Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2024; 41(3): 738-745
doi: 10.52142/omujecm.41.4.10

Assessing the relationship between liver and spleen volumes in patients with liver cirrhosis using the Cavalieri principle on cross-sectional images

Merve Nur OZGEN[1], Abdurrahman SAHIN [2], Ruken CELIKYAY [3], Bunyamin SAHIN[4*]

[1]Department of Anatomy, Faculty of Medicine, Tokat Gaziosmanpaşa University, Tokat, Türkiye
[2]Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Tokat Gaziosmanpaşa University, Tokat, Türkiye
[3]Department of Diagnostic Radiology, Sincan Research and Training Hospital, Ankara, Türkiye
[4]Department of Anatomy, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Türkiye

Received: 08.09.2024 • **Accepted/Published Online:** 19. 11.2024 • **Final Version:** 31.12.2024

Abstract

In the early stages of liver cirrhosis, hepatomegaly is observed, while in the later stages, enlargement of the spleen is observed due to shrinkage of the liver and increased pressure in the portal circulation. This study examined liver and spleen volumes and their proportional relationship in healthy controls (HC) and patients with liver cirrhosis (LC) using computed tomography (CT) images. CT images from 52 LC patients (26 females, 26 males) and 52 HC individuals (26 females, 26 males) aged 18 to 85 years were analyzed. Liver and spleen volumes, as well as spleen/liver+spleen volume ratio were calculated using the Cavalieri principle. Volume and ratio data were compared between the HC and LC groups. In addition, volumes and ratios were analyzed according to the disease classes in patients. Liver volume was greater in LC patients (1488.9 ± 502.3 cm^3) than in HC individuals (1321.8 ± 277.1 cm^3) ($p = 0.038$). Spleen volume was significantly greater in LC patients (676.8 ± 347.02 cm^3) than in HC individuals (249.37 ± 101.16 cm^3) ($p < 0.001$). The spleen/liver+spleen volume ratio was significantly higher in LC patients (30.75 ± 12.22%) than in HC individuals (15.68 ± 5.09%) ($p < 0.001$). No significant difference in volume ratios was observed between LC and HC groups based on sex ($p > 0.05$). Liver volumes were 1670.7 cm^3, 1357.4 cm^3, and 1087.3 cm^3, while the spleen/liver+spleen volume ratios were 26.71%, 33.49%, and 40.26% in LC classes A, B, and C respectively. As the cirrhosis class progressed, liver volume decreased ($p = 0.010$), and the spleen/liver+spleen volume ratio increased ($p = 0.020$). Liver and spleen sizes, as well as the spleen/liver+spleen volume ratio did not vary by sex. These values can serve as baseline parameters independent of sex. Liver and spleen volumes, as well as their ratios, were greater in LC patients than in HC individuals. As the class of cirrhosis progressed, liver volume decreased, and the ratio increased. Our findings suggest that the spleen/liver+spleen volume ratio can be used to evaluate the classes of liver cirrhosis.

Keywords: liver, spleen, volume, cirrhosis, Cavalieri principle, computed tomography

1. Introduction

Cirrhosis is a chronic and progressive disease defined as a deterioration in the anatomical structure of the liver due to fibrosis and nodularization. In liver cirrhosis, the spleen enlarges as liver volume and pressure in the portal circulation increase. Decreased platelet count and accompanying splenomegaly in patients with chronic liver disease may be considered diagnostic for cirrhosis. In the early stage of liver cirrhosis (A), hepatomegaly is seen, whereas in the later stages (B-C), the liver shrinks in both weight and volume due to the increase in fibrous tissue and shrinkage of the liver. Therefore, hepatomegaly and splenomegaly often appear together (1-3).

The Child-Pugh score (CPS) is considered the gold standard for determining the prognosis of liver cirrhosis. Making a diagnosis of cirrhosis is critical for guiding the treatment process, determining prognosis, and for individuals with chronic liver disease (4, 5). According to this classification, patients are divided into three classes: A, B, and C. These classes directly impact the functional ability and anatomical changes of the liver. In Child-Pugh A class, there may be mild fibrosis of the liver structure, but nodular regeneration is minimal. Liver size is usually normal or slightly enlarged. In the spleen, splenomegaly is rare, and signs of portal hypertension are usually absent. In the Child-Pugh B class, fibrosis and nodular structure are more prominent in the liver. The surface of the liver may be hardened and asymmetrically enlarged. Splenomegaly occurs in the spleen due to portal hypertension. The liver is markedly shrunken, nodular, and hard in the Child-Pugh C class. Fibrosis is advanced. Splenomegaly is severe in the spleen (6-8). Accurate measurement of liver and spleen volumes is necessary to diagnose hepatomegaly and splenomegaly in the clinic. Many studies in the literature examine the effect of varying volumes of organs on clinical pictures (9-11).

Multidetector computed tomography (MDCT), ultrasonography (USG), and magnetic resonance imaging (MRI) techniques are used for radiologic evaluation of the liver

*Correspondence: bsahin@omu.edu.tr

and spleen (11, 12). Cavalieri principle, one of the stereological methods, is also used to measure the volume of organs. This method takes cross-sectional images of the organ whose volume is to be measured. Cross-sectional surface areas are calculated using point counting or planimetry methods. The volume of the organ is calculated by multiplying the cross-sectional surface areas along the entire series by the thickness of the cross-section. For quantitative measurements, the planimetry method is widely used. It is often considered the gold standard, while computed tomography (CT) images are used because they provide more distinct cross-sectional images (13, 14).

Physical examination does not provide accurate information about the volume of organs (15). Easy and accurate measurement of liver and spleen volumes is important for early diagnosis, follow-up, and treatment planning of cirrhosis (16). Knowing the normal range of liver and spleen volumes in healthy controls (HC) will help clinically assess organ volume increase or decrease in patients with liver cirrhosis (LC). Changes in organ volumes can be obtained using noninvasive cross-sectional imaging.

This study aimed to calculate liver and spleen volumes and their ratios to each other on CT images using the Cavalieri principle and to compare them between HC and LC. Liver and spleen sizes and the relationship between the size ratios of the two organs were analyzed in HC and LC individuals using a sex comparison. In addition, volumes and ratios were evaluated according to the disease classes in patients.

2. Materials and Methods

2.1. Study Population

HC and LC subjects were scanned with CT aging 18-85 years who were admitted to Tokat Gaziosmanpaşa University Research and Training Hospital between August 2014 and March 2023. Patients with a history of hepatocellular carcinoma, amyloidosis, acute liver failure, hemochromatosis, and hepatic resection were excluded from the study. In the HC group, patients with any abdominal pathology, hepatomegaly, or splenomegaly and those with a history of liver disease were excluded. The HC group was randomly selected to be age- and sex-matched with LC. As a result of this review, 52 LC (26 female, 26 male) and 52 HC (26 female, 26 male) were included in the study. A gastroenterologist performed CPS of LC for clinical evaluation. The distribution of the Child-Pugh class as a result of the score was 27 A (12 female, 15 male), 19 B (11 female, 8 male), and 6 C (3 female, 3 male). According to sex, there was no significant difference between LC and HC group ($p>0.05$) and between Child-Pugh classes A, B, and C of LC ($p=0.668$).

2.2. Data Collecting

All images were obtained with a 64-slice MDCT machine (Optima CT660, GE Healthcare, Milwaukee, USA). Acquisition parameters were as follows: 120 kV; 150 mAs; collimation 64×0.5; slice thickness 2.5 mm; slice reconstruction thickness 1.25 mm; matrix 512×512 pixels; gantry angle 0° (degrees). In all cases, iodinated contrast medium was administered peripherally via intravenous (IV) route (usually antecubital vein) at a dose of 1.5 ml/kg. The examinations were obtained in the portal venous phase from cranial to caudal direction approximately 60 seconds after IV iodinated contrast medium was administered. The evaluations were performed in the portal venous phase, in which the portal and hepatic veins formed the most contrast with the parenchyma. The abdominal CT images used in the study were obtained from the Picture Archiving and Communication System (PACS) of the university.

2.3. Image Analysis

CT images in the PACS archive system were converted to Digital Imaging and Communications in Medicine (DICOM) format. Image series were opened sequentially using ImageJ software. In the program, the "Image" "Adjust" "Window/Level" setting was set to Level: 40 Window: 400. Thus, contrast adjustment was made to distinguish adjacent tissues and organs visually. The image series were sampled so that at least 15-20 image slices of the spleen and liver of the HC and LC remained.

2.4. Volumetric Analysis

The cross-sectional surface areas of the liver and spleen were drawn manually using the "polygon selection" tool of the program on each slice, excluding the inferior vena cava and gallbladder, as shown in Fig. 1. Thus, the program measures the cross-sectional surface areas using the planimetry method. Liver and spleen volumes were calculated in cm^3 by multiplying the sum of the cross-sectional surface areas by the section thickness according to the Cavalieri principle (13, 17). The coefficient of error (CE) for the volume calculation of each objects were estimated as described in the literature (18). In addition, the spleen volume was divided by the sum of the spleen and liver volumes and then multiplied by 100 to calculate the spleen/liver+spleen volume ratio. All calculations were performed using the sheets containing the formulas we prepared in the Microsoft Excel program.

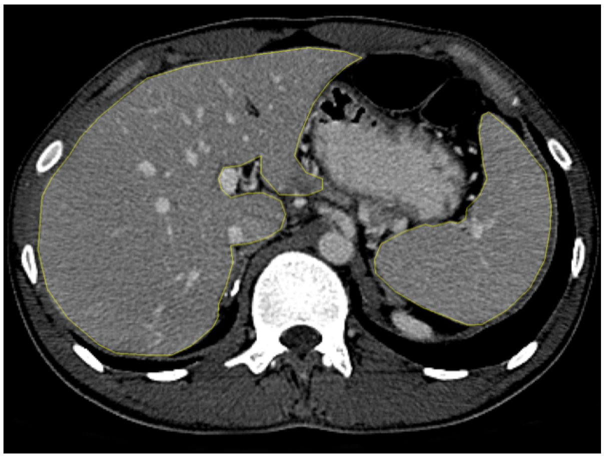

Fig. 1. Delineations of the cross-sectional surface areas of the liver and spleen in CT images using the "Polygon Selection" tool in the ImageJ program

2.5. Statistical Analysis

The data set represented quantitative variables using arithmetic mean and standard deviation. The normality of continuous variables was examined using Shapiro-Wilk's test. It was found that the variables were normally distributed. The homogeneity of variances, which is one of the assumptions for applying parametric tests, was also examined using Levene's test, and it was seen that the variances were homogeneous. The Chi-Square test analyzed the relationship between qualitative variables according to sex, and quantitative variables were analyzed by the Significance of the Difference Between Two Means test. When differences were sought between groups regarding continuous variables, the Significance of Difference Between Two Means test was used. One-way Analysis of Variance was used when differences were sought within groups regarding continuous variables. Tukey HSD test was used for multiple comparisons. All tests were considered statistically significant for p-values <0.05. Statistical analysis of the volume data and demographic data of the individuals obtained in the study were evaluated using SPSS software (SPSS 22.0 V.25, Chicago, IL, USA).

3. Results

3.1. Population

The mean age of the 52 LC in the study was 66.33±9.19 years, and the mean age of the 52 individuals in the HC group was 61.46±16.1 years, and there was no difference in the mean age of the groups (p=0.061). The mean ages of Child-Pugh classes A, B, and C were 65.41±9.49, 67.79±7.56 and 65.83±13.18, respectively. There was no difference between the classes regarding mean age (p=0.689).

3.2. Comparison of Volume and Volume Fraction Data between Groups

In this study, the liver and spleen volumes of the LC and HC were compared. The mean liver volume was 1321.8 cm^3 in the HC group and 1488.9 cm^3 in LC, and the livers of LC were larger than those of HC (p=0.038). The mean spleen volume was 249.37 cm^3 in the HC group and 676.8 cm^3 in the LC. Spleen volume was larger in LC than in the HC group (p<0.001). When the spleen/liver+spleen volume ratio was evaluated, the HC group had an average of 15.68%, while LC had an average of 30.75%. The spleen was proportionally larger in the LC than in the HC group (p<0.001). Details of liver and spleen volumes and spleen/liver+spleen volume ratios of LC and HC are given in Table 1.

Of the LC, 51.92% were in Child-Pugh A, 36.53% in Child-Pugh B, and 11.53% in Child-Pugh C class. The mean liver volumes of patients with Child-Pugh A, B, and C class cirrhosis were 1670.7 cm^3, 1357.4 cm^3, and 1087.3 cm^3, respectively. Liver volume was smaller in patients with Child-Pugh C class compared to other classes (p=0.010). The mean spleen volumes of patients with Child-Pugh A, B, and C liver cirrhosis were 635.7 cm^3, 700.2 cm^3, and 787.66 cm^3, respectively. Spleen volume did not differ between the classes (p=0.593). The spleen/liver+spleen volume ratio was 26.71% for Child-Pugh A, 33.49% for Child-Pugh B, and 40.26% for Child-Pugh C. The spleen/liver+spleen volume ratio increased from Child-Pugh A to Child-Pugh C (p=0.020). The details of liver and spleen volumes and spleen/liver+spleen volume ratios of the classes of LC are given in Table 2.

Table 1. Comparison of liver and spleen volumes and spleen/liver+spleen volume ratios of patients with liver cirrhosis and healthy controls between groups

	LC (n=52) Mean±SD	HC (n=52) Mean±SD	p
Liver Volume (cm^3)	1488.9±502.3	1321.8±277.1	0.038*
Spleen Volume (cm^3)	676.8±347.02	249.37±101.16	<0.001*
Spleen/Liver+Spleen Volume Ratio (%)	30.75±12.22	15.68±5.09	<0.001*

SD: Standard deviation, LC: Patients with liver cirrhosis, HC: Healthy controls, The significance of the difference between two means test, *p<0.05

Table 2. Comparison of liver and spleen volumes and spleen/liver+spleen volume ratios of patients with liver cirrhosis with Child-Pugh classification according to classes

	Child-Pugh A (n=27)		Child-Pugh B (n=19)		Child-Pugh C (n=6)		P
	Mean±SD	Min-Max	Mean±SD	Min-Max	Mean±SD	Min-Max	
Liver Volume (cm^3)	1670.7±489.7(a)	1329.4-2024.7	1357.4±472.3 (ab)	1052.8-1744.1	1087.3±292.9 (c)	923.6-1363.9	0.010*
Spleen Volume (cm^3)	635.7±340.85	345.65-911.44	700.2±355.6	400.65-976.2	787.66±378.16	460.44-1146.09	0.593
Spleen/Liver+Spleen Volume Ratio (%)	26.71±10.41 (a)	19.91-30.82	33.49±12.77 (ab)	24.47-39.65	40.26±12.09 (c)	32.5-52.89	0.020*

SD: Standard deviation, One-way analysis of variance, Tukey HSD test for multiple comparisons, (abc): A common letter in a row indicates statistical insignificance, *p<0.05

3.3. Comparison of Volume and Volume Fraction Parameters by Sex

The mean liver and spleen volumes of all female and male in the study were 1333.7 cm^3 and 432.45 cm^3 and 1477 cm^3 and 493.73 cm^3, respectively. Liver and spleen volume values did not differ between sexes (p>0.05). The spleen/liver+spleen volume ratio was 22.88% in female and 23.55% in male. Spleen volume showed similar values and did not differ between sexes (p>0.05). Details of liver and spleen volumes and spleen/liver+spleen volume ratios of male and female subjects are given in Table 3.

Table 3. Comparison of liver and spleen volumes and spleen/liver+spleen volume ratios of male and female individuals by sex

	Female (n=52) Mean±SD	Male (n=52) Mean±SD	p
Liver Volume (cm^3)	1333.7±384.3	1477±430.4	0.076
Spleen Volume (cm^3)	432.45±310.63	493.73±354.11	0.350
Spleen/Liver+Spleen Volume Ratio (%)	22.88±11.9	23.55±12.21	0.777

SD: Standard deviation, The significance of the difference between two means test

When liver and spleen volumes of LC were compared by sex, female had a mean volume of 1434.8 cm^3 and 636.58 cm^3, respectively, while male had 1543 cm^3 and 717.03 cm^3. Liver and spleen volumes of male and female LC did not differ between sexes (p>0.05). When the spleen/liver+spleen volume ratio was evaluated, it was 30.51% in female LC and 30.99% in male patients. The spleen/liver+spleen volume ratio did not differ between sexes (p=0.888). Details of liver and spleen volumes and spleen/liver+spleen volume ratios of male and female LC are given in Table 4.

Table 4. Comparison of liver and spleen volumes and spleen/liver+spleen volume ratios of male and female LC according to sex

	LC		
	Female (n=26) Mean±SD	Male (n=26) Mean±SD	p
Liver Volume (cm^3)	1434.8±465.5	1543±540.4	0.443
Spleen Volume (cm^3)	636.58±311.04	717.03±381.51	0.409
Spleen/Liver+Spleen Volume Ratio (%)	30.51±11.56	30.99±13.06	0.888

SD: Standard deviation, LC: Patients with liver cirrhosis, The significance of the difference between two means test

When the liver volumes of individuals in the HC group were compared according to sex, female had a mean volume of 1232.5 cm^3, while male had a mean volume of 1411 cm^3. Healthy male individuals have larger livers than healthy female individuals (p=0.019). The mean spleen volume of HC was 228.31 cm^3 in female and 270.43 cm^3 in male, with no difference between the sexes (p=0.135). The spleen/liver+spleen volume ratio was 15.26% in healthy females and 16.11% in healthy males, and this ratio did not differ between sexes (p=0.550). The details of liver and spleen volumes and spleen/liver+spleen volume ratios of the HC are given in Table 5.

Table 5. Comparison of liver and spleen volumes and spleen/liver+spleen volume ratios of the HC according to sex

	HC		
	Female (n=26) Mean±SD	Male (n=26) Mean±SD	p
Liver Volume (cm^3)	1232.5±251.6	1411±277.2	0.019*
Spleen Volume (cm^3)	228.31±115.82	270.43±80.86	0.135
Spleen/Liver+Spleen Volume Ratio (%)	15.26±5.84	16.11±4.29	0.550

SD: Standard deviation, HC: Healthy controls, The significance of the difference between two means test, *p<0.05

When the liver volume of female subjects was compared between groups, it was 1434.8 cm^3 in LC and 1232.5 cm^3 in HC. The liver volume of female did not differ between the groups (p=0.057). The mean spleen volume in female LC was 636.58 cm^3; in the HC, it was 228.31 cm^3, and the livers of female LC were larger than those of HC (p<0.001). Similarly, the spleen/liver+spleen volume ratio was 30.51% in female LC and 15.26% in the HC. The spleen/liver+spleen volume ratio was proportionally larger in female LC than in HC (p<0.001). The details of liver and spleen volumes and spleen/liver+spleen volume ratios of female LC and the HC are given in Table 6.

Table 6. Comparison of liver and spleen volumes and spleen/liver+spleen volume ratios of female subjects by groups

	Female		
	LC (n=26) Mean±SD	HC (n=26) Mean±SD	p
Liver Volume (cm^3)	1434.8±465.5	1232.5±251.6	0.057
Spleen Volume (cm^3)	636.58±311.04	228.31±115.82	<0.001*
Spleen/Liver+Spleen Volume Ratio (%)	30.51±11.56	15.26±5.84	<0.001*

SD: Standard deviation, LC: Patients with liver cirrhosis, HC: Healthy controls, The significance of the difference between two means test, *p<0.05

The liver volume of the male subjects LC was 1543 cm^3 and 1411 cm^3 in the HC. Liver volume did not differ between male with and without liver cirrhosis (p=0.273). The mean spleen volume was 717.03 cm^3 in male LC and 270.43 cm^3 in the HC, and the spleen volume was larger in male LC than in HC (p<0.001). Similarly, the spleen/liver+spleen volume ratio was 30.99% in male LC and 16.11% in the HC. The spleen/liver+spleen volume ratio was larger in male LC than in the HC (p<0.001). The details of liver and spleen volumes and spleen/liver+spleen volume ratios of male subjects LC and the HC are given in Table 7.

Table 7. Comparison of liver and spleen volumes and spleen/liver+spleen volume ratios of male individuals according to groups

	Male		
	LC (n=26) Mean±SD	HC (n=26) Mean±SD	p
Liver Volume (cm^3)	1543±540.4	1411±277.2	0.273
Spleen Volume (cm^3)	717.03±381.51	270.43±80.86	<0.001*
Spleen/Liver+Spleen Volume Ratio (%)	30.99±13.06	16.11±4.29	<0.001*

SD: Standard deviation, LC: Patients with liver cirrhosis, HC: Healthy controls, the significance of the difference between two means test, *p<0.05

4. Discussion

In the human body, it is difficult to precisely measure the size of the liver and spleen in vivo. Physical examination or radiological imaging techniques such as USG, CT, and MRI are used to detect changes in the size of these organs (4, 19, 20). These techniques help to determine the volumes of organs accurately. In this context, in clinical conditions such as liver cirrhosis, it is important to objectively and precisely determine the volume of both the organ and the pathological condition and to monitor the volume change. Studies in the literature have calculated liver and spleen volumes using different methods to indicate advanced liver disease and its complications (4, 9, 11, 21). However, the accuracy of the data obtained by measuring liver and spleen volumes with automatic measurement programs is important. Cavalieri's principle, one of the stereological methods, has recently been accepted as the gold standard due to its accurate calculation of the volumes of tissues and organs (11, 22). In this study, we aimed to calculate the volumes of the liver and spleen and the ratios of these organs to each other from CT images using the Cavalieri principle and compare them between LC and HC. In addition, the volumes and ratios were evaluated according to the disease classes in patients.

Using semi-automated software, Patel et al. (22) found that 584 LC with a mean age of 55.9 years had significantly lower liver volume than HC. The decrease in total liver volume in LC was mainly due to volume loss in the right lobe of the liver (segments 4-8). Zhou et al. (8) reported that the total liver volume manually measured using 16-MDCT in 101 patients with virus-induced cirrhosis and 113 HC subjects with an average age of 52 years was significantly smaller in LC than in HC subjects. Li et al. (23) manually measured the liver volume of 40 control subjects, 63 liver fibrosis subjects, and 24 liver cirrhosis subjects on CT images and reported that the liver volume was significantly smaller in LC than in HC. In LC, liver volume tended to decrease as fibrosis and cirrhosis increased. Contrary to the results in the literature, in our study, liver volume was 1488.9±502.3 cm^3 in LC with a mean age of 66.33 years and 1321.8±277.1 cm^3 in HC. Liver volume was higher in LC, and this difference was significant. This showed us that liver volume can be used for cirrhosis follow-up.

Liver morphology changes at different classes of cirrhosis. This change is partly due to changes in the volume and number of liver parenchymal cells. The CPS is the most widely used score to assess the severity of liver cirrhosis and predict prognosis (24). In a study by Zhou et al. (8) with 101 cirrhotic and 113 healthy subjects, the mean total liver volumes of cirrhotic patients with Child-Pugh A, B, and C were 1100.92±336.68 cm^3, 1043.88±364.75 cm^3, and 798.01±203.64 cm^3, respectively. It was concluded that all of these values were significantly smaller than those of HC subjects. Child-Pugh C patients had significantly smaller total liver volumes than Child-Pugh A and B patients. Although liver atrophy was observed in Child-Pugh A patients, certain regions, such as the caudate lobe and left lateral segment, may tend to grow to compensate for liver function.

On the other hand, in Child-Pugh B and C patients, the overall volume of the liver begins to decrease due to increased fibrosis. The liver of Child-Pugh C patients has been reported to change and shrink the most in size and volume. These data directly indicate that the low amount of liver cells in Child-Pugh C patients aggravates the pathophysiological state, leading to the worst clinical manifestations. In our study, the mean liver volumes of LC according to Child-Pugh classes A, B, and C were 1670.7 cm^3, 1357.4 cm^3, and 1087.3 cm^3, respectively, and there was a significant difference between the classes. The result that liver volume decreased from Child-Pugh A class to C class is similar to the results of studies in the literature (8, 22). However, the mean liver volume of HC was 1321.8±277.1 cm^3, which was less than Child-Pugh A and B and more than the C class. We think that the liver volumes in the study differ from the results in the literature due to a large number of Child-Pugh A class patients participating in the study and their older ages.

Spleen volume is important in determining spleen involvement in Hodgkin's disease and detecting diseases such as liver cirrhosis. In Hodgkin's disease and liver cirrhosis, the spleen usually enlarges with disease progression. Especially in advanced classes, the increase in splenic volume becomes prominent and is often characterized by multiple hypodense lesions (11, 25). In a study conducted on Hodgkin's disease, splenic involvement was observed in 15.6% and confirmed by imaging methods. Splenomegaly showed a strong correlation with advanced classes of the disease, and this finding emphasized the prognostic importance of splenomegaly in disease progression (25). In studies conducted in HC, the age factor affects spleen volume, and spleen volume decreases with age (21, 26). Li et al. (23) manually measured spleen volume on CT images and concluded that spleen volume was larger in LC than in HC. In LC, splenic volume tended to increase as cirrhosis increased. Splenic hypertrophy may be observed in LC accompanied by portal hypertension (9). The results of our study also support the findings in the literature. The splenic volume of LC was larger than that of HC. Although splenic volume increased as the cirrhosis class progressed, the difference between the classes was insignificant.

To the best of our knowledge, there is no study in the literature on measuring the ratio of spleen volume to total spleen and liver volume in LC. This shows us how much the spleen volume is enlarged in the total liver and spleen volume. In the present study, the spleen/liver+spleen volume ratio was 30.75% in LC and 15.68% in the HC. The spleen/liver+spleen volume ratio was higher in LC than in HC, and this difference was significant. In addition, this ratio increased as the classes of liver cirrhosis progressed. This finding suggests that the spleen/liver+spleen volume ratio can be used to evaluate classes of liver cirrhosis.

Comparing the accuracy of three different approaches to liver volume measurement in living donor transplants, Kalshabay et al. (27) reported a significant difference between the average error rate of manual and semi-automated applications, while there was no significant difference between manual and automated applications. They showed that the semi-automated method had the highest error rate among all three methods. The manual measurement method requires more time and effort than other methods and demands high precision from radiologists; however, it is recommended that this method is preferred due to the accuracy of the measurements. Automated liver volume calculation programs may give inaccurate results, especially when the density of liver parenchyma matches the density of adjacent organs such as the spleen, pancreas, and kidney. Therefore, we preferred the Cavalieri principle for manual volume measurement in this study because it is precise and unbiased, and the mathematical error percentage of the data obtained with this method is less than 0.05%; that is, it gives results without deviating from the actual value and can be applied practically (28-34). It also offers high efficiency, confidence, and accuracy in volume calculations (17). The accuracy of this study was increased by performing measurements using the Cavalieri principle.

From a practical point of view, the time to perform liver and spleen volume measurements is an essential factor, mainly when measurements are performed manually or using semi-automated applications. Since manual and semi-automated methods require the determination of liver and spleen contours in sections, the time for volume measurement depends on the number of sections to be analyzed. Reiner et al. (35) reported that the mean estimated liver volume decreases with increasing slice thickness on CT. Therefore, in our study, volume measurements were performed on CT images with a slice thickness of 2.5 mm. Since the probability of false positive results decreases with decreasing slice thickness, it is thought that the thinner the slices, the more accurate the results (36). However, the disadvantage of using such thin sections is that the procedure takes time.

Our study has some limitations. It was a retrospective study with a limited sample size. Considering the differences in the distribution of patient groups stratified by stage and insufficient clinical data, this study did not perform more specific group analyses, such as factors causing liver cirrhosis. This feature can be defined as the primary limitation of our study. However, using the Cavalieri principle method, the study measured accurate and reliable values obtained from CT images in LC and HC. To our knowledge, this study is unique as it is the first to calculate the liver, spleen, and spleen/liver+spleen volume ratio in liver cirrhosis with the Cavalieri principle and to compare these values with the HC.

This study analyzed volumetric CT results by comparing liver, spleen, and spleen/liver+spleen volume ratios between 52 HC and 52 LC. In conclusion, volumetric changes in the liver and spleen parallel the natural history of cirrhosis and are associated with clinical classes. Liver volume, spleen volume, and spleen/liver+spleen volume ratio were larger in LC than HC. Among LC, 51.92% were in the Child-Pugh A class, 36.53% in the Child-Pugh B class, and 11.53% in the Child-Pugh C class. In LC, liver volume decreased, and the spleen/liver+ spleen volume ratio increased as the Child-Pugh class progressed. The spleen/liver+ spleen volume ratio during routine CT scanning showed it can be a discriminative parameter for LC. These data may be valuable for understanding disease progression, monitoring treatment, and planning transplantation procedures. The use of stereological methods in such studies provides high precision and accuracy. Therefore, the data obtained are reliable for clinical applications. Further studies are needed to confirm these findings and better understand their clinical utility.

Conflict of interest

The authors declared no conflict of interest.

Funding

The authors declared that this study has received no financial support.

Acknowledgments

The authors would like to thank Tokat Gaziosmanpaşa University Research and Training Hospital for the realization of the study and providing the data.

Authors' contributions

Concept: M.N.O., A.S., R.C., B.S., Design: M.N.O., B.S., Data Collection or Processing: A.S., R.C., M.N.O., B.S., Analysis or Interpretation: M.N.O., B.S., Literature Search: M.N.O., B.S., Writing: M.N.O., A.S., R.C., B.S.

Ethical Statement

Approval was obtained from Tokat Gaziosmanpaşa University Clinical Research Ethics Committee, the study started. The ethics committee decision date is 02/03/2023 and the number of ethical committee decisions is 2023/04.

References

1. Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. Lancet. 2021;398(10308):1359-1376. https://doi.org/10.1016/S0140-6736(21)01374-X

2. Karagiannakis DS, Stefanaki K. Spleen stiffness: a predictive factor of dismal prognosis in liver cirrhosis. Clin J Gastroenterol. 2023; 16(2): 121-129. https://doi.org/10.1007/s12328-022-01752-z

3. Wilson R, Williams DM. Cirrhosis. Med Clin North Am. 2022; 106(3): 437-446. https://doi.org/10.1016/j.mcna.2021.12.001

4. Patidar Y, Mittal K, Patel RK, Thomas SS, Sarin SK. Liver volumetry in cirrhotic patients with or without hepatocellular carcinoma: Its correlation with Child-Pugh, model for end-stage liver diseases and indocyanine green dye test. Indian J Gastroenterol. 2024; 43: 760-767. https://doi.org/10.1007/s12664-023-01490-1

5. Xavier SA, Vilas-Boas R, Boal Carvalho P, Magalhães JT, Marinho CM, Cotter JB. Assessment of prognostic performance of Albumin-Bilirubin, Child-Pugh, and model for end-stage liver disease scores in patients with liver cirrhosis complicated with acute upper

gastrointestinal bleeding. Eur J Gastroenterol Hepatol. 2018; 30(6): 652-658. https://doi.org/10.1097/MEG.0000000000001087

6. Chen XL, Chen TW, Zhang XM, Li ZL, Zeng NL, Li T, et al. Quantitative assessment of the presence and severity of cirrhosis in patients with hepatitis B using right liver lobe volume and spleen size measured at magnetic resonance imaging. PloS One. 2014; 9(3): e89973. https://doi.org/10.1371/journal.pone.0089973

7. El-Khateeb E, Darwich AS, Achour B, Athwal V, Rostami-Hodjegan A. Review article: time to revisit Child-Pugh score as the basis for predicting drug clearance in hepatic impairment. Aliment Pharmacol Ther. 2021; 54(4): 388-401. https://doi.org/10.1111/apt.16489

8. Zhou XP, Lu T, Wei YG, Chen XZ. Liver volume variation in patients with virus-induced cirrhosis: findings on MDCT. AJR Am J Roentgenol. 2007; 189(3): W153-159. https://doi.org/10.2214/AJR.07.2181

9. Geng Y, Shao WQ, Lin J. Spleen to non-cancerous liver volume ratio predicts liver cirrhosis in hepatocellular carcinoma patients. Abdom Radiol. 2023; 48(2): 543-553. https://doi.org/10.1007/s00261-022-03727-7

10. Romero-Cristóbal M, Clemente-Sánchez A, Peligros MI, Ramón E, Matilla AM, Colón A, et al. Liver and spleen volumes are associated with prognosis of compensated and decompensated cirrhosis and parallel its natural history. United European Gastroenterol J. 2022; 10(8): 805-816. https://doi.org/10.1002/ueg2.12301

11. Patel M, Tann M, Liangpunsakul S. Liangpunsakul, CT-scan based liver and spleen volume measurement as a prognostic indicator for patients with cirrhosis. Am J Med Sci. 2021; 362(3): 252-259. https://doi.org/10.1016/j.amjms.2020.10.031

12. Ozturk A, Olson MC, Samir AE, Venkatesh SK. Liver fibrosis assessment: MR and US elastography. Abdom Radiol. 2022; 47(9): 3037-3050. https://doi.org/10.1007/s00261-021-03269-4

13. Sahin B, Ergur H. Assessment of the optimum section thickness for the estimation of liver volume using magnetic resonance images: a stereological gold standard study. Eur J Radiol. 2006; 57(1): 96-101. https://doi.org/10.1016/j.ejrad.2005.07.006

14. Mazonakis M, Damilakis J. Computed tomography: What and how does it measure?. Eur J Radiol. 2016; 85(8): 1499-1504. https://doi.org/10.1016/j.ejrad.2016.03.002

15. Zoli M, Magalotti D, Grimaldi M, Gueli C, Marchesini G, Pisi E. Physical examination of the liver: is it still worth it?. Am J Gastroenterol. 1995; 90(9): 1428-1432.

16. Labenz C, Arslanow A, Nguyen-Tat M, Nagel M, Wörns MA, Reichert MC, et al. Structured early detection of asymptomatic liver cirrhosis: results of the population-based liver screening program SEAL. J Hepatol. 2022; 77(3): 695-701. https://doi.org/10.1016/j.jhep.2022.04.009

17. Odaci E, Sahin B, Sonmez OF, Kaplan S, Bas O, Bilgic S, et al. Rapid estimation of the vertebral body volume: a combination of the Cavalieri principle and computed tomography images. Eur J Radiol. 2003;48: 316-326. https://doi.org/10.1016/s0720-048x(03)00077-9

18. Gundersen HJ, Jensen EB. The efficiency of systematic sampling in stereology and its prediction. J Microsc. 1987; 147(3): 229-263. https://doi.org/10.1111/j.1365-2818.1987.tb02837.x

19. Xu Z, Yang D, Luo J, Xu H, Jia J, Yang Z. Diagnosis of sarcopenia using the L3 skeletal muscle index estimated from the l1 skeletal muscle index on MR images in patients with cirrhosis. J Magn Reson Imaging 2023; 58(5): 1569-1578. https://doi.org/10.1002/jmri.28690

20. Zheng T, Qu Y, Chen J, Yang J, Yan H, Jiang H, et al. Noninvasive diagnosis of liver cirrhosis: qualitative and quantitative imaging biomarkers. Abdom Radiol. 2024; 49(6): 2098-2115. https://doi.org/10.1007/s00261-024-04225-8

21. Sahin NE, Oner Z, Oner S, Turan MK. A study on the correlation between spleen volume estimated via Cavalieri principle on computed tomography images with basic hemogram and biochemical blood parameters. Anat Cell Biol. 2022; 55(1): 40-47. https://doi.org/10.5115/acb.21.177

22. Patel M, Puangsricharoen P, Arshad HMS, Garrison S, Techasatian W, Ghabril M. Does providing routine liver volume assessment add value when performing CT surveillance in cirrhotic patients?. Abdom Radiol. 2019; 44(10): 3263-3272. https://doi.org/10.1007/s00261-019-02145-6

23. Li WX, Zhao XT, Chai WM, Zhu NY, DU LJ, Huang W, et al. Hepatitis B virus-induced liver fibrosis and cirrhosis: the value of liver and spleen volumetry with multi-detector spiral computed tomography. J Dig Dis. 2010; 11(4): 215-223. https://doi.org/10.1111/j.1751-2980.2010.00441.x

24. Durand F, Valla D. Assessment of the prognosis of cirrhosis: Child-Pugh versus MELD. J Hepatol. 2005; 42(1): S100-S107. https://doi.org/10.1016/j.jhep.2004.11.015

25. Arya LS, Dinand V, Bakhshi S, Thavaraj V, Singh R, Dawar R. Significance of splenomegaly in childhood Hodgkin disease. J Pediatr Hematol Oncol. 2004; 26(12): 807-812.

26. Caglar V, Alkoc OA, Uygur R, Serdaroglu O, Ozen OA. Determination of normal splenic volume in relation to age, gender and body habitus: a stereological study on computed tomography. Folia Morphol. 2014; 73(3): 331-338. https://doi.org/10.5603/FM.2014.0038

27. Kalshabay Y, Zholdybay Z, Di Martino M, Medeubekov U, Baiguissova D, Ainakulova A, et al. CT volume analysis in living donor liver transplantation: accuracy of three different approaches, Insights Imaging. 2023; 14(1): 82. https://doi.org/10.1186/s13244-023-01431-8

28. Canan S, Bahadır A, Yıldırım Ş, Odacı E, Şahin B, Baş O, et al. Stereolojik uygulamalarda kullanılan pratik gereçler ve bilgisayar destekli stereolojik analiz cihazları. Türkiye Klinikleri Tıp Bilimleri. 2004; 24: 672-680.

29. Canan S, Şahin B, Ünal B, Aslan H, Bilgiç S, Kaplan S. Parçacıkların toplam sayısının hesaplanması için bir metot: parçalama. Turkiye Klinikleri J Med Sci. 2002; 22(1): 30-46.

30. Odacı E, Bahadır A, Yıldırım Ş, Şahin B, Canan S, Baş O, et al. Cavalieri prensibi kullanılarak bilgisayarlı tomografi ve manyetik rezonans görüntüleri üzerinden hacim hesaplanması ve klinik kullanımı. Türkiye Klinikleri Tıp Bilimleri Dergisi. 2005; 25(3): 421-428.

31. Royet JP. Stereology: a method for analyzing images. Prog Neurobiol. 1991; 37(5): 433-474. https://doi.org/10.1016/0301-0082(91)90009-p

32. Sahin B, Aslan H, Unal B, Canan S, Bilgic S, Kaplan S, Tumkaya L. Brain volumes of the lamb, rat and bird do not show hemispheric asymmetry: a stereological study. Image Analysis & Stereology. 2001; 20(1): 9-13. https://doi.org/10.5566/ias.v20.p9-13

33. Sahin B, Emirzeoglu M, Uzun A, Incesu L, Bek Y, Bilgic S, et al. Unbiased estimation of the liver volume by the Cavalieri principle using magnetic resonance images. Eur J Radiol. 2003; 47(2): 164-170. https://doi.org/10.1016/s0720-048x(02)00152-3

34. Yaşar F, İmamoğlu, T, Adam G, Erdoğan N. Manyetik rezonans görüntüleme ile karaciğer hacminin hesaplanmasında formül ve Cavalieri yönteminin karşılaştırılması. Tepecik Eğitim Araştırma

Dergisi. 2011; 21(1): 19-24.

35. Reiner CS, Karlo C, Petrowsky H, Marincek B, Weishaupt D, Frauenfelder T. Preoperative liver volumetry: how does the slice thickness influence the multidetector computed tomography- and magnetic resonance-liver volume measurements?. J Comput Assist Tomogr. 2009; 33(3): 390-397. https://doi.org/10.1097/RCT.0b013e3181806c29

36. Hori M, Suzuki K, Epstein ML, Baron RL. Computed tomography liver volumetry using 3-dimensional image data in living donor liver transplantation: effects of the slice thickness on the volume calculation. Liver Transpl. 2011; 17(12): 1427-1436. https://doi.org/10.1002/lt.22419