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Utility of Platelet Count/Spleen Area Ratio to Predict the Presence of Esophageal Varices

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ABSTRACT

Background and Aim: Esophageal varices (EV) is well documented to be one of the major complications in cirrhotic patients. All cirrhotic patients should undergo screening for EV. There are several studies about non-invasive markers to predict the presence of EV including platelet count/spleen diameter ratio(P/D ratio). We postulated that whether platelet count/spleen area ratio (P/A ratio), should be better than P/D ratio to predict the presence of EV.

Patients and Methods: This is cross-sectional study in 164 cirrhotic patients without previous variceal hemorrhage. Biochemical study, endoscopic findings, splenic measurement by ultrasonography, P/D ratio and P/A ratio were collected in all patients.

Results: The prevalence of EV was 49% but high grade EV was only 10%. Receiver operating characteristic (ROC) curve was used for analysis, the value of P/D ratio ≤1,496 has sensitivity,specificity, negative predictive value (NPV), positive predictive value(PPV) and accuracy of test in about 100%, 36%, 100%, 60%, 67%, respectively. The value of P/A ratio ≤21.5 has sensitivity, specificity, NPV, PPV and accuracy of test of in about 100%, 68%, 100%, 75%, 84%, respectively.

Conclusion: The value of P/D ratio ≤1,496 and P/A ratio ≤21.5 were the good predictors for developing of EV. Moreover, the P/A ratio has a higher specificity than P/D ratio.

Key words : esophageal varices, platelet count/spleen area ratio, platelet count/spleen diameter ratio

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BACKGROUND

Esophageal varices (EV) related bleeding is the common caused of high morbidity and high mortality in cirrhotic patients with portal hypertension. Mortality rate in the first variceal bleeding ranged between 17-57%.[1] The prevalence of EV from endoscopic screening in cirrhotic patients is approximately 40-60%[2,3] and the prevalence of large EV is only found in about 10-20%.[4] From the recent data, non-selective beta-blockers decreased the risk of first variceal bleeding in cirrhotic patients with large EV.[5-10]

The Banevo IV concensus workshop on methodology of diagnosis and therapy in portal hypertension recommend that all cirrhotic patients should be screened for EV at the time of first diagnosis.[11] The

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AASLD single topic symposium on portal hypertension recommend that Child's A cirrhotic patients with evidence of portal hypertension (platelet count <140,000 and/or portal vein diameter >13 mm) should be screening for EV.[12] In the recent data, 50% of cirrhotic patients may not have developed EV 10 years after the diagnosis of cirrhosis.[13] Thus, It may be cost effective to screen for EV in high risk cirrhotic patients only.[14-18] To decrease the number of unnecessary endoscopic screening procedure in low risk cirrhotic patients, many of retrospective study have evaluated the possible noninvasive marker of EV formation in cirrhosis.[19-28] In these study; in high risk cirrhotic patients, low platelet count, splenomegaly are the two common noninvasive factors to predict of EV. There have been several studies about non-invasive markers to predict EV including platelet count/spleen diameter ratio (P/D ratio).[3] We postulated that whether platelet count/spleen area ratio (P/A ratio), should be better than platelet count/spleen diameter ratio to predict EV in cirrhotic patients. The aim of this study to evaluated the utility of the platelet count/spleen diameter ratio to predict for the presence of EV compared with the platelet count/spleen area ratio.

Patients and Methods

Patients

This is a cross-sectional study in 164 cirrhotic patients (age 25-80 years) without previous history of variceal bleeding from Division of Gastroenterology, Department of Medicine, Bangkok Metropolitant Medical College and Vajira Hospital. The period of this study is between 1 June 2004 to 30 January 2006. All patients were eligible if they had diagnosis liver cirrhosis base on criteria (1) or (2) [(1) physical examination and biochemical study expressed in chronic liver disease with or without evidence of portal hypertension confirmed by splenomegaly or thrombocytopenia / (2) one of the three of these findings in radiological study, liver biopsy and intraoperative findings compatible with liver cirrhosis]. All patients signed for informed consent and had no previous history of variceal hemorrhage. Patients with diagnosis of hepatocellular carcinoma, advanced other organ malignancy, or severe medical condition (end stage renal disease, congestive heart failure or severe respiratory syndrome) were excluded.

Patients with other caused of splenomegaly or thrombocytopenia (hematological disease, chronic illness or alcoholic consumption within 2 months) were also excluded. The history and biochemical investigation data in all patients were collected; age, sex, risk of cirrhosis, history of alcoholic consumption, other conditions associated with splenomegaly and thrombocytopenia. Complete blood count, platelet count, coagulogram, liver function test, HBsAg, anti-HBs, anti-HBc, anti-HCV, Child-Pugh classification and Child-Pugh score were evaluated in all patients.

Endoscopic evaluation was performed in 164 patients by a single endoscopist. The endoscopic finding of EV was classified by grading as F1-F3(F1; The varices can be depressed by endoscope, F2; The varices cannot be depressed by endoscope, F3; The varices are confluent around the circumferential).[29] From this study EV grade F2 and F3 was classified as large esophageal varices. The other endoscopic findings (gastric varices; GV or portal hypertensive gastropathy; PHG) were also recorded.

The ultrasonographic examination was performed by a single radiologist whom blinded to the basic characteristic and endoscopic findings in all patients. Upper ultrasonographic examination were imaged by the same unit of Phillips ATL (HDI 5000) with scanhead C4-240R (L10-5, 38 mm). Intraobserver reliability of the spleen measurement in one radiologist for 20 patients was 2.7%. The spleen measurement was performed in the same position (left anterior oblique) during the deepest inspiration.

The definition of spleen diameter is the maximum transverse distance between two pole in millimeters, spleen height is the maximum vertical distance across the splenic hilum at the same level of spleen diameter in millimeters, spleen area was calculated from spleen diameter multiplied by spleen height, platelet count / spleen diameter ratio was calculated by platelet count (/mcl) devided by spleen diameter (mm) and platelet count/spleen area ratio was calculated by platelet count (/mcl) devided by spleen area (mm^2). The splenic measurement and spleen height and spleen diameter evaluation was shown in Figure 1. The duration of initial biochemical study, endoscopic evaluation and spleen measurement was performed within 2 weeks.

Statistical analysis

The qualitative variables were compared by using the Chi-square test. The quantitative variable were compared by Man-Whitny U test at significant level

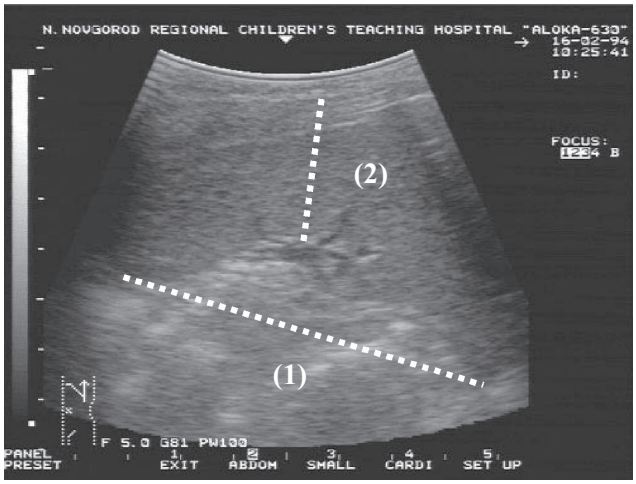


Figure 1 The picture of splenic measurement by ultrasound
(1) spleen diameter in mm.
(2) spleen height in mm.

of P value <0.05. Quantitative variable data of 164 cirrhotic patients presented in means ± standard deviation. Univariate analysis was performed in all basic biochemical characteristics, spleen diameter, spleen height, spleen area,portal vein diameter, platelet count / spleen diameter ratio and platelet count / spleen area ratio. Receiver operator characteristics (ROC) curve was performed to evaluate the best value of platelet count / spleen diameter ratio and the best value of platelet count / spleen area ratio for predicted EV. Diagnostic accuracy, negative predictive value (NPV) and positive predictive value (PPV) were calculated from each of best sensitivity and specificity in platelet count / spleen diameter ratio and platelet count / spleen area ratio. Data was collected and analyzed by using the SPSS version 13 for Window (SPSS Inc, Chicago, Ilinois, USA).

RESULTS

Data were collected from 164 patients,104 were male (63%), 60 were female (37%). The mean of age was 54.0 ± 11.6 (25-80) years [mean ± SD. (range)] other variables-result was shown in Table 1, 2.

We found the etiology of cirrhosis ; alcoholic was 103 (63%), HBV was 28 (17%), HCV was 18 (11%) and other caused was 15 (9%), as shown in Figure 2. Child's classification in Child A, B, C was 77 (47%), 74 (45%), 13 (8%) respectively. Prevalence of no EV, EV grade F1, EV grade F2 and EV grade F3 was 84 (51%), 63 (39%), 15 (9%) and 2 (1%) respectively and as shown in Figure 3. Endoscopic findings showed EV in about 49% and large EV was 10%. The prevalence of gastric varices (GV) was found in 17 (10%) and all of them also had EV. The portal hypertensive gastropathy (PHG) was found in 118 (72%). The prevalence of EV in Child A, B, C was 50%, 45%, 70% respectively, as shown in Figure 4. The basic characteristics of 164 cirrhotic patients with or without esophageal varices are shown in Table 1.

We also study to compare among the spleen diameter in normal volunteers, cirrhotic patients without esophageal varices and cirrhotic patients with esophageal varices. The results were 85.6103.4127.8

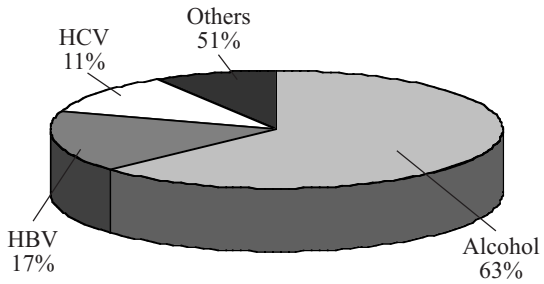


Figure 2 Etiology of cirrhosis

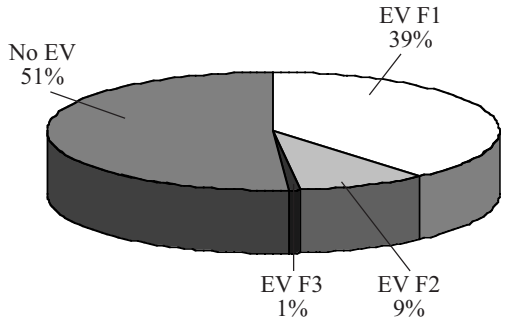


Figure 3 Endoscopic finding in 164 patients

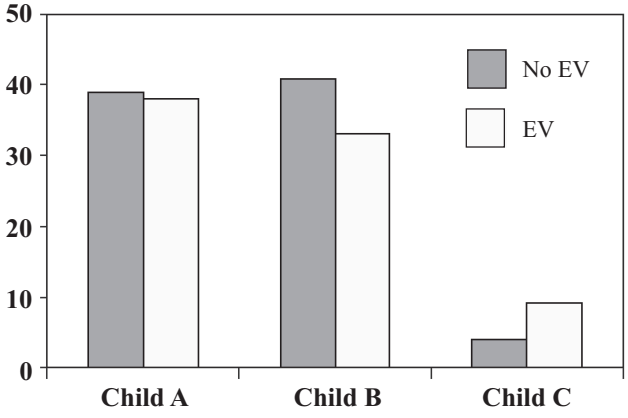


Figure 4 Number of patients with or without EV according to Child's classification

mm. respectively. We compared the spleen height in normal volunteers, cirrhotic patients without esophageal varices and cirrhotic patients with esophageal varices. The results were 33.0, 3.1, 5.6 mm. respectively. We compared the platelet count / spleen diameter ratio in normal volunteers, cirrhotic patients without esophageal varices and cirrhotic patients with esophageal varices, the results were 3458, 1426, 723 respectively. We compared the platelet count / spleen area ratio in normal volunteers, cirrhotic patients without esophageal varices and cirrhotic patients with esophageal varices, the results were 109.6, 6.4, 3.1 respectively, as shown in Table 2.

We used the receiver operator characteristics (ROC) curve to evaluated platelet count / spleen diameter ratio to select the best cut off value for sensitivity and specificity to predict the esophageal varices formation in cirrhotic patients. By ROC curve, the platelet count / spleen diameter ratio at 1,496 is the best value to predict the presence of esophageal varices in cirrhotic patients and the area under the curve (AUC) was 0.7857, as shown in Figure 5. From this value we found, the sensitivity was 100%, the specificity was 36%, the negative predictive value (NPV) was 100%, the positive predictive value (PPV) was 54% and the accuracy of test was 67%. We used the receiver operator characteristics (ROC) curve to evaluated the platelet count / spleen area ratio for the best cut off value

Table 1 Basic characteristics of 164 cirrhotic patients

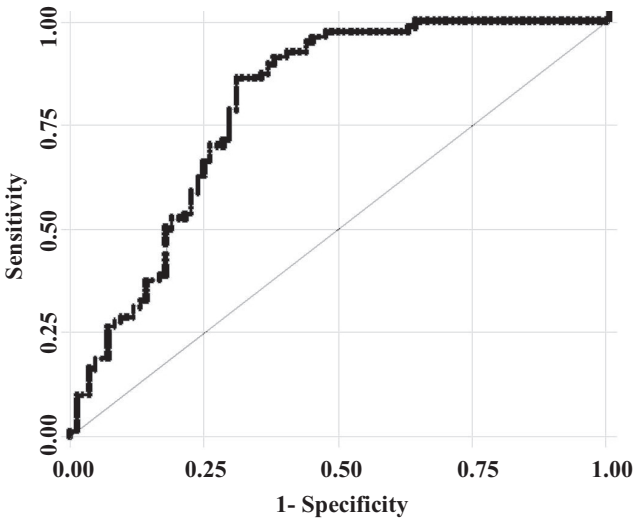
Charateristics	EV (n = 80)	Non-EV (n = 84)	P value
Age (y)	53.5 (36-80)	54.5 (25-78)	0.84
Hct (%)	33.7 (19.1-48.9)	33.8 (19.2-48.5)	0.69
Hb (g/dL)	11.3 (6.8-16.9)	11.3 (6.2-16.0)	0.73
WBC (/mcL)	5, 668 (1,200-16,900)	6, 474 (2,900-15,100)	0.01
Platelet count (/mcL)	88, 925 (26,000-192,000)	137,892 (33,000-408,000)	<0.01
AST (0-40 U/L)	65 (16-218)	66 (17-216)	0.87
ALT (0-35 U/L)	36 (7-176)	42 (4-172)	0.54
ALP (98-279 U/L)	308 (108-828)	309 (67-861)	0.77
Alb (3.8-5.0 g/dL)	3.0 (1.7-4.2)	3.1 (1.7-4.6)	0.53
Glob (1.2-3.0 g/dL)	4.5 (2.6-7.3)	4.3 (2.4-7.0)	0.83
TB (0.3-1.0 mg/dL)	2.1 (0.5-5.2)	1.8 (0.2-5.0)	0.03
DB (0.06-0.25 mg/dL)	1.0 (0.2-2.9)	0.9 (0.1-3.2)	0.07
Child score	7 (5-11)	7 (5-11)	0.58
PVD (mm.)	12.2 (6.8-17.8)	11.3 (7.0-16.3)	0.01
Spleen diameter (mm.)	127.8 (73.7-193.0)	103.4 (63.0-193.4)	<0.01
Spleen height (mm.)	55.6 (34.2-103.1)	43.1 (24.5-102.6)	<0.01
Spleen area (mm^2)	7,261.4 (3,225.-17,351.7)	4,643.3 (1,614.5-19,842.8)	<0.01
P/D ratio	723.4 (154.5-1,495.2)	1,426.7 (267.9-4,184.8)	<0.01
P/A ratio	13.1 (1.5-21.1)	36.4 (3.3-129.4)	<0.01

P/D ratio: platelet count / spleen diameter ratio
P/A ratio: platelet count / spleen area ratio

Table 2 The mean of spleen measurement and both ratio in normal volunteers and cirrhotic patients with or without EV

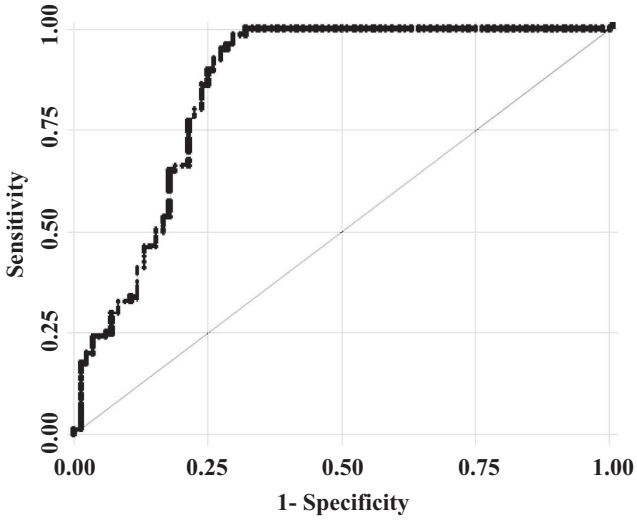
Characteristics	Normal Volunteers (n = 40)	Cirrhotic patients		P value
		No-EV (n = 84)	EV (n = 80)	
Spleen diameter (mm)	85.6	103.4	127.8	<0.01
Spleen height (mm)	33.0	43.1	55.6	<0.01
P/D ratio	3,458	1,426	723	<0.01
P/A ratio	109.6	36.4	13.1	<0.01

P/D ratio: platelet count / spleen diameter ratio
P/A ratio: platelet count / spleen area ratio



Area under ROC curve = 0.7960

Figure 5 ROC curve of the platelet count / spleen diameter ratio in all patients (n = 164)



Area under ROC curve = 0.8560

Figure 6 ROC curve of the platelet count / spleen area ratio in all patients (n = 164)

Table 3 The best value of 2 ratios to predict EV

Percent (%)	Sensitivity	Specificity	NPV	PPV	Accuracy of test
P/D ratio <1,496	100	36	100	60	67
P/A ratio <21.5	100	68	100	75	84

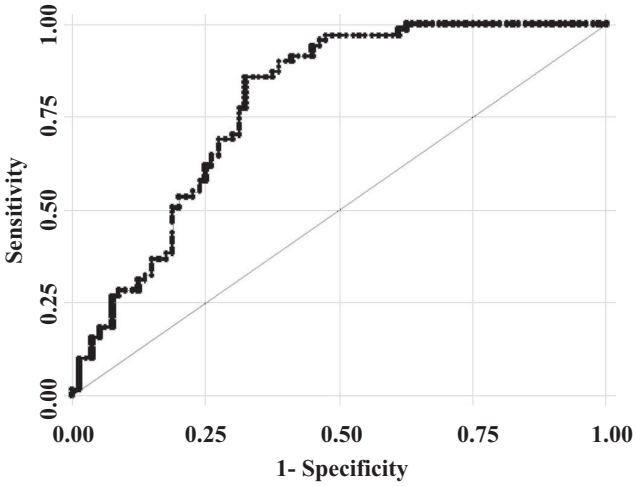
P/D ratio: platelet count / spleen diameter ratio
P/A ratio: platelet count / spleen area ratio

for sensitivity and specificity to predict the EV formation in cirrhotic patients. The platelet count / spleen area ratio at 21.5 was the best value for predicted the EV formation in cirrhotic patients and area under the curve (AUC) was 0.8492, as shown in Figure 6. The sensitivity was 100%, the specificiity was 68%, the negative predictive value (NPV) was 100%, the positive predictive value (PPV) was 75% and the accuracy of test was 84%, as shown in Table 3. Subgroup analysis in Child's A and B (n = 151) found that at the platelet count / spleen diameter ratio of 1,496 and the platelet count / spleen area ratio at 21.5 were also the best value to predict the EV formation in cirrhotic patients, as shown in Figure 7 and 8. Subgroup analysis in alcoholic group only (n = 103), the platelet count / spleen diameter ratio at 1,496 was the best value to predict the EV formation in cirrhotic patients and area under the curve (AUC) was 0.7983. The platelet count / spleen area ratio at 21.5 was the best value for predicted the EV formation in cirrhotic patients and area under the curve (AUC) was 0.8567. And subgroup analysis in non-alcoholic group [HBV, HCV and other] (n = 61) found that atthe platelet count / spleen diameter ratio of 1,034 was the best value for predicted the EV formation in cirrhotic patients and area under the curve (AUC) was 0.7985. The platelet count / spleen area ratio at 20.5 was the best value for predicted the esophageal varices formation in cirrhotic patients and area under the curve (AUC) was 0.8524.

The ROC curve was performed to evaluate the platelet count level for the best cut off in sensitivity and specificity to predict the esophageal varices formation in cirrhotic patients. The best platelet count level in all cirrhotic patients (n = 164), Child's A and B patients (n = 151), alcoholic group (n = 103) and non- alcoholic [HBV, HCV and others] group (n = 61) was 110, 000 / 102, 000 / 104, 000 / 106, 000 respectively. All of these platelet counts level had comparable sensitivity and specificity (about 75%, 67% respectively).

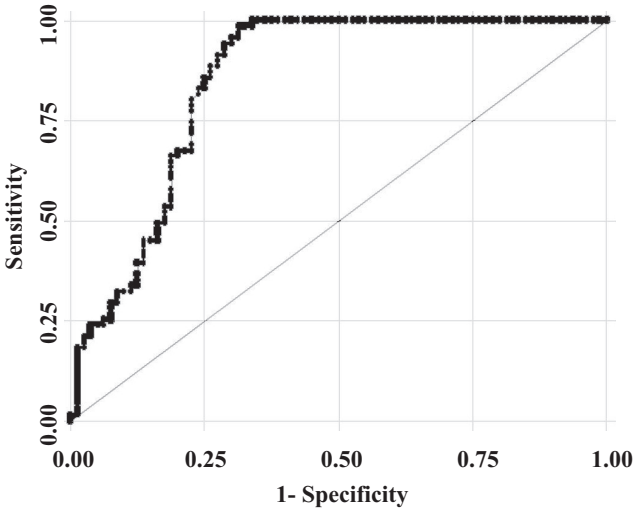
DISCUSSION

From previous studies regarding non-invasive



Area under ROC curve = 0.7857

Figure 7 ROC curve of the platelet count / spleen diameter ratio in Child's A and B patients (n = 151)



Area under ROC curve = 0.8492

Figure 8 ROC curve of the platelet count / spleen area ratio in Child's A and B patients (n = 151)

markers to predicted EV including platelet count, spleen diameter, spleen index and platelet count/spleen diameter ratio[3,4,31]. All of these markers may be related to hypersplenism. It seems that platelet count/spleen diameter ratio had very high sensitivity and specificity that may predict EV in cirrhotic patients. We interested in platelet count/spleen area ratio and postulated that whether platelet count/spleen area ratio should be better than platelet count/spleen diameter ratio to predict EV.

From the result of our study, both ratio can predict the presence of EV in cirrhotic patients. We found that the sensitivity of both parameter were excellent (100%) and suitable for screening EV in cirrhotic patients. However, we found that platelet count/spleen diameter ratio has a lower specificity. We believed that the difference in shape of spleen in difference cirrhotic patients might affect the specificity in platelet count/spleen diameter ratio. In addition, when splenomegaly occurred, its could be enlarged in all directions.

In the past, there was insufficient data for normal value of spleen diameter, spleen height, platelet count/spleen diameter ratio and platelet count/spleen area ratio in healthy Thai population. All of these data were additionally presented in this study. The result from the additional data; spleen diameter, spleen height, spleen area, platelet count/spleen diameter ratio and platelet count/spleen area ratio in healthy volunteers were significantly different from those in the cirrhotic patients. We found that the spleen area in alcoholic group was significantly lower ($P < 0.01$) and platelet count in alcoholic group was significantly higher ($P < 0.01$) than the normed. From this finding, we need larger population to confirm the result of this ratio. Peck-Radosavljevic M *et al*.,[30] found that thrombocytopenia in cirrhotic patients was caused by the reduction of hepatic production of thrombopoietin due to severe liver impairment.

Splenomegaly is a well recognized physical finding in cirrhotic patients There are three factors that contributed to the pathogenesis of hypersplenism: spleen size, reticuloendothelial activity and portal pressure. Westaby *et al*.,[31] found that the relationship between spleen size and portal pressure, measured both directly by splenic pulp pressure or indirectly by radiology can assess the size of EV. From the study of Markel *et al*.,[32] found that the splenomegaly in cirrhotic patients is mainly due to reticuloendothelial hyperplasia. From the same study, hemodynamic studies have shown that the consequent increase in the splenic portal blood flow does not contribute to increase portal pressure. Khishen *et al*.,[33] who assessed spleen volume by computer tomography scanning, found significant negative correlations to platelet count. The degree of hypersplenism of cirrhotic patients may related to a significantly increase splenic pooling of platelet.

It may be cost effective to screen for EV only in high risk patients. High grade EV was suitable for primary prophylaxis treatment and from our study the high grade EV was found in only10%. In addition, the best non-invasive marker for predict the EV should had very

high sensitivity and specificity. In conclusion, the platelet count/spleen diameter ratio <1,495 and of the platelet count/spleen area ratio <21.5 are a good screening test to detect EV in cirrhotic patients. Moreover, the platelet count/spleen area ratio has a higher specificity than platelet count/spleen diameter ratio to predict the presence of EV.

REFERENCES

1. Graham D, Smith JL. The course of patients after variceal hemorrhage. Gastroenterology 1981; 80: 800-9.
2. De franchis R, Primignani M. Natural history of portal hypertension in patients with cirrhosis. Clin Liver Dis 2001; 5: 645-63.
3. Egiannini, F Botta, P Borrc, *et al*. Platelet count/spleen diameter ratio ; proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut 2003; 52: 1200-5.
4. Thompoulos KC, Labropoulou K, *et al*. Non-invasive predictors of the presense of large EV in cirrhosis. Dig Liver Dis 2003; 35: 473-8.
5. D'Amico G, Pagliaro L, Bosch J. Pharmacologic treatment of portal hypertension : an evidence - based approach. Semin Liver Dis 1999; 19: 475-505.
6. Garcia - Pagan JC, Navasa M, Bosch J, *et al*. Enhancement of portal Pressure reduction by the association of isosorbide -5 mononitrate to propranolol administration in patients with cirrhosis. Hepatology 1990; 11: 330-8.
7. De Franchis R. Evaluation and follow-up of patients with cirrhosis and oesophageal varices. J Hepatol 2003; 38: 361-3.
8. Cales P, Oberti F, Payen JL, *et al*. Lack of effect of propranolol in the prevention of large oesophageal varices in patients with cirrhosis : a randomized trial. Eur J Gastroenterol Hepatol 1999; 11: 741-5.
9. Groszmann R, Garcia-Tsao G, Makuch R, *et al*. Multicenter randomized trial of non-selective beta-bllockers in the prevention of complications of portal hypertension : final results and identification of a predictive factor. Hepatology 2003; 38 (Suppl 1): 206.
10. Feu F, Garcia-Pagan JC, Bosch J, Luca A, *et al*. Relation between portal pressure response to pharmacotherapy and risk of recurrent variceal hemorrhage in patients with cirrhosis. Lancet 1995; 346: 1056-9.
11. De Franchis R. Update in consensus in portal hypertension : report of the Baveno IV consensus workshop on methodology of diagnosis, and therapeutic strategies in portal hypertension. J Hepatol 2005; 43: 167-76.
12. Grace ND, Grozmann RJ, Garcia Tsao G, *et al*. Portal hypertension and variceal bleeding : an AASLD single topic symposium. Hepatology 1998; 28: 868-80.
13. Garrceau AJ, Chalmers TC, The Boston Inter-Hospital Liver Group. The natural history of cirrhosis : I. Survival with oesophageal varices. N Engl J Med 1963; 268: 469-73.
14. Teran JC, Imperiale TF, Mullen KD, *et al*. Primary prophylaxis of variceal bleeding in cirrhosis : a cost-effectiveness analysis. Gastroenterology 1997; 112: 473-82.
15. Aoki N, Kajiyama T, Beck JR, *et al*. Decision analysis of prophylactic treatment for patients with high-risk esophageal varices. Gastrointest Endosc 2000; 52: 707-14.
16. Arguedas MR, Heudebert GR, Eloubeidi MA, *et al*. Cost-effectiveness of screening, surveillance and primary prophylaxis strategies for esophageal varices. Am J Gastroenterol 2002; 97: 2441-52.
17. Saab S, De Rosa V, Nieto J, *et al*. Costs and clinical outcomes of primary prophylaxis of variceal bleeding in patients with hepatic cirrhosis: a decision analytic model. Am J Gastroenterol 2003; 98: 763-70.
18. Spiegel BMR, Targownik L, Dulai GS, *et al*. Endoscopic screening for esophageal varices in cirrhosis: is it ever cost-effective? Hepatology 2003; 37: 366-77.
19. Pagliaro L, D'Amico G, Pasta L, *et al*. Portal hypertension in cirrhosis : natural history. In: Bosch J, Groszmann RJ, editors. Protal hypertension, pathophysiology and treatment. Oxford: Blackwell Scientific; 1994: 72-92.
20. Garcia-Tsao G, Escorsell A, Zakko M, *et al*. Predicting the presence of significant portal hypertension and esophageal varices in compensated cirrhotic patients (abstr). Hepatology 1997; 26: 360A.
21. Pilette C, Oberti F, Aube C, *et al*. Ni-invasive diagnosis of esophageal varices in chronic liver disease. J Hepatol 1999; 31: 867-73.
22. Chalasani N, Imperiale TF, Ismail A, *et al*. Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol 1999; 94: 3285-91.
23. Schepis F, Camma C, Niceforo D, *et al*. Which patients should undergo endoscopic screening for esophageal varices detection? Hepatology 2001; 33: 333-8.
24. Zaman A, Becker T, Lapidus J, *et al*. Risk factors for the presence of varices in cirrhotic patients without history of variceal hemorrhage. Arch Intern Med 2001; 161: 2564-70.
25. Madhotra R, Mulcahy HE, Willner I, *et al*. Prediction of esophageal varices in patients with cirrhosis. J Clin Gastroenterol 2002; 34: 81-5.
26. Zein CO, Lindor K, *et al*. Prevalence and predictors of EV in PSC. Hepatology 2004: 204-10.
27. Ng FH, Wong SY, Loo CK, *et al*. Prediction of esophageal varices in patients with liver cirrhosis. J Gastroenterol Hepatol 1999; 14: 785-90.
28. Watanabe S, Hosomin, Kitade, *et al*. Assessment of the presence and severity of EV by splenic index in patient with liver cirrhosis. J Comput Assist Tomogr 2000; 24: 788-94.
29. North - Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. N Engl J Med 1988; 319: 983-9.
30. Peck-Radosavljevic M. Thrombocytopenia in liver disease. Can J Gastroenterol 2000; 14 (Suppl D): 60-6D.
31. Westaby S, Wilkinson SP, Warren R, *et al*. Spleen size and portal hypertension. Digestion 1978; 17: 63-8.
32. Markel C, Gatta A, Anaboli L, *et al*. Splenic hemodynamic and portal hypertension in patients with liver cirrhosis and spleen enlargement. Clin Physiol 1985; 5: 531-9.
33. El-Khishen MA, *et al*. Splenectomy is contraindication for thrombocytopenia secondary to portal hypertension. Surg Gynecol Obstet 1985; 160: 233-8.