VALIDITY OF PLATELET COUNT / SPLEEN DIAMETER RATIO IN CIRRHOTIC PATIENTS

Uzma Qayyum, Batool Butt, Khurshid Uttra

Military Hospital/ National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To assess validity of platelet count/spleen diameter ratio in cirrhotic patients, as a non-invasive predictor of high risk esophageal varices (EVs).
Study Design: Cross sectional validation study.
Place and Duration of Study: Department of Medicine, Military Hospital Rawalpindi.
Material and Methods: A total of 160 cases with cirrhosis due to any cause were included in this study. The study included both male and female subjects and was restricted to age 35-70 years. Exclusion criteria were also applied to this group of patients. All these patients underwent blood test for platelet count and ultrasound abdomen for splenic diameter. For each patient calculation of platelet/splenic ratio was determined with a cut off value of 909 determined. Values greater than this cut off were supposed not to have high risk esophageal varices. Upper gastrointestinal endoscopies were performed on all patients and then on the basis of endoscopy results the patients were divided into two groups, first group in which high risk EVs (grade 2 and grade 3) were present and second group in which they were absent. Subsequently sensitivity, specificity, predictive values and accuracy were calculated, keeping in view the calculated cut off value and endoscopy findings.
Results: In our study, 60% (n=96) were between 35-50 years of age and 40% (n=64) were between 51-70 years of age, mean ± SD was calculated as 50.15 ± 9.28 years, 55.63% (n=89) were male and 44. 37% (n=71) were females. Validity of platelet count/spleen diameter ratio in cirrhotic patients for diagnosis of high risk EVs, keeping endoscopy as gold standard was recorded which showed that 58.13% (n=93) were true positive, 5.63% (n=9) were false positive, 27.5% (n=44) were true negative and 8.75% (n=14) were false negative. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate were calculated as 86.92%, 83.01%, 91.18%, 75.86% and 85.63% respectively.
Conclusion: Our results suggest that the platelet count/spleen diameter ratio may be a useful tool for detecting EVs in patients with hepatic cirrhosis but some-other trials in our local population are required to further authenticate its accuracy.

Keywords: Cirrhosis, High risk esophageal varices, Platelet count/spleen diameter ratio.

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INTRODUCTION

Portal hypertension and esophageal varices (EVs) are common major complications of liver cirrhosis with a high mortality rate and occur in approximately 24% to 80% of cases[1]. According to size esophageal varices are graded into three types:[2] A) Grade I EVs: These collapse to inflation of the esophagus with air. (B) Grade II EVs: These are varices between grades 1 and 3. (C) Grade III EVs: These are large enough to occlude the lumen[2]. In newly diagnosed cirrhotic patients the prevalence of EVs is approximately 60–80%[3]. EVs are likely to ulcerate and bleed. Factors that determine the risk of variceal haemorrhage include the severity of liver disease, size of varices, and presence of red signs[2]. Mostly first bleeding episodes happen during the first year after the detection of the varices[4]. It occurs at a rate of approximately 5% for small EVs and 15% for large EVs[3]. It implies mortality of 5%-10% mortality. Due to this reason, early recognition of EVs is a main part of the diagnostic work-up in patients with cirrhosis[4]. It also helps in prognosis of the disease[4]. The gold standard in the diagnosis of varices is upper gastrointestinal endoscopy[5]. Steps to reduce the incidence of

Correspondence: Dr Uzma Qayyum, 54-C, Askari 7, Adyala Road Rawalpindi Pakistan *(Email: uzma54@hotmail.com)*
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variceal bleeding include introduction of nonselective beta-blockers and prophylactic endoscopic variceal ligation of large varices[5]. Therefore, screening with endoscopy should be performed every year for patients with small EVs and every two years in patients with liver cirrhosis without previously diagnosed varices[5]. Endoscopy is however a costly, invasive and time -consuming procedure many patients will not have varices, rendering this method cost-ineffective[3]. Prediction of EVs by non invasive methods would result in performing endoscopic studies only in those with a high probability of having varices[4].

Clinically, portal hypertension is nearly always manifested as increase in spleen size in patients with chronic liver disease. According to a study, 60-65% of patients with cirrhosis and portal hypertension may have splenomegaly. Splenomegaly is caused by congestion under high blood flow that causes reactive and hyperplastic changes in the reticulocytes of splenic red pulp[5]. The etiology of thrombocytopenia in liver disease include portal hypertension (through hypersplenism), antibody-mediated platelet destruction (mainly in viral hepatitis), decreased thrombopoietin production by diseased liver and myelotoxic effects of alcohol and hepatitis virus[6].

The rationale of our study was to explore the recommendation for use of platelet count/splenic diameter ratio for prediction high risk EVs in cirrhosis non endoscopically, as the data available shows variable results in terms of specificity and sensitivity for platelet count /splenic diameter. Although endoscopy is gold standard for diagnosis of high risk EVs, it is unavailable at most of the health centers of our country. Also endoscopy is invasive, unpleasant, costly and there is fear of introducing infection, all these factors inturn reduce compliance. This ratio can help us to screen high risk patients with esophageal varices so that these patients can be put on primary prophylaxis against bleeding or transferred to higher health centres for invasive endoscopy for necessary banding if required.

PATIENTS AND METHODS

The cross section validation study of patients fulfilling the inclusion and exclusion criteria was carried out from 01 January 2014 to 30 June 2014 at Military Hospital Rawalpindi. Inclusion criteria included male/female gender, age 35-70 years and cirrhosis due to any cause. Patients were excluded if they had any of the following; hepatocellular carcinoma detected by ultrasonography and/or elevated alpha-fetoprotein (more than 10 times the upper normal limit of normal), primary hematologic disorders, active gastrointestinal bleeding on admission, previously known gastrointestinal bleeding, taking drugs for primary prophylaxis of variceal bleeding, taking alcohol less than 6 months before enrollment, history of parenteral drug addiction, history of sclerosis or band ligation, trans-jugular intrahepatic portosystemic stent shunt, history of surgery for portal hypertension, other diseases with life expectancy of less than one year and unstable medical condition.

A total of 160 patients were included in this study. Sample size was calculated by world health organization (WHO) sample size calculator, keeping sensitivity: 88.5%[15], specificity: 83%[15], expected prevalence: 41%[15], desired prevalence: 8% and confidence level: 95%. Sampling technique was non probability consecutive sampling. Written informed consent for participation was taken from patient or accompanying attendant after explaining the objectives of the study.

All these patients coming to medical outpatient department or admitted in wards underwent blood test for platelet count. About 5ml of freshly collected blood specimen from patient's vein, was added to bottle to which a chemical ethylenediaminetetraacetic acid (EDTA) had been added. Blood specimens were sent to laboratory where platelet count was done manually using hemocytometer. Ultrasound abdomen for splenic diameter was done by radiologist for which the patient was sent to radiology department. The spleen was visualized

with the patient in right lateral decubitus position and measurement taken in longitudinal axis. For each patient calculation of platelet/splenic ratio was done. A cut off value of 909 was kept. Values greater than this cut off were supposed not to have high risk esophageal varices. All endoscopies were performed by endoscopist who was blinded to the patients. On the basis of endoscopy results the patients were divided into two groups, first group in which high risk EVs (grade 2 and grade 3) were present and second group in which they were absent. First group in which high risk EVs were present included grade 2 varices defined as enlarged tortuous veins occupying less than one third of the esophageal lumen diagnosed by endoscopy and grade 3 varices defined as enlarged tortuous veins occupying more than one third of the esophageal lumen, large enough to occlude the esophageal lumen, diagnosed by endoscopy. Second group in which high risk esophageal varices were absent included grade 1 varices defined as small straight varices and no varices at all. Subsequently sensitivity, specificity, predictive values and accuracy were calculated, keeping in view the calculated cut off value and endoscopy findings. Data were collected on a performa. Receiver operating characteristic curve for platelet spleen diameter ratio 909 was also performed. Area under curve was: 0.824 [95% CI

Table-I: Age distribution (n=160).

Age (in years)	No. of patients	%
35-50	96	60
51-70	64	40
Total	160	100

Mean ± SD: 50.15 ± 9.28

Table-II: Gender distribution (n=160).

Gender	No. of patients	%
Male	89	55.63
Female	71	44.37
Total	160	100

Table-III: Frequency of high risk esophageal varcies in cirrhotic patients (n=160).

High Risk Esophageal varices	No. of patients	%
Yes	107	66.88
No	53	33.12
Total	160	100

Table-IV: Validity of platelet count/spleen diameter ratio in cirrhotic patients for diagnosis of high risk esophageal varices, keeping endoscopy as gold standard (n=160).

Platelet count/spleen diameter ratio	Gold Standard (Endoscopy)	
	High risk esophageal varices (+)	High risk esophageal varices (-)
Predictable platelet count /splenic diameter ratio of <909 (+)	True positive (a) 93 (58.13%)	False positive (b) 9 (5.63%)
Predictable platelet count/splenic diameter ratio of <909 (-)	False negative(c) 14 (8.75%)	True negative (d) 44 (27.5%)
Total	a + c 107 (66.88%)	b + d 53(33.12%)

Sensitivity	= a / (a + c) x 100 = 86.92%,
Specificity	= d / (d + b) x 100 = 83.01%
Positive predictive value	= a / (a + b) x 100 =91.18%
Negative predictive value	= d / (d + c) x 100 =75.86%
Accuracy rate	= a + d / (a + d + b + c) x 100 =85.63%

(0.81-0.91)] (fig). All the data were analyzed using SPSS Version 17.0. 2x2 table was constructed to calculate sensitivity, specificity, predictive values and accuracy. Mean and standard deviation (mean ± SD) was calculated for quantitative variables like age. Frequency and percentages were calculated for qualitative variables like gender.

RESULTS

A total of 160 cases fulfilling the inclusion/exclusion criteria were enrolled to determine validity of platelet count/spleen diameter ratio in cirrhotic patients for diagnosis of high risk EVs, keeping endoscopy as gold standard.

Age and gender distribution of the patients was done as shown in table-I and II. Frequency of high risk EVs in cirrhotic patients was recorded (table-III). Sensitivity, specificity, positive predictive value, negative predictive value and accuracy rate were calculated (table-IV). Receiver operating characteristic curve for platelet spleen diameter ratio 909 was performed. Area under curve was: 0.824 [95% CI (0.81-0.91)] (figure).

Of EVs of the platelet count/spleen diameter. Area under the ROC curve (AUROC) is 0.824. 1.00 represents perfect prediction with 100% sensitivity and 100% specificity (i.e. the top left corner). Thee diagnostic accuracy is generally defined as "Useful" (if AUROC >0.7) and "Excellent" (if AUROC is between 0.8-0.9).

DISCUSSION

Endoscopic screening for EVs is currently recommended in all patients at the time of diagnosis of cirrhosis[2]. Surveillance should be performed every 2 year on patients if at the time of first endoscopy no varices are seen. Large varices are developed at a rate of 8% per year in patients with small varices[2]. Thats why, endoscopy should be repeated every year when screening endoscopy reveals small varices[2]. Such policy eventually places a strong burden on medical resources as many patients may not have varices and may be hampered by the lack of compliance as it is invasive. Thus noninvasive parameters associated with high-risk EVs will result in reducing the number and thus the cost of endoscopies[4]. These parameters could be used to differentiate between high and low-risk patients; and thus the endoscopic examination will be limited to the high-risk patients only[4]. A lot of non-invasive parameters associated with portal hypertension have been assessed in various studies for predicting high risk EVs for example splenic diameter, liver stiffness, platelet count, spleen thickness, Platelet/Spleen diameter ratio, Right liver lobe diameter/serum albumin ratios, international normalized ratio, serum albumin, portal vein diameter (PVD), Child-Pugh score and elastography.

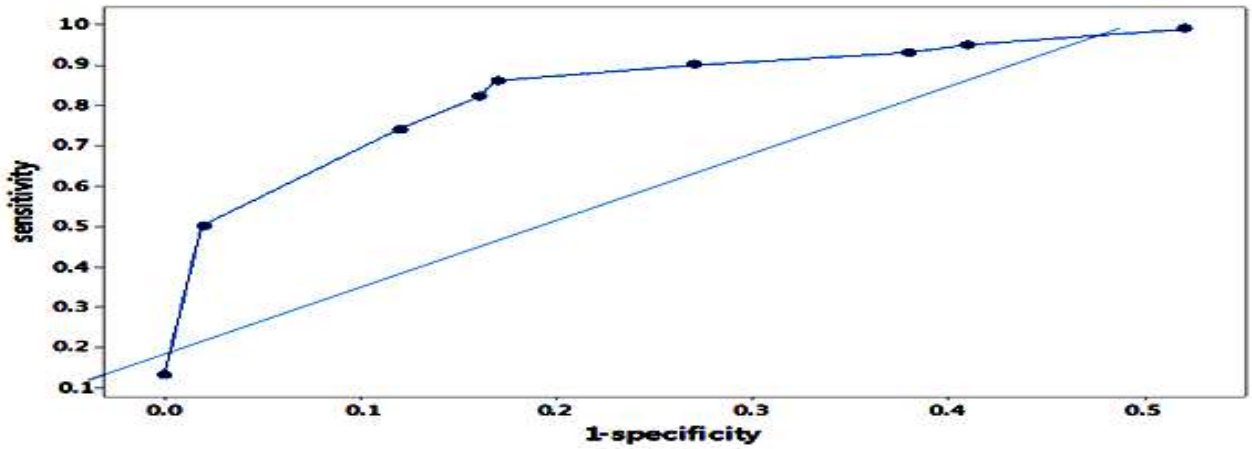

Figure: Receiver operating characteristic curves for the diagnosis.

There have now been a number of studies assessing this. In different studies various cut off values are used and various non invasive parameters other than platelet count by splenic diameter ratio are used. In a study conducted in egypt cut off of platelet count by splenic diameter of 587.9 was kept that showed sensitivity of 100% and specificity of 50%[7]. El Ray et al used cut off value of 1847 that showed 95% sensitivity and 93% specificity[8]. Similarly an African study considered this ratio useful in treatment in African regions lacking endoscopic facilities[3]. A Mexican study also considered it useful tool with 84% sensitivity and 70% specificity[4].

In a Chinese study, the model for predicting EV was composed of liver stiffness, platelet count, spleen thickness, platelet/spleen thickness ratio and Child-Pugh Score, The sensitivity of the model was 96.5% and the specificity was 99.2%. The model for predicting EV was composed of liver stiffness, platelet count, spleen thickness, platelet count /spleen thickness and Child-Pugh score which was accurate and sensitive and could be used to predict EVs in clinic[9]. Manohar et a concluded that multivariate prediction of large varices based on a combination of non-endoscopic parameters including the grade of spleen, blood parameters, platelet count, international normalized ratio, serum albumin, spleen size, PVD and platelet count to spleen diameter ratio can be utilized in place of single parameter based predictions[10]. Another study in China concluded that instead of a single variable, a comprehensive model using multiple variables significantly improves the predictive accuracy in screening the most at risk patients with potential variceal hemorrhage[11]. Berzigotti et al also used combined data including liver stiffness, spleen diameter and platelet count to identify patients with high risk EVs[12]. Instead of single parameter, above mentioned four studies used combined non invasive parameters for predicting high risk esophageal varices. A Spanish study used the cut-off of 1.010 for the ratio platelets /spleen showing sensitivity of 72.15% and specificity of 71.74% for the presence of varices and finally concluded that its implementation would entail a risk of not diagnosing large varices in almost a quarter of the population studied[13]. A meta- analysis yielded a pooled sensitivity of 89% and a pooled specificity of 74% and concluded that platelet count to spleen diameter (PC/SD) ratio of 909 may not be adequate to completely replace esophagogastroduodenoscopy as a noninvasive screening tool for EVs[14].

Almost all studies mentioned above has concluded that non invasive parameter can be used as a tool for predicting high risk EVs except the two above mentioned studies i.e. The Spanish study and the meta-analysis.

In our study, single non invasive parameter of platelet count by splenic diameter is used. Like in most of the above mentioned studies in which specificities and sensitivities are between 80 to 95%, our study also concluded sensitivity and specificity of 86.92% and 83.01% respectively.

Our findings are in agreement with a recent study conducted in SaudiArabia that showed that a cut off value of 909 for platelet count / splenic diameter ratio had a sensitivity and specificity of 88.5%, 83% respectively[15]. In this study prevalence of high risk EVs was 41.1%, while in our study, the prevalence of esophageal varices was higher i.e. 66.88%, but this was not the comparable variable.

CONCLUSION

Our results suggest that the platelet count/ spleen diameter ratio may be a useful tool for detecting EVs in patients with hepatic cirrhosis but some other trials in our local population are required to authenticate its accuracy.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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