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Platelet count/spleen diameter ratio for the non-invasive diagnosis of esophageal varices in Iranian patients with cirrhosis

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Abstract

Introduction: Esophageal varices (EVs) carry a significant risk of rupture and subsequent life-threatening bleeding. While previous research has investigated the effectiveness of the platelet count to spleen diameter ratio (PC/SD) as a non-invasive predictor of EVs in various populations, this study specifically focuses on the Iranian population to assess the applicability and effectiveness of this parameter in this region.

Materials and Methods: Upper gastrointestinal endoscopy was performed on 147 cirrhotic patients to screen for EVs. Biochemical tests and ultrasonography were done to measure spleen diameter (SD) and calculate the PC/SD ratio. ROC analysis was done to determine the predictive performance of the parameters.

Results: Among the patients, 73% had EVs. The analysis showed the following: platelet count (PC) had an AUC of 0.695 with 78.7% sensitivity and 56.4% specificity; SD had an AUC of 0.750 with 49.1% sensitivity and 89.7% specificity; and the PC/SD ratio had an AUC of 0.734 with 60.2% sensitivity and 79.5% specificity. The PC/SD ratio exhibited a high positive predictive value of 93% but a low negative predictive value of 41.9%. Optimal cutoff values were determined as follows: PC≤ 100,000, SD< 163, and PC/SD ratio≤ 523.

Conclusion: By identifying high-risk patients who may benefit from targeted endoscopic screening, this non-invasive method could contribute to improving overall patient care and reducing the need for invasive procedures. However, due to suboptimal performance results, it is crucial to use this approach with caution, as endoscopic screening remains the standard practice for the diagnosis and management of esophageal varices.

Keywords: Platelet count, Spleen diameter, Platelet count/spleen diameter ratio, Hepatic cirrhosis, Esophageal varices

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Introduction

Portal hypertension, a consequence of chronic liver disease and cirrhosis, represents a significant clinical challenge, with the development of esophageal varices (EV) being one of its most serious complications (1, 2). EVs are abnormally dilated veins in the lower portion of the esophagus, and their rupture can lead to life-threatening variceal bleeding, a primary factor contributing to morbidity and death in cirrhotic patients (3, 4).

Epidemiological studies have reported that the prevalence of EVs in cirrhotic patients can range from 60% to 80%, depending on the underlying etiology and severity of the liver disease. Furthermore, among patients with established EVs, the annual risk of experiencing a first episode of bleeding is estimated to be 10% to 15%, with a mortality rate as high as 20% associated with this event (5).

The gold standard for diagnosing EVs is upper endoscopy, which enables direct inspection and grading of the varices (6). However, this invasive procedure requires specialized equipment and skilled personnel, potentially limiting its accessibility and cost-effectiveness, especially in resource-constrained healthcare settings (5, 7).

In order to address these issues, scientists have looked into the use of non-invasive techniques to determine high-risk cirrhotic patients who would most benefit from targeted endoscopic screening. One such approach is the Platelet Count/Spleen Diameter (PC/SD) ratio, which has been proposed as a reliable predictor of the presence and severity of EVs (7-10). This simple, cost-effective, and easily obtainable parameter has the potential to optimize resource allocation and improve access to necessary care for cirrhotic patients.

However, it is important to note that the performance of predictive models, such as the PC/SD ratio, may vary across different populations due to factors like underlying disease etiology, genetic differences, and environmental influences (10). Therefore, it is crucial to assess the clinical utility of these non-invasive diagnostic tools in particular populations, such as the Iranian population in this study, to ensure their validity and clinical utility.

In light of the aforementioned situation, the current investigation was carried out to explore the correlation between platelet count (PC), spleen diameter (SD), and their ratio (PC/SD) in cirrhotic patients within the Iranian population. By focusing on this unique group, we seek to determine how effectively the PC/SD ratio functions in different healthcare settings and geographic regions. Our goal is to establish a non-invasive, cost-effective tool that can enhance early detection and improve patient management strategies in local healthcare environments.

Methods

Study Design and Population

This analytical cross-sectional study was conducted at Razi Hospital, a tertiary care center in the north of Iran, Rasht city. The study population comprised cirrhotic patients referred to the gastroenterology department at the study site between September 15, 2023, and March 15, 2024. A combination of clinical, laboratory, and imaging results led to the diagnosis of cirrhosis in the patients and all adult individuals with a confirmed diagnosis of cirrhosis, regardless of the underlying etiology, were included. However, patients diagnosed with acute liver failure, those requiring urgent liver transplantation, pregnant women, and individuals unable or unwilling to comply with study procedures were excluded from this study.

Data Collection

A thorough clinical evaluation that included a physical examination, a medical history, and laboratory testing was performed on each recruited individual. The age, sex, and marital status of the participants were documented. As part of the study protocol, the PC was measured for each participant and reported in the unit of × 10^9/L. All participants underwent abdominal ultrasonography, performed by an expert radiologist. The bipolar diameter of the spleen was precisely measured and recorded in millimeters (mm). Also, an experienced gastroenterologist performed upper endoscopy. The presence of EVs was meticulously assessed and documented. The ratio of PC to SD was computed by dividing the PC (× 10^9/L) by the SD (mm) measured during the abdominal ultrasonography.

Statistical Analysis

When applicable, the mean ± standard deviation or median (interquartile range) were used to express continuous variables. Frequencies and percentages were used to display the categorical variables. To assess the normality of the key variables (PC, SD, and PC/SD ratio), the Kolmogorov-Smirnov test was used. This informed the choice of appropriate statistical tests for the subsequent analyses. The Mann-Whitney test, a non-parametric method, was used to compare the values of PC, SD, and their ratio between participants with and without EVs. This test was chosen due to the non-normal distribution of the variables. The diagnostic efficacy of PC, SD, and PC/SD ratio in predicting the presence of EVs was evaluated with the use of receiver operating characteristic (ROC) curve analysis. Youden's J index was used to identify the ideal cut-off values, and the resulting sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed. The data analyses were conducted using SPSS version 16, MedCalc Version 19.5.3, and GraphPad Prism version 8.0.1 software. The significance level was set at 0.05.

Results

The study included a total of 147 patients diagnosed with cirrhosis. The mean age of participants was 56.18 ± 11.98 years, with 16 patients (10.9%) being older than 70 years. The majority of the study population was male (61.9%) and married (77.6%). The average duration of the disease among the participants was 3.31 ± 1.93 years, and 43 patients (29.3%) had a disease duration of more than four years (Table 1).

The most frequent underlying causes for cirrhosis were non-alcoholic steatohepatitis (NASH) (23.8%), hepatitis C virus (HCV) (19.7%), and alcohol-related (17.0%) liver disease. Based on the Child-Pugh classification, 31 patients (21.1%) were categorized as Class A, 81 (55.1%) as Class B, and 35 (23.8%) as Class C. EVs were discovered in 108 (73.5%) of the 147 patients during endoscopic screening. Interestingly, the study found that the average duration of cirrhosis was significantly longer in patients with EVs compared to those without (p<0.001). While the group with EVs had a larger percentage of women (65.7%) than the group without EVs (51.3%), the difference in percentages between the two groups was not statistically significant (p=0.111) (Table 2).

Table 1. Demographic and clinical characteristics of patients with cirrhosis presenting to the Razi Hospital of Rasht in 2023.

Variable	Total (n=147)	with EVs (n=108)	without EVs (n=39)	P value
Age (year)				
≤ 50	48 (32.7)			
50-70	83 (56.5)			
> 70	16 (10.9)			
Mean (SD)	56.18 (11.98)	56.62 (11.65)	54.95 (12.93)	0.457
Sex				
Male	91 (61.9)	37 (34.3)	19 (48.7)	0.111
Female	56 (38.1)	71 (65.7)	20 (51.3)	
Marital Status				
Single	33 (22.4)	19 (17.6)	14 (35.9)	0.019
Married	114 (77.6)	89 (82.4)	25 (64.1)	
Duration of disease (year)				
≤ 2	59 (40.1)			
3-4	45 (30.6)			
> 4	43 (29.3)			
Mean (SD)	3.31 (1.93)	3.64 (1.91)	2.38 (1.68)	<0.001

Table 2. Comparison of platelet count (PC), spleen diameter (SD), and platelet count to spleen diameter (PC/SD) ratio between individuals with and without esophageal varices in patients with cirrhosis.

Variable	Total (N=147)	Individuals without EVs (N=39)	Individuals with EVs (N=108)	P value
PC (n/mm^3)	85000 (69000-105000)	105000 (83000 - 113000)	81000 (65250 - 96000)	<0.001
SD (mm)	160 (150-175)	155 (130 - 160)	162 (155 - 180)	<0.001
PC/SD ratio	533.7 (418.2-687.5)	652 (550 - 942)	484 (389 - 625)	<0.001

To evaluate these parameters' ability to predict the diagnosis of EVs, ROC analysis was performed. The area under the ROC curve (AUROC) for PC was 0.695 (95% CI: 0.603-0.787), for SD 0.750 (95% CI: 0.663-0.837), and the PC/SD ratio 0.734 (95% CI: 0.646-0.822) (Figure 1).

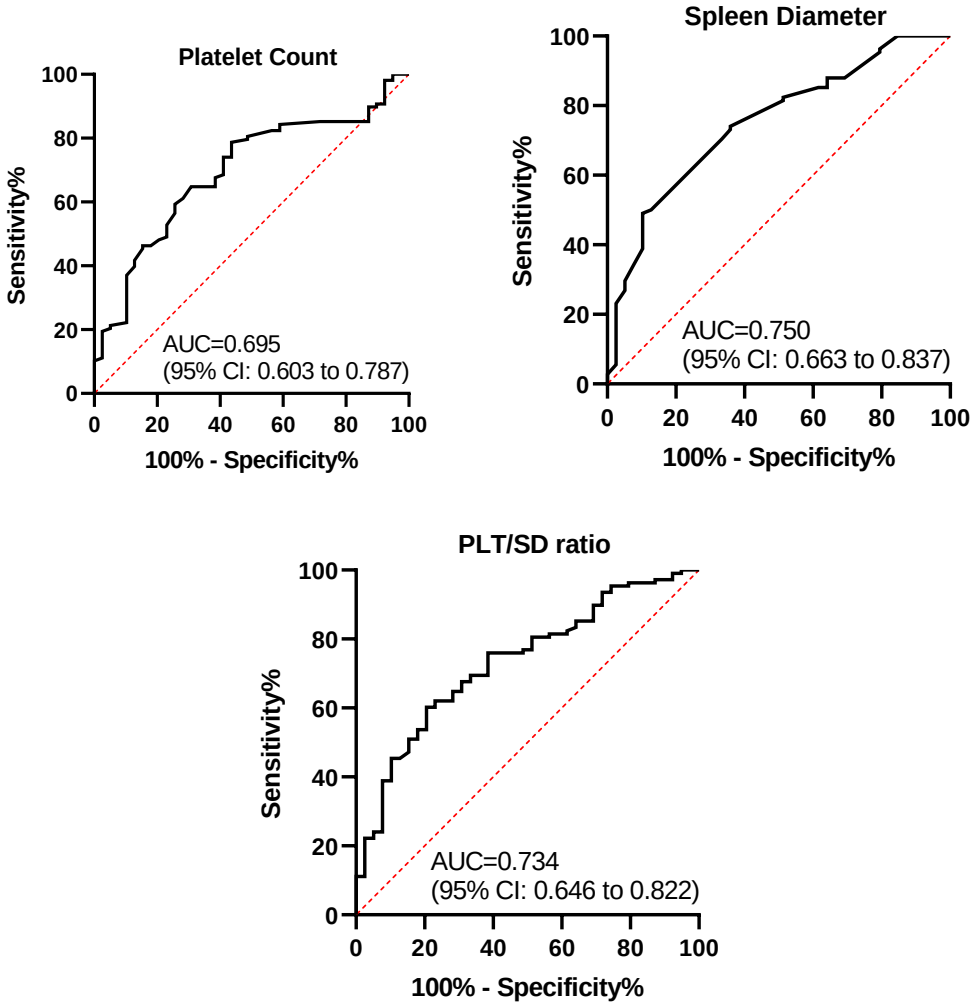

Figure 1. The predictive power of platelet count (PLT), spleen diameter (SD), and the ratio of platelet count to spleen diameter (PLT/SD Ratio) in the diagnosis of esophageal varices using the area under the curve (ROC).

AUC: Area Under Curve. CI: Confidence Interval

The following is the determination of the ideal cut-off values: PC > 100,000 (sensitivity 78.7%, specificity 56.4%), SD < 163 mm (sensitivity 49.1%, specificity 89.7%), and PC/SD ratio ≥ 523 (sensitivity 60.2%, specificity 79.5%).

Patients with a PC/SD ratio below the cut-off value of 523, a PC below the cut-off of 100,000, and an SD above the cut-off of 163 mm were more likely to have EVs. The PPV of these cut-off values were 89%, 83.3%, and 93%, respectively (Table 3).

Table 3. The best cut-off points of platelet count, spleen diameter, and platelet count to spleen diameter ratio in the diagnosis of esophageal varices.

	PC (n/mm^3)	SD (mm)	PC/SD ratio
Area under curve	0.695	0.750	0.734
Best cutoff point	≤ 100000	> 163	≤ 523
Sensitivity	78.7	49.1	60.2
specificity	56.4	89.7	79.5
Positive predictive value	83.3	93.0	89.0
Negative predictive value	48.9	38.9	41.9
Positive likelihood value	1.81	4.78	2.93
Negative likelihood value	0.38	0.57	0.50

Discussion

The present investigation aimed to evaluate the prevalence of EVs among cirrhotic patients and assess the utility of PC, SD, and the PC/SD ratio in predicting the presence of EVs. The study found that 108 (73.5%) of the 147 participants had EVs. According to the study results, cirrhotic individuals with EVs had considerably smaller PC, greater SD, and lower PC/SD ratios than those without EVs. Furthermore, the diagnostic utility of these parameters in predicting EVs was assessed using ROC analysis.

The prevalence of EVs in this study was consistent with those from other areas, such as southern India (77.7%), Mexico (80.2%), and China (74.7%) (10-12). However, lower prevalence rates were reported in studies conducted in Tanzania (39.5%) and South Carolina (51%) (13, 14). This variation in the occurrence of EVs across different patient populations could be attributed, in part, to differences in the underlying causes of liver cirrhosis. For instance, patients with biliary cirrhosis exhibited a lower prevalence of EVs (26.0%), while those with hepatitis B-related liver cirrhosis had a considerably higher rate (74.7%) (12, 15).

The results of the present investigation suggest that SD may represent a more reliable individual non-invasive marker for the prediction of EVs compared to PC or the PC/SD ratio in the study population, as evidenced by the AUROC values reported herein. These findings contrast with the conclusions of certain prior studies, which have proposed the PC/SD ratio as a more accurate non-invasive marker relative to PC or SD individually (8, 9).

The predictive power of the PC/SD ratio in the current study was satisfactory but not optimal. However, a number of previous investigations have documented higher discriminative ability of this marker (5, 16-18). Specifically, Giannini et al., who first introduced the PC/SD ratio as a promising non-invasive tool, reported an AUROC of 0.86 in predicting the presence of EVs (17). Similarly, Patil et al. observed an AUROC of 0.84 for the PC/SD ratio, a value exceeding that obtained in the present investigation (18).

The differences in the diagnostic utility of these non-invasive markers for predicting EVs across studies can be attributed to several factors. Firstly, the study populations may have varied in terms of the underlying etiologies of cirrhosis, disease severity, and the prevalence of EVs. Secondly, the cut-off values used for PC, SD, and PC/SD ratio varied across studies, which can affect the sensitivity and specificity of these

parameters in predicting the presence of EVs. Furthermore, the discrepancies observed in the diagnostic performance of these non-invasive parameters may be partially attributed to the influence small sample size of this study.

Despite the mixed findings, the present study demonstrated that the PC/SD ratio had a high PPV of 93%, indicating that patients with a ratio below the cut-off are highly likely to have EVs. However, the relatively low NPV of 41.9% suggests that a ratio above the cut-off may not accurately exclude the presence of EVs.

This emphasizes the potential utility of the PC/SD ratio as a screening tool for identifying high-risk patients. By employing this method, healthcare providers can effectively stratify patients according to their risk levels, facilitating a more focused approach to endoscopic screening and monitoring. This prioritization is crucial, as it enables clinicians to concentrate their resources and efforts on individuals who are most likely to benefit from early intervention.

The ability of a non-invasive predictor to accurately identify high-risk patients can help prevent serious complications, such as variceal hemorrhage, which is vital in managing conditions like cirrhosis. Early intervention not only enhances patient outcomes by averting adverse events but also improves the overall quality of care provided.

Moreover, this targeted approach contributes to the efficient allocation of healthcare resources. By ensuring that high-risk individuals receive timely care, healthcare systems can minimize unnecessary procedures for patients at lower risk, thereby alleviating the burden on medical facilities and personnel. This efficiency is particularly important in environments where healthcare resources are constrained, as it allows for better management of patient loads and enhances the overall effectiveness of the healthcare system.

It is imperative to acknowledge that although the PC/SD ratio exhibits potential as a non-invasive marker for predicting EVs and can assist in prioritizing patients for endoscopy, it is crucial to emphasize that it cannot replace traditional endoscopic procedures. Although previous studies have reported a high predictive ability for this marker (5, 16-18), our findings did not achieve that level of performance, indicating that its effectiveness was not optimal in this context. Therefore, the use of the PC/SD ratio should be approached with caution until sufficient evidence supports their efficacy.

The most reliable method for identifying EVs and determining their severity is still endoscopy, as it allows for direct visualization and grading of the varices (19).

In addition to the PC/SD ratio, other non-invasive indicators have been explored for the prediction of EVs in cirrhotic patients, such as various serum biomarkers (20-22). The combination of these biomarkers with the PC/SD ratio may further improve the diagnostic accuracy in predicting the presence of EVs, and this should be investigated in future studies.

The current research has certain limitations. Firstly, the fact that the study was limited to a single tertiary care facility may limit the applicability of the findings in other contexts. Secondly, the cross-sectional design of the study precluded the assessment of the long-term predictive value of the PC/SD ratio in identifying the development or progression of EVs. Prospective longitudinal studies would be valuable in evaluating the utility of the PC/SD ratio for monitoring the risk of EVs over time.

Conclusion

In conclusion, the present study suggests that PC, SD, and PC/SD ratio can be considered as beneficial non-invasive markers for predicting the presence of EVs in patients with hepatic cirrhosis. These parameters may help identify individuals who should prioritize undergoing upper gastrointestinal endoscopy for EV screening. However, comprehensive endoscopic examination should remain the standard approach for the identification and treatment of EVs in cirrhotic patients.

Author contribution

Concept development (provided idea for the research): **SKHGh** and **SF** Design (planned the methods to generate the results): **SM**, **SKHGh**, **FJ**, **ASh** Supervision (provided oversight, responsible for

organization and implementation): **FJ**, **AH** and **NL** Data collection/processing (responsible for experiments, patient management, organization, or reporting data) and data analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): **NL**, **AH**, **SKHGh**, **SF** Literature search (performed the literature search and writing of the manuscript): **NL**, **AH** and **SKHGh** Drafting the manuscript (responsible for writing a substantive part of the manuscript): All authors.

Conflict of interest

The authors declare that they have no competing interests.

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Ethics approval and consent to participate

This study was approved by the ethics committees of the Guilan University of Medical Sciences [IR.GUMS.REC.1403.052]. Informed consent was obtained from all individual participants

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