Iran Red Crescent Med J. 2023 May; 25(5):e1647 doi: 10.32592/ircmj.2023.25.5.1647

Published online 2023 May 15 **Original Article**

A Simple Approach to Predict Spleen Volume in Patients with Splenomegaly Due to Portal Hypertension

Tiancheng, Luo[1], Xinhua Huang[2,3], Wei Lei[2,3], Yujen Tseng[3], Ji Zhou[2], Shiyao Chen[1,4], Jian Wang[1] and Lili Ma[4,5*]

[1] Department of Gastroenterology, Zhongshan Hospital, Fudan University, Shanghai, China
[2] Department of Nursing, Huashan Hospital, Fudan University, Shanghai, China
[3] Department of Digestive Diseases, Huashan Hospital, Fudan University, Shanghai, China
[4] Department of Endoscopy Center, Zhongshan Hospital, Fudan University, Shanghai, China
[5] Department of Endoscopy Center, Wusong Branch of Zhongshan Hospital, Fudan University, Shanghai, China

*** *Corresponding author:*** Lili Ma, Department of Endoscopy Center, Zhongshan Hospital, Wusong Branch of Zhongshan Hospital, Fudan University, Shanghai, China. Tel: +8613816370677; Email: ma.lili@zs-hospital.sh.cn

Received 2021 November 01; **Revised** 2022 January 04; **Accepted** 2023 April 23.

Abstract

Background: Splenomegaly and hypersplenism are common presentations of portal hypertension and can result in severe comorbidities. The degree of splenomegaly is associated with disease severity and has been established as a reliable noninvasive indicator for disease surveillance.

Objectives: This study aimed to propose a simple and repeatable splenic measurement model to estimate the splenic volume in patients with portal hypertension.

Methods: In total, 161 patients with portal hypertension were admitted to our hospital from March 2017 to August 2020, with a final enrollment of 106 subjects. The splenic volume calculated via IQQA-Liver software was used for reference. Radiological data were retrospectively reviewed to measure the height, length, and width of the spleen. Different volume prediction models were constructed based on statistically significant laboratory and radiological parameters.

Results: The average spleen volume measured by the IQQA-Liver software was 852.29±362.26cm^3. Model 0 was constructed based on hematological and radiological parameters, while Models 1 and 2 were based on radiological parameters alone. Model 1 was superior to the others according to the Bland-Altman scatterplot and correlation analysis.

Conclusion: The proposed estimation model is a reliable predictor for splenic volume, providing valuable information in patients with portal hypertension. The simple technique allows for widespread clinical application.

Keywords: Computer tomography, Diagnostic model, Portal hypertension, Spleen volume, Volume rendering

1. Background

The prevalence of splenomegaly in patients with portal hypertension ranges from 60%-65% with varying degrees of severity, often attributed to hyper-inflow congestion (1, 2). Hypersplenism and splenomegaly can result in anemia, thrombocytopenia, and leukopenia in patients with end-stage liver disease, posing risks for severe comorbidities (3). Pathohistological evidence has demonstrated splenomegaly as a combination of blood pooling in the red pulp, hyperplasia of histocytes, and the eventual evolution of diffuse fibrosis extending to the entire parenchyma. Historically, the direct correlation between splenomegaly and portal hypertension has been contested due to its congestive-hyperplastic changes (4, 5). However, recent studies have established a significant relationship between spleen volume and the degree of portal hypertension through hepatic venous pressure gradient (HVPG) measurements, which is a well-established indicator for assessing disease severity (6). Clinically significant portal hypertension (CSPH) defined as HVPG ≥ 10mmHg, is often associated with severe complications, including ascites, hepatic encephalopathy, and gastroesophageal variceal bleeding, resulting in high morbidity and mortality rates in patients with portal hypertension (7, 8). Some studies have also established the direct correlation between spleen size and the presence of gastroesophageal varices, providing a non-invasive diagnostic alternative (9, 10).

Splenic measurements can be achieved through different imaging modalities, including ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI), with promising accuracy (11-13). Although 3-dimensional volume rendering technology has gained popularity in recent years, the lack of widespread availability in primary healthcare facilities and secondary hospitals limits its application. The process of volume rendering not only requires adequate equipment but can also be operator-reliant and time-consuming depending on the automatic or interactive nature of the volume rendering software (14).

2. Objectives

Therefore, this study aimed to propose an easy, accurate, and repeatable method for predicting splenic volume in patients with splenomegaly secondary to portal hypertension.

3. Methods

3.1. Study Design and Participants

A total of 161 patients diagnosed with gastroesophageal variceal hemorrhage secondary to portal hypertension were admitted to our hospital for the treatment of gastroesophageal varices from March 2017 to August 2020. All patients with available abdominal CT imaging studies were included in this study, with a final enrollment of 106 subjects. In total, 55 patients were excluded due to incomplete radiological data (n=11) or a prior history of splenectomy (n=44). Patients with previous endoscopic treatment for gastroesophageal varices, such as band ligation or sclerotherapy, as well as those with portovenous, portocaval, or portosplenic shunts were not excluded from the study. We were concerned with the prediction of splenic volume and did not correlate it with splenic volume; therefore, we did not have strict exclusion criteria. Written informed consent was obtained from each patient included in the present study. The study was not double-blinded. However, the author responsible for measuring the CT parameters was unaware of the splenic volume. The institutional review board (IRB) approval was obtained from the Ethics Committee of Zhongshan Hospital, Fudan University, Shang Hai Shi, China (B2015-133R).

3.2. CT Technique

All CT examinations were commenced after an overnight fast. Volume measurements were achieved based on the analysis of abdominal contrast CT images via IQQA-Liver software (EDDA Technology, Shanghai, China). The area of the spleen was manually traced on the sagittal, coronal, and transverse planes. IQQA-Liver allows for an automatic calculation of the 3-dimensional volume of the traced region, which calculates the actual spleen volume. Each window was then meticulously reviewed and corrected for any inconsistencies by two physicians (YJT and LLM). All volume measurements were measured in cubic centimeters (cm^3). A sample of the volume calculation process is shown in Figure 1. All available CT studies were retrieved for splenic volume construction for reference purposes, with a final enrollment of 106 subjects.

The radiological data were retrospectively reviewed on the Centricity Enterprise Web V3.0 (GE Healthcare, Illinois, USA). The height (H) of the spleen was calculated based on the number of consecutive 5mm slices containing the spleen. Due to the large variability of the organ, two different methods were tested for the measurement of the splenic length (L) and width (W). Method A employed a straight horizontal line drawn across the left and right border (L_A), and a second perpendicular line was drawn across the hilum between the superior and inferior borders (W_A). Method B includes an anterior-posterior diagonal line to determine the maximum length (L_B), and a second perpendicular line was drawn across the hilum to determine the splenic width (W_B) (Figure 2) (15). Method A was depicted by the green lines, while method B was depicted by the purple lines.

3.3. Data collection

Respective laboratory parameters were collected upon hospital admission, including total bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase, hemoglobin, platelet, prothrombin time, and serum creatinine. The Child-Pugh Score and Child-Pugh Class of each patient were also calculated, which is a system for assessing the prognosis and severity of the chronic liver disease. It includes the assessment of five clinical and laboratory criteria: serum bilirubin, serum albumin, ascites, neurological disorder, and INR. Comorbidities including hepatocellular carcinoma, portal venous thrombosis, spontaneous portosystemic shunt, ascites, and hepatic encephalopathy were documented.

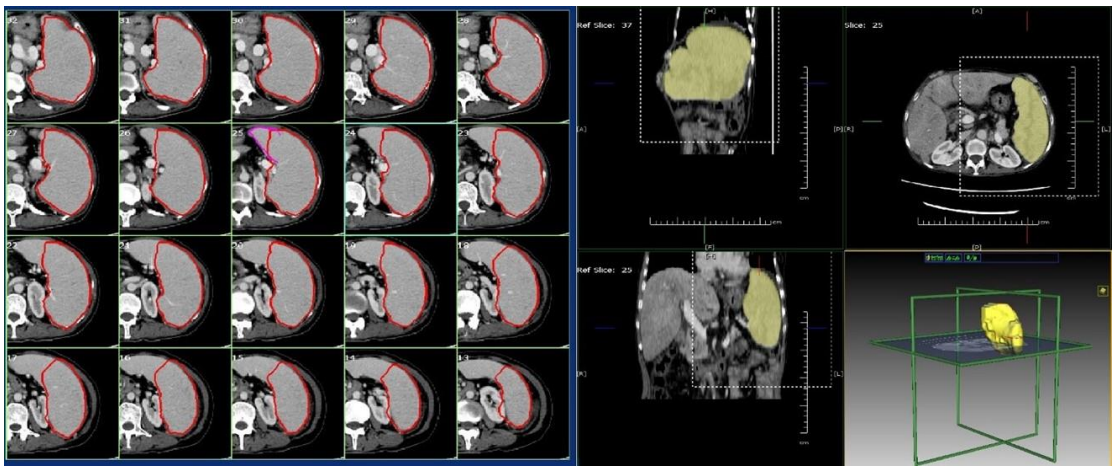

Figure 1. Semi-automated volume calculation of spleen volume with IQQA-Liver software
Formulation of Splenic Volume Estimation Models

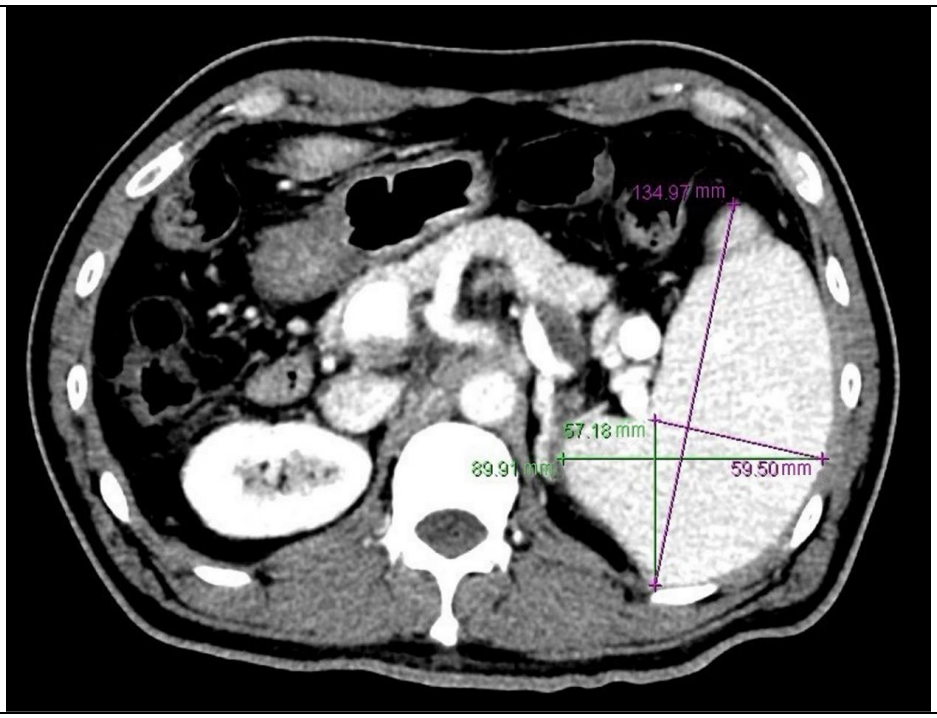

Figure 2. Two different methods used to measure splenic length (L) and splenic width (W)

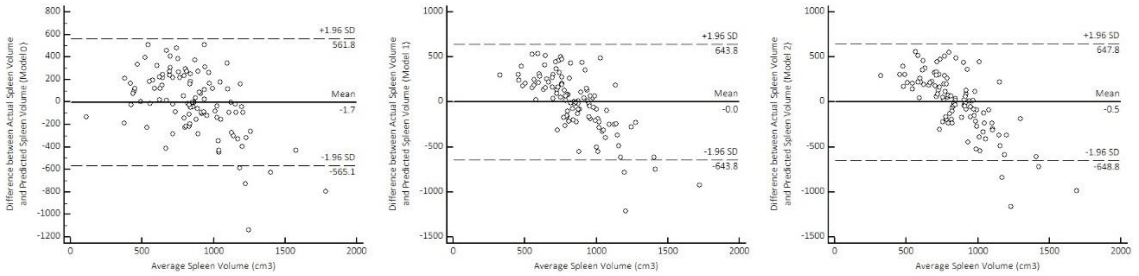

Figure 3. Bland Altman scatterplot comparing the differences between the actual splenic volume and the predicted splenic volume derived from Models 0, 1, and 2

3.4. Statistical Analyses

A correlation analysis was conducted to identify significant correlations between independent variables and splenic volume. All variables were tested via the one-sample Kolmogorov-Smirnov Test for normal distribution. Parameters that abided by normal distribution were assessed based on Pearson's *rho*, while the contrary was assessed with Spearman's *rho*. All significant variables from the correlation analysis were entered into a multivariate regression analysis to identify an independent association, and a subsequent predictive equation was constructed with the automatic linear modeling function in SPSS software. A Bland-Altman scatterplot was used to assess the difference between actual spleen volume and estimated spleen volume. Finally, a reassessment of the degree of correlation was performed to further validate the predictive abilities of the proposed estimation models. All analyses achieving A *P*-value of <0.05 were considered statistically significant.

4. Results

Of the included subjects, 68 (64.2%) patients were male, and 38 (35.8%) were female with a mean age of 58.50±11.47 years old. The mean HVPG measurement of the study subjects was 14.04±6.06 mmHg, with 66 (62.3%) patients classified as Child-Pugh Class A, 38 (35.8%) patients as Child-Pugh Class B, and 2 (1.9%) cases as Child-Pugh Class C. The mean spleen volume measured by the IQQA-Liver software was 852.29±362.26cm^3, which was referenced for constructing a predictive model. Radiological parameters included splenic height, splenic length, and width, wherein the latter was measured by two different methods. The mean splenic height is 15.71±3.77cm; moreover, the mean values of splenic length and width measured by method A were obtained at 8.41±1.42cm and 6.02±1.28cm, respectively, whereas the corresponding values of method B are 14.16±2.22cm and 5.44±1.35cm. A summary of patient characteristics was listed in Table 1.

The laboratory parameters, Child-Pugh score, as well as class and comorbidities, are shown in Table 2.

A univariate correlation analysis was conducted between all variables and actual spleen volume measured with IQQA-Liver software. The following laboratory and radiological parameters achieved a statistical significance of $P<0.05$: hemoglobin, platelet, prothrombin time, splenic height (H), method A splenic width (W_A), method B splenic length (L_B), and method B splenic width (W_B).

Table 1. Summary of Patient Characteristics (n=106)

Variable	Mean±SD or n (%)
Gender	
Male	68 (64.2%)
Female	38 (35.8%)
Age (y)	58.50±11.47
HVPG (mmHg)	14.04±6.06
Laboratory Findings	
Total Bilirubin (μmol/L)	18.35±18.67
Albumin (g/L)	34.49±4.88
ALT (U/L)	27.93±17.04
AST (U/L)	39.46±27.21
Creatinine (μmol/L)	68.67±17.59
Hemoglobin (g/L)	92.48±25.09
Platelet (×10^9/L)	69.58±35.49
Prothrombin Time (s)	14.13±1.52
Radiologic Findings	
Spleen Volume (cm^3)	852.29±362.26
Spleen Height, H (cm)	15.71±3.77
Method A: Spleen Length, L_A (cm)	8.41±1.42
Method A: Spleen Width, W_A (cm)	6.02±1.28
Method B: Spleen Length, L_B (cm)	14.16±2.22
Method B: Spleen Width, W_B (cm)	5.44±1.35
Child-Pugh Score	6.32±1.39
Child-Pugh Class	
A	66 (62.3%)
B	38 (35.8%)
C	2 (1.9%)
Comorbidities	
Portal Venous Thrombosis	28 (26.4%)
Hepatocellular Carcinoma	2 (1.9%)
Spontaneous Portovenous Shunt	28 (26.4%)
Ascites	55 (51.9%)
Hepatic Encephalopathy	0 (0%)
Gastroesophageal Varices Classification	
GOV Type 1	58 (54.7%)
GOV Type 2	29 (27.4%)
IGV Type 1	8 (7.5%)
IGV Type 2	0 (0%)
Esophageal Varices	10 (9.4%)

* HVPG: hepatic venous pressure gradient, ALT: Alanine transaminase, AST: Aspartate Transferase, GOV: gastroesophageal varies, IGV: isolated gastric varices.

Table 2. Correlation analysis of continuous variables and actual spleen volume with Pearson's and Spearman's correlation

Variable	Pearson's rho	P-value	Spearman's rho	P-value
Age	-0.122	0.211	-0.131	0.180
HVPG (mmHg)	-0.026	0.792	0.027	0.782
Laboratory Findings				
Total Bilirubin (μmol/L)	0.023	0.813	0.043	0.664
Albumin (g/L)	0.133	0.173	0.120	0.221
ALT (U/L)	-0.023	0.818	-0.008	0.939
AST (U/L)	-0.149	0.136	-0.125	0.211
Creatinine (μmol/L)	0.072	0.481	0.060	0.553
Hemoglobin (g/L)	**-0.228**	**0.019**	-0.135	0.168
Platelet (×10^9/L)	-0.481	<0.001	**-0.562**	**<0.001**
Prothrombin Time (s)	0.239	0.014	**0.265**	**0.006**
Child-Pugh Score	-0.081	0.410	-0.018	0.853
Radiological Findings				
Spleen Height, H (cm)	**0.392**	**<0.001**	0.387	<0.001
A: Spleen Length, L (cm)	**0.180**	**0.065**	0.136	0.166
A: Spleen Width, W (cm)	**0.257**	**0.008**	0.278	0.004
B: Spleen Length, L (cm)	**0.268**	**0.005**	0.284	0.003
B: Spleen Width, W (cm)	0.205	0.035	**0.335**	**<0.001**

* HVPG: hepatic venous pressure gradient, ALT: Alanine transaminase, AST: Aspartate Transferase. Univariate correlation analysis with Pearson's rho or Spearman's rho

All significant variables were entered into the automatic linear modeling, generating the following predictive equation.

Model 0: Splenic Volume=24.838 (splenic height, H, cm) – 3.840 (Hemoglobin, g/L) – 4.627 (Platelet, $\times 10^9$/L) + 1137.469

Two subsequent models were constructed excluding hematological variables to assess the predictive ability of radiological parameters according to two independent proposed measurement methods (Method A and Method B):

Model 1 (Method A): Splenic Volume=33.392 (splenic height, H, cm) + 45.888 (Splenic Width A, W_A, cm) + 51.453

Model 2 (Method B): Splenic Volume=32.110 (splenic height, H, cm) + 22.426 (Splenic Length B, L_B, cm) + 29.588

The mean values of the predicted spleen volume based on the above-listed models 0, 1, and 2 were 850.63±226.10 cm^3, 852.28±152.75 cm^3, and 851.76±149.08 cm^3, respectively. To further assess the predictive abilities of the three different proposed models, a Bland-Altman scatterplot was constructed to assess the differences between actual spleen volume measured via IQQA-Liver software and predicted splenic volume. The arithmetic means between the actual spleen volume and predicted spleen volume by models 0, 1, and 2 were -1.66 (95% CI: -57.02-53.71), -0.004 (95% CI: -63.27-63.26), and -0.53 (95% CI: -64.23-63.18), respectively (Figure 3).

Validation of model accuracy of the two radiological-based models (Models 1 and 2) was assessed based on the correlation between predicted spleen volume and laboratory parameters and was further compared to that of actual spleen volume measured via IQQA-Liver software. The correlation between platelet and the predictive spleen volume by Models 1 and 2 was statistically significant, with a respective correlation coefficient of -0.320 and -0.272. However, significant correlations among hemoglobin, prothrombin time, and both predicted volumes were not retained (Table 3).

Table 3. Reassessment of correlation analysis between two radiological-based models (Model 2 and Model 3) and significant hematological variables

	Actual Spleen Volume		Model 1		Model 2	
Hematologial Variable	Rho	P-value	Rho	P-value	Rho	P-value
Hemoglobin (g/L)	-0.228	0.019	-0.112	0.255	-0.118	0.226
Platelet ($\times 10^9$/L)	-0.562	<0.001	-0.320	0.001	-0.271	0.005
Prothrombin Time (s)	0.265	0.006	0.182	0.062	0.116	0.237

* Multivariate regression analysis was used to construct predictive models.

5. Discussion

The present study explored the construction of different models in the prediction of splenic volume with reference to the results derived from the IQQA software. Splenic volume prediction models were based on a different combination of laboratory and radiological parameters. Splenomegaly is a common clinical presentation in patients with portal hypertension, especially in those who suffer from end-stage liver diseases. Subsequent hypersplenism can often result in anemia, thrombocytopenia, and leukopenia, which can contribute to portal hypertension-related bleeding (1-3).

Hepatic vein catheterization for HVPG measurements is currently considered the gold standard for assessing portal pressure with an accurate reflection of disease severity. Although the technique has been employed for decades, its invasive nature and high costs limit its repeatability (16-18). According to the Baveno VI consensus, the therapeutic goal for decreasing portal pressure is defined as a decrease in HVPG of at least 10% from baseline, or to ≤ 12mmHg (7). Unfortunately, this method is an unrealistic surveillance modality in clinical practice because it requires multiple repetitions of the catheterization procedure. In recent years, many researchers have focused on exploring different noninvasive alternatives with comparable accuracy. Among the many proposed replacements, spleen size and volumetry showed a substantial correlation with portal hypertension (6, 19). Others have established the novel use of volumetric measurements in predicting patient prognosis or the presence of gastroesophageal varices, expanding the clinical value of spleen volume measurements (10, 20).

Based on the current study, we aimed to develop an easy and accurate replacement for estimating splenic volume in patients with portal hypertension. A univariate correlation analysis unveiled several statistically significant variables associated with actual spleen volume measured by IQQA-Liver software. Based on the automatic linear modeling analysis, the following equation was generated based on both laboratory and radiological parameters: Splenic Volume=24.838 (splenic height, H, cm) – 3.840 (Hemoglobin, g/L) – 4.627 (Platelet, $\times 10^9$/L) + 1137.469.

Due to the large individual variation of spleen size, we attempted two different methods of measuring splenic length and width. Model 1 Splenic Volume=33.392 (splenic height, H, cm) + 45.888 (Splenic Width A, W_A, cm) + 51.453, Model 2: Splenic Volume=32.110 (splenic height, H, cm) + 22.426 (Splenic Length B, L_B, cm) + 29.588, wherein Model 1 was based on radiological measurements of method A, while Model 2 was based on radiological measurements of method B.

The predicted spleen volume generated via the three different models listed above was assessed with a Bland-Altman scatterplot. Based on the arithmetic mean, we can conclude that Model 1 is superior to Models 0 and 2 although the difference is rather subtle. Model 1 has fewer outliers beyond the ±1.96 standard deviation, with a mean difference of -0.004 (95% CI: -63.27-63.26).

Further confirmation of model accuracy was achieved based on correlation analysis with laboratory parameters. Actual spleen volume measured with IQQA-Liver software is significantly correlated with hemoglobin, platelet, and prothrombin time. We reevaluated the correlation between the predicted spleen volume and the above-mentioned laboratory variables. Although the predicted volumes did not retain statistical significance with hemoglobin and platelet, based on the trend of *rho* value, or correlation coefficient, Model 1 is superior to Model 2.

The present study explored the estimation of splenic volume based on CT parameters. Similar studies have been conducted based on ultrasound results. However, ultrasound studies can be heavily reliant on the operators' experience, patients' cooperation, and gas disturbances. CT on the other hand, can provide a more objective measurement of the splenic dimensions. However, unlike ultrasound, CT is not a truly noninvasive surveillance method, especially when CT with contrast is ordered.

There are several limitations to this study. First, there was no direct correlation between the measured HVPG and splenic size in our study subjects, which may be due to inaccurate measurements of HVPG. During the study period, our center lacked a uniform protocol for HVPG measurement apparatuses (end-hole versus balloon-occlusion catheter). The balloon-occlusion tip catheter has been proven to be superior to the end-hole catheter and is recommended for HVPG measurements with high precision (18, 21). Second, the subjects included in this study had no available weight and height data, which made it impossible to caliber the organ size according to the patient's body mass index (BMI) (15). Third, the small sample size limits the confirmation of the study results on a validation cohort. A larger sample size is warranted to evaluate the repeatability and accuracy of the study results.

6. Conclusion

Splenic volume can provide valuable clinical information in patients with splenomegaly secondary to portal hypertension. However, the lack of widespread availability of 3-dimensional rendering technology and software limits its novelty. The current study provides an easy approach for accurately predicting splenic volume based on CT imaging, which is readily available in most patients with portal hypertension. The simple technique allows for volume measurement even without adequate radiological training, promoting its application in clinical settings.

Acknowledgments

Tiancheng Luo, Wei Lei, and Xinhua Huang contributed equally and share first authorship.

The authors would like to thank the patients who participated in the present study, and to the staff of the Gastroenterology department and Endoscopy Center for their support.

Footnotes

Conflicts of Interest: All authors declare no conflict of interest.

Authors' Contributions: Tiancheng Luo, Wei Lei, and Ji Zhou performed the acquisition, analysis, and interpretation of data; Tiancheng Luo and Yujen Tseng drafted the manuscript; Jian Wang and Lili Ma provided critical revision of the manuscript; Shiyao Chen and Lili Ma performed endoscopic treatment for all patients. All authors have reviewed and approved the final version manuscript for submission.

Ethical Approval: Institutional review board (IRB) approval was obtained from the Ethics Committee of Zhongshan Hospital, Fudan University, Shang Hai Shi, China (B2015-133R).

Funding/Support: This study was supported by the Natural Science Foundation of Shanghai, Grant, 21ZR1447600.

References

1. Peck-Radosavljevic M. Thrombocytopenia in chronic liver disease. *Liver Int.* 2017;**37**(6):778-93. doi: 10.1111/liv.13317. [PubMed: 27860293].
2. Yoshida H, Shimizu T, Yoshioka M, Matsushita A, Kawano Y, Ueda J, et al. The Role of the spleen in portal hypertension. *J Nippon Med Sch.* 2023;**90**(1):20-5. doi: 10.1272/jnms.JNMS.2023_90-104. [PubMed: 36908126].
3. Boyer TD, Habib S. Big spleens and hypersplenism: fix it or forget it?. *Liver Int.* 2015;**35**(5):1492-8. doi: 10.1111/liv.12702. [PubMed: 25312770].
4. Catucci D, Obmann VC, Berzigotti A, Gräni C, Guensch DP, Fischer K, et al. Noninvasive assessment of clinically significant portal hypertension using ΔT1 of the liver and spleen and ECV of the spleen on routine Gd-EOB-DTPA liver MRI. *Eur J Radiol.* 2021;**144**:109958. doi: 10.1016/j.ejrad.2021.109958. [PubMed: 34571458].
5. De Gottardi A, Sempoux C, Berzigotti A. Porto-sinusoidal vascular disorder. *J Hepatol.* 2022;**77**(4):1124-35. doi: 10.1016/j.jhep.2022.05.033. [PubMed: 35690264].
6. Yan SP, Wu H, Wang GC, Chen Y, Zhang CQ, Zhu Q. A new model combining the liver/spleen volume ratio and classification of varices predicts HVPG in hepatitis B patients with cirrhosis. *Eur J Gastroenterol Hepatol*. 2015;**27**(3):335-43. doi: 10.1097/MEG.0000000000000269. [PubMed: 25563138].
7. de Franchis R; Baveno VI Faculty. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. *J*

Hepatol. 2015;**63**(3):743-52. doi: 10.1016/j.jhep.2015.05.022. [PubMed: 26047908].
8. Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. *Dig Dis*. 2016;**34**(4):382-386. doi: 10.1159/000444551. [PubMed: 27170392].
9. Ying L, Lin X, Xie ZL, Hu YP, Shi KQ. Performance of platelet count/spleen diameter ratio for diagnosis of esophageal varices in cirrhosis: a meta-analysis. *Dig Dis Sci.* 2012;**57**(6):1672-81. doi: 10.1007/s10620-012-2058-y. [PubMed: 22367112].
10. Chen XL, Chen TW, Zhang XM, Li ZL, Zeng NL, Zhou P, et al. Platelet count combined with right liver volume and spleen volume measured by magnetic resonance imaging for identifying cirrhosis and esophageal varices. *World J Gastroenterol.* 2015;**21**(35):10184-91. doi: 10.3748/wjg.v21.i35.10184. [PubMed: 26401083].
11. Kihira S, Kagen AC, Vasudevan P, Jajamovich GH, Schiano TD, Andrle AF, et al. Non-invasive prediction of portal pressures using CT and MRI in chronic liver disease. *Abdom Radiol (NY).* 2016;**41**(1):42-9. doi: 10.1007/s00261-015-0614-6. [PubMed: 26830610].
12. Zhang QW, Wang Y, Wang J, Zhao HB, Yu H, Liu SY, et al. A non-invasive magnetic resonance imaging-based model predicts portal venous pressure. *J Dig Dis*. 2016;**17**(3):175-185. doi: 10.1111/1751-2980.12325. [PubMed: 26860821].
13. Rezai P, Tochetto SM, Galizia MS, Yaghmai V. Splenic volume model constructed from standardized one-dimensional MDCT measurements. *AJR Am J Roentgenol.* 2011;**196**(2):367-72. doi: 10.2214/AJR.10.4453. [PubMed: 21257889].
14. Pattanayak P, Turkbey EB, Summers RM. Comparative evaluation of three software packages for liver and spleen segmentation and volumetry. *Acad Radiol.* 2017;**24**(7):831-9. doi: 10.1016/j.acra.2017.02.001. [PubMed: 28258903].
15. 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 (Warsz).* 2014;**73**(3):331-8. doi: 10.5603/FM.2014.0038. [PubMed: 25465038].
16. Cheng Y, Gu L, Yin X, Wang X, Xiao J, Wang Y, et al. Agreement between wedged hepatic venous pressure and portal pressure in hepatic sinusoidal obstruction syndrome. *J Pers Med*. 2022;**13**(1):4. doi: 10.3390/jpm13010004. [PubMed: 36675665].
17. Ferrusquía-Acosta J, Bassegoda O, Turco L, Reverter E, Pellone M, Bianchini M, et al. Agreement between wedged hepatic venous pressure and portal pressure in non-alcoholic steatohepatitis-related cirrhosis. *J Hepatol*. 2021;**74**(4):811-18. doi: 10.1016/j.jhep.2020.10.003. [PubMed: 33068638].
18. Kulkarni AV, Rabiee A, Mohanty A. Management of portal hypertension. *J Clin Exp Hepatol.* 2022;**12**(4):1184-99. doi: 10.1016/j.jceh.2022.03.002.
19. Hayashi H, Beppu T, Okabe H, Nitta H, Imai K, Doi K, et al. Combined measurements of serum bile acid level and splenic volume may be useful to noninvasively assess portal venous pressure. *J Gastroenterol*. 2012;**47**(12):1336-41. doi: 10.1007/s00535-012-0599-7. [PubMed: 22569764].
20. Romero-Cristóbal M, Clemente-Sánchez A, Ramón E, Téllez L, Canales E, Ortega-Lobete O, et al. CT-derived liver and spleen volume accurately diagnose clinically significant portal hypertension in patients with hepatocellular carcinoma. *JHEP Rep.* 2022;**5**(3):100645. doi: 10.1016/j.jhepr.2022.100645. [PubMed: 36691569].
21. Maleux G, Willems E, Fieuws S, Heye S, Vaninbroukx J, Laleman W, et al. Prospective study comparing different indirect methods to measure portal pressure. *J Vasc Interv Radiol*. 2011;**22**(11):1553-8. doi: 10.1016/j.jvir.2011.08.003. [PubMed: 22024115].