Study of the Right Liver Lobe Size/albunin Ratio as a Noninvasive Predictor of Oesophageal Varices Compared to: Spleen Size, Platelet count and Platelet count/spleen Diameter Ratio in Post Hepatitis C Virus Liver Cirrhosis in Egypt

Serag Esmat
Department of Internal Medicine, Faculty of Medicine, Cairo University. Cairo, Egypt
seragesmat@hotmail.com

Abstract: Background and aim: Hepatic C Virus (HCV) is considered the most common aetiology of chronic liver disease in Egypt. Portal hypertension is a major complication of liver cirrhosis, and leads to the development of portosystemic shunts. Oesophageal varices are the most important among these shunts. Bleeding from oesophageal varices is the most serious complication of cirrhosis, with a high risk of death. The prevention of variceal bleeding is very important, non-selective beta blockers and prophylactic band ligation decrease the risk of bleeding by 50%. The current guide lines recommend screening of all cirrhotic patients by endoscopy, to identify patients at risk of bleeding so prophylactic treatment should be started to them. But repeated endoscopic examinations are unpleasant for patients, and carries high cost impact and more burden on endoscopic units, while only 50% of cirrhotic patients have esophageal varices, and up to 30% have large varices. For these reasons many non-invasive predictors for the presence and size of varices have been studied. The aim of this study to evaluate prospectively the right liver lobe size /albumin ratio and to compare it with spleen size, platelet count and platelet count/spleen diameter ratio as noninvasive predictors of oesophageal varices in post hepatitis C virus liver Cirrhosis in Egypt. Patients and methods: This prospective study included one hundred patients with post hepatitis C virus liver Cirrhosis. All studied subjects underwent a detailed history taking, clinical examination and a biochemical workup, including total bilirubin, aspartate aminotransferase, alanine aminotransferase, serum albumin, prothrombin activity, complete blood count and viral markers for hepatitis C and hepatitis B viruses. Child-Pugh score was calculated for all patients. An upper gastrointestinal endoscopy and abdominal ultrasound were performed for all patients. The platelet count to spleen diameter ratio and the right liver lobe to albumin ratio were calculated. Results: All the 4 predictors showed high statistically significant correlation with the presence and the grade of oesophageal varices (P values <0.001) Among the 4 noninvasive predictors the platelet count/spleen diameter ratio gave the highest accuracy at a cut-off value of 1326.58 (sensitivity 96.34% and specificity 83.33%) followed by the RT liver lobe/albumin concentration ratio at a cut-off value of 44.2 (sensitivity 91.46% and specificity 77.78%) followed by the spleen size at a cut-off value of 131.5mm (sensitivity 90.24% and specificity 83.33%) then lastly the platelet count at a cut-off value of 131000/mm$^3$ (sensitivity 84.15% and specificity 83.33%).

1. Introduction:

Egypt has a very high prevalence of hepatitis C virus (HCV) and a high morbidity and mortality from chronic liver disease(1). HCV is considered the most common aetiology of chronic liver disease in Egypt, where prevalence of antibodies to HCV (anti-HCV) is 10-fold greater than in the United States and Europe (2).

Portal hypertension is a major complication of liver cirrhosis, and leads to the development of portosystemic shunts. Oesophageal varices are the most important among these shunts due to its clinical effects and play a major role in transforming the disease from a pre-clinical to a clinical phase. Longitudinal studies have shown that oesophageal and/or gastric varices eventually develop in all cirrhotic patients (3,4) and that once they have developed they tend to increase in size and to bleed (4). The yearly rate of development of new varices is about 5–10% (3,5); the rate of growth of varices from small to large ranges between 5% and 30% in different studies (5–8). Bleeding from oesophageal varices is the most serious complication of cirrhosis, with a high risk of death (9). The mortality from each episode of variceal bleeding is 17%–57% (4, 10, 11). On endoscopic examination the presence of red spots on the varices equals high risk of bleeding which is also related to the size of varices (12, 13).
The prevention of variceal bleeding is very important, non-selective beta blockers and prophylactic band ligation decrease the risk of bleeding by 50% (14,15). It is recommended that all cirrhotic patients should undergo endoscopic screening for the presence of varices (16–21), patients who have large or medium sized varices should be treated to prevent bleeding.

Patients who don’t have varices and with compensated cirrhosis should repeat endoscopy every 2-3 years, and every 1-2 years for those with small varices (17). It is also recommended for patients with decompensated cirrhosis to repeat endoscopy every 1 year even if there is no varices (17,19). But repeated endoscopic examinations are unpleasant for patients, and carries high cost impact and more burden on endoscopic units, while only 50% of cirrhotic patients have esophageal varices, and up to 30% have large varices. For these reasons many non-invasive predictors for the presence and size of varices have been studied.

This study attempts to evaluate prospectively the right liver lobe size /albumin ratio and to compare it with spleen size, platelet count and platelet count/spleen diameter ratio as non-invasive predictors of esophageal varices in post hepatitis C virus liver Cirrhosis in Egypt.

2. Materials and methods:

This prospective study included one hundred patients with post hepatitis C virus liver Cirrhosis who were under investigations and treatment at the Gastroenterology & Hepatology outpatient clinics or those who were admitted to the Internal Medicine departments of the Cairo university hospitals.

Diagnosis of cirrhosis was based on physical findings, laboratory investigations and imaging findings. Patients who previously underwent injection sclerotherapy, band ligation, surgery for oesophageal varices, and those who were receiving beta blockers were excluded from the study. All patients with liver cirrhosis due to causes other than HCV were also excluded.

All studied subjects underwent a detailed history taking, clinical examination and biochemical workup, including total bilirubin, aspartateaminotransferase, alanine aminotransferase, serum albumin, prothrombin activity, complete blood count and viral markers for hepatitis C and hepatitis B viruses. Child-Pugh score was calculated for all patients using the 5 parameters (ascites, albumin, bilirubin, prothrombin activity and encephalopathy) (22). An upper gastrointestinal endoscopy and abdominal ultrasound were performed in all patients.

The right liver lobe diameter in the midclavicular line and the maximum spleen bipolar diameter were measured and the values were recorded. The platelet count to spleen diameter ratio and the right liver lobe to albumin ratio were calculated.

All endoscopies were performed in a single endoscopy unit by an experienced endoscopist and a grading classification I – IV was used (23). Grade I was used for varices in the level of mucosa, grade II for varices smaller than 5 mm filling less than 1/3 of the oesophageal lumen, grade III for varices larger than 5 mm filling more than 1/3 of the oesophageal lumen and grade IV for varices occupied more than 2/3 of oesophageal lumen.

All the data were recorded, analyzed and correlated.

Data were statistically described in terms of range, mean ± standard deviation (± SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney U test for independent samples when comparing 2 groups and Kruskal Wallis analysis of variance (ANOVA) test with Mann Whitney U test for independent samples as post hoc multiple 2-group comparisons when comparing more than 2 groups. For comparing categorical data, Chi square (χ²) test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms sensitivity, specificity, +ve predictive value, -ve predictive value, overall accuracy, the likelihood ratio of a positive test and the likelihood ratio of a negative test. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results:

48 men and 52 women were included in the study, all with post HCV liver cirrhosis. The main clinical characteristics of all patients are shown in table 1.

The mean values of platelet (PLT) count, spleen diameter, PLT count/spleen diameter ratio and the right liver lobe diameter/albumin concentration ratio were correlated to the presence and grade of varices and they all highly significantly correlated to the presence and grade of varices as shown in table 2 and table 3.

The sensitivity, specificity and accuracy of PLT count, spleen diameter, PLT count/spleen diameter and splenomegaly were compared to the presence and grade of varices. The correlation of these parameters with the presence and grade of varices is shown in table 4.
diameter ratio and the right liver lobediameter/albumin concentration ratio as noninvasive predictors of oesophageal varices were studied by applying the ROC curve to detect the cut off values with the best sensitivity and specificity.

Among the 4 noninvasive predictors the platelet count/spleen diameter ratio gave the highest accuracy at a cut-off value of 1326.58 followed by the RT liver lobe/albumin concentration ratio at a cut-off value of 44.2 followed by the spleen size at a cut-off value of 131.5mm then lastly the platelet count at a cut-of value of 131000/mm³ as shown in table 4 and figures 1-5.

Table 1: showing the patients clinical characteristics

<table>
<thead>
<tr>
<th>Main clinical characteristics of all patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
</tr>
<tr>
<td>Gender (M/F)</td>
</tr>
<tr>
<td>Age (mean ±SD)</td>
</tr>
<tr>
<td>Age (range)</td>
</tr>
<tr>
<td>Child class.(A/B/C)</td>
</tr>
<tr>
<td>Varices present (yes/no)</td>
</tr>
<tr>
<td>Grade of varices(I/II/III/IV)</td>
</tr>
<tr>
<td>Varices type (small/large)</td>
</tr>
<tr>
<td>Mean PLT count,mm³ (mean ±SD)</td>
</tr>
<tr>
<td>Mean spleen diameter, mm (mean ±SD)</td>
</tr>
<tr>
<td>Mean PLT count/spleen ratio(mean ±SD)</td>
</tr>
<tr>
<td>Mean right liver lobe diameter, mm (mean ±SD)</td>
</tr>
<tr>
<td>Mean albumin concentration,gm/dl (mean ±SD)</td>
</tr>
<tr>
<td>Mean right lobe/ albumin ratio (mean ±SD)</td>
</tr>
</tbody>
</table>

Table 2: Correlation between all parameters with and without varices

<table>
<thead>
<tr>
<th>Varices presence</th>
<th>PLT count</th>
<th>Spleen diameter</th>
<th>PLT/spleen ratio</th>
<th>Right lobe/albumin ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Mean</td>
<td>215,055.56</td>
<td>121.22</td>
<td>1,838.389</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>69,772.295</td>
<td>13.584</td>
<td>707.1507</td>
</tr>
<tr>
<td>Yes</td>
<td>Mean</td>
<td>95,560.98</td>
<td>157.44</td>
<td>624.820</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>41,519.919</td>
<td>19.745</td>
<td>301.3943</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3: Correlation between all predictors and grades of varices

<table>
<thead>
<tr>
<th>Grade of varices</th>
<th>PLT count</th>
<th>Spleen diameter</th>
<th>PLT/spleen ratio</th>
<th>Right lobe/albumin ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mean</td>
<td>167,428.57</td>
<td>136.29</td>
<td>1,204.285</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>59,969.040</td>
<td>15.966</td>
<td>364.5529</td>
</tr>
<tr>
<td>II</td>
<td>Mean</td>
<td>99,466.67</td>
<td>149.87</td>
<td>668.750</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>37,015.183</td>
<td>16.296</td>
<td>246.9659</td>
</tr>
<tr>
<td>III</td>
<td>Mean</td>
<td>96,000.00</td>
<td>160.60</td>
<td>600.033</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>31,167.479</td>
<td>14.136</td>
<td>199.6266</td>
</tr>
<tr>
<td>IV</td>
<td>Mean</td>
<td>72,480.00</td>
<td>163.48</td>
<td>470.914</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>25,932.798</td>
<td>24.395</td>
<td>237.9270</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>0.007</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table 4: Comparison of accuracy of the 4 parameters in predicting the presence of oesophageal varices

<table>
<thead>
<tr>
<th>Predictor</th>
<th>AUROC</th>
<th>Cut off point</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>(+)ve PV (%)</th>
<th>(-)ve PV (%)</th>
<th>Accuracy (%)</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLT count</td>
<td>0.912</td>
<td>131000</td>
<td>84.15</td>
<td>85.33</td>
<td>95.83</td>
<td>53.57</td>
<td>84.00</td>
<td>5.05</td>
<td>0.19</td>
</tr>
<tr>
<td>Spleen size</td>
<td>0.934</td>
<td>131.5</td>
<td>90.24</td>
<td>85.33</td>
<td>96.10</td>
<td>65.22</td>
<td>89.00</td>
<td>5.41</td>
<td>0.12</td>
</tr>
<tr>
<td>PLT count/spleen ratio</td>
<td>0.927</td>
<td>1326.58</td>
<td>96.34</td>
<td>85.33</td>
<td>96.34</td>
<td>83.33</td>
<td>94.00</td>
<td>5.78</td>
<td>0.04</td>
</tr>
<tr>
<td>Right liver lobe/Albumin conc.ratio</td>
<td>0.912</td>
<td>44.22</td>
<td>91.46</td>
<td>77.78</td>
<td>94.94</td>
<td>66.67</td>
<td>89.00</td>
<td>4.12</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Figure 1: ROC curve for sensitivity and specificity of platelet count for the prediction of varices.

Figure 2: ROC curve for sensitivity and specificity of spleen size for the prediction of varices.

Figure 3: ROC curve for sensitivity and specificity of platelet count/spleen diameter ratio for the prediction of varices.

Figure 4: ROC curve for sensitivity and specificity of RT liver lobe size/albumin concentration ratio for the prediction of varices.
Figure 5: Comparison between sensitivity & specificity of the 4 parameters in predicting the presence of oesophageal varices

4. Discussion:

Bleeding oesophageal varices is still the leading cause of death in patients with cirrhosis. In recent studies, mortality rates vary between 11% and 20% within six weeks of the bleeding episode (24-27).

Endoscopy is still the gold standard method for diagnosis of oesophageal varices and is recommended every two to three years in cirrhotic patients without varices, and every one to two years in patients with small varices (14,28,29). Several studies have been performed to find noninvasive parameters that can predict the presence of oesophageal varices in liver cirrhosis to reduce the cost and burden on endoscopy units (28).

The prevention of bleeding from oesophageal varices is an important goal. Identification of patients who are at risk of variceal bleeding is the first step in prevention of bleeding so the patients can be selected to start prophylactic treatment.

The prevalence of oesophageal varices among cirrhotics is variable, ranging from 24% to 80% (30). The value of diagnosing oesophageal varices by a noninvasive predictor is to save endoscopy to patients who have high probability of having varices.

In the present study as shown in tables 2-4 and figures 1 and 2 like many other previous studies (31-37) have shown that platelet count and spleen diameter correlate well with the presence of oesophageal varices. However, in cirrhotic patients, the presence of thrombocytopenia may be due to several factors other than portal hypertension, as shortened mean platelet lifetime, decreased thrombopoietin production or myelotoxic effects of hepatitis C virus (38). The presence of splenomegaly in cirrhotic patients is mainly related to portal hypertension.

In 2003 Giannini et al (28) introduced the use of the platelet count/spleen diameter ratio as a predictor of oesophageal varices. This ratio links thrombocytopenia to splenomegaly to introduce a variable that takes into consideration that thrombocytopenia is mainly due to hypersplenism secondary to portal hypertension. In his study with a cut-off value of 909 the sensitivity was 100% and specificity was 93%. In 2006 Giannini et al (39) reported the results of a multicenter study to validate the use of platelet count/spleen diameter ratio in the prediction of oesophageal varices. In this study the cut-off value of 909 showed sensitivity 92% and specificity 67%. Many studies (23, 39-42) have been done using different best cut-off values to investigate this parameter as a noninvasive predictor for oesophageal varices.

In the present study the cut-off value of 1326.58 for the platelet count/spleen diameter ratio was used which showed sensitivity 96.34% and specificity 83.33% as shown in tables 3 and figure 2. In 2007 Alempijevic et al (24) investigated the right liver lobe diameter/albumin concentration ratio as a noninvasive predictor of oesophageal varices and at a cut-off value of 44.25 the sensitivity was 83.1% and the specificity was 73.9%. In the present study at a cut-off value of 44.22 for the right liver lobe diameter/albumin concentration ratio, the sensitivity was 91.46% and the specificity was 77.78% as shown in table 4 and figure 4.

5. Conclusion:

Among the noninvasive parameters studied in this study, the platelet count/spleen diameter ratio had the highest accuracy for diagnosing oesophageal varices (sensitive to 96.34% and specificity 83.33%). For the right liver lobe diameter/albumin concentration ratio, the sensitivity was 91.46% and the specificity was 77.78% and can be considered as a noninvasive predictor of oesophageal varices that can provide accurate information as well as the platelet count/spleen diameter ratio.

The use of the 4 studied predictors in this study can help the physicians to restrict endoscopy on those who are highly suspected to have oesophageal varices to start the prophylactic therapy and not to use the endoscopy for all the patients.

Of course endoscopy still is the gold standard for the diagnosis of oesophageal varices, but the use of the noninvasive predictors specially...

http://www.americanscience.org

editor@americanscience.org
platelet count/spleen diameter ratio and the right lobe liver size/albun concentration ratio will be of a great help to reduce the number of endoscopies in patients with post hepatitis C virus liver cirrhosis in Egypt. More studies are required in a larger sample of post hepatitis C cirrhosis patients for validation of the right lobe liver size/albun concentration ratio as a noninvasive predictor of oesophageal varices as well as the platelet count/spleen diameter ratio and to determine a cut-off value that can be safely recommended for the noninvasive diagnosis oesophageal varices.

The limitation of the present study includes: relatively small number of patients, liver biopsy was not done and the diagnosis of cirrhosis was based on clinical and laboratory results.

Corresponding author
Serag Esmat
Department of Internal Medicine, Faculty of Medicine, Cairo University. Cairo, Egypt
seragesmat@hotmail.com

6. References:


30-de Franchis R. Noninvasive diagnosis of esophageal varices: Is it feasible? Am J Gastroenterol 2006; 101:25202?
38-Peck-Radosavljevic M. Thrombocytopenia in liver disease. Can J Gastroenterol 2000;14(Suppl D):60D-6D.
42-Korula J. Platelet count/spleen diameter ratio predicted the presence of esophageal varices in liver cirrhosis. ACP J Club 2004; 140:53.

1/5/2011