VIA MEDICA
RESEARCH PAPER
ISSN 2450–7458
e-ISSN 2450–8187

Ümmügülsüm Durak[1], Miraç Vural Keskinler[1], Gunes Alkaya Feyizoglu[1], Furkan Durak[2], Cundullah Torun[1], Tahsin Karaaslan[3], Aytekin Oğuz[1]

[1]Istanbul Medeniyet University, Department of Internal Medicine, Istanbul, Türkiye
[2]Prof. Dr. Ilhan Varank Training and Research Hospital, Department of Cardiology, Istanbul, Türkiye
[3]Istanbul Medeniyet University, Department of Nephrology, Istanbul, Türkiye

An Observational Study on the Association Between Surrogates of Visceral Adiposity and Albuminuria in Type 2 Diabetes

ABSTRACT

Objective: This study aimed to investigate the associations between albuminuria and visceral adiposity in patients with type 2 diabetes (T2D).

Materials and methods: This single-center cross-sectional study included patients with T2D. Anthropometric measurements, urine analyses, and fasting blood tests, were conducted. Patients diagnosed with hepatosteatosis within the past 3 months were invited to undergo transthoracic echocardiography to measure epicardial fat thickness (EFT). The clinical, laboratory, and imaging findings of patients with microalbuminuria (> 30 mg/day) were compared with those of patients without microalbuminuria using chi-square tests and t-tests.

Results: The study included 702 patients with a mean age of 58.9±10.9 years and a male predominance (57.8%). Microalbuminuria was present in 253 patients (36%). In the group with microalbuminuria, age, levels of glucose, triglycerides, HbA1c, FIB-4, and visceral adiposity index (VAI) scores were higher, while glomerular filtration rate (GFR), high-density lipoprotein (HDL) cholesterol levels, and the frequency of hypertension were lower compared to the patients without microalbuminuria ($p < 0.05$ for all). Out of 169 patients who underwent liver ultrasonography, hepatosteatosis was observed in 138 individuals (81.7%). Among the 59 patients who underwent echocardiography, an increased EFT was found in 25 (42.4%) patients. No significant differences were observed in EFT, hepatic steatosis presence, or stage between the microalbuminuria and non-microalbuminuria groups ($p = 0.807$, 0.834, and 0.351, respectively).

Conclusions: While no associations were found between microalbuminuria and hepatosteatosis or EFT, patients with microalbuminuria showed higher VAI and FIB-4 scores. The findings underscore the potential of these scores in predicting microalbuminuria in patients with T2D. (Clin Diabetol 2024; 13, 4: 216–223)

Keywords: diabetic nephropathy, albuminuria, epicardial adipose tissue, visceral adiposity

Address for correspondence:
Cundulah Torun, MD
Istanbul Medeniyet University, Department of Internal Medicine, Istanbul, Türkiye
Fahrettin Kerim Gokay Street, 34722 Kadikoy/Istanbul
Phone: + 905497949993
E-mail: cundullaht@gmail.com
Clinical Diabetology 2024, 13; 4: 216–223
DOI: 10.5603/cd.100161
Received: 15.04.2024 Accepted: 24.06.2024
Early publication date: 13.08.2024

Introduction

Obesity is a global epidemic, and it is widely recognized that increased visceral adipose tissue is closely associated with metabolic disorders. Renal lipid accumulation is a manifestation of increased visceral adiposity. The presence of albuminuria in individuals

with obesity is explained by renal injury associated with renal lipid accumulation [1].

Metabolic dysfunction-associated steatotic liver disease (MASLD), one of the most well-established conditions associated with increased visceral adiposity, stands as a prominent cause of liver-related morbidity and mortality [2, 3]. There are also studies indicating an association between microalbuminuria and MASLD [4, 5].

The association between epicardial fat thickness, a manifestation of increased visceral adipose tissue, and cardiometabolic diseases has recently been investigated. Epicardial fat is a visceral deposit of adipose tissue located between the myocardium and the visceral pericardium. Adipose tissue is involved in the production of proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-) and interleukin-6 (IL-6). These adipose tissue inflammation mediators may promote endothelial dysfunction [6]. Although there are many studies that demonstrate a link between abdominal adiposity and cardiometabolic risk factors, studies on the association between epicardial fat tissue and cardiometabolic risk factors are limited.

The aim of this study was to investigate whether indicators of increased visceral adiposity, such as epicardial fat thickness (EFT), visceral adiposity index (VAI), and hepatosteatosis, are associated with microalbuminuria in patients with type 2 diabetes (T2D).

Materials and methods

Study design

This single-center observational study included patients with T2D, who were regularly attending our hospital's internal medicine outpatient clinics. Between November 2021 and June 2022, the medical records of patients with T2D were reviewed every 2 weeks using the hospital's electronic database.

Study participants

Patients diagnosed with malignancies, chronic inflammatory or autoimmune diseases, advanced chronic kidney disease (stages 4 and 5), chronic liver disease, congestive heart failure, and those who were pregnant or lactating were excluded from the study. Eligible patients were contacted by phone and invited to participate in the study. Patients who experienced a weight change equivalent to 5% of their body weight within the last 3 months were also excluded from the study. The study workflow, incorporating inclusion and exclusion criteria, is shown in Figure 1.

Ethical approval

The study was approved by the Istanbul Medeniyet University Clinical Research Ethics Committee (Decision No. 2022/0636). Informed consent was obtained from the patients, and the study adhered to the principles of the Helsinki Declaration throughout its duration.

Data collection

Patients who signed the informed consent form underwent a series of anthropometric measurements, including height, weight, and waist circumference (WC). The body mass index (BMI) was then calculated by dividing the patient's weight by the square of their height in meters (kg/m^2). After an 8–12-hour fast, blood samples were collected for analysis, which included measurements of glucose, insulin, glycated hemoglobin (HbA1c), creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

Urine analyses were performed, and based on their spot urine microalbumin/creatinine ratio, patients were categorized into 2 groups: those with values above 30 mg/day were placed in the microalbuminuria group, while those with values below this threshold were classified as the normoalbuminuria group.

The fibrosis-4 (FIB-4) score was calculated using the following formula:

(Age [years] × AST [IU/L])/(Platelet count [10^9/L] × √ALT [IU/L]) [7]

The visceral adiposity index (VAI) score was calculated using gender-specific equations as follows:

VAI in male = WC (cm)/(39.68 + (1.88 × BMI) × (TG (mmol/L)/1.03) × (1.31/HDL-C (mmol/L))

VAI in female = WC (cm)/(36.58 + (1.89 × BMI) × (TG (mmol/l)/0.81) × (1.52/HDL-C (mmol/l)) [8]

MASLD diagnosis and evaluation

Two radiologists evaluated patients who underwent abdominal ultrasonography for different reasons, adhering to the guidelines established by Saverymuttu et al. [9]. This evaluation considered the presence of variations in echo amplitude between the liver and kidney, the extent of echo penetration into the deeper areas of the liver, and the clarity of the liver's blood vessel structure. Based on these criteria, patients with MASLD were classified into grades 1 (mild), 2 (moderate), and 3 (severe).

Epicardial fat thickness measurement

Patients who had undergone abdominal ultrasound for any reason in the last 3 months and were found to have hepatosteatosis underwent transthoracic echocardiography (TTE).

Epicardial fat thickness was measured by a cardiologist with 7 years of professional experience. Patients

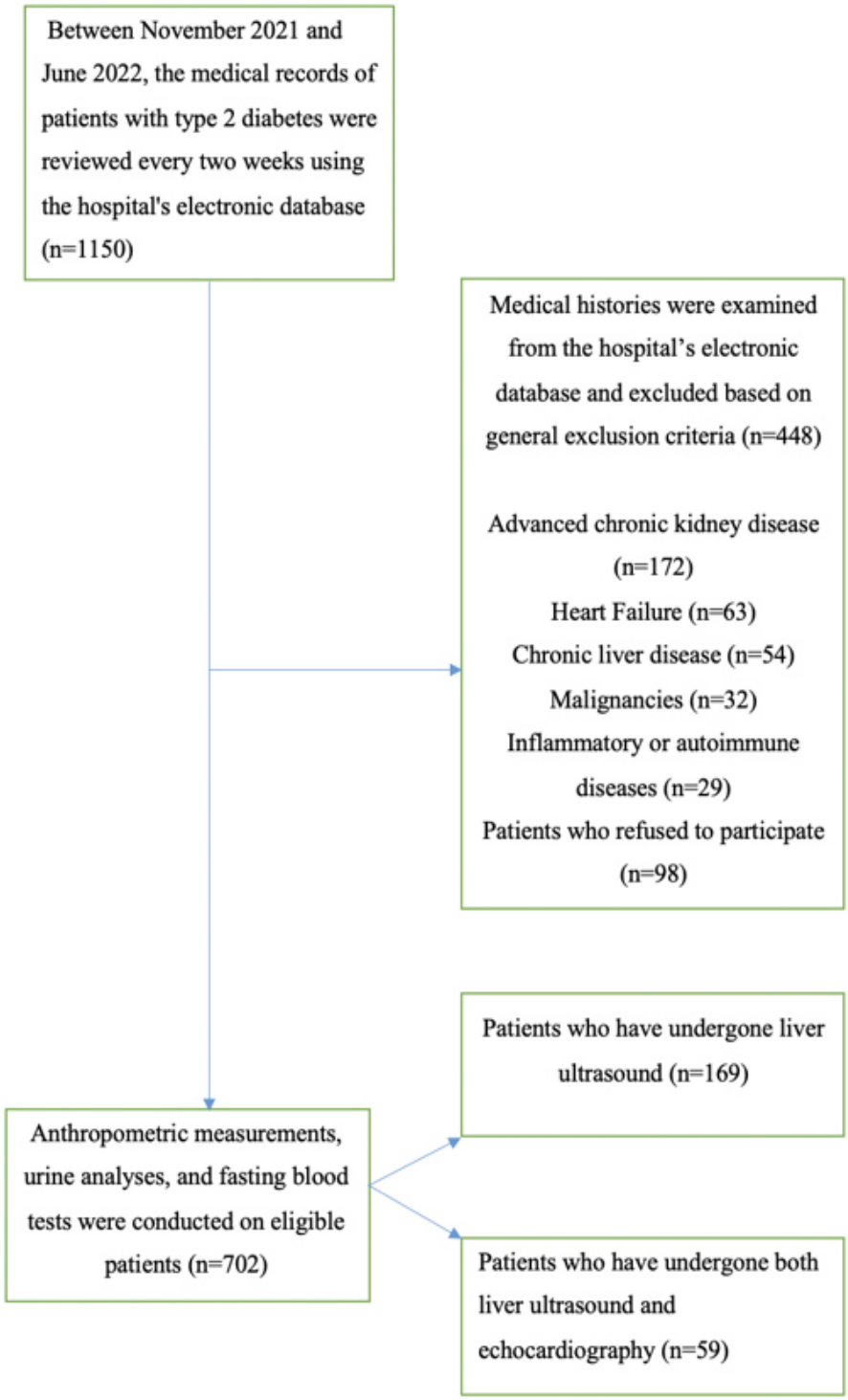

Figure 1. Flow Diagram of the Study Participants

underwent a minimum of 15 minutes of rest in a supine position, and EFT measurements were carried out using a 2.5-MHz probe on an echocardiography device (General Electric — Vivid S60 Echocardiography Device, Norway). EFT was defined as the echo-free space between the visceral and parietal pericardium along the anterior wall of the right ventricle. EFT was measured at end-diastole from the parasternal long-axis view of patients lying on their left side. The mean value covering 3 consecutive cardiac cycles was utilized for statistical analysis, and EFT was categorized into 2 groups: those with EFT below 7 mm and those with EFT 7 mm or greater [10].

Table 1. Baseline Clinical Characteristics of the Patients

Variable	n (%), median (min–max)
Gender (male)	406 (57.8)
Age [year]	59 (25–87)
Body mass index [kg/m^2]	31 (17.5–66.5)
Height [cm]	162 (138–196)
Weight [kg]	82 (43–181)
Waist circumference [cm]	101 (68–173)
Smoking	160 (22.8)
Alcohol consumption	10 (1.42)
Diabetes duration [year]	11 (1–42)
Hypertension	412 (58.7)
Hyperlipidemia	421 (60)
Leukocyte [mm^3]	8000 (4000–21,000)
Hemoglobin [gr/dL]	14 (8.9–18)
Platelet count [× 109/L]	269 (13–707)
ALT [U/L]	18 (4–128)
AST [U/L]	16 (5–223)
Glucose [mg/dL]	152 (61–558)
Uric acid [mg/dL]	4.4 (1.39–7.7)
Creatinine [mg/dL]	0.75 (0.38–1.7)
GFR [ml/min/1.73 m^2]	95.6 (40–152)
Triglycerides [mg/dL]	149 (39–1607)
HDL-C [mg/dL]	47 (12–133)
LDL-C [mg/dL]	104 (16–271)
HbA1c [mmol/mol]; [%]	65 (33–163); 8.1(5.2–17)
C-peptide [ng/mL]	2.5 (0.02–8.17)
Albuminuria [mg]	19.9 (0.2–940)
Microalbuminuria [n, %]	253 (36)

The results were presented in the form of nouns and percentages, or median values and minimum and maximum values

ALT — alanine aminotransferase, AST — aspartate aminotransferase, GFR — glomerular filtration rate, HDL-C — high-density lipoprotein cholesterol, LDL-C — low-density lipoprotein cholesterol, HbA1c — glycated hemoglobin

Statistical analysis

Descriptive statistics were presented as counts and percentages for categorical variables, and as mean ± ± standard deviation or median (minimum-maximum) for continuous variables. The presence of normal distribution was assessed through histograms, Q-Q plots, and normal distribution tests (Kolmogorov-Smirnov or Shapiro-Wilk). For categorical variables, Pearson's chi-square test was used, or in cases where assumptions were not met, Fisher's exact test was employed. In tables larger than 2 × 2, the Fisher-Freeman-Halton test was utilized when the number of observed values with expected values < 5 was substantial. In comparing continuous variables between 2 groups, either the independent samples t-test or Mann-Whitney U test was employed based on the normality of the distribution. Spearman or Kendall correlation analysis was conducted for assessing linear relationships between continuous variables. Situations in which the 2-sided p-value was < 0.05 were considered statistically significant. Data analysis was performed using SPSS (Statistical Package for the Social Sciences) version 20.

Results

The study included 702 patients with T2D with a mean age of 58.9 ± 10.9 years and a male predominance (57.8%). The mean body mass index was 1.8 ± 6.3 kg/m^2, and the mean duration of T2D was 11.8 ± 8.1 years. A total of 253 patients (36%) had microalbuminuria. The frequency of microalbuminuria was significantly lower in the metformin group (p = 0.019). No significant relationship was found between other antidiabetic drugs and microalbuminuria.

The clinical and laboratory characteristics of the patients are presented in Table 1. Metformin was used by 78.9% (n = 551), dipeptidyl peptidase-4 (DPP-4) inhibi-

Table 2. Comparison of Clinical Characteristics Between Patients With and Without Microalbuminuria

Characteristic	Microalbuminuria (–) (n = 449)	Microalbuminuria (+) (n = 253)	p-value
Gender (Male)	261 (64.3)	145 (35.7)	0.896
Age (year)	58.1±11.0	60.3 ± 10.7	0.009
Body mass index (kg/m^2)	31.2 (19.7–56.1)	30.9 (17.5–66.5)	0.599
Waist circumference (cm)	101 (68–160)	101 (70.0–173)	0.199
Smoking	100 (62.5)	60 (37.5)	0.731
Alcohol use	5 (50)	5 (50)	0.508
Diabetes duration	11 (1–41)	12.0 (1–42)	0.350
Hypertension	244 (59.2)	168 (40.8)	0.002
Hyperlipidemia	267 (63.4)	154 (36.6)	0.776
FIB-4	0.83 (0.24–19.4)	0.87 (0.26–7.29)	0.008
VAI	5.03 (0.51–50.1)	6.30 (0.11–49.7)	0.001
Leukocyte (mm^3)	8000 (4000–15,000)	8000 (4000–21,000)	0.559
Hemoglobin (gr/dL)	14 (8.9–18)	14 (9–18)	0.396
Platelet count (× 10^9/L)	270 (13.0–707)	268 (96–520)	0.669
ALT (U/L)	17 (5–113)	19 (4–128)	0.360
AST (U/L)	16 (5–98)	17 (6–223)	0.055
Glucose (mg/dL)	144 (61–452)	170 (70–558)	<0.001
Uric acid (mg/dL)	4.3 (1.39–7.7)	4.4 (1.7–7.5)	0.319
GFR (mL/min)	96.4 (40–131)	93.4 (42.4–152)	0.022
Triglycerides (mg/dL)	144 (39–930)	167 (46–1607)	0.002
HDL-C (mg/dL)	47 (12–133)	45.0 (22–94)	0.043
LDL-C (mg/dL)	102 (16–254)	109 (31–271)	0.146
HbA1c (mmol/mol); (%)	62 (37–163); 7.80 (5.5–17.0)	74 (33–162); 8.90 (5.2–16.9)	<0.001
C-peptide (ng/mL)	2.5 (0.02–8.17)	2.50 (0.21–8.11)	0.179

The results were presented in the form of nouns and percentages, or median values and minimum and maximum values.

ALT — alanine aminotransferase; AST — aspartate aminotransferase; FIB-4 — the fibrosis-4 score; GFR — glomerular filtration rate; HbA1c — glycated hemoglobin; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; VAI — visceral adiposity index

tor by 55.3% (n: 388), sodium glucose co-transporter-2 (SGLT-2) inhibitor by 66.1% (n: 464), pioglitazone by 19.2% (n: 135), glucagon-like peptide-1 (GLP-1) analog by 7.69% (n: 54), and insulin by 51.4% (n: 361).

A total of 169 patients underwent liver ultrasonography. Hepatosteatosis was not detected in 31 individuals (18.3%). Among the 138 patients with hepatosteatosis, 55 had grade 1 hepatosteatosis (39.9%), 67 had grade 2 hepatosteatosis (48.5%), and 16 had grade 3 hepatosteatosis (11.6%). A total of 59 patients underwent transthoracic echocardiography, and the median ejection fraction was 60%. Among them, 40 patients had stage 1 diastolic dysfunction (67.8%), 18 patients had stage 2 dysfunction (30.5%), and one patient had stage 3 diastolic dysfunction (1.7%). The median EFT was 6 mm (ranging from 3 to 14). Of the 59 patients, 34 had an EFT less than 7 mm (57.6%), while 25 had an EFT equal to or greater than 7 mm (42.4%). The EFT was ≥ 7 mm in 34.7% of the group using metformin and ≥ 7 mm in 80% of the group not using metformin. The difference was statistically significant (p = 0.013). There was no statistical significance between other drugs and EFT.

In the group with microalbuminuria, age, levels of glucose, urea, triglycerides, HbA1c, FIB-4, and VAI scores were higher, while HDL levels and the frequency of hypertension were lower compared to the patients without microalbuminuria (p < 0.05 for all). A comparison of clinical and laboratory characteristics between the 2 groups is presented in Table 2.

There were no significant differences in EFT and the frequency of hepatosteatosis between the group with microalbuminuria and the group without microalbuminuria (p = 0.807 and 0.834, respectively). A comparative presentation of the liver ultrasound and TTE results for these 2 groups is provided in Table 3.

Table 3. Comparison of Liver Ultrasonography and Transthoracic Echocardiography Between Patients With and Without Microalbuminuria

Characteristic	Microalbuminuria (–)	Microalbuminuria (+)	P-value
Hepatosteatosis (n = 138)	88 (63.8)	50 (36.2)	0.834
Hepatosteatosis Grade			
Grade 1	34 (61.8)	21 (38.2)	
Grade 2	46 (68.7)	21 (31.3)	0.351
Grade 3	8 (50)	8 (50)	
Ejection fraction	60 (60–60)	60 (40–60)	0.074
Diastolic dysfunction			
Stage 1	24 (60)	16 (40)	
Stage 2	12 (66.7)	6 (33.3)	0.536
Stage 3	0 (0)	1 (100)	
Epicardial fat thickness [mm]	6 (3–14)	6 (3–10)	0.807
Epicardial fat thickness			
< 7 mm	20 (58.8)	14 (41.2)	0.894
≥ 7 mm	16 (64)	9 (36)	

The results were presented in the form of nouns and percentages, or median values and minimum and maximum values

In the correlation analysis between EFT and albuminuria levels in patients who underwent echocardiography, no significant correlation between the 2 variables was observed. (Spearman r = 0.1, p = 0.447).

Discussion

This study investigated the association between albuminuria and visceral adiposity surrogates in patients with T2D. The finding of a 36% frequency of microalbuminuria is a noteworthy result of the study. There were no differences in EFT, the presence of hepatic steatosis, and its stage between the microalbuminuria and non-microalbuminuria groups. The group with microalbuminuria had higher FIB-4 scores and VAI values compared to the group without microalbuminuria.

Studies have shown an association between microalbuminuria and the presence of MASLD in both patients with and without T2D. In a study with patients with pre-diabetes and newly diagnosed T2D, Kasapoglu et al. found a significant relationship between MASLD and microalbuminuria, independent of BMI [5]. In a study conducted by Li et al. [11] involving elderly individuals without T2D they also found a higher frequency of microalbuminuria in the MASLD group compared to the group without MASLD.

In our study, although the frequency of microalbuminuria was higher in patients with hepatic steatosis (36.2%) compared to those without hepatic steatosis (32.3%), this difference did not reach statistical significance (p = 0.834). The primary reason for this situation could be the relatively small sample size of patients who underwent abdominal ultrasound (n = 138). Additionally, in our study, it is notable that the level of microalbuminuria in patients without hepatic steatosis was considerably higher compared to control groups in other studies. For instance, in Kasapoglu's study, the frequency of microalbuminuria in the control group was found to be 2%. In our study, all patients had T2D, the duration of which was longer compared to other studies (11 years), with a higher median age (59 years). These factors appear to account for this discrepancy. It is believed that conducting this study with individuals without T2D or those with a shorter duration of T2D may reveal a significant relationship between hepatic steatosis and microalbuminuria.

In this study, no relationship was observed between the stage of hepatic steatosis and microalbuminuria. Among those with grade 3 hepatic steatosis, 50% had microalbuminuria, whereas in the group with grade 1 hepatic steatosis, 38.2% had microalbuminuria (p = 0.351). Upon reviewing the literature, no significant relationship was found between the degree of hepatosteatosis and microalbuminuria. Although not statistically significant, a higher frequency of microalbuminuria was observed in patients with grade 3 hepatosteatosis, which requires further clarification through comprehensive studies with larger sample sizes.

The relationship between EFT and microalbuminuria has been investigated in studies involving patients with hypertension and diabetes. Ozturk et al. [12] found a significant relationship between EFT and microalbuminuria in their study of 75 hypertensive patients. In a study with patients with T2D, Akbaş et al. [13] found that EFT was higher in patients with microalbuminuria compared to those with normoalbuminuria. However, in our study, no significant correlation was found

between EFT and microalbuminuria. This can be explained, in part, by the significantly higher prevalence of hypertension in patients without microalbuminuria in our study, compared to those with microalbuminuria.

In our study, the group with microalbuminuria had a higher FIB-4 score compared to the group without microalbuminuria. The FIB-4 score is a non-invasive alternative to liver biopsy for diagnosing and managing liver disease, serving as a liver fibrosis biomarker. In a study by Xu et al. [14] investigating the association between microalbuminuria and the FIB-4 score in patients with T2D, they found that in individuals with MASLD, a FIB-4 score below 1.1 is a highly specific predictor for CKD, allowing for the exclusion of CKD. Similarly, Saito et al. [15] demonstrated that an FIB-4 score > 1.3 has a prognostic impact on the development of CKD and proteinuria in patients with T2D. In a recent study, Kuma et al. [16] found that the FIB-4 score was independently associated with eGFR decline in metabolically healthy men during a 5-year follow-up. When the results of these studies are considered together with our findings, it becomes apparent that the FIB-4 score is a useful method for predicting the development of both microalbuminuria and CKD in individuals with and without T2D.

There is a strong relationship between visceral adiposity and T2D. The visceral adiposity index (VAI) is commonly used to predict the magnitude of visceral adipose tissue. In 1982, Moorhead delineated the concept of lipid nephrotoxicity, and later, studies examining the role of visceral adiposity in the development of chronic kidney disease shed light on the underlying mechanisms [17, 18]. It is known that increased visceral fat and insulin resistance exist in individuals with T2D years before the development of microvascular complications like microalbuminuria [19]. Therefore, the finding of high VAI values in the group with microalbuminuria in our study is an important result. In a study conducted by Qi et al., the relationship between VAI values and microalbuminuria in newly diagnosed diabetes patients was examined, and it was found that VAI successfully predicted microalbuminuria in newly diagnosed T2D patients [20]. In a study conducted by Sun et al., it was determined that visceral fat accumulation evaluated by VAI is independently associated with increased urinary albumin excretion in middle-aged and elderly Chinese individuals. Considering these findings together, VAI appears to be an easy and reliable method for evaluating kidney damage in both metabolically healthy individuals and patients with T2D.

The relationship between the progression of diabetic kidney disease and poorly controlled diabetes is well-established. Previous studies have demonstrated an association between elevated HbA1c levels and albuminuria [21]. In our study, the elevated HbA1c levels in patients with microalbuminuria corroborate this data. Similarly, the higher mean age within the microalbuminuria group in our study reinforces the concept of an association between microvascular complications and the duration of T2D [22, 23]. In our study, the fact that both microalbuminuria and EFT were less in patients using metformin may be explained by the first-line therapy of metformin in T2D for many years and thus the short duration of T2D in the group using metformin.

The study's retrospective design, a limited number of patients evaluated with TTE, and the unequal distribution of age and hypertension frequency among the groups are some of the limitations of the study.

In conclusion, in individuals with T2D, the presence of microalbuminuria was associated with high VAI and FIB-4 scores, while no significant association was found with hepatic steatosis or EFT. To validate the study's findings, prospective and randomized trials are needed.

Article information

Data availability statement

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

Ethical approval

Istanbul Medeniyet University Clinical Research Ethics Committee June 18, 2021 (Decision No. 2022/0636).

We confirm that Ethical Committee approval was sought where necessary and guidelines on patient consent have been met and any details of informed consent obtained are indicated within the text of the submitted manuscript.

Author contribution

Author 1: conceptualization (lead), writing — original draft (lead), review and editing (equal); Author 2: methodology (lead) — review and editing (equal); Author 3: Conceptualization (supporting) — review and editing (equal); Author 4: software (lead), writing — review and editing (equal); Author 5: formal analysis (lead); writing — review and editing (equal); Author 6: writing — original draft (supporting), review and editing (equal); Author 7: conceptualization (supporting) — review and editing (equal).

Funding

No funding was received for this work.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Kume S, Uzu T, Araki Si, et al. Role of altered renal lipid metabolism in the development of renal injury induced by a high-fat diet. J Am Soc Nephrol. 2007; 18(10): 2715–2723, doi: 10.1681/ASN.2007010089, indexed in Pubmed: 17855643.
2. Targher G, Marra F, Marchesini G. Increased risk of cardiovascular disease in non-alcoholic fatty liver disease: causal effect or epiphenomenon? Diabetologia. 2008; 51(11): 1947–1953, doi: 10.1007/s00125-008-1135-4, indexed in Pubmed: 18762907.
3. Kaya E, Yilmaz Y. Metabolic-associated Fatty Liver Disease (MAFLD): A Multi-systemic Disease Beyond the Liver. J Clin Transl Hepatol. 2022; 10(2): 329–338, doi: 10.14218/JCTH.2021.00178, indexed in Pubmed: 35528971.
4. Vuppalanchi R, Chalasani N. Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis: Selected practical issues in their evaluation and management. Hepatology. 2009; 49(1): 306–317, doi: 10.1002/hep.22603, indexed in Pubmed: 19065650.
5. Kasapoglu B, Turkay C, Yalcın KS, et al. Increased microalbuminuria prevalence among patients with nonalcoholic fatty liver disease. Ren Fail. 2016; 38(1): 15–19, doi: 10.3109/0886022X.2015.1106845, indexed in Pubmed: 26540639.
6. Katsiki N, Mikhailidis DP, Wierzbicki AS. Epicardial fat and vascular risk: a narrative review. Curr Opin Cardiol. 2013; 28(4): 458–463, doi: 10.1097/HCO.0b013e3283605fba, indexed in Pubmed: 23591557.
7. Sterling RK, Lissen E, Clumeck N, et al. APRICOT Clinical Investigators. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology. 2006; 43(6): 1317–1325, doi: 10.1002/hep.21178, indexed in Pubmed: 16729309.
8. Amato MC, Giordano C, Galia M, et al. AlkaMeSy Study Group. Visceral Adiposity Index: a reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care. 2010; 33(4): 920–922, doi: 10.2337/dc09-1825, indexed in Pubmed: 20067971.
9. Saverymuttu SH, Joseph AE, Maxwell JD. Ultrasound scanning in the detection of hepatic fibrosis and steatosis. Br Med J (Clin Res Ed). 1986; 292(6512): 13–15, doi: 10.1136/bmj.292.6512.13, indexed in Pubmed: 3080046.
10. Eroglu S, Sade LE, Yildirir A, et al. Epicardial adipose tissue thickness by echocardiography is a marker for the presence and severity of coronary artery disease. Nutr Metab Cardiovasc Dis. 2009; 19(3): 211–217, doi: 10.1016/j.numecd.2008.05.002, indexed in Pubmed: 18718744.
11. Li X, Xia M, Ma H, et al. Liver fat content is independently associated with microalbuminuria in a normotensive, euglycaemic Chinese population: a community-based, cross-sectional study. BMJ Open. 2021; 11(6): e044237, doi: 10.1136/bmjopen-2020-044237, indexed in Pubmed: 34187816.
12. Ozturk MT, Ebinç FA, Okyay GU, et al. Epicardial Adiposity is Associated with Microalbuminuria in Patients with Essential Hypertension. Acta Cardiol Sin. 2017; 33(1): 74–80, doi: 10.6515/acs20160418a, indexed in Pubmed: 28115810.
13. Akbas EM, Demirtas L, Ozcicek A, et al. Association of epicardial adipose tissue, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. Int J Clin Exp Med. 2014; 7(7): 1794–1801, indexed in Pubmed: 25126182.
14. Xu HW, Hsu YC, Chang CH, et al. High FIB-4 index as an independent risk factor of prevalent chronic kidney disease in patients with nonalcoholic fatty liver disease. Hepatol Int. 2016; 10(2): 340–346, doi: 10.1007/s12072-015-9690-5, indexed in Pubmed: 26676626.
15. Saito H, Tanabe H, Kudo A, et al. High FIB4 index is an independent risk factor of diabetic kidney disease in type 2 diabetes. Sci Rep. 2021; 11(1): 11753, doi: 10.1038/s41598-021-88285-6, indexed in Pubmed: 34083571.
16. Kuma A, Mafune K, Uchino B, et al. Potential link between high FIB-4 score and chronic kidney disease in metabolically healthy men. Sci Rep. 2022; 12(1): 16638, doi: 10.1038/s41598-022-21039-0, indexed in Pubmed: 36198747.
17. Moorhead JF, Chan MK, El-Nahas M, et al. Lipid nephrotoxicity in chronic progressive glomerular and tubulo-interstitial disease. Lancet. 1982; 2(8311): 1309–1311, doi: 10.1016/s0140-6736(82)91513-6, indexed in Pubmed: 6128601.
18. de Vries APJ, Ruggenenti P, Ruan XZ, et al. ERA-EDTA Working Group Diabesity. Fatty kidney: emerging role of ectopic lipid in obesity-related renal disease. Lancet Diabetes Endocrinol. 2014; 2(5): 417–426, doi: 10.1016/S2213-8587(14)70065-8, indexed in Pubmed: 24795255.
19. Zatterale F, Longo M, Naderi J, et al. Chronic Adipose Tissue Inflammation Linking Obesity to Insulin Resistance and Type 2 Diabetes. Front Physiol. 2019; 10: 1607, doi: 10.3389/fphys.2019.01607, indexed in Pubmed: 32063863.
20. Qi L, Kang N, Li Y, et al. The Predictive Value of Visceral Adiposity Index and Lipid Accumulation Index for Microalbuminuria in Newly Diagnosed Type 2 Diabetes Patients. Diabetes Metab Syndr Obes. 2021; 14: 1107–1115, doi: 10.2147/DMSO.S302761, indexed in Pubmed: 33737822.
21. Chiu WC, Lai YR, Cheng BC, et al. HbA1C Variability Is Strongly Associated with Development of Macroalbuminuria in Normal or Microalbuminuria in Patients with Type 2 Diabetes Mellitus: A Six-Year Follow-Up Study. Biomed Res Int. 2020; 2020: 7462158, doi: 10.1155/2020/7462158, indexed in Pubmed: 32047814.
22. Olivarius Nd, Andreasen AH, Keiding N, et al. Epidemiology of renal involvement in newly-diagnosed middle-aged and elderly diabetic patients. Cross-sectional data from the population-based study "Diabetes Care in General Practice", Denmark. Diabetologia. 1993; 36(10): 1007–1016, doi: 10.1007/BF02374492, indexed in Pubmed: 8243848.
23. Ruggenenti P, Remuzzi G. Nephropathy of type-2 diabetes mellitus. J Am Soc Nephrol. 1998; 9(11): 2157–2169, doi: 10.1681/ASN.V9112157, indexed in Pubmed: 9808106.