MASLD and fibrosis.[33]

In addition, higher triglycerides and lower HDL-C were associated with the elevation of LS in T1D. Higher triglycerides was also

**TABLE 3** Associations of liver fat fraction (%) with biomedical variables in patients with type 1 diabetes and type 2 diabetes.

| | Type 1 diabetes | | | | Type 2 diabetes | | | |
|---|---|---|---|---|---|---|---|---|
| | Model 1 | | Model 2 | | Model 1 | | Model 2 | |
| Variable | β (95% CI) | *P* | β (95% CI) | *P* | β (95% CI) | *P* | β (95% CI) | *P* |
| ALT (u/L) | 0.15 (0.09, 0.21) | < .001 | 0.14 (0.08, 0.20) | < .001 | 0.24 (0.12, 0.36) | < .001 | 0.28 (0.17, 0.40) | < .001 |
| AST (u/L) | 0.09 (0.01, 0.17) | .02 | 0.09 (0.01, 0.17) | .03 | 0.47 (0.25, 0.70) | < .001 | 0.51 (0.29, 0.72) | < .001 |
| GGT (u/L) | 0.05 (0.02, 0.07) | .003 | 0.04 (0.01, 0.07) | .005 | 0.14 (0.07, 0.22) | < .001 | 0.14 (0.07, 0.22) | < .001 |
| FIB-4 index | 1.64 (−2.76, 6.04) | .46 | 1.88 (−3.95, 7.71) | .52 | 1.34 (−4.00, 6.68) | .62 | 2.03 (−3.92, 7.98) | .50 |
| Triglycerides (mmol/L) | 2.29 (0.92, 3.66) | .001 | 2.08 (0.70, 3.46) | .004 | 3.42 (1.14, 5.70) | .004 | 3.30 (1.02, 5.58) | .01 |
| LDL-cholesterol (mmol/L) | 0.50 (−0.78, 1.79) | .44 | 0.44 (−0.92, 1.79) | .53 | −0.09 (−2.06, 1.88) | .93 | −0.57 (−2.69, 1.56) | .60 |
| HDL-cholesterol (mmol/L) | −3.82 (−6.90, −0.73) | .02 | −4.17 (−7.64, −0.70) | .02 | −4.53 (−9.45, 0.39) | .07 | −6.43 (−12.64, −0.22) | .04 |
| Total cholesterol (mmol/L) | 0.66 (−0.55, 1.86) | .28 | 0.60 (−0.64, 1.85) | .34 | 0.21 (−1.61, 2.02) | .82 | −0.10 (−2.14, 1.94) | .92 |
| HbA1c (%) | 1.42 (0.52, 2.33) | .002 | 1.29 (0.36, 2.22) | .01 | 0.99 (−0.35, 2.34) | .15 | 0.86 (−0.48, 2.19) | .20 |
| Total tissue fat (%) | 0.05 (−0.11, 0.21) | .54 | 0.05 (−0.21, 0.32) | .69 | 0.24 (−0.05, 0.53) | .11 | −0.07 (−0.72, 0.58) | .83 |
| Android tissue fat (%) | 0.16 (0.03, 0.29) | .02 | 0.15 (−0.02, 0.31) | .08 | 0.37 (0.17, 0.57) | .001 | 0.31 (0.07, 0.56) | .01 |
| Gynoid tissue fat (%) | −0.02 (−0.16, 0.12) | .76 | −0.09 (−0.34, 0.15) | .45 | 0.02 (−0.21, 0.25) | .84 | −0.49 (−0.90, −0.08) | .02 |
| Total mass (kg) | 0.20 (0.10, 0.29) | < .001 | 0.27 (0.09, 0.45) | .004 | 0.11 (−0.01, 0.24) | .08 | −0.02 (−0.37, 0.32) | .89 |
| Total lean mass (g) | 0.0002 (0.00003, 0.0003) | .01 | 0.0002 (−0.00002, 0.0004) | .08 | 0.0001 (−0.0001, 0.0003) | .40 | 0.0001 (−0.0004, 0.001) | .80 |
| BMC (g) | 0.004 (0.001, 0.01) | .02 | 0.004 (0.0001, 0.01) | .04 | 0.0004 (−0.004, 0.005) | .85 | −0.00 (−0.01, 0.01) | .79 |
| AG ratio | 10.37 (4.39, 16.36) | .001 | 14.37 (2.36, 26.39) | .02 | 7.82 (2.23, 13.42) | .01 | 11.38 (5.16, 17.60) | .001 |
| Liver stiffness (kPa) | 2.33 (−0.36, 5.02) | .09 | 2.00 (−0.84, 4.84) | .16 | 2.13 (−0.15, 4.40) | .07 | 1.60 (−0.72, 3.92) | .17 |

*Note*: Model 1: unadjusted. Model 2: adjusted for sex, age, BMI and diabetes duration.
Abbreviations: AG, android-to-gynoid fat; ALT, alanine transaminase; AST, aspartate transaminase; BMC, bone mineral content; BMI, body mass index; CI, confidence interval; FIB-4 index, fibrosis-4 index; GGT, gamma-glutamyl transferase.

associated with FF in both T1D and T2D. This is consistent with previous studies showing higher triglycerides associated with liver fibrosis in patients with T2D,[34] steatosis and MASLD in both T1D and T2D.[34,35]

Poor glycaemic control has been suggested as an independent predictor of LS in T2D,[36] but this is not consistently found in either T1D or T2D.[25] Also, we did not find an association between HbA1c and LS in either T1D or T2D. HbA1c was positively associated with the liver FF in T1D, in both univariate and multivariate logistic regression analysis. One possible explanation for this is that patients with T1D had a significantly higher HbA1c level compared with patients with T2D. The poorly controlled blood glucose levels in diabetes can stimulate the conversion of excess sugars into fat in the liver.[37] On the other hand, intensification of glucose-lowering medication by T2D patients might mask this association.[25]

LS was not associated with total tissue fat, android fat, gynoid fat, lean mass or BMC with either univariate or multivariate logistic regression in T1D or T2D. However, these variables (except for gynoid fat) were associated with the liver FF in T1D. In T2D, android tissue fat and the AG ratio were positively associated, whereas gynoid fat was negatively associated, with the liver FF. This is consistent with previous work showing that android fat was positively associated with MASLD, whereas gynoid fat was negatively associated with MASLD.[38]

Our study has several limitations. We did not compare our findings with liver histology because there was no clinical indication to perform a liver biopsy in our patients. We did, however, use state-of-the art imaging to investigate our patients. Although our patients were matched for BMI, the cohort with T1D had a longer duration of diabetes and worse glycaemic control, suggesting that we may have overestimated MASLD in our T1D cohort. However, matching T1D and T2D participants based on waist/height ratios, waist/hip ratios or age and comparing them with people without diabetes may provide important insights.

In conclusion, patients with T1D have lower liver fat content and LS compared with patients with T2D, despite having similar levels of obesity, a longer duration of diabetes and worse glycaemic control. As obesity increases in patients with T1D, more patients will be diagnosed with MASLD, but patients with T1D appear to be at a lower risk compared with patients with T2D.

## AUTHOR CONTRIBUTIONS

Conceptualization and design: EAO and CWLR. Acquisition of data: MI, JAK, AM and DA. Analysis and interpretation of data: MI, EAO and CWLR. All the authors contributed to writing the manuscript, verified the underlying manuscript data and approved the final version of the manuscript for publication.

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## CONFLICT OF INTEREST STATEMENT

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## PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.15760.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ORCID

*Ebaa Al-Ozairi* https://orcid.org/0000-0001-5006-4369
*Mohammad Irshad* https://orcid.org/0000-0002-7520-0221
*Carel W. le Roux* https://orcid.org/0000-0001-5521-5445

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## SUPPORTING INFORMATION

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