

Nonendoscopic predictors of large esophageal varices

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Background

There is a particular need for noninvasive predictors of esophageal varices (EV) that might help reduce medical, social, and economic costs. Our study aimed at studying the noninvasive predictors of EV.

Patients and methods

A total of 100 live cirrhotic patients with compensated liver functions were subjected to full clinical, laboratory, and imaging investigations.

Results

A total of 55% of the studied groups showed EV; 39% showed high-grade EV (grades III, IV, and V). Platelet count and platelet count/splenic diameter ratio have the highest accuracy and specificity for predicting EV, whereas platelet count/splenic diameter ratio has the highest predictive accuracy for the presence of large EV.

Conclusion

The platelet count/splenic diameter ratio can predict the presence of EV and large-sized EV.

Keywords:

liver cirrhosis, platelet count, splenic diameter, varices

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Introduction

The most common clinical manifestations of portal hypertension in patients with liver cirrhosis are esophageal varices (EV) [1]. Large esophageal varices (LEV) are at a higher risk of bleeding, which is possibly because of a higher variceal wall tension. The availability of non-invasive methods for the detection of LEV may help limit the number of endoscopic procedures. This study aimed at assessing the noninvasive predictors of LEV in Egyptian patients with liver cirrhosis.

Patients and methods

Consecutively diagnosed patients with cirrhosis of the liver admitted to the internal medicine department of Kasr El-Aini University Hospital in the period between January 2007 and April 2008 were included in our study after a written informed consent was approved. Individuals presenting with variceal bleeding, portal vein thrombosis, hepatoma, or with a current or a past history of treatment with β -adrenergic receptor blockers, endoscopic variceal sclerotherapy, or band ligation or those with a history of surgical intervention for portal hypertension were excluded from the study. All the patients were subjected to a detailed clinical evaluation, appropriate investigations, imaging studies (conventional ultrasonography and Doppler studies), and upper gastrointestinal endoscopic examination at our center. The diagnosis of cirrhosis was made on the basis of clinical, biochemical, and ultrasonographic findings, investigations of the cause of liver cirrhosis. Platelet count/splenic size ratio was calculated for each patient by dividing the platelet

count/ml by splenic bipolar diameter in millimeters. EV were classified according to Dagradi's grading system [2].

Statistical analysis

Patients' data were analyzed using SPSS 17.0 (SPSS Inc., Chicago, Illinois, USA) for windows 7. Quantitative variables were expressed by mean and SD, compared using an unpaired Student's *t*-test and the Mann-Whitney test. Qualitative variables were expressed by numbers (frequency) and percent compared between groups using the χ^2 -test and exact test when appropriate. An ROC curve was constructed and the optimal cutoff points with accuracy, sensitivity, specificity, PPV, and NPV were calculated. A *P* value was considered to be significant if less than 0.05.

Results

There were 100 eligible liver cirrhosis patients with compensated liver functions, mean age of 54.67 years, ranging between 15 and 75 years; 54% were males. Investigations for the etiology of liver cirrhosis showed that 90% of the studied group were hepatitis C virus (HCV)-infected patients, 4% were hepatitis B virus (HBV)-infected patients, 2% were coinfecting with both HCV and HBV, 1% had Wilson disease, 1% had congenital hepatic fibrosis, and 1% had primary biliary cirrhosis. Upper endoscopic examination was performed, and the results showed that 55% of the studied group of patients had EV; 16% of the studied group was found to have low-risk bleeding EV (grades I and II) and 39% had high-risk bleeding EV (grades III, IV, and V).

Table 1 Factors predicting the presence of esophageal varices and large esophageal varices

Items	Cutoff	T+	F-	T-	F+	Sensitivity	Specificity	Accuracy
Diagnosis of EV								
Hemoglobin	11.5	53	2	12	33	96.36	26.67	65
Platelets	110 444	41	14	40	5	74.55	88.89	81
Albumin	3.3	53	2	21	24	96.36	46.67	74
Bilirubin	2.1	38	17	32	13	69.09	71.11	70
INR	1.4	51	4	18	27	92.73	40	69
Splenic size	16.1	38	17	36	9	69.09	80	74
Splenic vein size	8.5	33	22	30	15	60	66.67	63
Platelet count/splenic diameter ratio	684.7	41	14	39	6	74.55	86.67	80
Child score	B, C	52	3	17	28	94.55	37.78	69
Ascites	+	35	20	28	17	63.64	62.22	63
Diagnosis of high risk EV								
Platelets	98 136	32	7	15	1	82.05	93.75	85.45
Splenic vein velocity	21.1	20	19	15	1	51.28	93.75	63.64
Platelet count/splenic diameter ratio	589.8	34	5	14	2	87.18	87.50	87.27
Child score	B, C	39	0	3	13	100	18.75	76.36

EV, esophageal varices; INR, international normalized ratio.

Univariate analysis of the studied parameters was carried out and it was found that decreased hemoglobin levels, platelet count, albumin levels and platelet count/splenic diameter ratio and increased bilirubin levels, INR levels, splenic size, splenic vein size, Child score B and C, and ascites were significantly associated with the presence of EV. On carrying out logistic regression analysis for the presence of EV using these parameters, they were found to be statistically significant predictors. The platelet count and platelet count splenic size ratio had the highest predictive accuracy and specificity, whereas the hemoglobin and albumin levels had the highest sensitivity. Logistic regression analysis for the presence of LEV showed that platelet count, splenic vein velocity, platelet count/splenic size ratio, and Child score B or C were the only significant predictors, with the platelet count/splenic size ratio having the highest predictive accuracy, the platelet count and splenic vein velocity having the highest specificity, and the Child score B and C having the highest sensitivity.

An ROC curve was constructed and the cutoff values were calculated for each variable; the optimum cutoff point for the platelet count/splenic size ratio for diagnosing EV was 684.7, but this cutoff point was 589.8 for diagnosing LEV (Table 1).

Discussion

There is a particular need for noninvasive predictors of the presence of EV as they might help reduce medical, social, and economic costs. Nevertheless, most of the studies on the noninvasive diagnosis of EV have been carried out in a particular subgroup of patients, that is, patients who were going to be placed on a liver transplantation waiting list, whereas some studies lacked uniformity in EV classification or adequate statistical analysis [1]. Several studies in the past have shown independent parameters such as splenomegaly [2], ascites [3], spider naevi [4], Child's grade [5], platelet count [6,7], prothrombin time/activity, portal vein diameter, platelet count/spleen diameter ratio [8], serum albumin [9], and serum bilirubin [3] as significant

predictors for the presence of EV. Spleen size is becoming increasingly important because both splenomegaly and EV may be related to high portal pressure; also, splenomegaly may increase platelet sequestration and lead to a low platelet count.

The present study was carried out on patients with compensated liver disease and it corroborates the results of earlier studies. Giannini *et al.* [8] proposed that a platelet count/spleen diameter ratio of 909 or less is an accurate noninvasive marker for the presence of EV. This was further validated in a multicenter trial. The study population predominantly included patients with hepatitis C-related cirrhosis. A similar study by Agha *et al.* [10], from Pakistan, made identical observations in the same subset of patients. Sen *et al.* [11] found a platelet count-spleen diameter ratio of 650 or less to be a sensitive noninvasive marker (area under curve of 0.81) in HCV-related cirrhosis.

In our study, univariate analysis showed that platelet count 110 444 or less was associated with the presence of EV in a predominant HCV-related cirrhosis subset, and had the highest accuracy and specificity in predicting EV. Schepis *et al.* [7] made similar observations, platelet count 100 000 or less were predictors for the presence of EV, and recommended that patients should undergo screening upper endoscopy if these findings are present. However, for Doppler ultrasound parameters, they found that portal vein diameter greater than 13 mm was the only significant predictor that was not consistent with our findings as we found that portal vein diameter had no significance (their Doppler parameters included portal vein diameter, mean flow velocity, and congestive index) and they did not consider other parameters, namely, CBC, Child-Pugh score, and liver functions, in their study.

Moreover, in our study, platelet count 98 136 or less also had a high accuracy and specificity in predicting LEV.

Platelet count/splenic size ratio has been found to have the next highest accuracy and specificity in predicting EV in addition to being the most accurate significant predictor of LEV. Gianni *et al.* [8] concluded that the platelet count/spleen diameter ratio may be an effective means for ruling out the presence of EV even in the

longitudinal follow-up of patients. However, Gianni *et al.* [8] showed that the platelet count/spleen diameter ratio could help in differentiating between patients with no EV and those with EV with a cutoff value of 909, which is different from the cutoff value in our study, probably because of the different grading system used in their study. We believe that the use of this ratio is very helpful, and this hypothesis is supported by the fact that from a clinical point of view, the platelet count may decrease for several reasons in patients with chronic liver disease [12].

Thrombocytopenia may occur in patients with portal hypertension by more than one mechanism. Splenic sequestration and antibody-mediated destruction of platelets are known to occur in patients with cirrhosis [13], in addition to the role of thrombopoietin [12], making the cutoff of the platelet count reported in our study different from that reported by other studies carried out on patients with liver cirrhosis with different cause.

Other factors assessed in our study were found to have no statistical significance in the prediction of EV (irrespective of the varices size) including TLC, transaminases level, hepatic vein wave pattern, portal vein blood velocity, and the cause of cirrhosis.

Conclusion

Platelet count was the most accurate and specific method for predicting EV; hemoglobin and albumin levels were the most sensitive, platelet count/splenic size ratio was the most accurate and specific for predicting LEV, and platelet count and CTP class B and C were the most sensitive.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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