Liver–Spleen Ratio: Can It Be Used for the Prediction of Coronary Artery Disease?

ABSTRACT

Background: Considering that ectopic fat accumulation in various organs, especially the heart and liver, is a cardiometabolic risk factor, the need for easily accessible markers of ectopic fat accumulation is inevitable. The main starting point of the study is based on the hypothesis of predicting cardiovascular disease risk through the link that can be established between the liver–spleen ratio, which is one of the strong indicators of hepatosteatosis, and epicardial adipose tissue volume.

Methods: This was a retrospective study. The records of 283 consecutive patients who underwent coronary computed tomography angiography in our Radiology Department were reviewed retrospectively from our hospital’s system. All patients’ epicardial adipose tissue volume and liver–spleen ratio were calculated using appropriate criteria on non-contrast computed tomography images. Additionally, the Coronary Artery Disease–Reporting and Data System was calculated on contrast computed tomography images. The participating patients were divided into groups according to the liver–spleen ratio and Coronary Artery Disease–Reporting and Data System score.

Results: We found that while there was a negative correlation between the liver–spleen ratio and epicardial adipose tissue volume in the hepatosteatosis group, this relationship was not observed in the non-steatosis group. In addition, we observed that the family history of cardiovascular disease and the frequency of cardiovascular disease were higher in the hepatosteatosis group than in the other group, and there was a correlation between cardiovascular disease and the liver–spleen ratio. Also, we found that age and liver–spleen ratio values were found to be independent predictors of coronary artery disease.

Conclusion: In our study, we found that the frequency of cardiovascular disease was lower in patients with a high liver–spleen ratio. We also demonstrated in the study that the liver–spleen ratio, which indicates a low level of epicardial adipose tissue volume accumulation, is an independent predictor of cardiovascular disease. In addition, the use of liver–spleen ratio, which is more valuable than liver attenuation in predicting hepatic steatosis, may be more useful in evaluating the risk of hepatosteatosis-related cardiovascular disease.

Keywords: Liver–spleen ratio, hepatosteatosis, epicardial adipose tissue, cardiovascular disease

INTRODUCTION

Epicardial adipose tissue (EAT) is an accumulation of adipose tissue located between the outer wall of the myocardium and the visceral layer of the pericardium. Epicardial adipose tissue volume accounts for 15–20% of average heart volume, and EAT mass accounts for approximately 1% of total adipose tissue (AT) mass.1 Age, waist circumference, ethnicity, and heart mass are independent predictors of EAT volume.1 Epicardial adipose tissue consists of adipocytes and neurohumoral, inflammatory, stroma-vascular, and immune system cells.1 EAT has a physical protective barrier role for the heart. It causes anti-inflammatory effects in periods when EAT accumulation is low and pro-inflammatory effects that cause cardio-metabolic events in later periods when accumulation increases.1

In obese individuals, visceral adipose tissue accumulation causes metabolic diseases and increased inflammatory events.4 Studies have shown that EAT volume is associated with the development of cardiovascular events, but it is not yet clear
whether the role of EAT accumulation in cardiovascular disease (CVD) is independent of other visceral adipose tissue deposits.\textsuperscript{5,6}

Although it is not a measurement method recommended by the guidelines in EAT measurement, transthoracic echocardiography methods are frequently preferred methods.\textsuperscript{7} Echocardiography is the most commonly used method for EAT measurement because it is easily accessible, non-invasive, and cost-effective, but this method has some limitations. The lack of equal intensity of EAT in all areas of the heart and the fact that the experience of the echocardiographer changes the measurement results are the most significant limitations of EAT measurement by echocardiography. The volume of epicardial adipose tissue is the most consistent measurement method for determining the amount of EAT.\textsuperscript{7} EAT volume can also measure with computed tomography (CT) and magnetic resonance (MR), and both methods provide a more accurate and volumetric measurement of epicardial fat tissue than transthoracic echocardiography. Although both methods are more sensitive and specific, they are more expensive and laborious than echocardiography.\textsuperscript{7} It is still unclear which EAT measurement method best reflects metabolic risk.

Hepatosteatosis is the accumulation of fatty tissue in and around the liver and is the most common liver disease. Hepatosteatosis is estimated to affect 25% of the general population.\textsuperscript{8,9} Hepatosteatosis, a type of visceral adipocyte tissue (VAT) deposition, correlates significantly with all components of the metabolic syndrome, regardless of body mass index (BMI), and can be considered the hepatic expression of the metabolic syndrome.\textsuperscript{10,11} Hepatic steatosis is also known to be associated with increased cardiovascular risk in CVD and diabetic individuals.\textsuperscript{12,18} Ultrasonography, CT scans, and magnetic resonance imaging (MRI) are the most common methods for diagnosing hepatosteatosis, but liver biopsy is the gold standard for diagnosis.\textsuperscript{15,26} On CT, hepatosteatosis is diagnosed with a hypodense image, which occurs due to lower than expected liver attenuation. One of the most critical limitations of this method is that additional deposits such as iron or copper in the liver and inflammatory events can cause changes in liver density.\textsuperscript{16,17} Liver–spleen (L/S) attenuation ratio is valuable in the diagnosis of hepatosteatosis because of its advantages, such as being in the same cross-section and not being affected by most systemic diseases.\textsuperscript{15,18} The accepted value for the L/S ratio in the detection of steatosis involving more than 30% of the liver parenchyma is approximately 1.1-1.2.\textsuperscript{18}

The relationship between EAT and hepatosteatosis was firstly demonstrated in 2014. Iacobellis et al. revealed that obese individuals with steatohepatitis have higher EAT, epicardial fat is a good predictor of hepatic steatosis in obese persons; furthermore, echocardiographic epicardial fat measurement predicts ultrasound-measured hepatic steatosis better than BMI or waist circumference.\textsuperscript{19} Ectopic fat accumulation in and around critical organs, especially the heart and liver, is a cardiometabolic risk factor. Given this result, the need for easily accessible markers of ectopic fat accumulation is also inevitable. While hepatosteatosis is a traditional and established pattern of organ-specific fat deposition, recent research and clinical interest have focused on the heart’s fat infiltration. Liver and cardiac steatosis may co-exist and influence each other as previously described.\textsuperscript{20,21}

Defining the relationship between EAT and hepatosteatosis and revealing it with simple radiological measurement methods will provide a more accurate association of the cardiometabolic risks attributed to both adipose tissue accumulations and a more accurate interpretation of the relationship between the 2 visceral adipose tissue accumulations. While the measurement of EAT volume with CT stands out as the most essential method for the determination of the amount of EAT,\textsuperscript{7} the determination of the L/S ratio is one of the measurement methods with proven effectiveness in detecting hepatosteatosis.\textsuperscript{18,22} Based on this idea, we aimed to reveal the L/S ratio and EAT volume and their relationship with CVD by using the liver spleen density measurement technique with CT.

**HIGHLIGHTS**

- Epicardial adipose tissue (EAT) volume was higher in the steatosis group than in the non-steatosis group, and there is a negative correlation between liver–spleen (L/S) ratio and EAT volume in the hepatosteatosis group.
- The family history of cardiovascular disease (CVD) and CVD frequency is higher in the hepatosteatosis group than in the other group.
- Liver–spleen ratio value was found to be an independent predictor of coronary artery disease.
- There is no relationship between the L/S ratio and EAT volume in the group without steatosis. This situation was attributed to the change in properties with the increase in EAT accumulation.
- Due to various limitations in the evaluation of hepatosteatosis by liver attenuation, it may be more beneficial to use the L/S ratio, especially in determining the risk of cardiovascular disease.

**METHODS**

The study protocol was approved by the Medical Ethics Committee of our hospital (Ethics Committee number: 14567952-050/460; March 25, 2020). Written informed consent was obtained from all subjects.

The records of 283 consecutive patients who underwent coronary computed tomographic angiography in our Radiology Department between July 2012 and February 2020 were reviewed retrospectively from our hospital’s HBYS and PACS (Enilil) system. Data on CVD presence, family history of CVD, hypertension, weight, height, BMI, and biochemical blood lipid profiles were collected. Patients with a cardiac history such as coronary bypass surgery, valve replacement, pericardial effusion, volunteers with chronic liver disease, liver metastasis, or primary liver tumor, who used alcohol, and
whose clinical laboratory data were insufficiently available were excluded from the study.

The patients participating in the study were divided into 2 groups according to the L/S ratio. Those with an L/S ratio above 1.2 were considered the non-steatosis group, and those below 1.2 were considered the steatosis group. In the steatosis group, those with the L/S ratio between 1.1 and 1.2 were mild steatosis; Those below 1.1 were accepted as severe steatosis group and divided into 2 groups.

**Radiological Evaluation**

All CT examinations were performed on the third-generation Siemens dual-energy Computed Tomography scanner (Somatom Drive; Siemens Healthcare, Forchheim, Germany). Non-contrast images were acquired using the following scanning parameters: tube voltage, 120 kV; 80 mAs tube current; high-pitch spiral acquisition mode; reconstructed slice thickness, 1.5 mm; prospectively electrocardiography-triggered; scanning range, from the tracheal carina to portal vein level of the liver. If the heart rate was > 65 beats per minute, heart rate control was achieved with a β-blocker. All reconstructions were transferred to Syngo Via workstation (Siemens Healthcare, Forchheim, Germany) to quantify EAT volume and hepatosteatosis. Measurements of EAT, hepatosteatosis and Coronary Artery Disease—Reporting and Data System (CAD-RADS) scores were evaluated by 2 radiologists (with 10 years and 6 years of cardiovascular imaging experience, respectively) blinded to the study protocol. The interobserver variability was 10%.

The data obtained from coronary computed tomography angiography (CCTA) images were evaluated for grading of stenosis severity. The CAD-RADS classification system is used for CVD presence and CAD-RADS scores of the patients were calculated according to the reference values. Table 1 shows the scoring of the scale. They range from CAD-RADS 0 (absence of atherosclerosis) to CAD-RADS 5 (presence of at least 1 total occlusion).

On the CACS images, hepatic CT attenuation was measured by drawing 3 different regions of interest (ROI) (approximately 1.5 × 1.5 cm²) at the portal vein level of the liver (left lobe, right anterior lobe, and right posterior lobe of the liver, respectively). All ROIs were distributed in the hepatic parenchyma, and the biliary, vascular, and extrahepatic structures were excluded. Spleen attenuation was obtained by averaging 3 ROIs (approximately 1.5 × 1.5 cm²) from 3 different areas in the same section. The attenuation index—the liver-to-spleen attenuation ratio (CT L/S) was calculated as L/S, where L is the hepatic attenuation, and S is the splenic attenuation

Semi-automatic quantification of EAT volume in non-contrast CT images. All data sets were checked for coverage of the entire epicardial sac. First, the reader identified the upper and lower limits of the pericardial sac as the bifurcation of the pulmonary trunk and, respectively, the slice caudal to the posterior descending artery. Next, the contour of the pericardial sac is automatically traced and adjusted by the reader, if necessary. The EAT volume (green) (in mL) is automatically calculated by the inclusion of all contiguous 3D voxels with CT attenuations between the specified upper threshold (here −40 HU) and the lower threshold of −200 HU (Figures 2 and 3).

**Statistical Analysis**

The data obtained were evaluated using the Statistical Package for Social Sciences for Windows 21.0 (SPSS Inc., Chicago, Ill, USA) statistical program. Descriptive statistics were determined for each variable. Data were expressed as mean ± standard deviation or median and interquartile range. A statistically significant difference between the groups was determined by the χ² test for categorical variables. Nonparametric statistics (Mann–Whitney U test) and parametric statistics (independent sample t-test) were all used for continuous variables. Associations between the variables were explored using Spearman’s rho test. Binary logistic regression analysis was performed to determine independent predictors for CAD. Factors with a P value of <.2 were included in the univariate analysis in the regression test, while those that were significant in the univariate analysis were included in the multivariable evaluation. If the P value is less than .05; was considered statistically significant.

**RESULTS**

A total of 236 patients, 108 women and 128 men were included in the study. There were 154 patients without hepatosteatosis and 82 patients in the hepatosteatosis group.
There was no significant difference between the 2 groups in total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) cholesterol, and triglyceride levels ($P > .05$) (Table 2).

The mean age of the hepatosteatosis group (56.25 ± 10.74) was significantly higher than the group without hepatosteatosis (43.6 ± 11.16) ($P < .001$). When the BMI of the 2 groups was compared, it was found that the hepatosteatosis group (30.62 ± 5.03) was significantly higher than the other group (25.93 ± 2.96) ($P < .001$).

When the 2 groups were evaluated in terms of atherosclerotic heart disease, the family history of CVD and the frequency of CVD were significantly higher in the hepatosteatosis group than in the other group ($P < .001$). The incidence of HT in the hepatosteatosis group was also more frequent than in the other group ($P < .001$).

Eighty-two patients with hepatosteatosis were divided into 2 groups: mild and severe steatosis. There were 24 patients with mild steatosis and 58 patients with severe steatosis. There was no significant difference between the 2 groups regarding age, gender variables, and total cholesterol, HDL, LDL, triglyceride, and BMI levels. While there was no significant difference in terms of family history of CVD in the 2 groups evaluated for atherosclerotic heart disease, it

Table 2. Demographic and Biochemical Characteristics of the Group with And Without Hepatosteatosis

|                          | Non-Hepatosteatosis Group (n = 154) | Hepatosteatosis Group (n = 182) | $P$  |
|--------------------------|------------------------------------|---------------------------------|------|
| Age                      | 43.6 ± 11.16                       | 56.25 ± 10.74                   | <.001|
| Gender (F/M)             | 73/80                              | 35/48                           | .258 |
| Total cholesterol (mg/dL)| 201.12 ± 45.51                     | 200.75 ± 47.27                  | .960 |
| HDL cholesterol (mg/dL)  | 45.96 ± 11.97                      | 44.11 ± 11.23                   | .328 |
| LDL cholesterol (mg/dL)  | 123 (52.75)                        | 121.5 (40.33)                   | .565 |
| Triglyceride (mg/dL)     | 135.5 (100.75)                     | 145.5 (99)                      | .516 |
| BMI (kg/m²)              | 25.93 ± 2.96                       | 30.62 ± 5.03                    | <.001|
| HT (mm Hg)               | 61 (39.8%)                         | 61 (73.4%)                      | <.001|
| CVD                      | 5 (3.2%)                           | 46 (55.4%)                      | <.001|
| CVD family history       | 57 (37.2%)                         | 50 (60.2%)                      | .001 |
| Liver attenuation (HU)   | 62.05 ± 6.15                       | 50.32 ± 7.93                    | <.001|
| L/S ratio                | 1.32 ± 0.9                         | 1.01 ± 0.13                     | <.001|
| EAT volume (mm³)         | 69.03 (30.95)                      | 112.24 (44)                     | <.001|

HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index; HT, hypertension; CVD, cardiovascular disease; L/S, liver–spleen ratio; EAT volume, epicardial adipose tissue volume.
was found that the patient group with severe steatosis had a higher history of CAD (P < .001). When the epicardial adipose tissue volume was examined, the EAT volume was significantly higher in patients with severe steatosis (P = .023) (Table 3).

The groups with and without hepatosteatosis were also evaluated separately in terms of L/S ratio and EAT volume. In the group with hepatosteatosis, L/S ratio was inversely correlated with EAT volume (r = -0.241 P = .028). No significant correlation was found between EAT volume and L/S ratio in the group without hepatosteatosis (P = .675).

The patients were divided into 2 groups in terms of CVD according to the CAD-RADS score. 185 patients with a CAD-RADS score of 0 were included in the non-CVD group, and 51 patients with a CAD-RADS score of ≥1 were included in the CVD group. We also performed binomial logistic regression analysis to define variables that are independently associated with CAD (Table 4). Age, L/S ratio, EAT volume, and BMI were included in this model. As a result of our multivariable analysis, age and L/S ratio values were found to be independent predictors of CAD (Table 4).

### DISCUSSION

In our study, in which the relationship between EAT and CVD of patients diagnosed with hepatosteatosis according to the L/S ratio, the following results were obtained was evaluated: (1) EAT volume was higher in the steatosis group than in the non-steatosis group; (2) There is a negative correlation between the L/S ratio and EAT volume in the hepatosteatosis group; (3) The family history of CVD and CVD frequency is higher in the hepatosteatosis group than in the other group; (4) L/S ratio value was found to be an independent predictor of CAD. Other aspects of our study worthy of attention are as follows. The use of the CT method, which provides high reproducibility, for epicardial fat measurements. In the EAT measurement, EAT volume was measured rather than the thickness of EAT, which is not equal in all regions of the heart, and the L/S ratio, which is more valuable than liver attenuation, was used in predicting liver steatosis.

In our study, EAT volume was nearly 2 times higher in the patient group with hepatosteatosis than in patients without steatosis. Many studies have shown that the amount of EAT is higher in patients with hepatosteatosis. 18,21,23-25 Our EAT volume measurements with the CT method are consistent with the data of similar studies in the literature when evaluated by taking into account the local distribution of EAT, regional variability, and the measurements of patients with different ethnic origins. 18,26-28 Pathogenetic processes in which insulin resistance, oxidative stress, and inflammation play a role-play a role in the relationship between fatty liver and the amount of EAT. 29-31

These processes cause liver and cardiac adiposity to be seen together with the increase of visceral adipocyte tissue. Our finding that the patient group with hepatosteatosis had much higher EAT volume measurements than the other group in our study is consistent with similar data in the literature. Our study found a negative correlation between the L/S ratio and EAT volume in the hepatosteatosis group. The L/S ratio is a measurement method with proven effectiveness in detecting hepatosteatosis radiologically and histologically. 18,22,32,33 Determination of steatosis with the L/S ratio is more valuable than using only liver attenuation in the diagnosis of hepatosteatosis due to its advantages, such as having the liver and spleen in the same cross-section and not being affected by most systemic diseases. 15,18 The accepted reference value for the L/S ratio in detecting severe steatosis involving more than 30% of the liver parenchyma is 11.18 We interpreted our data by considering the reference ratio of 1.1 in the differentiation of mild and severe hepatosteatosis. 18 In the light of the literature, we accepted that

### Table 3. Evaluation of Patient Groups According to The Severity of Hepatosteatosis

| Parameters            | Mild Steatosis (n = 24) | Severe Steatosis (n = 58) | P     |
|-----------------------|------------------------|--------------------------|-------|
| Age                   | 53.44 ± 11.67          | 57.46 ± 10.19            | .118  |
| Gender (F/M)          | 30.52 ± 4.92           | 30.67 ± 5.11             | .899  |
| Total Cholesterol (mg/dL) | 13/12                 | 22/36                    | .134  |
| HDL Cholesterol (mg/dL) | 206.53 ± 34.9         | 198.38 ± 51.66           | .542  |
| LDL Cholesterol (mg/dL) | 45.97 ± 11.12        | 43.35 ± 11.31            | .410  |
| Triglyceride (mg/dL)  | 131.03 ± 29.35         | 120.65 ± 42.59           | .349  |
| BMI (kg/m²)           | 157.55 (57.55)         | 144.5 (148)              | .213  |
| HT (mm Hg)            | 15 (60%)               | 46 (79.3%)               | .102  |
| CVD                   | 6 (24%)                | 40 (68.9%)               | <.001 |
| CVD family history    | 12 (48%)               | 38 (65.5%)               | .150  |
| Liver attenuation (HU) | 54.72 ± 5.49          | 48.43 ± 8.1              | .001  |
| L/S ratio             | 1.15 ± 0.3             | 0.95 ± 0.11              | <.001 |
| EAT volume (mm³)      | 93.85 (43)            | 112.11 (42)              | .023  |

HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index; HT, hypertension; CVD, cardiovascular disease; L/S, liver–spleen ratio; EAT volume, epicardial adipose tissue volume.

### Table 4. Binary Logistic Regression Analysis of Cardiovascular Disease

| Parameters | Univariate Analysis | Multivariable Analysis |
|------------|---------------------|------------------------|
|            | OR (95% CI) | P     | OR (95% CI) | P     |
| Age        | 0.88      | <.001 | 0.91      | <.001 |
| L/S ratio  | 3276.44   | <.001 | 6312.15   | <.001 |
| EAT volume | 0.96      | <.001 | 0.98      | .119  |
| BMI (kg/m²)| 0.83      | <.001 | 1.09      | .131  |

L/S ratio, liver–spleen ratio; EAT volume, epicardial adipose tissue volume; BMI, body mass index.
patients with L/S ratio above 1.2 do not have hepatosteatosis, those between 1.2 and 1.1 have mild hepatosteatosis, and those below 1.1 have severe hepatosteatosis.\textsuperscript{18,34} We found that the severity of hepatosteatosis, which can be calculated according to liver attenuation, increased with the decrease in the L/S ratio. There was no relationship between the L/S ratio and EAT volume in the group without steatosis. There was a negative correlation between EAT volume and the L/S ratio in the steatosis group. The most important reason for this difference between the L/S ratio and EAT volume between groups with and without steatosis is the change in inflammatory properties due to the change in the amount of accumulation of EAT. This adipose tissue shows anti-inflammatory properties in the early stages when EAT volume accumulation is low; when the accumulation increases, its properties change and inflammatory molecules are released.\textsuperscript{33,35} EAT volume, whose inflammatory properties increase, causes an increase in visceral adipose tissue accumulations over time.

The family history of CVD and the frequency of CVD were higher in the hepatosteatosis group than in the other group. As a result of our multivariable analysis, age and L/S ratio values were found to be independent predictors of CAD. As the L/S ratio decreases, EAT volume and incidence of CVD increase. The increase in the frequency of CVD is an important known consequence of increased visceral adipose tissue and secondary hepatic and epicardial adipose tissue.\textsuperscript{36–38} In explaining the role of hepatosteatosis and increase in the amount of EAT in the development of CVD, there are pathogenetic processes in which insulin resistance, oxidative stress, and inflammation play a role.\textsuperscript{29–31} EAT, which is found in low amounts in healthy people, has beneficial effects on both immunological and coronary blood flow and has cardio-protective properties with the functions of using and storing free fatty acids. Under conditions of low oxidative stress, normal epicardial adipocytes secrete adiponectin, that is, anti-inflammatory properties, which protect cardiomyocytes from hypertrophic stimuli, minimize inflammation and fibrosis in the coronary arteries and myocardium, thereby reducing the likelihood of adverse clinical events.\textsuperscript{39,40} In physiological conditions, EAT carries out tasks such as removing and storing excess free fatty acids that are toxic to the myocardium, while it is involved in the increased supply of free fatty acids required for the myocardium with increasing ischemia.\textsuperscript{38} With the changing biological structure of EAT, the release of adiponectin from EAT to the systemic circulation decreases, and pro-inflammatory adipocytokines such as leptin, adipin, TNF-\(\alpha\), IL-1\(\beta\), IL-6, IL-18, and resistin are released. It causes a systemic inflammatory response. Systemic inflammation also triggers a positive feedback mechanism that causes epicardial adipose tissue to accumulate.\textsuperscript{32} In many previous studies conducted by some researchers in our group, it was concluded that the relationship between EAT and CVD frequency was the result of concomitant inflammatory events.\textsuperscript{25,41–46} Studies in subjects with CVD or at high risk of CVD have shown that pro-inflammatory cytokines are released from EAT rather than from subcutaneous adipose tissue.\textsuperscript{2} It means that EAT is more closely associated with cardiovascular events than the amount of total body adipose tissue. In a meta-analysis evaluating more than 40,000 patients, EAT was also an independent risk factor for CVD, and EAT volume correlates with coronary artery calcification and myocardial ischemia.\textsuperscript{46} In recent studies, it has been concluded that EAT is an independent predictor of coronary events and left ventricular dysfunction, but visceral adipocyte tissue accumulation is not an independent risk factor for cardiovascular events.\textsuperscript{47–50} In patients with CVD, pro-inflammatory adipokine production of epicardial adipose tissue is considerably higher than subcutaneous adipose tissue.\textsuperscript{3} It indicates that epicardial adipose tissue is a better predictor of CVD than subcutaneous fat deposition.

In our study, the mean BMI was higher in the hepatosteatosis group compared to the other group and also, BMI was an independent predictor for CVD. There is a close relationship between BMI and visceral adipose tissue; as the weight gain increases, the amount of visceral adipose tissue, liver steatosis, and epicardial adipose tissue also increases.\textsuperscript{51,52} Inflammation caused by increased adipose tissue also causes an increase in local adipose tissue accumulations with positive feedback. Our data showing BMI is higher in patients with hepatosteatosis, and the increase in the frequency of concomitant CVDs supports these pathophysiological processes and similar data in the literature. Compared with BMI and waist circumference, EAT thickness is more valuable in demonstrating hepatosteatosis.\textsuperscript{53} The patient population of most of the studies investigating the relationship between hepatosteatosis and EAT consists of obese individuals.\textsuperscript{19,39,53} In obese individuals, like many visceral adipocyte tissue accumulations, EAT also increases, and the biological structure and anti-inflammatory properties of EAT also change.\textsuperscript{39} In obese individuals, EAT has inflammatory properties rather than anti-inflammatory properties.\textsuperscript{2} Although obesity is a severe risk factor for CVD, the correlation of epicardial fat with the risk of CVD and the development of high-risk obstructive plaque is independent of obesity.\textsuperscript{54–56} Only 23.7% (n=56) of our patient group are obese individuals. Considering the studies in the literature showing that EAT thickness is higher in obese patients with steatosis than in obese patients without steatosis and studies showing that the role of EAT in the development of CVD is independent of VAT, our study shows that the relationship between EAT and hepatosteatosis cannot be explained only by obesity or VAT accumulations.\textsuperscript{19}

There was no significant difference in total cholesterol, HDL, LDL cholesterol, and triglyceride levels between groups with and without hepatosteatosis in the study. Another known traditional risk factor for CVD is dyslipidemia. While there was no difference in cholesterol levels between the 2 groups in our study, the significant difference in cardiovascular events may raise the idea that CVDs may be associated with the EAT relationship independent of hyperlipidemia. In studies examining the relationship between cholesterol levels, CVH, and EAT, EAT was found to be inversely correlated with HDL cholesterol and positively correlated with LDL cholesterol and triglyceride.\textsuperscript{25,46,49,57,58}
Among the exciting aspects of our study are (1) the use of the CT method, which provides high reproducibility for epicardial fat measurements; (2) more consistent measurements can be made by measuring the volume of EAT, which is not found in equal amounts in each area on the heart, rather than the thickness, (3) the liver-spleen attenuation ratio can be measured in hepatosteatosis; (4) Finally, by comparing the L/S ratio with EAT, factors that may cause an increase in EAT volume, such as visceral adipose tissue accumulation caused by structural causes, can be ignored. Although it is not a measurement method recommended by the guidelines in EAT measurement, transthoracic echocardiography is often the preferred method because it is easily accessible, non-invasive, and low cost. This method has some limitations.

The biggest limitations of EAT measurement with echocardiography are that EAT is not equal in all areas of the heart, the experience of the echocardiographer changes the measurement results, and the difficulty of the procedure in obese individuals. Epicardial adipose tissue volume can also be measured with CT and MR, and both methods provide a more accurate and volumetric measurement of epicardial fat tissue than transthoracic echocardiography. CT and MR imaging are more sensitive and specific than echocardiography, but they are more expensive and laborious. In studies comparing volume and thickness measurements of EAT from different cross-sectional areas, EAT volume was found to be correlated with intra-abdominal visceral adipose tissue deposition compared to other measurements. In line with all this information, the measurement of EAT volume stands out as the best method to determine the amount of EAT. In the meta-analysis of 9 studies published by Nerlekar et al., EAT volume was found to be more valuable in CVD risk assessment than other EAT measurement methods. In most studies examining the relationship between EAT and hepatosteatosis, liver attenuation is used to diagnose hepatosteatosis. Non-contrast CT is the most effective method for demonstrating fatty liver. In contrast-enhanced CT, attenuation is affected by contrast agent concentration, volume, rate of administration, and timing of measurements. The spleen is unaffected by most common pathological processes and is located on the same CT scan as the liver, facilitating liver and spleen measurements. In diagnosing hepatosteatosis with computed tomography, a more hypodense image is obtained due to the decrease in liver attenuation compared to expected. The average liver density is 50–57 HU on non-contrast computed tomography and 40–48 HU in the spleen. Liver density below 48 HU also suggests fatty liver. In the light of these data, we would like to state that in determining the presence and severity of hepatosteatosis with liver density, iron accumulation in the liver or inflammatory events may cause a change in liver density. Therefore, the risk of error may increase by determining steatosis only by density measurement. Our study aimed to eliminate the effect of possible iron accumulation in the liver and spleen or density changes caused by the inflammatory disease using the L/S ratio.

The authors declare that they have no competing interest.

CONCLUSION

In conclusion, we showed in the study that the L/S ratio was an independent predictor for CVD, EAT volume was negatively correlated with the L/S ratio, and the frequency of CVD is much lower in patients with a high L/S ratio. Use of L/S ratio, which is more valuable than liver attenuation in predicting hepatic steatosis, may be more useful in evaluating the risk of hepatosteatosis-related CVD.

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