PLATELET COUNT/SPLEEN DIAMETER RATIO:  
A NONINVASIVE PARAMETER TO PREDICT 
THE PRESENCE OF ESOPHAGEAL VARICES 

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ABSTRACT 

Introduction: Variceal bleeding is one of the most dreaded complications of cirrhosis because of its 
attendant high mortality. The prevalence of varices in patients with cirrhosis is approximately 60- 
80% and the risk of bleeding is 25-35%. Incidence of first variceal hemorrhage ranges from 20 to 
40% within 2 years. Recurrent bleeding occurs in 30% to 40% of patients within the next 2 to 3 days 
and in up to 60 % within 1 week. Thus, prevention of esophageal variceal bleeding remains at the 
forefront of long-term management of cirrhotic patients. However, subjecting all patients with 
cirrhosis to screening endoscopy may not be cost effective. If patients at low or high risk of having 
esophageal varices (EV) could be identified from easily obtainable clinical variables, a more affordable 
approach for screening would be possible. The study was conducted to identify clinical, biochemical 
and ultrasonographic parameters associated with the presence of esophageal varices in patients with 
compensated cirrhosis. 

Methodology: This is a cross-sectional study of patients aged 20-84 y/o admitted at the FEU-NRMF 
Medical Center and the Chinese General Hospital between January 2002 to July 2004 with a diagnosis 
of cirrhosis based on clinical, biochemical, and/or histopathological data. All patients underwent a 
complete biochemical work-up, gastroscopy and ultrasonographic measurement of spleen bipolar 
diameter. Platelet count/spleen diameter ratio was calculated for all patients, tabulated and analyzed. 

Results: 150 patients underwent blood extractions, ultrasound and upper endoscopy. The prevalence 
rate of EV was 46%. In the study, the authors found out that age, sex, protime, platelet/spleen 
diameter ratio, platelet count and spleen diameter were significantly different among patients with 
or without esophageal varices (NEV), although the platelet count/spleen diameter ratio was the only 
parameter which was independently associated with the presence of EV in a univariate analysis. A 
platelet count/spleen diameter ratio cut off value of <160 was highly predictive in the diagnosis EV 
with a sensitivity of 88.4% (95% CI, 77.9, 94.5) and specificity of 80.2% (95% CI 69.6, 88). Positive 
and negative predictive values were 79.2% (95% CI 68.2, 87.3) and 89% (95% CI 79, 94.8), respectively.
INTRODUCTION

Chronic liver disease generally progresses slowly from hepatitis to cirrhosis, often over 20 to 40 years. Some forms of liver disease are non-progressive or only slowly progressive. Other, more severe forms are associated with scarring and architectural disorganization, which, if advanced, lead to cirrhosis. The scarring causes increased resistance to blood flow through the portal vein leading to ascites, esophageal varices, and increased risk of infection. Portal hypertension, a common complication of cirrhosis, results in the development of collaterals to bypass the increased resistance to flow within the portal bed to return blood to the systemic circulation. Gastrointestinal bleeding is the most severe complication of portal hypertension, and esophageal and gastric varices are by far the most common sources of bleeding in these patients. Thirty percent of patients with compensated cirrhosis and 60% of patients with decompensated cirrhosis have gastroesophageal varices at the time of presentation. Mortality is highest in the first 5 days after the index episode of variceal bleeding and returns to baseline levels by 3 to 4 months. This is the critical window for optimal treatment to improve the survival of variceal bleeders. The rate of early rebleeding translates into an increased risk of mortality. It appears that the rate of growth of varices from small to large in compensated cirrhotic patients is faster than the rate of de novo appearance of varices. Therefore, the presence of esophageal varices (EV) is considered a prognostic indicator and a factor affecting the morbidity and mortality of surgical procedures.

The American College of Gastroenterology (ACG) recommends endoscopic screening to detect varices in patients with cirrhosis with no previous variceal hemorrhage. If initial endoscopy shows no varices, the examination should be repeated at 2-3 year intervals and at 1-2 year intervals in patients with small varices so as to evaluate its development or progression.

In order to reduce the increasing burden of invasive procedures, some studies have attempted to identify noninvasive parameters to predict the presence of esophageal varices. Overall, the most common finding of these studies was that parameters directly linked to portal hypertension such as splenomegaly and decreased platelet count were predictors of the presence of esophageal varices. In patients with chronic liver disease, several factors other than portal hypertension such as myelotoxic effects of alcohol or hepatitis, shortened platelet mean lifespan and decreased thrombopoietin production may decrease platelet count. On the other hand, the presence of splenomegaly in cirrhotic patients is likely the result of vascular disturbance. The study was conducted to determine the association of esophageal varices and platelet count/spleen diameter ratio in patients with compensated cirrhosis.

METHODOLOGY

This is a cross-sectional study of patients with a diagnosis of cirrhosis based on clinical, biochemical, and/or histopathological data to determine the association of esophageal varices and platelet count/spleen diameter ratio. The study group consisted of patients aged 20-84 years old diagnosed to have cirrhosis who were admitted at the FEU Medical Center or the Chinese General Hospital from January 2002 to July 2004. Patients were asked to sign an informed consent prior to enrollment in the study.

Patients were excluded if they had any of the following:

1. hepatocellular carcinoma detected by ultrasonography and/or elevated alpha-feto protein (more than 10 times the upper normal limit of normal)
2. primary hematologic disorders
3. active gastrointestinal bleeding on admission
4. previously known gastrointestinal bleeding
5. taking drugs for primary prophylaxis of variceal bleeding
6. taking alcohol less than 6 months before enrollment
7. history of parenteral drug addiction
8. history of sclerosis or band ligation, trans-
jugular intrahepatic portosystemic stent shunt
9. history of surgery for portal hypertension
10. other diseases with life expectancy of less than one year
11. unstable medical condition

At entry, all patients underwent a complete physical examination, laboratory tests which included prothrombin activity, total bilirubin, and platelet count, upper gastrointestinal endoscopy and ultrasonography. Spleen diameter was determined through ultrasonography and was read by one reader. Minimum spleen bipolar diameter was expressed in millimeters (mm). All endoscopy were performed in a single endoscopy center using a video endoscope and esophageal varices were identified by two gastroenterologists who were unaware of the clinical, laboratory and ultrasonographic findings using a consistent single classification. Platelet count/spleen ratio was calculated for all patients.

Definition of Terms
1. Compensated cirrhosis — patients without ascites and/or hepatic encephalopathy
2. Splenomegaly — diameter of >100mm by ultrasound
3. Normal platelet count: 150-450 x 10^3/ul
4. Esophageal varices were graded as absent or present and classified using the small and large classification
   Small: varices in the lower 3rd of the esophagus and occupied less than a third of the esophageal lumen or minimally protrude into the lumen but did not flatten with air insufflation
   Large: varices in the lower 3rd of the esophagus that occupied at least a third of the lumen or protrudes into the esophageal lumen and touch each other (presence of confluence) and did not flatten with air insufflation

RESULTS
One hundred-fifty (150) patients were enrolled in the study. One hundred-six (106) patients were men and 44 were women. Using endoscopy, esophageal varices were detected in 69 of the 150 patients examined (46%). The mean age was 51 years among those with esophageal varices and 57 years among those without esophageal varices. Table 1 shows the main variables of the 150 patients included in the univariate comparison of variables between those with and without esophageal varices. Cirrhosis was caused by alcohol ingestion in 135 patients while the cause was hepatitis B in 15 patients. By ultrasonography, 69 were found to have splenomegaly while 81 were found to have normal spleen dimensions. Patients with esophageal varices had significantly lower prothrombin activity and platelet count compared to those without. Spleen diameter was greater while platelet count/spleen diameter ratio was lower in patients with esophageal varices.

Using the platelet count/spleen diameter ratio cut off determined by Giannini et al, a 91.3% prevalence adjusted positive predictive value and a 74% prevalence adjusted negative predictive value for the presence of esophageal varices was obtained. However, using the said cut-off resulted in a 60.9% (95% CI 48.4, 72.2) sensitivity and a 95% (95% CI 87.2, 98.4) specificity. Using the receiver operating characteristic (ROC) curve to assess the platelet count/spleen diameter ratio cut off in this study (Figure 1), a cut-off of 160 was noted to give the best sensitivity and specificity of 88.4% (95% CI 77.9, 94.5) and 80.2% (95% CI 69.6, 88.0), respectively. Using this cut-off, the prevalence adjusted positive and negative predictive values were 79.2% and 89%, respectively. Moreover, accuracy of this platelet/spleen diameter ratio cut off as evaluated by the kappa coefficient was 0.681 (Table 2). Both spleen diameter and platelet count cut-off with the best sensitivity and specificity for a diagnosis of esophageal varices that were identified by means of ROC curves had prevalence adjusted positive and negative predictive values that were lower than those of the platelet count/spleen diameter ratio. It was determined therefore that a different cut-off of < 160 for the platelet count/spleen diameter was better than the cut-off determined by the previous study when applied to this population.
TABLE 1. Main characteristics according to the presence of esophageal varices.

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>NEV</th>
<th>EV</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>49 / 32</td>
<td>57 / 12</td>
<td>0.005</td>
</tr>
<tr>
<td>Age (y)</td>
<td>57</td>
<td>51</td>
<td>0.02</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>6.7 + 11.3</td>
<td>7.4 + 10.8</td>
<td>NS</td>
</tr>
<tr>
<td>Prothrombin activity</td>
<td>85.3 + 16.7</td>
<td>73.5 + 20.2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Platelet count (n/mm³)</td>
<td>202.2 + 84.2</td>
<td>100.33 + 40.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Spleen diameter (mm)</td>
<td>88.6 + 17.4</td>
<td>121.5 + 16.8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Platelet count / spleen ratio</td>
<td>240.9 + 119.0</td>
<td>86.3 + 43.1</td>
<td>&lt;.000</td>
</tr>
</tbody>
</table>

NVE: no esophageal varices; EV: esophageal varices
Data are ± SE: standard of error

TABLE 2. Platelet count, spleen diameter and platelet count/spleen diameter ratio of 150 patients according to the presence and absence of esophageal varices

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>NEV</th>
<th>EV</th>
<th>P value</th>
<th>Cut off</th>
<th>Kappa coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count (n/mm³)</td>
<td>202.235</td>
<td>100.333</td>
<td>&lt;.0001</td>
<td>&lt; 115</td>
<td>0.63</td>
</tr>
<tr>
<td>Spleen diameter (mm)</td>
<td>88.62</td>
<td>121.46</td>
<td>&lt;.0001</td>
<td>&gt; 88</td>
<td>0.507</td>
</tr>
<tr>
<td>Plt ct /spleen ratio</td>
<td>240.87</td>
<td>86.267</td>
<td>&lt;.0001</td>
<td>&lt; 160</td>
<td>0.681</td>
</tr>
</tbody>
</table>

NVE: no esophageal varices; EV: esophageal varices
Parameter cut off were identified by means of ROC curves

FIGURE 1A
Receiver operating characteristic curve using spleen diameter
DISCUSSION

Due to the increasing prevalence of chronic liver diseases, variceal hemorrhage is associated with significant morbidity, mortality, and health care costs. Numerous studies have demonstrated the efficacy of pharmacotherapy for primary prevention of variceal bleeding in patients with high-risk varices indicating the importance of screening for the presence of esophageal varices. Therefore, there is a particular need for non-invasive predictor for the presence of esophageal varices as that might ease the medical, social and economic burden of the disease.

Based on the present study it was found that a simple non-invasive technique may be used as a reliable predictor for the presence of esophageal varices among cirrhotic patients. The platelet count/spleen diameter ratio was deemed to be the appropriate parameter to be used as splenomegaly is implicated in thrombocytopenia of cirrhosis with spleen size being inversely correlated with platelet count. The use of this ratio normalizes platelet count to splenic sequestration since platelet count alone maybe misleading and cannot be solely attributed to portal hypertension. Likewise, the measurement of the spleen bipolar diameter using ultrasonography is easily obtainable, reproducible and non-invasive and is routinely performed on patients with cirrhosis. The focus was on the presence of any esophageal varices whether it be small or large as this is the first step in the diagnostic/prognostic work-up of
cirrhotic patients which later will prove important in the decision-making process. Moreover, analysis of the presence and absence of esophageal varices prevents misinterpretation of data and allows generalization of the results.

Although this study had a small sample population, based on the inferred results, the use of platelet count/spleen diameter ratio showed a good result in discriminating absence or presence of esophageal varices. From the statistical standpoint, it is the only independent parameter associated with the presence of esophageal varices. It should be noted that even among patients with compensated cirrhosis, platelet count/spleen diameter ratio were significantly different between those with and without esophageal varices. The use of platelet count/spleen diameter ratio would have avoided unnecessary endoscopy in all patients without running a significant risk of missing the presence of esophageal varices. The use of this strategy of using non-invasive tests would necessarily lower the cost of management of cirrhotic patients since no additional expense would be entailed with the use of ultrasonography as cirrhotic patients usually undergo annual/biannual abdominal ultrasonography as part of the surveillance program for hepatocellular carcinoma. As the yearly incidence of esophageal varices in patients with cirrhosis is approximately 5%, it is felt that the use of these non-invasive diagnostic modality would provide an affordable alternative to detection of esophageal varices among cirrhotic patients.

REFERENCES


7. Garcia tsao et al Predicting the presence of significant portal hypertension and varices in cirrhotic patient, Hepatol 1997;26:360.

