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RESEARCH ARTICLE

Comparative evaluation of hepatosteatosis in patients with type 2 diabetes mellitus using non-contrast abdominal CT and laboratory findings

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ABSTRACT

Aim: This study aims to underscore the significance of employing multiple parameters from non-contrast abdominal CT scans for the assessment of hepatosteatosis in patients with Type 2 Diabetes Mellitus.

Methods: Non-enhanced Computed Tomography of the diabetic subjects were analyzed. Control subjects were selected from non-diabetic patients who had undergone abdominal tomography within the same period. The craniocaudal length of the liver and liver, spleen, pancreas densities, and epicardial adipose tissue were measured. Additionally, patient demographics and laboratory values were retrospectively obtained.

Results: The craniocaudal length of the liver was significantly greater in the diabetes mellitus group compared to the control group (168.3 ± 17.2 mm vs 152.3 ± 14.8 mm, $p < 0.001$). Hepatosteatosis was observed in 22 individuals with diabetes mellitus, whereas only one participant in the control group had this condition ($p < 0.001$). The diabetes mellitus group exhibited significantly lower median liver density ($p < 0.001$), liver-spleen density ratio ($p = 0.004$), pancreatic head density ($p = 0.001$), and pancreatic body density ($p = 0.013$). Additionally, the average thickness of epicardial adipose tissue was markedly higher in the diabetes mellitus group compared to the control group (8.1 ± 1.9 mm vs 4.9 ± 1.1 mm, $p < 0.001$).

Conclusions: These data indicate an association between hepatosteatosis and increased epicardial adipose tissue thickness, liver and pancreatic densities in individuals with diabetes mellitus. These findings suggest that non-contrast abdominal CT findings such as epicardial adipose tissue thickness and relevant laboratory tests may aid in evaluating metabolic disorders and fat accumulation in diabetic patients.

Keywords: Type 2 diabetes mellitus, hepatosteatosis, liver/spleen ratio, adipose tissue, liver/diagnostic imaging, pericardium/diagnostic imaging, risk factors, spleen/diagnostic imaging

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INTRODUCTION

Diabetes mellitus (DM), with a rapidly escalating prevalence and projections indicating a significant surge in cases by 2030, poses a critical threat to liver health. Characterized by disruptions in metabolism due to insulin abnormalities, DM leads to chronic hyperglycemia and predominantly affects individuals with type-2 DM (90%-95%) (1,2). Previous research has established a clear link between DM and an increased risk of chronic liver conditions and hepatosteatosis (3).

Hepatosteatosis is a prevalent liver disorder characterized by the accumulation of fat within hepatocytes, with estimates suggesting that approximately 25% of the population is affected by this condition (4). Hepatosteatosis is considered a component of metabolic syndrome independent of increased body mass index (5). Additionally, hepatosteatosis has been associated with an increased risk of cardiovascular disease in diabetic patients (6).

In the diagnosis of hepatosteatosis, radiological methods such as magnetic resonance imaging (MRI), ultrasonography, and computed tomography (CT) are utilized. While liver biopsy is considered the gold standard for diagnosis, its invasive nature makes it unsuitable for screening purposes (7). The most commonly used radiological method for diagnosing hepatosteatosis is ultrasonography, which relies on visual comparisons of liver and right kidney echogenicities. Classification is based on increased echogenicity, loss of periportal echogenicity, and loss of diaphragmatic echogenicity, and it is categorized as mild, moderate, or severe (8). MRI is helpful in diagnosing focal hepatosteatosis and distinguishing it from masses. On CT scans, fatty liver appears hypodense, and the liver-to-spleen attenuation ratio is useful in diagnosing hepatosteatosis (9). The measurement of liver density alone may be disadvantageous in differentiating diseases that involve iron or copper deposition. Therefore, in routine clinical practice, the measurement of the liver-to-spleen density ratio is utilized for the diagnosis of hepatosteatosis (10,11).

Epicardial adipose tissue (EAT) is increasingly recognized as a component of metabolic syndrome, particularly in conjunction with hepatosteatosis (12). It is believed that an increase in EAT contributes to an elevated risk of cardiovascular diseases. Furthermore, numerous studies have demonstrated increased EAT in diabetic patients (12,13). Key components of metabolic syndrome, such as insulin resistance and lipid metabolism disorders, may lead to fat accumulation within hepatocytes and in the epicardial region, potentially influencing the development and severity of hepatosteatosis (14,15). Therefore, identifying the presence of hepatosteatosis and noting any associated increase in EAT, especially in diabetic patients, could aid in predicting associated conditions and managing patient care.

In this study, our objective is to comparatively evaluate CT findings of hepatosteatosis in diabetic patients. Additionally, we aim to explore the association between EAT and diabetic subjects.

METHODS

This retrospective study was carried out at the radiology department of Abant İzzet Baysal University İzzet Baysal Training and Research Hospital, following ethical approval (2023/298). After receiving approval from the ethics committee, patients diagnosed with diabetes mellitus who attended our institution between January 1, 2021, and January 31, 2023, were included in the study.

Demographic information including age, gender, height, weight, Hip and Waist Circumference (HC and WC), BMI, Waist to Hip Ratio (WHR), comorbidities, etc., as well as laboratory data such as glucose levels, HbA1C, alanine and aspartate transaminases (ALT and AST), triglyceride, HDL-cholesterol, serum uric acid, etc., were collected. Triglyceride was divided by HDL cholesterol to determine the Triglyceride/HDL ratio (THR), and serum uric acid was divided by HDL cholesterol to determine the UHR.

CT images of patients undergoing follow-up for diabetes mellitus were retrospectively retrieved from the PACS system of our hospital. The study included two groups: patients with diabetes mellitus and those without. The control group consisted of volunteers whose abdominal CT scans were reported as normal. Patients were excluded if they had incomplete or inadequate investigations, suboptimal CT imaging, a history of surgery, or a history of malignancy. Following the application of these exclusion criteria, a total of 85 cases were included in the study.

Every CT scan of the abdomen was performed with a 64-slice scanner (General Electric Revolution EVO, 64x2 slices). The scanning range extended from the base of the lung to the symphysis pubis. Scans were performed during deep inspiration and breath-hold without the use of contrast agents. The CT scanning protocol employed the following parameters: a tube voltage of 120 kVp, a tube current ranging from 70 to 400 mA, a rotation time of 0.5 seconds, a pitch of 1.375, and a slice thickness of 5 mm. Quantification of liver, spleen, and pancreas densities was performed on abdominal CT images by delineating a circular Region of Interest (ROI) with an approximate diameter of 1 cm (Image 1). The density measurements were obtained by averaging the values from three different areas in both the liver and spleen, and arithmetic means were then calculated for both the liver and spleen. In the liver parenchyma, a region of interest (ROI) was selected while excluding blood vessels, bile ducts, and focal liver lesions. Similarly, in the spleen parenchyma, an ROI was chosen excluding blood vessels. Regions affected by artifacts were also excluded. The liver-to-spleen density ratio (LSR) was computed by dividing the mean density of the hepatic ROI by the mean density of the spleen ROI. Hepatosteatosis on CT images was defined by either relative hypoattenuation (where liver attenuation is more than 10 HU lower than spleen attenuation) or absolute low attenuation (where liver attenuation is less than 40 HU). Density measurements for the pancreas were acquired separately for the head and body sections. Additionally, the examination encompassed the assessment of EAT thickness from thoracic sections.

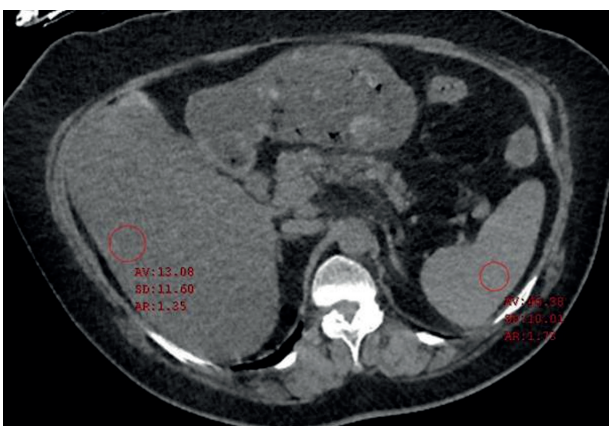

Image 1. Density measurements of liver and spleen in non-contrast abdominal CT examination.

EAT was defined as the adipose tissue located between the surface of the heart and the visceral layer of the pericardium (visceral epicardium). EAT thickness (mm) was measured on the anterior free wall of the right ventricle. Measurements were conducted exclusively at the ventricular base (basal level) due to being derived from the lower thoracic sections of abdominal CT scans. The level at the base of the ventricles was designated as the basal level.

Statistical analyses

SPSS version 18 for Windows was used to conduct the statistical analysis (IBM Corp, Chicago, IL, USA). The study variables' normality was evaluated using the Kolmogorov-Smirnov test. Independent samples t-tests were used to assess variables that fit into a normal distribution. The results are shown as means and standard deviations. The Mann-Whitney U test was used to examine variables that did not have a normal distribution. These variables were expressed as medians (range). The chi-square test was used to compare categorical variables between study groups, and the results were presented as frequencies and percentages. Receiver operating characteristic (ROC) analysis was used to assess the study parameters' specificity and sensitivity in identifying diabetes mellitus. Less than 0.05 was the threshold for statistical significance.

RESULTS

The study population comprised 85 subjects, with 44 in the DM group. Patient characteristics are given in Table 1. Briefly, age and gender distribution were similar. However abdominal obesity indicators were significantly different.

Furthermore, significantly lower values were noted between the DM and control groups for median liver density (p<0.001), liver-spleen density ratio (p=0.004), pancreas head density (p=0.001), and pancreas body density (p=0.013). Refer to Table 2 for a summary of the data from the study and control groups.

Table 1. Demographic characteristics of the study population

		Diabetes Mellitus	Control	p
Gender (n, %)	Women	22 (50%)	21 (51.2%)	0.91
	Men	22 (50%)	20 (48.8%)	0.91
Age (years)		57.9 ± 8.8	55.9 ± 7.6	0.26
BMI (kg/m^2)		32.6 ± 7	29.2 ± 4.9	0.01
WC (cm)		110.7 ± 13	101.6 ± 13	<0.001
WHR (%)		1.09 ± 0.07	0.90 ± 0.08	<0.001

BMI: Body Mass Index, WC: Waist Circumference, WHR: Waist-hip ratio.

Table 2. Data of study and control groups

	Diabetes Mellitus	Control	p
	Median (min-max)		
Glucose (mg/dL)	130.5 (90-320)	98 (80-132)	**<0.001**
HbA1C (%)	6.8 (5.4-19.2)	5.4 (5-6.2)	**<0.001**
AST (U/L)	20.5 (11-53)	20 (7-31)	0.55
ALT (U/L)	19.5 (9-60)	18 (9-44)	**0.07**
HDL Cholesterol (mg/dL)	46.4(20-131)	48.8 (28-156)	0.45
Triglyceride (mg/dL)	141 (49-432)	108 (55-281)	0.09
THR (%)	2.9 (1-21.6)	2.3 (1-9)	0.09
Liver density (HU)	41.5 (12-68)	54 (21-66)	**<0.001**
Spleen density (HU)	46 (28-53)	47 (39-58)	0.07
LSR	0.9 (0.3-1.5)	1.1 (0.5-1.6)	**0.004**
Pancreas head density (HU)	32 (-8-56)	42 (22-53)	**0.001**
Pancreas body density (HU)	34 (-25-54)	38 (25-51)	**0.013**
	Mean ± Std		
Serum Uric Acid (mg/dL)	6.1 ± 1.8	5.3 ± 1.3	**0.023**
UHR (%)	0.14 ± 0.07	0.12 ± 0.06	0.07
Liver length (mm)	168.3 ± 17.2	152.3 ± 14.8	**<0.001**
EAT (mm)	8.1 ± 1.9	4.9 ± 1.1	**<0.001**

AST: Aspartate transaminases, ALT: Alanine transaminases, HDL: High density lipoprotein, THR: Triglyceride/HDL ratio, LSR: Liver/spleen density ratio, UHR: Uric Acid/HDL ratio, EAT: Epicardial adipose tissue, HbA1C: Hemoglobin A1c.

Table 3. Correlation analysis

	Liver density	LSR	EAT	Pancreas head density	Pancreas body density
BMI	r = -0.44	r = -0.31	r = 0.38		
	p < 0.001	p = 0.003	p < 0.001		
Glucose	r = -0.32	r = -0.27	r = 0.34	r = -0.34	r = -0.38
	p = 0.003	p = 0.013	p = 0.001	p = 0.001	p < 0.001
HbA1C	r = -0.24	r = -0.22	r = 0.41	r = -0.24	r = -0.22
	p = 0.02	p = 0.04	p < 0.001	p = 0.026	p = 0.04
WC	r = -0.49	r = -0.33	r = 0.38		
	p < 0.001	p = 0.002	p < 0.001		
WHR	r = -0.44	r = -0.28	r = 0.57		
	p < 0.001	p = 0.003	p < 0.001		

LSR: Liver/spleen density ratio, EAT: Epicardial adipose tissue, BMI: Body Mass Index, WC: Waist Circumference, WHR: Waist-hip ratio, HbA1C: Hemoglobin A1c.

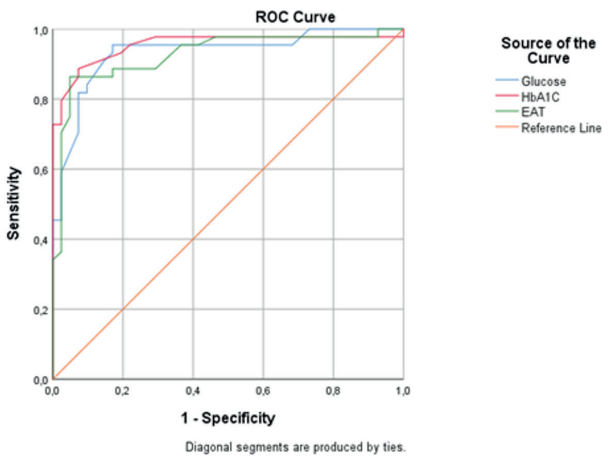

Figure 1. ROC analysis EAT >5.4mm: 89% sensitivity, 83% specificity (AUC: 0.93, p<0.001, 95% CI: 0.87-0.99). Serum glucose >111.5 mg/dL: 93% sensitivity, 83% specificity (AUC: 0.93, p<0.001, 95% CI: 0.87-0.98). Serum HbA1C >5.75%: 93% sensitivity, 81% specificity (AUC: 0.95, p<0.001, 95% CI: 0.90-1).

EAT: Epicardial adipose tissue, HbA1C: Hemoglobin A1c, ROC: Receiver operating characteristic, AUC: Area under the curve.

Correlation analysis revealed significant negative correlations between liver density and BMI, serum glucose levels, serum HbA1C levels, WC, and WHR. Similarly, the LSR exhibited significant negative correlations with BMI, serum glucose levels, serum HbA1C levels, WC, and WHR. Pancreas head density was negatively correlated with serum glucose levels and HbA1C levels, while pancreas body density exhibited negative correlations with serum glucose levels and HbA1C levels. EAT showed significant positive correlations with BMI, serum glucose levels, serum HbA1C levels, WC, and WHR (Table 3).

In ROC analysis, an EAT thickness greater than 5.4 mm demonstrated 89% sensitivity and 83% specificity for detecting diabetes mellitus (DM) (Area under the curve (AUC): 0.93, p < 0.001, 95% CI: 0.87-0.99). Similarly, a serum glucose level exceeding 111.5 mg/dL exhibited 93% sensitivity and 83% specificity for DM detection (AUC: 0.93, p < 0.001, 95% CI: 0.87-0.98). Additionally, a serum HbA1C level above 5.75% showed 93% sensitivity and 81% specificity for detecting DM (AUC: 0.95, p < 0.001, 95% CI: 0.90-1) (see Figure 1).

DISCUSSION

Our study revealed a significant increase in liver sizes among individuals diagnosed with DM, aligning with existing literature and underscoring the prevalent issue of hepatosteatosis within the diabetic population, indicative of notable fat accumulation in the liver (16). This enlargement of the liver in diabetic individuals may serve as a potential indicator of hepatosteatosis, recognized as a component of metabolic syndrome. Moreover, the augmentation in liver sizes correlates with diminished liver functional capacity and heightened susceptibility to progressive liver diseases.

Hence, vigilance in monitoring and assessing liver sizes in diabetic patients holds crucial importance for implementing prospective preventive and therapeutic interventions.

In our study, hepatosteatosis was detected in 22 diabetic patients, whereas only one patient in the control group exhibited this condition. Our findings are consistent with the literature, demonstrating an increased risk of hepatosteatosis in diabetic individuals (17).

In the ROC analysis, we evaluated the diagnostic performance of EAT thickness, serum glucose levels, and serum HbA1C levels in detecting DM. An EAT thickness greater than 5.4 mm demonstrated high sensitivity (89%) and specificity (83%) in identifying DM. Similarly, elevated serum glucose levels (>111.5 mg/dL) and HbA1C levels (>5.75%) showed high sensitivity (93%) and specificity (83% and 81%, respectively) in detecting DM. These findings align with existing literature, emphasizing the interconnectedness between DM, metabolic parameters, and imaging findings. Such observed correlations underscore the potential utility of non-invasive imaging techniques and metabolic markers in the early detection and management of DM and associated complications (18-20).

Our study showed that increased EAT may serve as an indicator of hepatosteatosis. This finding is clinically significant as it suggests that measuring EAT could provide a non-invasive marker to alert physicians to the presence of hepatosteatosis in diabetic patients. The clinical utility of this marker extends further; an increase in EAT has been associated with heightened CV risk, making it a dual-purpose marker that could inform both hepatic and cardiovascular health management. In diabetic patients, particularly those with hepatosteatosis, monitoring EAT could thus facilitate early identification of individuals at greater risk for CV events. This is crucial because recent studies have consistently reported a correlation between elevated EAT and increased CV risk, underscoring the importance of comprehensive risk assessment and proactive management strategies in this population. By incorporating EAT measurement into routine clinical practice, healthcare providers can enhance their ability to detect and mitigate the multifaceted risks associated with diabetes, ultimately improving patient outcomes (21).

The retrospective nature of this study, involving the retrospective collection of data, may introduce limitations in establishing causal relationships. Moreover, the single-center design of the study might restrict the generalizability of the findings and could imply limitations concerning diversity, as it relies on a solitary population sample. The constrained sample size could also pose limitations in terms of statistical power and reliability. Furthermore, having all measurements conducted by a single individual may be less dependable compared to independent verification by another evaluator to ensure consistency in measurements. These limitations could influence the interpretation of the study's results and underscore the necessity for larger-scale, prospective studies.

In conclusion, our findings reveal a significant increase in hepatosteatosis and EAT thickness in individuals diagnosed with DM. Additionally, noteworthy discrepancies in the densities of the liver, pancreas, and other organs were observed. These outcomes underscore the effective utilization of non-contrast abdominal CT scans and pertinent laboratory tests in evaluating metabolic disorders and fat accumulation in diabetic patients. Consequently, early identification and management of heightened hepatosteatosis and EAT thickness in diabetic individuals are imperative for averting metabolic health complications and associated issues. Yet, studies in diabetic subjects that evaluate EAT in subgroups according to the presence of hepatosteatosis are still needed.

Ethical approval

This study has been approved by the Bolu Abant İzzet Baysal University Clinical Researches Ethic Committee (approval date 05/09/2023, number 2023/298). Written informed consent was obtained from the participants.

Author contribution

Concept: ZC, MEK; Design: ZC, MEK; Data Collection or Processing: ZC, MEK; Analysis or Interpretation: ZC; Literature Search: ZC, MEK; Writing: ZC, MEK. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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