Correlation between Aspartate Aminotransferase to Platelet Ratio Index Score and the Degree of Esophageal Varices with Liver Cirrhosis

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ABSTRACT

Background: *Esophageal varices is the most common complication in liver cirrhosis. Bleeding varices is a serious complication causing increased mortality rate. In anticipation of those complications, the role of screening test is essential. Endoscopy is the standard method for assessing esophageal varices, but it carries certain risks for patients if it is contraindicated. Moreover, it is an invasive, expensive and uncomfortable procedure. Accordingly, a non-invasive method, aspartat aminotransferase to platelet ratio index (APRI) score, has been developed for evaluating esophageal varices.*

Method: *An analytic cross-sectional observational study was conducted in patients with liver cirrhosis who underwent endoscopy between March 2011 and August 2012. Data were obtained from medical records of hospitalized patients in Mohammad Hoesin General Hospital. The degree of esophageal varices was assessed based on endoscopic findings and APRI score. Spearman test was performed to analyze the correlation between APRI score and the degree of esophageal varices.*

Results: *There were 55 patients, 30 (54.5%) male and 25 (45.5%) female patients, with a range of age between 15-70 years and a mean value of age of 47.09 ± 12.8. APRI score < 0.5 was found in 21.81% subjects, APRI score of 0.5-1.5 was obtained in 41.81% subjects and APRI score > 1.5 was noted in 36.36% subjects with a mean value of 2.32 ± 3.92. There was a correlation between APRI score and degree of esophageal varices with p = 0.011*

Conclusion: *APRI score can indirectly predict esophageal varices in patients with liver cirrhosis.*

Keywords*: APRI score, the degree of esophageal varices, liver cirrhosis*

ABSTRAK

Latar belakang: *Varises esofagus merupakan penyulit paling sering pada sirosis hati. Perdarahan varises esofagus merupakan komplikasi serius karena dapat meningkatkan mortalitas. Oleh karena itu skrining varises esofagus penderita sirosis hati penting untuk mengantisipasi penyulit. Endoskopi merupakan salah satu metode untuk menilai varises esofagus, tetapi beresiko pada penderita yang mengalami kontraindikasi karena bersifat invasif, mahal dan kurang nyaman. Berdasarkan hal ini, maka dikembangkan metode non invasif seperti skor aspartat aminotransferase to platelet ratio index (APRI) untuk menilai varises esofagus. Tujuan penelitian untuk menilai korelasi antara skor APRI dengan derajat varises esofagus penderita sirosis hati.*

Metode: *Penelitian observasi analitik dengan desain penelitian potong silang pada penderita sirosis hati yang menjalani prosedur pemeriksaan endoskopi dari Maret 2011 sampai Agustus 2012. Data diperoleh dari rekam medik pasien rawat inap di Rumah Sakit Muhammad Hoesin. Derajat varises esofagus dinilai dari hasil endoskopi serta skor APRI. Dilakukan tes Spearman untuk menganalisis korelasi antara skor APRI dengan derajat varises esofagus.*

Hasil: *Terdapat 55 penderita sirosis hati terdiri dari laki-laki 30 (54,5%) dan perempuan 25 (45,5%) dengan usia antara 15 – 70 tahun, rerata 47,09 ± 12,8. Didapatkan skor APRI < 0,5 = 21,81%, skor APRI 0,5 – 1,5*

= 41,81% dan skor APRI > 1,5 = 36,36% dengan rerata 2,32 ± 3,92. Didapatkan penderita varises esofagus derajat I sebanyak 15 (27,3%), derajat II sebanyak 20 (36,4%), derajat III sebanyak 15 (27,3%) dan derajat IV sebanyak 5 (9,1%). Diketahui terdapat korelasi antara skor APRI dengan derajat varises esofagus dengan p = 0,011.

***Simpulan:** Terdapat korelasi antara skor APRI dengan derajat varises esofagus penderita sirosis hati.*

***Kata kunci:** skor APRI, derajat varises esofagus, sirosis hati*

INTRODUCTION

Liver cirrhosis is the end stage of chronic liver disease characterized by the presence of several complications caused by portal hypertension. Esophageal varices is a frequent complication of cirrhosis with incidence rates reach 90%.[1] Bleeding from esophageal varices is a serious and dangerous complication with incidence of 5% on small varicose veins and 15% at large ones. Mortality rate due to variceal bleeding episode is about 10-20% and the life expectancy is around 63%.[2,3] Therefore, screening of esophageal varices in patients with liver cirrhosis is essential to anticipate the complications that arise.[3,4]

The method currently used for screening of esophageal varices is endoscopic examination performed every 2-3 years in patients with liver cirrhosis without varices and every 1-2 years in patients with small varices. Endoscopy is an invasive, less expensive and less acceptable method. Therefore, screening test for patients with large esophageal varices who have high bleeding risk will be a growing problem. To overcome the problem, some experts have developed several non-invasive methods such as serum markers, ultrasonography and transient elastrography, which can be used as alternative measures to assess the presence of esophageal varices indirectly.[5]

Based on the concept that the occurrence of portal hypertension is due to hepatic fibrosis, an important factor that results in vascular resistance in the liver, then the non-invasive examination of serum markers can be used to predict esophageal varices in liver cirrhosis with good results.[6,7] Aspartate aminotransferase to platelet ratio index (APRI) score is one of the serum markers that can be used to assess the presence of liver fibrosis. APRI score can be obtained from the calculation of two laboratory results, namely the aspartate aminotransferase (AST) level and platelet counts. APRI score has an advantage in that it only covers two laboratory tests, which are low cost and routinely performed for all patients.[8] The purpose of our study was to determine the correlation between APRI score and the degree of esophageal varices in patients with liver cirrhosis.

METHOD

This study design was observational, analytic and cross-sectional conducted in patients with liver cirrhosis who underwent endoscopic procedure in Mohammad Hoesin Hospital, Palembang between March 2011 and August 2012. Data were retrieved from medical records of hositalized patients with liver cirrhosis in the hospital. Diagnosis of liver cirrhosis was established based on clinical findings and results of laboratory and ultrasound examinations. Symptoms of liver cirrhosis usually include enlarged stomach and leg swelling, weakness, loss of appetite, weight loss, satiety, epigastric discomfort, nausea, bloating, upper right abdominal pain, vomiting blood and passage of black stool. Signs of liver cirrhosis were associated with failure of liver function and the presence of portal hypertension. Laboratory results might indicate the presence of anemia, thrombocytopenia, hemostasis disorders, liver dysfunction, hypoalbuminemia, electrolyte disturbances and the presence of serological markers for viral hepatitis.

Ultrasonography included examination on the size, the structure of liver parenchyma, the liver edge, homogeneity and presence of mass. In patients who have advanced liver cirrhosis, their liver ultrasonography would showed a smaller size and presence of nodules, uneven surfaces, as well as an increase in parenchymal echogenicity.[9]

APRI score is an index ratio of aspartate aminotransferase (AST) and platelets counts. Wai CT et al formulate the equation as follows:

$$\frac{\text{Aspartate aminotransferase (AST)/upper normal limit x 100}}{\text{Platelet counts } (10^9/\text{L})}$$

APRI score value of < 0.5 indicated no or minimal fibrosis, APRI score from 0.5 to 1.5 indicated significant fibrosis and APRI score > 1.5 indicated liver cirrhosis.[8]

Examinations of esophageal varices were performed using Olympus® GIF Q 150 endoscope. There are several methods to determine the degree of esophageal varices. In this study, the degree of

esophageal varices was determined by subjective methods, which divided into esophageal varices into: (1) grade I when small veins were seen with valsava maneuvering; (2) grade II if varices was found with a diameter of 1-3 mm; (3) grade III when varices was 3-6 mm in size and (4) grade IV when the varices size was > 6 mm.

Inclusion criteria for this study were: (1) all patients with liver cirrhosis. The diagnosis was established based on clinical symptoms, laboratory and ultrasound results; (2) patients with esophageal varices evaluated by endoscopic examination. Exclusion criteria were patients with a history of variceal ligation and sclerotherapy, a thrombus in portal vein ultrasonography, history of taking beta-blockers, nitrates, hepatoprotective and antifibrotic agents.

Spearman correlation test was used to analyze the correlation between APRI score and the degree of esophageal varices with $p < 0.05$ considered as the significance limit. Statistical analysis was performed using SPSS version 2.0.

RESULTS

In this study, there were 55 patients with liver cirrhosis who underwent endoscopy, consisting of 30 (54.5%) male and 25 (45.5%) female patients with the age range of 15-70 years and a mean age of 47.09 ± 12.8. The major causes of patients with liver cirrhosis were hepatitis B virus (61.8%) and hepatitis C virus (7.3%). Patient characteristics are shown in Table 1.

Data on the degree of esophageal varices were obtained. There were 15 (27.3%) patients with of patients with esophageal varices grade I, 20 (36.4%) patients with grade II, 15 (27.3%) patients with grade III, and 5 (9.1%) patients with grade IV esophageal varices with a mean value of 2.18 ± 0.94. APRI score < 0.5 was found in 12 (21.81%) patients, APRI score of 0.5-1.5 was obtained in 23 (41.81%) patients and APRI score > 1.5 was noted in 12 (36.36%) patients with a mean value of 2.32 ± 3.92 (Figure 1 and 2). The statistical Spearman test showed a correlation between APRI score and the degree of esophageal varices in patients with liver cirrhosis with $p = 0.011$ ($p < 0.05$).

Table 1. Characteristics of patients

Variable	n (%)	Mean ± SD
Sex		
Male	30 (54.5)	
Female	25 (45.5)	
Age (year)		
15-70	55	47.09 ± 12.8
Ascites		
Present	46 (83.6)	
None	9 (16.4)	
Laboratory		
Albumin (mg/dL)		2.60 ± 0.68
Globulin (mg/dL)		3.79 ± 1.10
Platelet (10^9/L)		153.74 ± 12.8
AST (17 - 327 IU/L)		83.22 ± 68.29
ALT (11 - 344 IU/L)		57.4 ± 58.93
Indirect bilirubin (0.26 - 11.72 mg/dL)		1.47 ± 2.24
Direct bilirubin (0.12 - 31.70 mg/dL)		3.50 ± 6.24
Etiology		
HbsAg positive	34 (61.8)	
Anti HCV positive	4 (7.3)	
Others	17 (30.9)	

AST: aspartate aminotransferase; ALT: alanine transaminase; HCV: hepatitis C virus

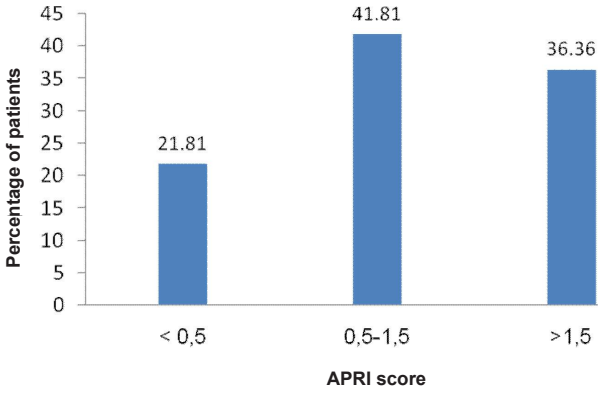

Figure 1. Frequency of APRI score

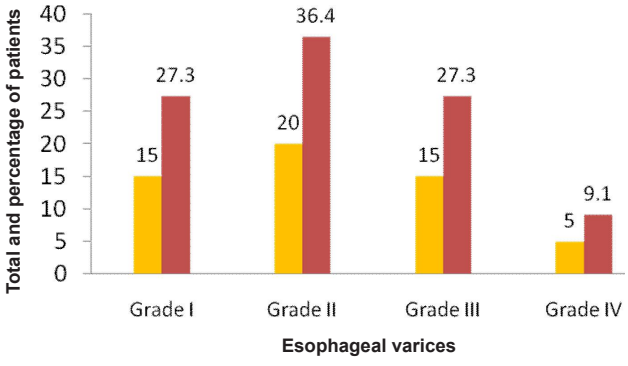

Figure 2. Degree of esophageal varices

DISCUSSION

Esophageal varices is one of complications of portal hypertension caused by liver cirrhosis.[10] Assessment of esophageal varices degree can be done indirectly by identifying liver fibrosis. Several methods can be used to assess liver fibrosis indirectly by using serum

markers such as fibrotest, fibro index, APRI score, Lok score, Forns index, etc.[11] APRI score has several advantages compared with other indirect markers because it is cheaper, easy to performed and routinely examined in all patients with liver cirrhosis.[8]

Several studies have shown that APRI score can be used to depict hepatic fibrosis. Shaheen et al reported the identification of fibrosis in patients with chronic hepatitis C virus infection, APRI score < 0.5 had a negative predictive value (NPV) of 72%, while the APRI score >1.5 had a positive predictive value (PPV) of 87%.[12] Wai CT et al concluded that APRI score can predict accurately significant fibrosis and cirrhosis in 51% and 81% respectively, potentially avoiding the need for liver biopsis in patients.[13]

Study on the prediction of esophageal varices by non-invasive parameters is very important in order to avoid endoscopy which is an invasive, expensive, and less convenient procedure for every liver cirrhotic patient. Thabut et al, in their manuscript on the non-invasive assessment of portal hypertension have stressed out the role of serum markers in establishing diagnosis of esophageal varices in the future. Therefore, the cheaper, easier and higher sensitivity and specificity marker is required.[14]

In our study, most patients had second grade esophageal varices (36.4%) and APRI score from 0.5 to 1.5 was found as much as 41.81%. The statistical Spearman test showed a correlation between APRI score and the degree of esophageal varices with $p = 0.011$ ($p < 0.05$). The results are similar to previous study results, which show a correlation between APRI score and esophageal varices. Tafarel et al examined 300 patients with liver cirrhosis and they also found a correlation between APRI score and esophageal varices ($p = 0.02$).[15] Sanyal et al in 2006 examined 1,016 patients with compensated liver cirrhosis and reported a correlation between APRI score and the presence of esophageal varices ($p = 0.01$).[16] Sebastian et al got strong correlation between APRI score in the presence of esophageal varices (APRI = 1.4, sensitivity 54%, specificity 69%) and on a large varices (APRI score = 15, sensitivity 59% and specificity 63%).[7]

CONCLUSION

There is a correlation between APRI score and the degree of esophageal varices. APRI score can indirectly predict the degree of esophageal varices in patients with liver cirrhosis.

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