Original Article

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Platelet count/spleen diameter ratio as a predictor of high-risk esophageal varices in patients with liver cirrhosis

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Abstract

Background: Non-invasive parameters for the prediction of large esophageal varices among patients with liver cirrhosis is of greatest importance as it may decrease both the medical and economic load related to screening. The aim of this study is to evaluate platelet count/spleen diameter ratio as a non-invasive predictor of high-risk esophageal varices.

Patients and methods: This observational cross-sectional study included forty eight cirrhotic patients underwent screening endoscopy for EV. All participants were subjected to full history taking, clinical examination, laboratory investigations, abdominal ultrasonography (US) and upper gastrointestinal endoscopy and EV grading classification according to AASLD practice guidelines criteria. Calculation of spleen bipolar diameter and platelet count /bipolar spleen diameter ratio for all patients and its diagnostic accuracy was done.

Results: The patients were divided into two groups according to esophageal varices; risky group, included twenty four patients with large risky varices and non-risky group, included twenty four patients with small non risky varices. Compared to patient with non-risky varices, patient with large risky varices had a significant higher mean abdominal US spleen bipolar diameter and lower mean platelet count/spleen diameter ratio. Platelet count/spleen diameter ratio at cut off point equal to or less than 809.45 had sensitivity and specificity 95.8% (for each) to differentiate between high and low risk groups with area under ROC 0.99. Furthermore, spleen bipolar diameter ≥138.7 mm cutoff point had sensitivity of 95.8% and specificity 62.5% in detecting high risky varices with total accuracy was 79.2% and area under ROC 0.94.

Conclusions: The platelet count/spleen diameter ratio and spleen bipolar diameter in cirrhotic patients may be proposed as safe and reproducible tools to improve the management of cirrhotic patients who should undergo screening endoscopy for EV.

Introduction

Liver cirrhosis represents the final common histologic pathway for a wide variety of chronic liver diseases[1]. The complications of cirrhosis include, portal hypertension, ascites, hepatorenal syndrome, and hepatic encephalopathy [2].

Portal hypertension is a pathological condition that onsets with abnormal increase (>5mm mercury[hg]) in hepatic venous pressure gradient and causes dilatation of portosystemic collaterals [3].

One of the most serious complications of portal hypertension is the development of esophageal varices (EV). The prevalence of esophageal varices among these patients may range from 60-80%[4].

Incidence of variceal bleeding varies between 5-15% and life-threatening variceal bleeding can develop in 30-40% of patients with varices [5]**.** Most often it is esophageal varices that bleed; however, gastric varices are responsible for 10-36% of bleeding episodes [6]**.** Therefore, the prevention of variceal bleeding is an important goal in management of patients with liver cirrhosis [4]. The most important predictor of variceal hemorrhage is the size of varices, with the highest risk of first hemorrhage (15% per year) occurring in patients with large varices. Other predictors of hemorrhage are decompensated cirrhosis (Child B/C) and the endoscopic presence of red wale marks. Although, bleeding from esophageal varices occurs spontaneously in up to 40% of patients, and despite improvements in therapy over the last decade, it is associated with a mortality of at least 20% at 6 weeks[7]. Esophagogastroduodenoscopy (EGD) is the gold standard for the diagnosis of esophageal varices, and the carrying out the most suitable measures to treat esophageal varices depends on the findings sophagogastroduodenoscopy[8]. Several non-invasive methods have been developed to diagnose esophageal varices in patients with cirrhosis, such as platelet count in peripheral blood, measurement of serum albumin levels, Child-Pugh classification, right liver lobe diameter/albumin ratio, and platelet count/ spleen diameter ratio (PC/SD)[9-11]. Baveno VI consensus commends grouping of liver stiffness and platelet count to choice patients who do not need endoscopic screening for esophageal varices. However, Baveno VI Meeting Consensus recommends the endoscopy screening for all cirrhotic patients at the time of their diagnosis and periodical endoscopy examination in patients with EV [12]. However, the upper endoscopy is an invasive and painful technique which may not be acceptable for the patients. Therefore, predicting the presence of EV through non-endoscopic and non-invasive markers is essential in order to classify the patients who benefit from routine

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endoscopy screening and may reduce considerably the number of avoidable endoscopies [13]. Furthermore, precise identification of patients at highest risk of bleeding documents stratification in an attempt to avoid potentially harmful preventive treatments in patients who will never have variceal bleeding. The aim of this study is to evaluate the platelet count / spleen diameter ratio as a predictor of high-risk esophageal varices in patients with liver cirrhosis.

Patients and methods

This observational cross-sectional study included forty eight patients with liver cirrhosis aged 18-70 years who were admitted to the Hepatic and Gastroenterology Clinics at Specialized Medical Hospital of Mansoura University for upper gastrointestinal endoscopic screening for the presence of esophageal varices after obtaining approval from the medical ethical committee in Mansoura Faculty of Medicine. Diagnosis of liver cirrhosis depends on typical clinical, laboratory, and ultrasound features. All the participants were subjected to, full history taking included medication use (beta-blockers, diuretics or nitrites), clinical examination and Child Pugh classification. All patients supplied informed consent before participating in this study. **Inclusion Criteria**: Patients aged 18-70 years old with liver cirrhosis. **Exclusion criteria:** Patients less than 18 years old and more than 70 years old, previous attack of active upper gastrointestinal bleeding, previous endoscopic sclerotherapy, band ligation or variceal occlusion therapy of EV, previous surgery for portal hypertension or transjugular intrahepatic portosystemic shunt (TIPS) procedure or shunt surgery, renal impairment, severe psychosis. **Laboratory investigations:** Complete blood count (CBC) including platelets count, Liver function tests [Alanine transaminase (ALT) and Aspartate transaminase (AST), serum albumin, serum bilirubin (total and direct) and prothrombin time], serum creatinine, viral markers (Anti-HCV Ab, HBsAg and anti HIV antibody).

Upper gastrointestinal endoscopy (EGD):

All patients underwent an upper gastrointestinal endoscopy using a videoscope. All endoscopies were performed by experienced endoscopists, and a grading classification according to AASLD practice guidelines criteria was used**,** (no varices, small varices and large varices). High risky esophageal varices included; small varices with red signs (cherry-red spots, red wale marks, hematocytic spots or diffuse erythema) and large varices with or without red signs[14].

Abdominal ultrasonography:

Patients were prepared for abdominal ultrasound by fasting for eight hours, and then the maximum spleen bipolar diameter was measured in millimeters. While the patient is in the right lateral decubitus position with the left arm raised away from the abdomen, the transducer was placed between the ribs at the level of the ninth intercostal space, and then the patient was asked to take a deep breath and hold it. The transducer was manipulated in the coronal plane or the coronal oblique plane until a suitable longitudinal view of the spleen is obtained, then the length of the spleen was measured between the superior and the inferior borders of the spleen. Gel was applied to the upper abdomen before scanning for better resolution.

Calculation of platelet count /bipolar spleen diameter ratio: Platelet count / spleen bipolar diameter ratio for all patients were calculated.

Grouping of the patients: The patients were retrograde divided into two groups according to esophageal varices: Risky group: included twenty four patients with large risky varices. Non-risky group: included twenty four patients with small non risky varices.

Statistical analysis

Data were analyzed using IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for non-parametric data and mean, standard deviation for parametric data after testing normality using Kolmogrov-Smirnov test. Significance of the obtained results was judged at the 0.05 level and all tests were 2 tailed. Chi-square test was used for categorical variables, to compare between different groups as appropriate. Student-t test was used for parametric quantitative variables, to compare between two studied groups. Mann Whitney test was used for non-parametric quantitative variables, to compare between two studied groups. Binary stepwise logistic regression analysis was used for prediction of independent variables of high risk variceal bleeding. Significant predictors in the Univariate analysis were entered into regression model using forward Wald method. Adjusted odds ratios and their 95% confidence interval were calculated. Receiver Operating Characteristics (ROC) curve was used to detect best cut off point , sensitivity and specificity of the studied marker ten cross tabulation to detect positive and negative predictive values and accuracy.

Results

Table 1 shows that, the two studied groups were matched as regarding age and sex. There was a statistically significant higher mean hemoglobin, WBCS, platelets count and serum albumin among cases with low risky varices versus high risk group while, serum bilirubin, AST and INR were significantly higher among high risk group compared to low risk group. Furthermore, a non-statistically significant difference was found as regarding, MCV, MCHC, serum creatinine and ALT.

Table 2 shows that, patients in low risk group had a significant lower mean abdominal US spleen bipolar diameter and higher mean platelet count/ spleen diameter ratio compared to patients in higher risk group.

Table 3 shows the validity of abdominal US spleen bipolar diameter in differentiating high and low risky varices, where was spleen bipolar diameter equal to or more than cutoff point 138.7 mm had sensitivity of 95.8% and specificity 62.5% in detecting high risky varices, with total accuracy was 79.2%. **Figure 1** illustrates receiver operator characteristics curve for abdominal US spleen

bipolar diameter/mm to differentiate between high and low risk groups with the best cut-off point was 0.94.

Table 4 level and area under ROC of platelet count/spleen diameter ratio in differentiating high and low variceal risk. At cut off point equal to or less than 809.45, the sensitivity and specificity were 95.8% for each to differentiate between high and low risk groups with best cu-off point was 0.99 **Figure 2**

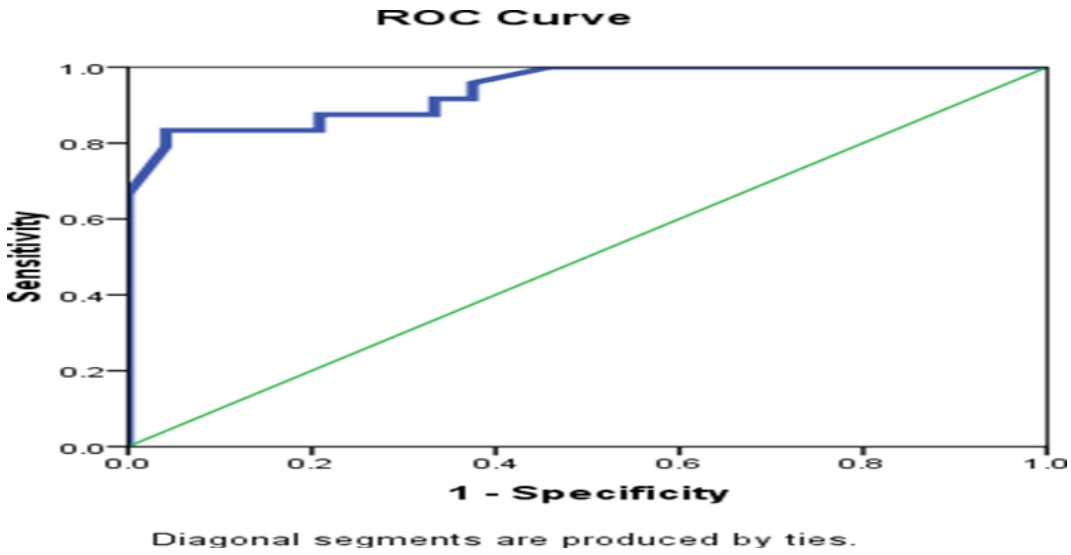

Figure 1. Receiver operator characteristics curve for abdominal US spleen bipolar diameter/mm to differentiate between high and low risk groups.

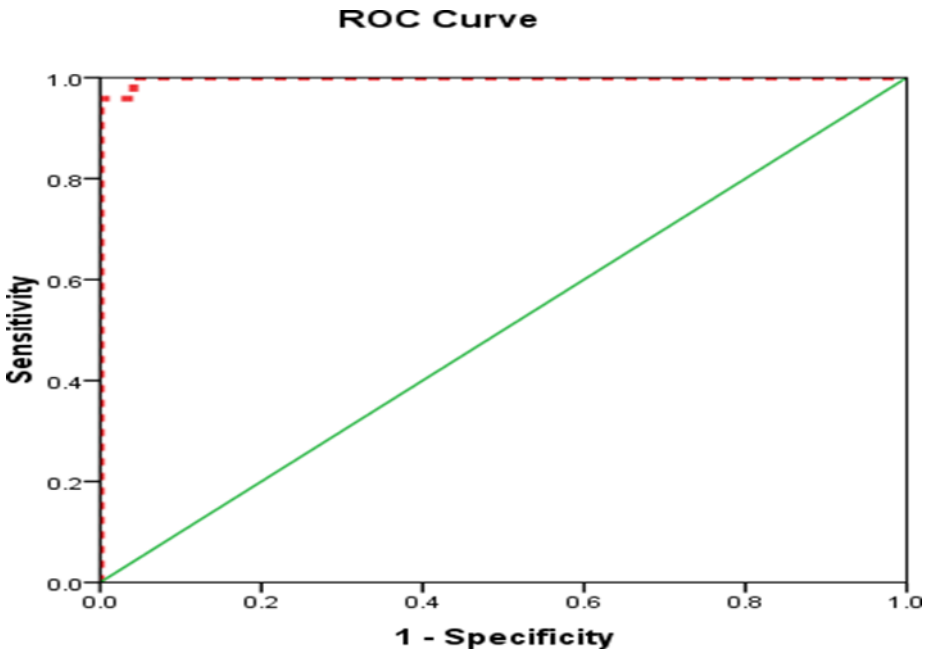

Figure 2. Receiver operator characteristics curve for platelet count/spleen diameter ratio in differentiating high risky group.

Table 1. Demographic and laboratory data of studied group

	Low risky group N=24	High risky group N=24	P value
	Mean ±SD	Mean ±SD	
Age/years	48.42±6.43	51.17±5.99	0.13
Sex: M/F	17/7	16/8	0.75
HB (gm/dl)	11.98±1.12	9.38±1.15	<0.001
MCV	84.29±6.01	80.96±5.80	0.06
MCHC	34.79±3.11	33.92±3.13	0.34
WBCS	6704.2±1716.5	4620.8±1543.8	<0.001
Platelet	151381.0±15.3	136810.0±23.6	<0.001
Serum Creatinine mg/dl	0.98±0.15	1.01±0.21	0.51
Albumin g/dl	3.63±0.54	3.15±0.59	0.004
Serum bilirubin	1.11±0.19	2.20±0.68	<0.001
ALT IU/L	42.17±9.17	41.67±10.18	0.86
AST IU/L	39.54±6.92	47.38±12.81	0.01
INR	1.32±0.27	1.98±0.63	0.001

Table 2: Abdominal US and platelet /spleen diameter ration among studied group.

	Low risky group N=24	High risky group N=24	P value
Abdominal US spleen bipolar diameter Mean ±SD	137.08±14.02	176.12±24.39	<0.001
Platelet count/ spleen diameter ratio Mean ±SD	1157.7±221.31	492.17±189.75	<0.001

Table 3: Validity of Abdominal US spleen bipolar diameter in differentiating high and low risk variceal risk.

	AUC,p	Cut off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Abdominal US/spleen bipolar diameter/mm	0.94 <0.001*	≥138.7	95.8	62.5	71.9	93.8	79.2

AUC: Area Under curve, PPV: Positive predictive value, NPV: Negative predictive value.

Table4. Level and area under ROC of platelet count/spleen diameter ratio in differentiating high and low variceal risk.

	AUC,p	Cut off point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Platelet count spleen diameter ratio	0.99 <0.001*	≤809.45	95.8	95.8	95.8	95.8	95.8

Discussion

This study shows that, patients in low risk esophageal varices (EVs) group had a significant lower mean abdominal ultrasonography spleen bipolar diameter and higher mean platelet count/ spleen diameter ratio compared to patients in higher risk EVs group. Platelet

count/Spleen diameter ratio (PC/SD) is proposed by Giannini et al, is one of the best non-invasive predictor of EVs, moreover, the platelet count/spleen diameter ratio seems to represent an acceptable surrogate for clinically relevant portal hypertension[15]

In accordance with our results, Barrera et al observed that, platelet count was significantly lower among patients with high risk esophageal varices. Also, the author demonstrated that, a larger spleen diameter was observed in high risk esophageal varices patients compared with small non- risk esophageal. Finally, the PC/SD ratio in patients with high risk esophageal varices was significantly lower compared with no high risk esophageal varices[16]. In contrast, Chawla et al. found that Platelet count to spleen diameter ratio has low grade evidence to replace upper gastrointestinal endoscopy as a noninvasive method for varices [17].

Also, Serag et al, showed a statistically significant increase as regarding splenic diameter and significant decrease in mean platelet count and mean PLT/SD ratio in patients with varices versus patients with no varices is 1838.39±707.15 [18].

In this study, the platelet count/spleen diameter ratio at cut off point equal to or less than 809.45 had sensitivity and specificity 95.8% (for each) to differentiate between high and low risk groups with area under ROC 0.99. In accordance with this result Giannini et al, found that platelet count / spleen diameter ratio correlated significantly with the presence and grades of esophageal varices with a cut-off value of 909 and the sensitivity was 100%, and the specificity was 93% [15]. Furthermore, Serag et al, found that platelet count and spleen diameter correlated significantly with the presence and grades of esophageal varices when a cut-off value of 1326.58 was used with a resulting 96.34% sensitivity, 83.33% specificity and 94% accuracy[18]. Interestingly, The PC/SD ratio was validated in a multicenter study with 91.5% sensitivity and 67% specificity and a second validation in a different group of patients was carried out with similar results. However, in a study carried out by Berzigotti et al, no independent association of spleen diameter or platelet count was demonstrated [19].

Furthermore, spleen bipolar diameter at cutoff point ≥ 138.7 mm had sensitivity of 95.8% and specificity 62.5% in detecting high risk variceal bleeding risk with total accuracy was 79.2% and area under ROC 0.94.

Conclusion

Platelet count/spleen diameter ratio can help physicians as a noninvasive predictor of high risk esophageal varices to restrict the use of endoscopic screening only to patients with a high probability of risky esophageal varices. This is especially useful in clinical settings where resources are limited and endoscopic facilities are not present in all areas.

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