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Evaluating the Relationship Between Liver and Spleen Volumes in Healthy Individuals Using the Cavalieri Principle on Computed Tomography Images

Bilgisayarlı Tomografi Görüntülerinde Cavalieri Prensibi Kullanılarak Sağlıklı Bireylerde Karaciğer ve Dalak Hacimleri Arasındaki İlişkinin Değerlendirilmesi

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Evaluating the Relationship Between Liver and Spleen Volumes in Healthy Individuals Using the Cavalieri Principle on Computed Tomography Images

ABSTRACT

Objective: Hepatomegaly and splenomegaly can occur independently due to many health problems. The liver and spleen size relationships with age, weight, height and body mass index have not yet been evaluated in detail. This study aims to calculate liver and spleen volumes in computed tomography (CT) images of healthy individuals using the Cavalieri principle and to determine their proportional relationships.

Materials and Methods: Liver and spleen volumes were measured in abdominal CT images of 51 individuals, 24 females and 27 males, without any intra-abdominal pathology. Liver and spleen volumes were calculated and compared using the ImageJ software based on the Cavalieri Principle. The relationships between liver and spleen volumes of the subjects and height, weight and waist circumference were also evaluated.

Results: A moderately significant correlation was found between liver and spleen volumes (*r=0.523; p<0.01*). In men, there was a negative correlation between liver volume and age (*r=-0.460; p=0.016*), and a positive correlation between BMI (*r=0.412; p=0.033*), weight (*r=0.754; p<0.001*), height (*r=0.534; p=0.004*) and waist circumference (*r=0.708; p<0.001*), while no relationship was found between these variables in women. In men, there was a positive correlation between spleen volume and body weight (*r=0.516; p=0.006*) and waist circumference (*r=0.606; p=0.001*), while in women, no significant relationship was found between spleen volume and other variables.

Conclusion: The moderate correlation between liver and spleen volumes indicates the structural and functional association of these two organs. The data obtained show that individual and gender-specific parameters should be taken into account in the evaluation of hepatosplenomegaly.

Keywords: Computed tomography, Cavalieri principle, Correlation, Liver, Spleen.

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ÖZ

Amaç: Hepatomegali ve splenomegali birçok sağlık sorunu nedeniyle bağımsız olarak ortaya çıkabilir. Karaciğer ve dalak boyut ilişkileri ile yaş, kilo, boy ve vücut kitle indeksi henüz ayrıntılı olarak değerlendirilmemiştir. Bu çalışma, Cavalieri prensibini kullanarak sağlıklı bireylerin bilgisayarlı tomografi (BT) görüntülerindeki karaciğer ve dalak hacimlerini hesaplamayı ve orantılı ilişkilerini belirlemeyi amaçlamaktadır.

Gereç ve Yöntem: Karın içi patolojisi olmayan 24 kadın ve 27 erkek 51 bireyde abdominal BT görüntülerinde karaciğer ve dalak hacimleri ölçüldü. Karaciğer ve dalak hacimleri Cavalieri Prensibi'ne dayalı ImageJ yazılımı kullanılarak hesaplandı ve karşılaştırıldı. Deneklerin karaciğer ve dalak hacimleri boy, kilo ve bel çevresiyle ilişkileri de değerlendirildi.

Bulgular: Karaciğer ve dalak hacimleri arasında orta düzeyde anlamlı bir korelasyon bulundu (*r=0,523; p<0,01*). Erkeklerde karaciğer hacmi ile yaş (*r=-0,460; p=0,016*) arasında negatif korelasyon, BKİ (*r=0,412; p=0,033*), kilo (*r=0,754; p<0,001*), boy (*r=0,534; p=0,004*) ve bel çevresi (*r=0,708; p<0,001*) değerleri arasında pozitif korelasyon bulunurken, kadınlarda bu değişkenler arasında ilişki bulunamamıştır. Erkeklerde dalak hacmi ile vücut ağırlığı (*r=0,516; p=0,006*) ve bel çevresi (*r=0,606; p=0,001*) arasında pozitif korelasyon bulunurken, kadınlarda dalak hacmi ile diğer değişkenler arasında anlamlı ilişki bulunamamıştır.

Sonuç: Karaciğer ve dalak hacimleri arasında tespit edilen orta düzeyde korelasyon, bu iki organın yapısal ve işlevsel birlikteliğine işaret etmektedir. Elde edilen veriler, hepatosplenomegali değerlendirmelerinde bireysel ve cinsiyete özgü parametrelerin dikkate alınması gerektiğini göstermektedir.

Anahtar Sözcükler: Bilgisayarlı tomografi, Cavalieri prensibi, Korelasyon, Karaciğer, Dalak.

Introduction

The interaction between the liver and spleen can lead to changes in organ size due to various factors such as tissue alterations, reduced metabolic activity, and age-related vascular changes. As a result, hepatomegaly and splenomegaly may develop, or both organs may undergo a gradual reduction in size over time. Understanding organ volumes is essential for identifying and diagnosing potential pathologies (1-3). Furthermore, the evaluation of treatment responses relies on the accurate measurement of these volumes both before and after clinical interventions (3, 4). To detect such changes, clinicians frequently use computerized tomography (CT) and magnetic resonance imaging (MRI) techniques in combination with physical examination (5).

It has been suggested that changes in liver and spleen volume reflect not only pathological processes but are also closely associated with an individual's metabolic status, anthropometric parameters, and systemic physiological responses (5-8). The literature emphasizes that incorporating these parameters into the evaluation of organ size variations through a holistic approach may improve the accuracy of both clinical assessments and diagnostic decisions. In this context, the relationship between body composition and organ morphology supports the use of liver and spleen volumes as dynamic biomarkers. Currently, stereological methods are commonly applied in clinical settings to obtain accurate measurements of organ sizes, particularly those of the liver and spleen (9-12).

Body mass index (BMI) and waist circumference are key anthropometric indicators used to monitor weight gain over time. According to the literature, an increase in waist circumference in parallel with weight gain is significantly associated with increased liver volume and hepatic steatosis (12, 13). Epidemiological and clinical studies, particularly over the last two decades, have shown that dietary habits, rising BMI, and changes in abdominal fat distribution, along with genetic predisposition and environmental influences, contribute to the increased incidence of various hepatobiliary pathologies, especially fatty liver disease. Moreover, structural and functional alterations in the liver have been observed to affect the spleen through circulatory mechanisms, potentially resulting in increased splenic volume (14-17).

Changes in organ volume can be detected using CT and MRI scans. Isolated organ volume can be calculated using the Cavalieri principle and applied clinically to support disease assessment. The Cavalieri principle is one of the most widely used stereological methods, allowing volume estimation of organs or structures from sectional images. It is preferred due to its low cost, unbiased nature, and reliability (17-20).

In this study, we aimed to calculate liver and spleen volumes in healthy individuals using the Cavalieri principle on CT images and to determine the proportional relationship between these two organs. Additionally, we evaluated the associations between liver and spleen volumes and the age, height, weight, BMI, and waist circumference of the participants.

Material and Method

Informed consent was not required for this retrospective study; therefore, an informed consent form was not applied. The current study has been approved by the Ondokuz Mayıs University Medical Research Ethics Committee on 12.01.2017 with the official number B.30.2.ODM.0.20.08/673. The images used in our study were from individuals who presented to the Department of Radiology, Faculty of Medicine at Ondokuz Mayıs University. The images used in our study were obtained from individuals who presented to the Ondokuz Mayıs University Health Research and Application Center with suspected urinary tract stones and were referred for radiological imaging. Cases in which no significant pathology was detected in the patient reports prepared by the Department of Radiology were included in the study. CT images were obtained from the Department of Radiology, Ondokuz Mayıs University Faculty of Medicine. CT images of a total of 51 participants, 24 females and 27 males, aged between 22 and 70 years, without any pathological condition in the abdomen and without signs of hepatomegaly or splenomegaly, were included.

Radiographic Image Protocol

The radiological images used in the study were obtained from supine abdominal CT images consisting of consecutive axially oriented 3 mm thick slices using a Toshiba TSX-101A, Aquilion 16 Slice, Tochigi, Japan model device. The imaging parameters were set to 120 kV and 75 mA, 150 mA current, and 3 mm slice thickness.

Measurement of liver and spleen volumes from computed tomography images

All images were converted to DICOM format and processed using the ImageJ software developed by the National Institutes of Health of the United States. Contrast adjustments were made to distinguish the spleen and liver from surrounding structures in each subject's images. The organ to be measured was outlined on the sections using the computer mouse and the polygon selection tool within ImageJ. Sections were sampled by selecting 13 to 15 sections in the series using systematic random sampling. The boundaries of the liver and spleen were drawn using the software's polygon selection tool, and the software automatically measured the cross-sectional surface areas of each image of the organs (Figure I). Cross-sectional surface area data were exported to Microsoft Excel spreadsheets containing formulas to estimate liver and spleen volumes. Liver and spleen volumes were calculated by multiplying the section thickness (including range) by the cross-sectional surface area of the organ according to Cavalieri's principle. In addition, the coefficient of error (CE) for each volume estimate was determined using the quadratic approximation formula (21, 22).

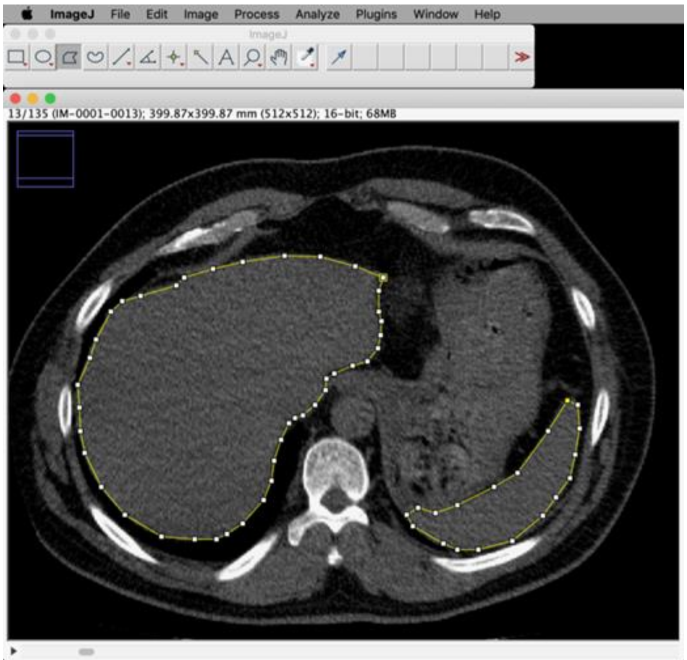

Figure I. Delineation of boundaries of the liver and spleen measured sectional surface areas in ImageJ

The waist circumferences of participants were measured by identifying the largest sectional area of the abdomen in the images using 'the wand tool' in ImageJ. This tool automatically outlines the outer boundary of the abdomen, allowing for the waist circumference to be measured automatically.

To determine the spleen-to-liver volume ratio, the volume of the spleen was divided by the volume of the liver, and this ratio was then converted into a percentage by multiplying the result by 100.

Statistical Analysis

The mean values for participants with known demographic characteristics were computed for age, height, weight, BMI, and waist circumference. These data were then analyzed in relation to the liver and spleen volumes to explore any potential correlations.

Statistical analyses were done using SPSS version 21. We assessed the variables using analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests) to determine their normal distribution. Variables that followed a normal distribution (height, body weight, body mass index, and waist circumference) were subjected to t-tests for independent samples. For variables that did not exhibit a normal distribution (spleen volume, liver volume, spleen/liver ratio), gender comparisons were conducted using the Mann-Whitney U test. The Pearson correlation test was utilized to identify the correlation between liver and spleen volumes. The relationships between numerical variables were also examined by calculating the Spearman correlation coefficient. Values of $p<0.05$ were considered statistically significant.

It is possible to calculate the error coefficient (CE) in measurements made with the Cavalier method. With this calculation, it is questioned whether the number of sections and the number of points counted, and therefore the sampling, are sufficient. If the error coefficient in the calculations is the targeted value, it is decided that the stereological operations performed are appropriate. In the study suggested by Gundersen and Jensen (1987) when performing volume calculations, if the error coefficient is 10% and below, it is stated that the stereological operation performed is calculated correctly (23).

Results

As a result of the PASS (Power Analysis and Sample Size Software) power analysis conducted using intraclass correlation coefficient values in the light of literature data during the preliminary preparation process of the study, the minimum number of individuals to be included in the study to be completed with a 95% confidence level and 90% power was calculated as 15.

The CE (± SD) for spleen and liver volume measurements across all participants was 1.96 ± 1.40 and 1.04 ± 0.39, respectively. Specifically, the Error Coefficient (CE) for spleen volume measurements was 2.21 ± 1.65 in female participants and 1.73 ± 1.13 in male participants. For liver volume measurements, the CE was 1.02 ± 0.41 in females and 1.05 ± 0.38 in males. This value is in the acceptable range.

Results regarding demographic characteristics

Demographic characteristics (the mean height, weight, body mass index (BMI) and waist circumference) of all individuals measured are shown in Table I below.

Table I. Height, weight, BMI and waist circumference values of the individuals

Measurements	Female (N=24)	Male (N=27)	Total (N=51)	*p-value*
Height (cm)	1.61±0.07	1.76±0.09	1.69±0.11	***<0.001***
Weight (kg)	68.92±11.08	89.11±14.10	79.61±16.23	***<0.001***
BMI	26.70±5.22	28.79±4.26	27.81±4.80	*0.121*
Waist circumference(mm)	1049.04±141.68	1080.15±123.25	1065.51±131.86	*0.121*

Height (mean ± SD cm), weight (mean ± SD kg), BMI (mean ± SD kg/m^2)

Radiological Findings

The mean liver volume, spleen volume and spleen-liver volume ratio for all individuals are given in Table II. We see that the liver and spleen volumes in male individuals are significantly larger than the values in females ($p<0.05$).

Table II. Spleen volume, liver volume, spleen/liver x 100 of the subjects

Volume/ Percentage	Female (N=24)	Male (N=27)	Total (N=51)	*p-value*
Spleen Volume (cm^3)	241.02 ± 108.36	301.39 ± 103.79	272.98 ± 109.22	***0.030****
Liver Volume (cm^3)	1477.49 ± 365.18	1700.82 ± 371.90	1595.72 ± 382.02	***0.043****
Percentage of Spleen	16.57 ± 6.55	17.89 ± 5.91	17.27 ± 6.20	***0.336***

*;$p<0.05$

Spleen volume (mean ± SD cm^3), liver volume (mean ± SD cm^3), spleen/liverx100 (mean ± SD %)

Correlation Findings

The Pearson correlation analysis showed a significant positive relationship between liver and spleen volumes for all participants ($r=0.523$, $p<0.01$). In male participants, a significant positive correlation was also observed between liver and spleen volumes ($r=0.554$, $p=0.03$). A positive relationship was found between liver and spleen volumes for female participants, but it was not statistically significant ($r=0.447$, $p=0.29$).

When the relationship between liver and spleen volumes and other variables (age, height, weight, BMI, waist circumference) was examined in female individuals, no significant relationship was found between the variables for female individuals.

There were significant correlations between liver and spleen volumes of male individuals with various physical and demographic characteristics.

Specifically, spleen volume showed a moderate positive correlation with body weight (*r=0.516, p=0.006*) and a strong correlation with waist circumference (*r=0.606, p=0.001*). On the other hand, the relationship between spleen and age, height and BMI is weak or not statistically significant (Table III).

When we look at the correlation relationships in male individuals, we see that liver volume decreases with age (*r=-0.460, p=0.016*). A positive correlation exists between height and liver (*r=0.534, p=0.004*). We see that liver volume increases as height increases. We see liver volume increase as body weight increases (*r=0.754, p<0.001*). We found an increased liver volume with increasing BMI depending on height and weight (*r=0.412, p=0.033*). As BMI and waist circumference values increase, their correlation with the liver is positively related (*r=0.708, p<0.001*). There was a significant relationship between age, height, weight, BMI, and waist circumference in male individuals (Table III).

Table III. Correlation between liver and spleen volumes of male individuals with age, height, weight, BMI, and waist circumference

Values Male		Age (year)	Height (cm)	Body Weight (kg)	BMI	Waist circumference (mm)
Spleen Volume	r	-0,313	0,327	0,516	0,265	0,606
	p	0,111	0,096	**0,006***	0,182	**0,001***
Liver Volume	r	-0,460	0,534	0,754	0,412	0,708
	p	**0,016***	**0,004***	**<0,001***	**0,033***	**<0,001***
Percentage of Spleen	r	-0,032	0,147	0,156	-0,006	0,238
	p	0,874	0,465	0,437	0,975	0,233

*; $p < 0.05$

However, it does not show a significant correlation between the (spleen/liver) x 100 ratio and the measured variables.

In female participants, no significant correlations were observed between liver and spleen volumes and other variables, including age, height, weight, BMI and waist circumference.

Discussion

In our study, the mean liver volume was 1595.72 cm^3 in all participants, 1477.49 cm^3 in females, and 1700.82 cm^3 in males. The liver volumes of male individuals were larger than those of female individuals. In males, liver volume showed a negative correlation with age but significant positive correlations with height, weight, body mass index (BMI), and waist circumference. No significant correlation was observed between liver volume and these variables in females. In our study, the mean spleen volume in all participants was 272.98 cm^3, 241.02 cm^3 in females, and 301.39 cm^3 in males. There was a difference in spleen volume between the genders, and male individuals had larger spleen volumes (p<0.030). In addition, a positive correlation was observed between liver and spleen volumes in both males and females, suggesting that changes in one organ may affect the other. Changes in liver size can indicate whether specific body functions are being met, with liver enlargement often signaling diseases such as hepatitis, cirrhosis, steatosis, or hepatomegaly. These conditions may cause liver swelling, impacting nearby organs and causing discomfort. Monitoring liver size is essential for planning and assessing treatment progress, as it helps determine the risk of liver disease.

When we look at the literature, we see that the studies carried out are similar to our results. Sharma et al., in their study where they determined liver volumes on 100 individuals, liver volume according to age groups: 21-25 years 2123 cm^3, 26-30 years 1633 cm^3, 31-35 years 1274 cm^3, 36-40 years 1395 cm^3, 41-45 years old 1702 cm^3, 46-50 years old 1306 cm^3, 46-50 years old 1306 cm^3, 51-55 years old 1045 cm^3, 56-60 years old 1168 cm^3, 61-65 years old 1184 cm^3, 66-70 years old 1022 cm^3 (24). Farraher et al. measured liver volumes in 27 individuals using two methods (25). They found a liver volume of 1768 cm^3 with manual measurement and 1747 cm^3 using semi-automatic segmentation, showing a high correlation between both methods (25).

In a study by Sahin et al. different section thicknesses (2.5 mm, 5 mm, 7.5 mm, and 10 mm) on MR images were compared using a point counting measurement tool and the planimetry technique to create a stereological gold standard (26). They found the point counting measurement tool was easy to use, allowing for faster volume calculations, including backward and forward estimations. However, the planimetry method produced more accurate results. They concluded that the most precise liver volume estimations were obtained from 4-5 mm thick images (26). Our study used section thicknesses aligned with Sahin et al.'s recommendations to achieve the most realistic results. Additionally, their findings indicated that water immersion is ineffective for measuring cavity organ volumes. Our results confirm that radiological imaging methods offer greater applicability and consistency in volume measurement. These findings suggest that increased liver volume is associated with concurrent spleen regeneration. In light of this study, our findings and other literature results show consistent, parallel liver and spleen interaction trends.

Changes in spleen size can indicate underlying health issues, as the spleen is closely linked to immune function. Conditions such as lymphoma, leukemia, infections, inflammatory disorders, hepatomegaly, and splenomegaly can all influence spleen size. These changes may also impact adjacent structures, causing discomfort and potential complications. In our study of healthy individuals, the average spleen volume was 272.98 cm^3, with females averaging 241.02 cm^3 and males 301.39 cm^3 a statistically significant difference indicating larger spleen volumes in males. However, no significant difference between genders was observed when evaluating the spleen-to-liver volume ratio. In male participants, spleen volume showed a positive correlation with body weight and waist circumference, suggesting that increases in these measurements are associated with increased spleen volume.

The spleen volume measurements in our study align closely with values reported in the literature, supporting the validity of our findings. Variations in liver and spleen volumes across studies likely stem from differences in measurement methods, sample sizes, age distributions, ethnicities, and volume calculation formulas.

In a study by Samir and colleagues, splenomegaly was described as a nonspecific finding in mild and severe COVID-19 cases. They observed a weak positive correlation between COVID-19 severity, spleen size, and lung CT severity scores, highlighting the importance of spleen volume changes in COVID-19 (27).

Similarly, a study conducted by Adam and colleagues utilized the Cavalieri method to assess spleen volume in individuals aged 21–40, reporting an average of 250 cm^3 (28).

The spleen, the largest organ in the reticuloendothelial system, has long been used to indicate disease activity in various reticuloendothelial disorders (29). Numerous studies have aimed to calculate spleen volume, but findings show considerable variation in reported spleen volumes.

Ando et al. reported that in 24 patients with gallbladder cancer who underwent liver resection, both the liver and spleen enlarged during regeneration, working together at specific common points. One year after the hepatectomy, the remaining liver volume had increased to 76% of its original size, while spleen volume had expanded to 174% of the original. Notably, one-month post-resection, spleen volume regeneration doubled as liver regeneration accelerated, underscoring the interdependent relationship between the liver and spleen in regenerative processes (30).

According to the literature, the preprandial spleen volume in individuals aged 23-35 was calculated using the Cavalieri method, finding an average volume of 200 cm^3 (31).

In another study using the ellipsoid formula on 1,230 healthy individuals aged 18-55, the average spleen volume was 166 cm^3 (32). Harris et al. reported an average spleen volume of 127 cm^3 in 230 Japanese subjects (33).

The results of Kaneko et al. examined correlations between spleen volume, age, gender, and body surface area in a study of 150 healthy liver transplant donors with an average age of 36 years (range 20-63). They found an average spleen volume of 112 cm^3 (32-209 cm^3). Spleen volume correlated with age but not with body weight or surface area, and gender did not impact spleen size (34).

In a study by Junji Ueda et al., spleen volumes were calculated for patients with and without liver cirrhosis, yielding averages of 496 ml (n = 67) and 143 ml (n = 54), respectively (35).

In contrast, Stiff et al., also using the ellipsoid formula on 309 participants aged 18-74, found an average spleen volume of 249 cm^3 (36).

In the study calculated by Şahin et al. with the Cavalier principle, the average spleen volume was found to be 303.4 cm^3 in men and 232.8 cm3 in women (37). The data of this study are similar to our study. The liver and spleen are functionally interconnected, playing active roles in the immune system by fighting infections, cleansing the blood, and participating in blood clotting. Consequently, dysfunction in one organ can impact the other. Our study observed a positive correlation between liver and spleen volumes, with both organs being larger in males than in females. Liver and spleen volumes decrease with age, especially in males, probably due to age-related tissue changes, vascular structure changes, and immune system decline. In addition, BMI and waist circumference showed positive correlations with liver and spleen volumes. This result supports the association of increased liver fat, decreased muscle mass, and spleen growth with weight gain.

This study's total sample consisted of 51 male and female participants, a relatively small sample size that may be perceived as a limitation. Increasing the sample size could enhance the power of the study. However, using the Cavalieri method strengthens our findings, as this technique is known for its low error rate, ease of application, and high reliability. The observed correlation between liver and spleen volumes in males and females supports our hypothesis regarding their interrelationship. It is expected that liver and spleen sizes would influence each other, particularly in relation to health issues. Our findings also reveal a positive correlation between BMI, waist circumference, and age-related changes, underscoring their impact on liver and spleen health. This study underscores the importance of evaluating liver and spleen health, as issues in one organ can affect the other. Monitoring both organs may help reduce potential health problems. Furthermore, our findings suggest that this combined approach could support treatment planning and prognosis, including liver transplant volume calculations and managing immune-related spleen conditions. Our study contributes valuable insights to the existing literature and can be a reference for future clinical research.

In clinical practice, accurate and reliable measurement of liver and spleen volumes constitutes not only a cornerstone of diagnostic processes but also a critical component of treatment planning. Alterations in organ volumes observed in a wide spectrum of conditions portal hypertension, cirrhosis, hematological malignancies, infections, and metabolic disorders provide essential insights for both early diagnosis and prognosis. Liver volume assessment is indispensable in evaluating candidates for liver transplantation, grading hepatic steatosis, and monitoring treatment responses in chronic liver diseases. Similarly, spleen volume measurement offers valuable clinical information for detecting splenic involvement in hematological malignancies, assessing the effectiveness of immunotherapies, and identifying complications such as hypersplenism or splenic infarction at earlier stages.

In this context, radiological volumetric analyses based on stereological techniques (e.g., the Cavalieri principle) provide a standardized, reproducible, and non-invasive approach that enhances the robustness of clinical decision making compared to traditional measurement methods. While existing studies in the literature have examined liver and spleen volumes in various patient groups, methodological heterogeneity and the lack of standardization limit comparability across findings. Thus, the integration of stereology-based volumetric assessments into clinical workflows not only contributes significant methodological value to the current body of literature but also holds the potential to improve patient management in hepatology and hematology. Incorporating regular volume evaluations into clinical routines may facilitate earlier diagnosis, enable more personalized treatment strategies, and directly enhance patient outcomes.

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