**ABSTRACT**

**Aim:** recent guidelines recommend that all cirrhotic patients without previous variceal hemorrhage undergo endoscopic screening to detect esophageal varices. The aim of this study is to evaluate clinical, laboratory and ultrasound parameters to detect esophageal varices.

**Methods:** this is a cross sectional study. Forty seven consecutive cirrhotic patients without history of variceal hemorrhage underwent upper endoscopy. Physical examination, laboratory and ultrasonography to find portal vein diameter and anteroposterior splenic measurement of each patient were also recorded.

**Results:** esophageal varices was detected in 36 of the 47 patients (76.6%). Using bivariate analysis we found that a platelet count of 82,000/ul (90.9% sensitivity; 41.7% specificity), portal vein diameter of 1.15 cm (75% sensitivity; 54.5% specificity) and an anteroposterior splenic measurement of 10.3 cm (83.3% sensitivity; 63.6% specificity) were predictive factors for esophageal varices in liver cirrhosis.

**Conclusion:** our data show that platelet count, portal vein diameter and anteroposterior splenic measurement can be used as non invasive parameters to detect esophageal varices in cirrhotic patients.

**Key words:** liver cirrhosis, esophageal cirrhosis, non-invasive parameters.

**INTRODUCTION**

Liver cirrhosis is a chronic liver disease characterized by inflammation, necrosis and regeneration processes with diffuse increase in connective tissue (fibrosis) and formation of nodules around the regenerating liver parenchyma.

Most common causes of death in liver cirrhosis are hemorrhage from esophageal varices, spontaneous bacterial peritonitis, septicemia, liver failure, hepatic encephalopathy, renal failure and hepatocellular carcinoma.1,2

Liver cirrhosis with portal hypertension can cause bleeding in the upper gastrointestinal tract due to rupture of esophageal varices. Data from abroad demonstrate that 50% of patients with liver cirrhosis will develop portal hypertension and esophageal varices.3,4,5 The prevalence of esophageal varices on liver cirrhosis is 50%-80%, while the mortality rate due to esophageal variceal bleeding is 17%-57%. The mortality rate from first-time bleeding is 40%.6

The prevalence of gastrointestinal bleeding due to rupture of esophageal varices reported by Djojoningrat was 70.2% in 1998 at Cipto Mangunkusumo Hospital Jakarta, with a mortality rate of 26.6%.7

The gold standard examination to establish the diagnosis of esophageal varices is endoscopy. However, not all healthcare centers, especially in rural areas, have such a facility. In addition, the competency of healthcare providers (doctors) in those places to perform endoscopy is limited. The available method in rural area is laboratory examination and ultrasonography.

Several studies have been performed to identify predictive factors for esophageal varices.

Fook-Hong et al.8 recommends endoscopic screening in liver cirrhosis in the presence of thrombocytopenia (<150,000/ul) or ascites.

The AASLD 1998 recommends endoscopic screening in patients with Child B and Child C liver cirrhosis. For Child A without portal hypertension, endoscopic screening is recommended only in the presence of thrombocytopenia of less than 140,000/ul, portal vein diameter of over 13 mm, or portosystemic collaterals on ultrasound examination.9,10

Schepis F et al10 recommends endoscopic examination in liver cirrhosis with prothrombin activity below 75%, platelet count is less than 100,000/UL, and...
portal vein diameter exceeds 13 mm on ultrasound examination. Zaman et al., in their study, found that a platelet count less than 88,000/μL significantly predicts the development of esophageal varices.

Chalasani et al., in a multivariate analysis found thrombocytopenia (< 88,000/μL) and splenomegaly to be strong predictors of esophageal varices.

Giannini et al., in their study in Italy in 2003, found a cut off point of platelet count ≥ 112,000 (p = 0.0001; 95% CI 0.815 – 0.928), splenic diameter > 121 mm (p = 0.0001; 95% CI 0.850 – 0.951).

This study was aimed to identify simple, non-invasive examination parameters to predict the presence of esophageal varices.

METHODS

The design of this study was cross sectional. The study subjects were patients with liver cirrhosis based on clinical, laboratory, ultrasound, and/or liver biopsy findings at the hepatology outpatient unit of Cipto Mangunkusumo Hospital who have never suffered from variceal bleeding. Subjects were selected consecutively from January 2003 to August 2003, and 47 patients have been included.

The exclusion criteria were contraindications for endoscopy, malignancy, and refusal to participate in the study.

The confidence interval was set at 95%. All eligible patients were briefed on the study procedure.

Physical laboratory examination for platelet count, albumin level, total bilirubin, prothrombin time, as well as ultrasound examination were performed to assess ascites, portal vein diameter, and anteroposterior splenic measurements.

The subjects were classified according to Child classification. Esophageal varices was assessed in accordance with the OMED classification as follows: 12

• 1st Degree: Variceal bulging almost undetectable, only demonstrated using the valsava maneuver
• 2nd Degree: Variceal bulging up to one fourth of the esophageal lumen
• 3rd Degree: Variceal bulging up to one half of the esophageal lumen
• 4th Degree: Variceal bulging of over half of the esophageal lumen.

Data were collected in the case record form and was then tabulated and processed using a personal computer using SPSS for windows 11.5. Descriptive data were presented in the form of text, tables, and figures. Study results were presented as mean and standard deviation. Analysis of quantitative data was performed using T-test, while qualitative data were analyzed using Chi square. A p value of < 0.05 was established as statistically significant. The cut-off point was determined using the receiver operator characteristic curve.

RESULTS

From January to August 2003, 47 patients with liver cirrhosis were found to meet the study criteria, comprising 29 (62%) males and 18 (38%) females. The age ranged from 22 to 79 years with a mean age of 56.6 ±12.3 years SD. The population distribution based on age can be found in Figure 1.

Based on Child classification, the 47 study subjects were classified as follows: 28 subjects (59.6%) Child A, 15 subjects (31.9%) Child B, and 4 subjects (8.5%) Child C.

Table 1. General Characteristics of The Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>29</td>
<td>62</td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>38</td>
</tr>
<tr>
<td>Child Classification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child A</td>
<td>28</td>
<td>59.6</td>
</tr>
<tr>
<td>Child B</td>
<td>15</td>
<td>31.9</td>
</tr>
<tr>
<td>Child C</td>
<td>4</td>
<td>8.5</td>
</tr>
<tr>
<td>Etiology of liver cirrhosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B (+)</td>
<td>17</td>
<td>36.2</td>
</tr>
<tr>
<td>Hepatitis C (+)</td>
<td>19</td>
<td>40.4</td>
</tr>
<tr>
<td>Hepatitis B and C (+)</td>
<td>7</td>
<td>14.9</td>
</tr>
<tr>
<td>Hepatitis B and C (-)</td>
<td>4</td>
<td>8.5</td>
</tr>
<tr>
<td>Esophageal varices (+)</td>
<td>36</td>
<td>76.6</td>
</tr>
<tr>
<td>(-)</td>
<td>11</td>
<td>23.4</td>
</tr>
</tbody>
</table>
The etiology of liver cirrhosis in the subjects of this study were: hepatitis B virus marker (+) was found in 17 subjects (36.2%), hepatitis C virus marker (+) in 19 subjects (40.4%), hepatitis B and C virus marker (+) in 7 subjects (14.9%), while no hepatitis B or C virus markers were detected in 4 subjects (8.5%). Table 1 shows the general characteristics of study subjects.

To see the correlation between independent variables and esophageal varices, Chi Square analysis was performed for qualitative variables while T-test was performed on quantitative variables. The results of these analyses can be found in Table 2.

The results of free variable analysis show that significant difference was observed for platelet count, portal vein diameter, and splenic measurement (mm).

Table 3 demonstrates Child classification with incidence of esophageal varices among the 47 study subjects. Esophageal varices was found in 36 subjects (76.6%) out of 47 study subjects, comprising 19 Child A subjects from 28 subjects (67.9%), 13 Child B subjects out of 15 subjects (86.7%), and 4 Child C subjects (100%). Eleven subjects (23.4%) were not found to have esophageal varices, comprising 9 Child A subjects and 2 Child B subjects.

Table 4 demonstrates Child classification and degree of esophageal varices in 36 study subjects, 1st degree esophageal varices was found in 10 subjects (27.8%), 2nd degree in 23 subjects (63.9%), and 3rd degree in 3 subjects (8.3%).

The cut off point was then calculated for the three variables with p value less than 0.05 from analysis (platelet count, portal vein diameter, as well as anteroposterior splenic measurement) based on the ROC curve, as found in Figures 2, 3 and 4.

From the ROC curves, the specificity and sensitivity of each cut off points can be seen. (Table 5)
DISCUSSION

Several similar studies to predict esophageal varices have been conducted abroad, such as by Fook Hong in Hongkong\(^8\), Schepis\(^10\) and Chalasani\(^11\) in Italy, as well as Zaman\(^4\) in the United States. These researchers used different inclusion and exclusion criteria, but they analyzed the same parameters.

The general characteristics of the subjects of this study (Table 1) are as follows: 29 males (62%) and 18 females (38%), which is not far from the results of the study by Fook Hong et al\(^8\), who found 38 males (66%) and 15 females (34%), and the study by Schepis et al\(^10\) who found 94 males (66%) and 49 females (34%). The age distribution of study subjects found in the fifth decade (Figure 1) was not much different from previous studies.

Based on Child Classification, Fook Hong et al\(^8\) in Hongkong found the following results: Child A 26%, Child B 55% and Child C 19%. Zaman et al\(^4\) in the United States found Child A 34%, Child B 51% and Child C 15%, while Chalasani et al\(^11\) in Italy found Child A 22%, Child B 48% and Child C 30%. This study found Child A 59.6%, Child B 31.9%, Child C 8.5%. The low number of cirrhotic patients with Child C in this study subject was because patients with history of previous variceal hemorrhage or other complications are not included in this study.

The etiology of liver cirrhosis among our study subjects were: 17 patients positive hepatitis B virus marker (36.2%), 19 patients positive hepatitis C virus marker (40.4%), 7 patients positive hepatitis B and C virus markers (14.9%), while 4 were not found with hepatitis B or C virus marker (8.5%). The same findings were found in the study by Schepis et al.\(^10\)

Fook Hong et al,\(^8\) on the other hand found hepatitis B as the most common cause of liver cirrhosis (62%). A multi-center study of 711 patients conducted in Italy and the Netherlands by the North Italian Endoscopic Club (NIEC)\(^13\) found that 53% of liver cirrhosis was due to alcohol-induced, and 47% due to virus.

In this study, we assessed for hepatitis B and C virus markers to identify the etiology of liver cirrhosis. The aim of conducting hepatitis B and C virus markers in this study is to compare the etiology of liver cirrhosis in this study with that of previous studies. To determine the etiology of liver cirrhosis other than hepatitis B and C, further assessments are needed, which were not conducted in this study due to financial limitations.

The endoscopic findings in this study were as follows: 36 patients (76.6%) were found to have esophageal varices of various degrees in line with OMED classifications, while 11 patients (23.4%) without esophageal varices. Chalasani et al,\(^11\) in their study found esophageal varices in 70%, while Zaman et al\(^4\) found 68%. The prevalence of esophageal varices in liver cirrhosis ranges around 50% and 80%,\(^6\) so that the endoscopic findings in this study is still within this range.
The high prevalence of esophageal varices on endoscopy probably due to the late of patients to seek treatment after signs and symptoms of portal hypertension were present.

Up to now, endoscopy has still been the gold standard modality to identifying esophageal varices. In this study, all of the subjects, 4 subjects with Child C were found to have esophageal varices; out of 15 Child B subjects, 13 subjects were found with esophageal varices (86.7%). Out of 28 subjects with Child A, 19 subjects were found with esophageal varices (67.9%). To determine the proportion of the incidence of esophageal varices in each Child classification, well-distributed samples should have be collected.

The results of analysis using T-test for quantitative variables and Chi Square for qualitative variables found the following variables to be significant for esophageal varices (p < 0.05) i.e.: platelet count (p = 0.003), portal vein diameter (p = 0.03), and anteroposterior splenic measurement (p = 0.007).

The mean platelet count in the group with varices was 101,000 ± 52,000/ul, while that of the group without esophageal varices was 161,000 ± 62,000/ul, with ± 60,000/ul difference in mean value. A similar finding was reported by Fook Hong et al, with a mean value of 110,000 ± 60,000/ul among those with esophageal varices and 160,000 ± 90,000/ul in the group without esophageal varices, with a difference of 50,000/ul in mean value. Thrombocytopenia in liver cirrhosis was due to microcirculation changes and hypersplenism related to portal hypertension as well as inadequate thrombopoietin synthesis.

On ultrasound examination, anteroposterior splenic measurement in the group with esophageal varices was 12.3 ± 2.39 cm, while in the group without esophageal varices the anteroposterior splenic measurement was 10.1 ± 1.74 cm. Almost similar findings were found in the study in Hongkong by Fook Hong et al, with a mean anteroposterior splenic measurement of 11.7 ± 3.2 cm in the group with esophageal varices, and 10.2 ± 2.8 cm in the group without esophageal varices. Previous data from the Division of Hepatology of Cipto Mangunkusumo Hospital in 1984 by Pridady found an anteroposterior splenic measurement of 7.6 ± 1.2 cm in normal subjects and 12.7 ± 2.1 cm among patients with liver cirrhosis. Schepis et al in Italy found a mean anteroposterior splenic measurement of 16.3 ± 2.7 cm in the group with esophageal varices, and 13.9 ± 2.5 cm in the group without esophageal varices. This difference in splenic size may be due to racial, genetic, and anatomical differences.

The mean portal vein diameter in the group with esophageal varices was 12.6 ± 2.7 mm, while that in the group without esophageal varices was 10.6 ± 2.2 mm, with a difference of mean value of 2 mm. Pridady found a mean portal vein diameter of 7 ± 1 mm among normal subjects and 12 ± 2 mm among cirrhotic patients. Fook Hong et al, in their study, found a portal vein diameter of 1.15 ± 0.24 cm among patients with esophageal varices, and 1.05 ± 0.26 cm among patients without esophageal varices. Schepis et al found a portal vein diameter of 13.82 ± 2.1 mm, among patients with esophageal varices, and 12.33 ± 2.04 mm among patients without esophageal varices.

On endoscopy, 36 patients were found with esophageal varices. After adjustment to the criteria from the British Society of Gastroenterology, 10 subjects were found with first degree esophageal varices, 23 with 2nd degree, and 3 subjects with 3rd degree esophageal varices. Referring to the primary prevention algorithm in esophageal varices bleeding, 26 (72.2%) of the subjects in this study required primary preventive management for esophageal varices bleeding.

Based on statistical analysis, we tried to obtain a cut off point for the variables with a p value of less than 0.05, which are platelet count, portal vein diameter, and anteroposterior splenic measurement, using the receiver operator characteristic curve. This was done because at the Division of Hepatology, there has still been no cut off point for any of these variables. In Europe and the United States, they use a cut off point of 1.3 mm for portal vein diameter, 12 mm for anteroposterior splenic measurement, and a variation for platelet count, from 80,000 to less than 150,000. In this study, the cut off point for platelet count was 82,000/ul, with a 90.9% sensitivity and 41.7% specificity; 11.5 mm for portal vein diameter, with a sensitivity of 75% and a specificity of 54.5%, 103 mm for anteroposterior splenic measurement with a sensitivity of 83.3% and a specificity of 63.6%.

CONCLUSION

In this study, the non-invasive parameters that can be used to detect esophageal varices in liver cirrhosis are: platelet count of equal to or less than 82,000/ul, portal vein diameter of 11.5 mm or more, and an anteroposterior splenic measurement of 103 mm or more.

The cut off value in this study can be used as reference to detect esophageal varices, until more ideal studies with a large sample size with well-distributed Child classification is performed.

Further studies need to be performed to determine the degree of esophageal varices and obtain a cut off
point in the degree of esophageal varices that requires prevention of esophageal varices bleeding.

REFERENCES


