Use of Platelet Count Combined with Magnetic Resonance Imaging to Measure Spleen Volume and Right Liver Volume to identify Cirrhosis and Esophageal Varices

Mostafa Mohamad Assy, Ayman Fathy Zeid, Hamed Abdel Hakim Gobran,
Sarah Al Sayed Mahmoud Metwally
Department of Radiodiagnosis, Faculty of Medicine, Zagazig University, Zagazig, Egypt
***Corresponding author:** Sarah Al Sayed Mahmoud Metwally, **Mobile:** (+20) 0127 134 3727, **Email:** sarahalsayed710@yahoo.com

ABSTRACT
Background: Low platelets count (PLT), high spleen volume on ultrasonography, and a high Child-Pugh score are among the most reported recent cirrhosis assessment characteristics. **Objective:** This study aimed to evaluate the utilization of platelet count combined with magnetic resonance imaging to measure spleen volume (SV) and right liver volume to identify cirrhosis and esophageal varices (EV).
Patients and methods: A total of 50 cirrhotic patients diagnosed by abdominal ultrasound and/or MRI. They were referred from the General Medicine and Tropical Departments of Zagazig University Hospitals. We studied platelet count combined with magnetic resonance imaging to measure spleen volume and right liver volume for detection of severity of cirrhosis and esophageal varices.
Results: The best cutoff value of SI/platelet count in prediction of cirrhosis and child C were ≥ 3.24 and ≥ 6.625 respectively. SV/platelet count and SI/platelet count differed significantly among groups. RVPS differed significantly between groups and was significantly lower in OV. The best cutoff value of SI/platelet count and SV/platelet count in prediction of OV were ≥ 5.05 and ≥ 3.24 respectively. RVPS differed significantly between studied groups as it was significantly lower in OV.
Conclusion: With the advancement of the Child-Pugh class, the ratio of SV/PLT and SI/PLT increased, as the Child-Pugh class progressed PLT and RVPS diminished. RVPS can be used as a new combination parameter to determine the occurrence of cirrhosis and discriminate between the CPS classes.
Keywords: Platelet count, Cirrhosis, Esophageal varices.

INTRODUCTION

Hepatic failure as well as esophageal varices (EVs) are two of the most common consequences of posthepatitis cirrhosis. In cirrhotic patients, they are associated with an increased risk of death. It is hard to conduct a liver biopsy every year or two in cirrhotic patients in order to monitor cirrhosis progression. Preventing clinical decompensation and stabilizing individuals with cirrhosis is now universally established. As a result, accurate therapy of cirrhosis requires a noninvasive and dependable assessment of severity [(1)]. As a result of the development of the Child-Pugh classification system (CPS) which is significant predictive index for cirrhotic patients, it is now widely used to assess the severity of the disease [(2)]. The disadvantages of CPS for cirrhotic patients, on the other hand, might be modified by a number of internal and external variables [(3)].

Cirrhosis severity has to be monitored and classified with more dynamic and repeatable non-invasive techniques. Low platelet count (PLT), big spleen size on ultrasonography, and a high Child-Pugh score are among the most commonly reported recent cirrhosis assessment characteristics [(4)]. Splenomegaly and the function of the spleen are increasingly being used to assess the severity of cirrhosis [(5)].

Based on routine laboratory and ultrasound tests, the PLT/spleen diameter ratio was also found to be a unique indicator of cirrhotic patients with EV [(6)].

Recent advances in magnetic resonance imaging (MRI) have made it safer and more reliable in the diagnosis of cirrhosis. The severity and prognosis of cirrhosis have been shown to be strongly linked with the reduction in right liver lobe volume (RV). RV, spleen volume, and PLT data have not yet been analyzed as an indicator of hepatic disease by combining them into a single score [(7)].

It was the goal of this trial to use platelet count combined with magnetic resonance imaging to measure spleen volume and right liver volume to identify cirrhosis and esophageal varices.

PATIENTS AND METHODS

Fifty cirrhotic patients diagnosed by abdominal ultrasound and/or MRI were included in this trial. They were referred from the General Medicine and Tropical Departments of Zagazig University Hospitals.

Inclusion Criteria: Cirrhotic patients, patients who received endoscope to detect EV and who were able to undergo (MR) scans.

Exclusion Criteria: Gastrointestinal hemorrhage of any kind, on the basis of clinical or imaging data, patients had hepatocellular cancer, portal vein thrombosis, or a hepatic vascular malformation, and contraindications for MRI (e.g. aneurysmal clips, pacemakers .. etc.).

All studied groups underwent the following:
- Complete history taking: including delivery (normal or C section).
- Full clinical examinations.
- Laboratory investigations including PLT count,

Received: 20/04/2022
Accepted: 19/06/2022

albumin level, bilirubin level, and prothrombin time. For Child-Pugh score calculation. 12, 26, and 12 patients were classed as having Child-Pugh Class A, B, and C, respectively, based on the Child-Pugh score computation.

- Endoscopic assessment is used by the endoscopy operators to demonstrate EV.

Imaging assessment:

- Abdominal ultrasound was done for patients for detection of liver cirrhosis.
- The 1.5-T MRI scanner was used to perform supine MRI scans on each subject.
- A single-shot fast SE sequence was used to acquire unenhanced T1- and T2-weighted images.
- Portal venous phase contrast-enhanced images were used for analysis better than an arterial or delayed phase in depicting contour of liver and spleen.
- The right liver lobe volume (RV) was computed by multiplying the total of all right hepatic lobe areas by the slice thickness. The same technique was used to assess spleen volume (SV).
- For the spleen volume index, measurements were taken of the spleen's maximum thickness (T), length (L), and width (W) [SI =W x T x L]. When measuring the size of the spleen, we believe SV or SI to be more accurate than simply measuring the width of the spleen at its largest point.
- Consequently, the MRI-to-PLT spleen volume parameter ratios based on SV, RV, and PLT (SV/PLT and SI/PLT are also included.) calculations were made in this study. In addition, we integrated the PLT/SV and RV characteristics into a single marker by multiplying them both (RVPS = RV × PLT/SV) for assessment of cirrhosis of the liver.

Ethical consent:

Research ethics council at Zagazig University approved the study (ZU-IRB#9734) as long as all participants provided informed consent forms. Ethics guidelines for human experimentation were adhered to by the World Medical Association's Helsinki Declaration.

Statistical analysis

In order to analyze the data acquired, Statistical Package of Social Sciences version 20 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed. The quantitative data were presented in the form of mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) was used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X^2) were used to assess qualitatively independent data. $P \leq 0.05$ was determined significant.

RESULTS

Age differed significantly between groups, with the case group showing a far greater disparity. Differences in gender across the research groups were found to be statistically insignificant (Table 1).

Table (1): Demographics

Parameter	Groups		Test	
	Case group N=50 (%)	Control group N=50 (%)	t/χ^2	P
Age (year): Mean ± SD	56.3 ± 10.76	33.86 ± 11.87	9.095	< 0.001**
Gender: Female Male	30 (60%) 20 (40%)	37 (74%) 13 (26%)	2.216	0.137

The platelet count in the case group was much lower, and this difference was statistically significant. According to the statistically significant differences in SV/platelet count and SI/platelet count, the case group had a considerably higher SI/platelet count than the control group. This study's case group's RVPS was much lower, and this difference was statistically significant (Table 2).

Table (2): Comparisons regarding SV/platelet count, SI/platelet count and RVPS between the studied groups

Parameter	Groups		Test	
	Case group Mean ± SD	Control group Mean ± SD	Z	P
Platelet count (mcL)	84.5 ± 18.51	250± 51.81	-6.93	<0.001**
SV/PLT	4.49 ± 1.01	1.09 ± 0.95	-5.094	<0.001**
SI/PLT	7.29 ± 1.41	1.68 ± 0.82	-5.087	<0.001**
RVPS	210.68 ± 47.81	855.78 ± 198.31	-5.28	<0.001**

In terms of age, there was a statistically significant difference between the two groups analysed. There was a statistically significant difference in the percentage of females across the groups tested, where 75% of those without and with OV were female, compared to 41.7% of those with OV. In OV group, the platelet count was statistically considerably lower than in the other groups tested, with a statistically significant difference between the groups. SV/platelet count and SI/platelet count are statistically significantly different amongst the groups studied, with OV having a much higher SV/platelet count. RVPS was much lower in OV compared to the other groups tested, and this difference was statistically significant (Table 3).

Table (3): Relation between presence of OV and the studied parameters

Parameter	OV		Test	
	Absent N=76 (%)	Present N=24 (%)	T	P
Age (year): Me1an ± SD	57.92 ± 12.34	41.03 ± 14.81	5.055	<0.001**
Gender: Female Male	57 (75%) 19 (25%)	10 (41.7%) 14 (58.3%)	9.166	0.002*
	Mean ± SD	**Mean ± SD**	**Z**	**P**
Platelet count (mcL)	170 ±38.51	74.5 ± 16.91	-5.479	<0.001**
SV/PLT	2.03 ± 0.42	5.25 ± 1.21	-5.163	<0.001**
SI/PLT	3.22 ± 0.64	11.55 ± 2.11	-5.212	<0.001**
RVPS	705.69 ± 166.51	157.43 ± 34.61	-5.163	<0.001**

There was statistically significant association between presence of OV and Child Pough class where out of patients with child C, 41.7% had OV versus 7.7% had no OV (Table 4).

Table (4): Relation between presence of OV and child class

Parameter	OV		Test	
	Absent N=26 (%)	Present N=24 (%)	χ^2	P
Child class: A B C	10 (38.5%) 14 (53.8%) 2 (7.7%)	2 (16.7%) 12 (46.2%) 10 (41.7%)	12.12	0.001**

In terms of platelet count, there was a large disparity across the groups that were examined. Compared to other groups, the difference between A and B was statistically significant. Between the three groups, there was a considerable variation in the SV/platelet, SI/platelet, and RVPS ratios. There was a substantial difference between child C and each of the other groups in a pairwise comparison (Table 5).

Table (5): Relation between child class and the studied parameters

Parameter	Child class			Test	
	A	B	C	χ^2	P
Age (year): Mean ± SD	55.42 ± 8.33	55.23 ± 10.3	59.5 ± 13.8	F 0.69	0.506
Gender: Female Male	6 (50%) 6 (50%)	18 (69.2 %) 8 (30.8 %)	6 (50%) 6 (50%)	0	>0.999
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**KW**	**P**
Platelet count (mcL)	165±37.51	77 ±17.52	54.5 ± 12.11	27.077	<0.001 **
Pairwise	P_1 <0.001**	P_2 0.461	P_3 <0.001 **		
SV/PLT	2.82±0.61	4.02 ± 0.81	25.44 ± 5.81	17.631	<0.001 **
Pairwise	P_1 0.424	P_2 0.003 *	P_3 <0.001 **		
SI/PLT	4.54 ± 0.92	5.99 ±1.12	42.33 ±8.12	16.174	<0.001 **
Pairwise	P_1 0.909	P_2 0.002 *	P_3 <0.001 **		
RVPS	370.94 ± 87.31	239.15 ± 54.21	60.97 ±13.51	16.12	<0.001 **
Pairwise	P_1 0.732	P_2 0.003 *	P_3 <0.001 **		

The best cutoff of SI/platelet count in prediction of cirrhosis is ≥ 3.24, overall accuracy 81% specificity 74%, sensitivity 88%, area under curve 0.795 , negative predictive value 86% and positive predictive value 77.2%, **(Figure 1)**

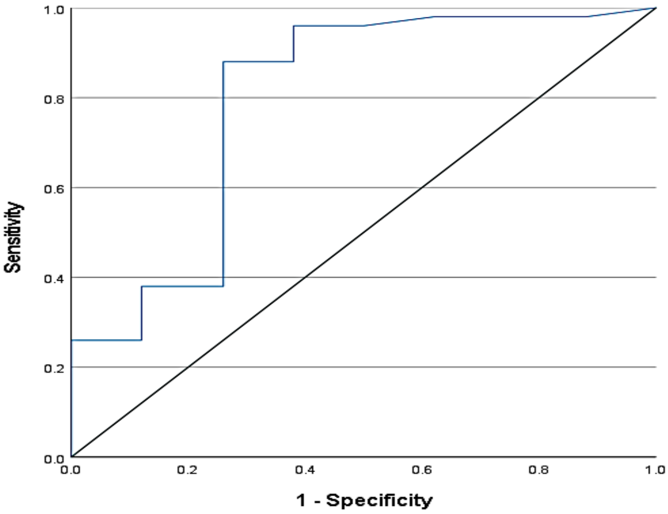
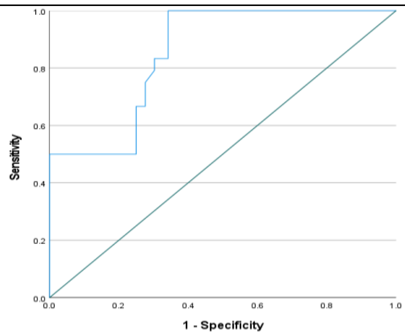
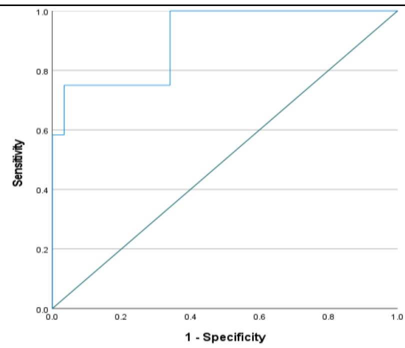


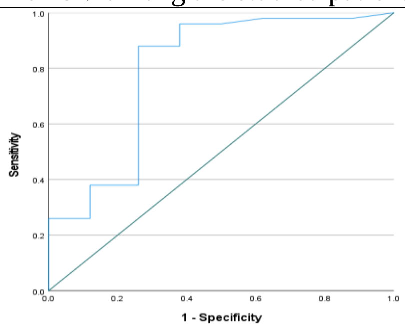
Figure (1): ROC curve showing performance of SI/platelet count in prediction of cirrhosis among the studied patients



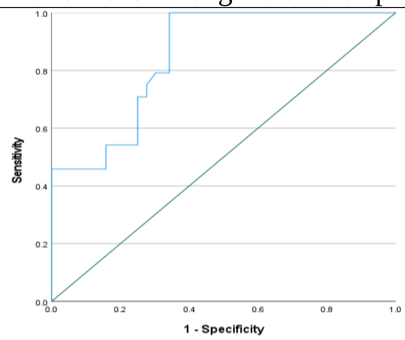
A- ROC curve to show performance of SI/platelet count for prediction of OV among the studied patients



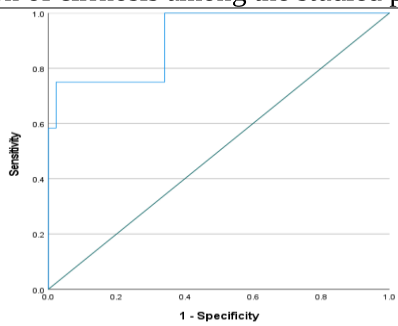
B- ROC curve to show performance of SI/platelet count for prediction of child C among the studied patients



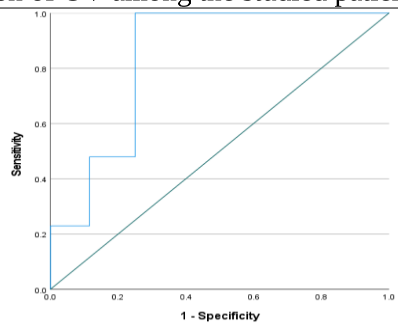
C-ROC curve to show performance of SV/platelet count for prediction of cirrhosis among the studied patients



D- ROC curve to show performance of SV/platelet count for prediction of OV among the studied patients



E-ROC curve to show performance of SV/platelet count for prediction of child C among the studied patients



F- ROC curve to show performance of RVPS for prediction of cirrhosis among the studied patients

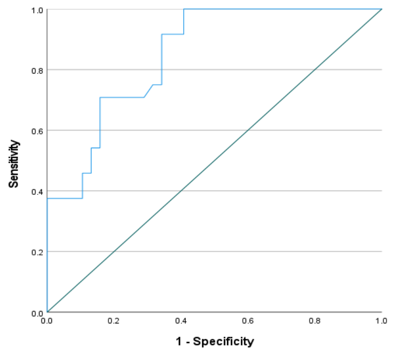
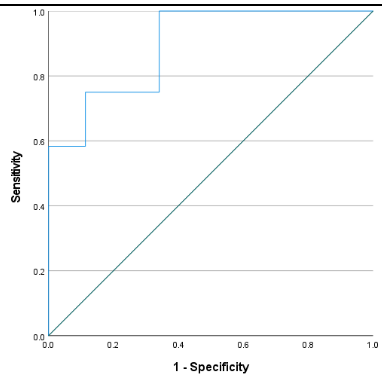
	
G- ROC curve to show performance of RVPS for prediction of OV among the studied patients	H- ROC curve to show performance of RVPS for the prediction of child C among the studied patients

Figure (2): The best cutoff of SI/platelet count in prediction of OV was ≥5.05 with area under curve 0.854, sensitivity 91.7%, specificity 65.8%, positive predictive value 45.8%, negative predictive value 96.2% and overall accuracy 72% ($p<0.001$) **(Figure 2-A).** The best cutoff of SI/platelet count in prediction of child C was ≥6.625 with area under **(figure 2-B).** The best cutoff of SV/platelet count in prediction of cirrhosis was ≥2.105 with area under curve 0.795, **(figure 2-C).** The best cutoff of SV/platelet count in prediction of OV was ≥3.24 with area under curve 0.85, **(Figure 2-D).** The best cutoff of SV/platelet count in prediction of child C was ≥5 with area under curve 0.911, **(Figure 2-E).** The best cutoff of RVPS in prediction of cirrhosis was ≤408.2 with area under curve 0.804, **(Figure 2-F).** The best cutoff of RVPS in prediction of OV was ≤277.225 **(figure 2-G).** The best cutoff of RVPS in prediction of child C was ≤ 213.43 with area under curve 0.896 **(figure 2-H).**

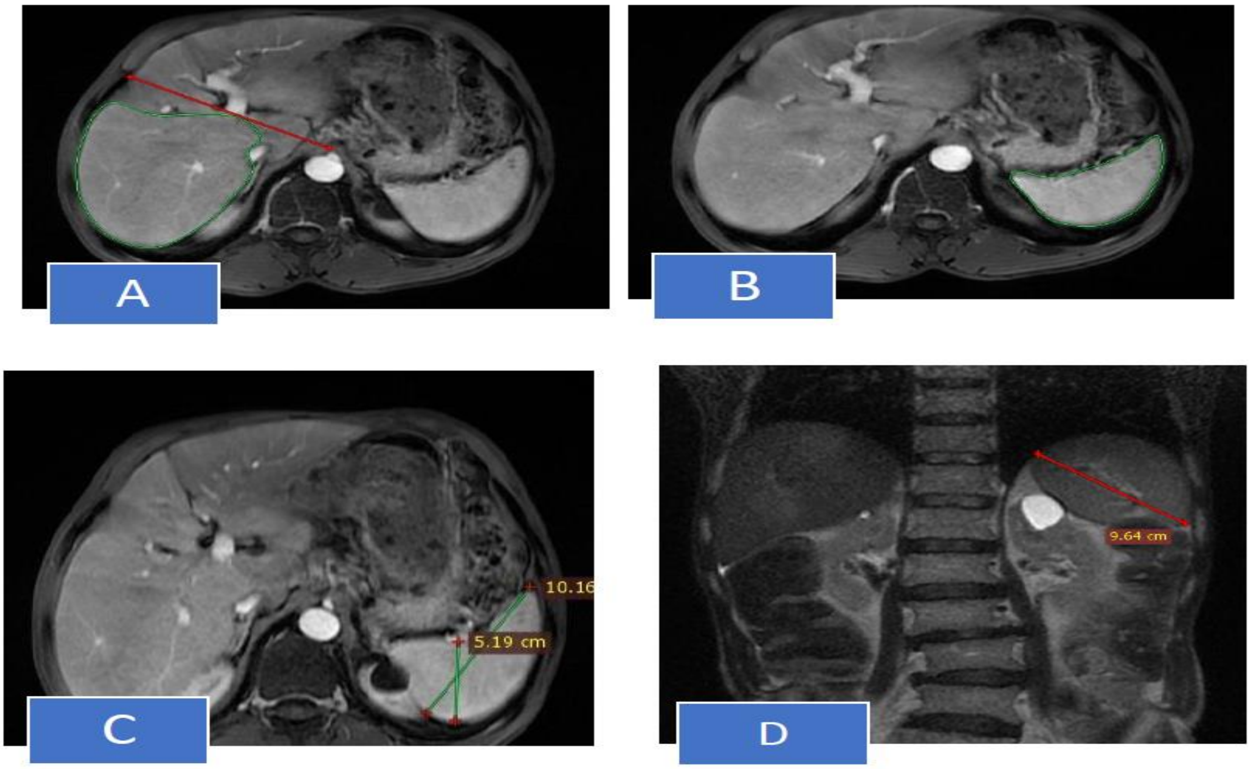


Figure (3): A 57-year- old patient with hepatitis c viral history and cirrhosis of the liver, and no history of hepatic encephalopathy and esophageal varices, or ascites. His platelet count was 200 x 10^9/l, albumin level was 3.3 g/dl, bilirubin was 0.6 mg/dl, and the prothrombin time was 14 sec, so the Child-Pugh score was 6 (class A). A: Outline of the right liver lobe (in green) was delineated on the axial enhanced magnetic resonance image portal phase. B: Outline of the spleen (in green) was improved (magnetic resonance imaging portal phase delineation). C: Spleen maximal width and maximal thickness on axial enhanced magnetic resonance image. D: Spleen maximal length on coronal cut magnetic resonance image. Findings: Spleen volume = 323.3, Spleen volume/platelet count = 1.62, Spleen index = spleen maximal width (W) x thickness (T) x length (L) = 505.68**,** Spleen index/platelet count = 2.53**,** RT liver volume = 843.51**,** RVPS = Rt liver vol x plt count / spleen volume = 521.81**.** The patient had no EV and low Child Pugh score (6), so SI/PL and SV/PL decreased, while RVPS increased.

DISCUSSION

Every year or two, a liver biopsy to check on the progression of cirrhosis is difficult to do in individuals who are cirrhotic. For chronic liver disease diagnosis, however, noninvasive methods such as laboratory examination and imaging proved to be reliable and repeatable [(3)].

MRI was used to quantify noninvasive variables such as liver volume (RV), SV, or SI, and PLT was used to determine whether and how these parameters were linked to cirrhosis's presence and severity. In order to assess liver cirrhosis, PLT and spleen volume data were combined into one measure (SV/PLT or SI/PLT). Studies have established a link between SV and SI levels evaluated by MRI and the Child-Pugh classification of cirrhosis [(8)].

It's possible that low PLT in cirrhosis patients has multiple causes. Because of the increasing number of false-positive results when relying solely on PLT to make a cirrhosis diagnosis, accuracy may suffer [(9)].

Concerns about costs could be raised. The expenses of routine MR usage in all cirrhotic patients must be weighed against the benefits of avoiding upper gastrointestinal endoscopies. However, even though MRI examinations are more expensive, for some individuals, particularly those who are unable to tolerate an invasive upper gastrointestinal endoscopic examination, MRI may be a better option.

PLT/SV and RV were integrated into a single marker in our investigation by multiplying both (RVPS = RV × PLT/SV) for assessment of liver cirrhosis, which agreed with **Ying *et al.*** [(10)] who showed that the platelet count/spleen diameter ratio (PSR) can accurately identify EV in cirrhosis. The use of this measure among cirrhotic patients may reduce the frequency of endoscopy.

Chen *et al.* [(11)] suggested that when it comes for diagnosing cirrhosis, RV/SV should be employed, and SI can be advised, whereas in our study we combined SI with platelet count to detect the occurrence of the disease and distinguish between distinct CPS classes.

Our study recommended the combination of RV and platelet count to assess degree of cirrhosis and EV, while **Li *et al.*** [(12)] described how liver lobe volume and ALB can be used to determine cirrhosis severity and the presence of an esophageal varices in cirrhotic patients.

In agreement with our study, **Abd-Elsalam *et al.*** [(13)] who found that platelet count is a noninvasive metric that has great accuracy in predicting EV, according to this study. These patients, especially in less-advantaged developing nations, can skip screening endoscopy since they have a low risk of variceal bleeding and large EV is considerably less common in them than it is in those who are hemolytic and have low platelet counts (below 150,000).

The combination of SV or SI with PLT was clearly superior to PLT alone in differentiating between cirrhosis and various CPS categories in our study.

Jamil *et al.* [(14)] found that the platelet count/spleen diameter ratio is the most reliable marker for the prediction of the development of esophageal varices. It is simple to collect and can be used in conjunction with other indicators to identify people at high risk of developing esophageal varices; as a result, endoscopic screening will be reduced, as well as the associated medical costs. When it comes for measuring spleen size, we believe that SV or SI are more accurate than spleen maximal width. Consequently, the MRI-to-PLT, spleen volume parameter ratios based on SV, RV, and PLT were calculated in our study.

EVs and liver failure are two of the more serious consequences that can arise from post-hepatitis cirrhosis, according to our research. Therefore, noninvasive and reliable evaluation of the severity of cirrhosis is critically important for management. The management of cirrhosis requires a noninvasive and accurate assessment of the disease's severity.

In agreement with this, **Chen *et al.***[(15)] the intravoxel incoherent motion (IVIM) is a promising magnetic resonance approach for assessing hepatic cirrhosis, which is a frequent chronic degenerative illness of the liver in clinical practice. In contrast to our study which depended on magnetic resonance contrast-enhanced imaging, **Han *et al.*** [(16)] Using dual-energy CT, researchers found that the iodine weight in the spleen (IW-S) can noninvasively predict and evaluate the severity of esophageal varices (EV) in cirrhotic individuals.

It has been shown that CT scans can be used to detect high-risk varices and to quantify the risk of varix bleeding, unlike our investigation, which relied on MRI to calculate the correct liver volume and spleen capacity [(17)].

Also, **Malek *et al.*** [(18)] found that the LSPS (liver stiffness-spleen-platelet ratio) is a useful method for detecting high-risk EV in patients with CLD, even though our study relied on ultrasound. A greater LSPS score indicates that the patient has CLD, which necessitates further endoscopic evaluation by doctors.

CONCLUSION

In line with the advancement of the Child-Pugh class, SV/PLT and SI/PLT have increased, whereas PLT and RVPS have dropped. Cirrhosis can be detected and the CPS class differentiated using RVPS as a new combination measure. Evaluating the existence of EV could be done by using the SV/PLT. A positive outcome of this study would be to aid in the selection of a suitable treatment strategy.

Conflict of interest: The authors declared no conflict of interest.
Sources of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Author contribution: Authors contributed equally in the study.

REFERENCES

1. **Berzigotti A, Piscaglia F (2011):** Ultrasound in portal hypertension- part 1. Ultraschall Med., 32: 548-568.
2. **Chuang Y, Ou H, Lazo M *et al.* (2018):** Predicting post-hepatectomy liver failure by combined volumetric, functional MR image and laboratory analysis. Liver Int., 38: 868-874.
3. **De Franchis R (2010):** Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol., 53: 762-768.
4. **Levick C, Phillips-Hughes J, Collier J *et al.* (2019):** Non-invasive assessment of portal hypertension by multi-parametric magnetic resonance imaging of the spleen: A proof of concept study. PloS One, 14: 66-71.
5. **Shi B, Wang X, Mu Q *et al.* (2005):** Value of portal hemodynamics and hypersplenism in cirrhosis staging. World J Gastroenterol., 11: 708-711.
6. **Taouli B**, **Ehman R, Reeder S (2009):** Advanced MRI methods for assessment of chronic liver disease. AJR Am J Roentgenol., 193: 14-27.
7. **Zhou W, Yang J**, **Zhang G *et al.* (2019):** Association between red cell distribution width-to-platelet ratio and hepatic fibrosis in nonalcoholic fatty liver disease: A cross-sectional study. Medicine, 98: 65-69.
8. **Chen X, Chen T, Li Z *et al.* (2013):** Spleen size measured on enhanced MRI for quantitatively staging liver fibrosis in minipigs. J Magn Reson Imaging, 38: 540-547.
9. **Peck-Radosavljevic M (2000):** Thrombocytopenia in liver disease. Can J Gastroenterol., 14: 60-66.
10. **Ying L, Lin X, Xie Z *et al.* (2012):** Performance of platelet count/spleen diameter ratio for diagnosis of esophageal varices in cirrhosis: a meta-analysis. Dig Dis Sci., 57 (6): 1672-81.
11. **Chen X, Chen T, Zhang X *et al.* (2014):** 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. DOI:10.1371/journal.pone.0089973
12. **Li H, Chen T, Li Z *et al.* (2015):** Albumin and magnetic resonance imaging-liver volume to identify hepatitis B-related cirrhosis and esophageal varices. World J Gastroenterol., 21 (3): 988-96.
13. **Abd-Elsalam S, Habba E, Elkhalawany W *et al.* (2016):** Correlation of platelets count with endoscopic findings in a cohort of Egyptian patients with liver cirrhosis. DOI:10.1097/MD.0000000000003853
14. **Jamil Z, Malik M, Durrani A (2017):** Platelet count to splenic diameter ratio and other noninvasive markers as predictors of esophageal varices in patients with liver cirrhosis. Turk J Gastroenterol., 28 (5): 347-352.
15. **Chen F, Chen Y, Chen T *et al.* (2020):** Liver lobe based intravoxel incoherent motion diffusion weighted imaging in hepatitis B related cirrhosis: Association with child-pugh class and esophageal and gastric fundic varices. doi: 10.1097/MD.0000000000018671
16. **Han X, An W, Cao Q *et al.* (2020):** Noninvasive evaluation of esophageal varices in cirrhotic patients based on spleen hemodynamics: a dual-energy CT study. Eur Radiol., 30 (6): 3210-3216.
17. **Lee C, Lee S, Choi W *et al.* (2021):** An index based on deep learning-measured spleen volume on CT for the assessment of high-risk varix in B-viral compensated cirrhosis. Eur Radiol., 31 (5): 3355-3365.
18. **Malek M, Hoque M, Azam M *et al.* (2021):** Prediction of Esophageal Varices in Chronic Liver Disease by Liver Stiffness-Spleen Size-to-Plalelet Ratio Risk Score. Mymensingh Med J., 30 (1): 115-122.