

Original Article

A STUDY TO COMPARE THE EFFICACY OF NON-INVASIVE PREDICTORS OF ESOPHAGEAL VARICES IN PATIENTS WITH PORTAL HYPERTENSION

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Objective: To study the predictive power and compare the various noninvasive investigative parameters for detection of esophageal varices in patients with Portal Hypertension as compared to invasive parameter.

Methods: Fifty consecutive patients meeting the inclusion and exclusion criteria were enrolled in the study. All patient were subjected to complete blood count, Liver function tests, total serum proteins, albumin and globulin levels, coagulation profile (APTT, PT, INR)HbsAg, anti HCV antibodies and abdominal ultrasonography to assess the spleen longitudinal diameter of spleen and portal vein diameter and upper gastrointestinal endoscopic examination. Elastography was determined using Fibrosan. Patients were assessed with Child Turcotte Pugh (CTP) score and the esophageal varices were graded using Westaby's Classification.

Results: Predominant age group was 51-60 years. Males were the most common to present with EV. Majority of patients were Hepatitis C antibodies positive and they were the most common cause for PHT. 48% had severe thrombocytopenia of count less than twenty thousand. 56% had spleen size of less than 130mm. 4% did not have EV, 26% had Grade-I varices, 34% had Grade-II varices and 36% had Grade-III varices. Higher Fibrosan score is associated with larger varices. (p-value -0.001). Low platelet count was seen in Grade-III varices. When the Right lobe diameter albumin ratio was high the varices were also larger. Patients who had large grade-III varices also had a low Platelet / spleen ratio with a mean of 190. (p-value -0.002)

Conclusions: Overall the non-invasive parameters had a significant ability to predict and estimate grade of varices and severity of PHT.

Keywords: portal hypertension (PHT), transient elastography, esophageal varices (EV).

Introduction

Portal hypertension is defined as a pathologic increase in the portal venous pressure gradient between the portal vein and the inferior vena cava.¹ Esophageal varices (EV) have been the troublesome complications of Portal Hypertension. The common and frequent cause of morbidity & mortality is variceal bleeding which is seen in around 30-50% of the patients. EV can be confirmed endoscopy. Esophageal varices are formed only when the Hepatic vein pressure gradient (HVPG) exceeds 10 mm Hg and bleeding occurs usually when the HVPG exceeds 12 mm Hg.³ However not all patients who have a HVPG greater than 12 mm Hg bleed. In order to reduce the burden of endoscopy, as the prevalence of EV bleeding has increased, studies have been done frequently to identify modalities to identify or predict EV noninvasively. Studies have evaluated the parameters of PHT as predictors of the presence of EV either directly or indirectly. They are splenomegaly, Thrombocytopenia and a poor Child pugh score.^{4,6} In patients with CLD the presence of thrombo-

cytopenia may be due to several other factors like the reduced lifetime of platelets, low thrombopoietin release or can also be due the myelotoxic effects of either alcohol or the hepatitis viruses. However the splenomegaly in cirrhotic patients is mainly due to PHT. Likewise studies have demonstrated the platelet count/spleen diameter ratio as a parameter predicting EV by linking thrombocytopenia to the size of spleen and Right lobe diameter/albumin ratio has also been used in the studies to predict EV.⁷ The recent noninvasive technique that has been used is transient elastography or Fibrosan that measures the liver stiffness or hepatic parenchymal elasticity using ultrasound elastic waves. Many studies have proved that Fibrosan is a useful and reliable method to the assess fibrosis of the liver parenchyma. Moreover PHT is due to liver fibrosis as proved in many studies of the cases with fibrosis. Thus it can also be used a method to assess PHT and can also be used to predict the EV.⁸

EV, most of the time is asymptomatic and this can be diagnosed easily with many noninvasive parameters. In a country where there is increased caseload & higher

financial constraint, there is a need for a reliable and reproducible non-invasive predictor which can be used.

Methods

This cross-sectional study was conducted at East medical ward, Mayo hospital Lahore from March 2019 to August 2019. Patients of either gender aged between 25-65 years who were diagnosed as case of Portal hypertension clinical, biochemical, radiological and endoscopies were included. Patients with HIV, Liver metastasis, Hepatocellular carcinoma, history of prior treatment for PHT in form of surgery or EVL and pregnancy were excluded. Ethical approval was sought from the institutional review forum and written informed consent taken in each case prior to commencing the study. All patients were subjected to complete blood count, activated partial thromboplastin time, prothrombin time and INR, Liver function tests [serum bilirubin, alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST)], total serum proteins, albumin and globulin levels, coagulation profile [APTT, PT, INR] serum electrolytes and blood urea, serum creatinine, random blood sugar, HbsAg, anti HCV and abdominal ultrasonography to assess the spleen longitudinal diameter and portal vein diameter and upper gastrointestinal endoscopic examination. Fibro-elastography was determined using FibroScan. Patients were assessed with Child Turcotte Pugh (CTP) score and the esophageal varices were graded using Westaby's Classification. Westaby classification⁹ (taken as it is)!

Grade-I: Varices appearing as slight protrusion above mucosa, which can be depressed with insufflations.

Grade-II: Varices occupying <50% of the lumen.

Grade-III: Varices occupying >50% of the lumen and which are very close to each other with confluent appearance.

Data was analyzed using SPSS version 21.0. Numerical values were reported using mean and standard deviation or median. Categorical values are reported using number and percentages. ANOVA was used to compare the mean scores. A p value of < 0.05 was taken as statistically significant.

Results

50 patients took part in the study with males accounting for 72% of the study population. Majority of the subjects were between the age group

51 to 60 years (44%) followed by the age group 41 to 50 years (36%), very few were below the age of 40 years (4%). Viral Hepatitis including hepatitis B and C were the commonest cause of portal hypertension (22% and 64% respectively). Rest of the causes included non cirrhotic portal hypertension, alcoholism and other cryptogenic causes. Predominantly the patients had thrombocytopenia and the mean was around 35,061 and the mean hemoglobin was 10.11g/dL. Around 56% of the patients had splenomegaly of more than 130 mm. Right lobe diameter was measured and most of the patients (around-70%) had a diameter of more than 140mm. Majority of the patients about 46% had a right lobe diameter albumin ratio between 6 -10 followed by 4-6, very few found (6%) in the group 2-4. Majority of the patients had a CTP score of C, around 68%, very few had a score of A. 36% of the study group had grade-III EV, followed by 34% of patients with grade II. Only 2 patients did not have EV.

Patients with grade-III varices had mean Fibroscan score of 62.43 and grade-II varices had a mean score of 44.77. The mean score of grade I varices is around 38.34. The relationship with Fibroscan and EV was significant as the p-value is around 0.001. When Fibroscan was compared with CTP score the p value was significant 0.003. The mean score for CTP C is 51.96, CTP B is 43.58 and CTP 30.2 (p-value 0.003). Patients with grade-III varices had mean Right lobe / albumin ratio of 7.61 and grade II varices had a mean ratio of 7.4. The mean score of grade I varices is around 6.03. The relationship with Right lobe/ albumin ratio and EV was significant as the p value is around 0.05. When Right lobe/albumin ratio was compared with CTP score the p value was significant 0.003. The mean score for CTP C is 7.49, CTP B is 5.64 and CTP 4.56. Patients with grade III varices had mean Platelet/spleen ratio of 190 and grade-II varices had a mean ratio of 253. The mean score of grade I varices is around 289. The relationship with platelet/spleen ratio and EV was significant as the p value is around 0.002. When platelet/spleen ratio was compared with CTP score the p value was significant 0.001. The mean ratio for CTP C is 169.3, CTP B is 421.8 and CTP 649.2. Patients with grade-III varices had mean Platelet count of 28411 and grade-II varices had a mean count of 31705. The mean score of grade I varices is around 38076. The relationship with platelet count and EV was significant as the p value is around 0.017. When platelet count was compared with CTP score the p value was significant 0.001. The mean count for CTP C is 23212, CTP B is 55000 and CTP 79000. **(Table-1 and 2)**

Table-1: Comparing varices grade with various non invasive markers of predicting esophageal varices.

Varices Grade	Bibroscan score	Right lobe/ albumin ration	Platelet/ spleen ratio	Platelet count
Zero	25.45±1.34	3.8±0.15	858±189	100500±41719
One	38.34±3.7	6.03±2.2	289±249	38076±36518
Two	44.77±7.0	7.4±1.7	253±250	31705±29546
Three	62.43±6.95	7.6±2.2	190±143	28411±20633
p-value	0.001	0.05	0.002	0.017

Table-2: Comparing CTP score with various non invasive markers of predicting esophageal varices

C T P Score	Bibroscan score	Right lobe/ albumin ration	Platelet/ spleen ratio	Platelet count
A	30.2±8.28	4.56±1.27	649.2±386.3	79000±47507
B	43.58±10.21	5.64±0.98	421.8±255.5	55000±32812
C	51.96±11.93	7.4±1.7	169.3±156.9	23212±19617
p-value	0.003	0.003	0.001	0.001

Discussion

Fifty patients participated in the study. Overall the non-invasive parameters had a significant ability to predict and also identify the estimated grading of variceal size. Commonest age group involved was people aged between 51-60 years and the majority (about 4/5ths) were men. These findings are consistent with previous similar studies.

Authors

Predominant age group

Waleed K. Al-Hamoudi et al ¹⁰	57.2 ± 15.3
Alempijevic et al ¹¹	55.14 ± 7.71
El Makarem et al ¹²	51.09 ± 5.1
Borro, et al ¹³	62
Montasser et al ¹⁴	53.9 ± 8.3
Bulat et al ¹⁵	52.32 ± 13.60
Cherian et al ⁵	42

The most frequent etiology was hepatitis C (64%) followed by hepatitis B (22%), alcoholism and other cryptogenic causes. This can be attributed to the alarmingly high prevalence rates of hepatitis C in Pakistan (6.8%).¹⁶ Invariably the study population had thrombocytopenia which was similar to other studies. Thrombocytopenia also had significant relationship between the CTP score and grading of varices. The p value was 0.001 and 0.017 respectively.

Authors

Platelet count and EV

Waleed K. Al-Hamoudi et al ¹⁰	p value -0.004
El Makarem et al ¹²	p value - 0.001
Borro, et al ¹³	p value-0.0001
Cherian et al ⁵	p value - 0.003
Present study	p value - 0.017

Only Alempijevic et al¹¹ reported the relation between platelet count EV grade as statistically insignificant. (p value-0.987) Patients who had large EV grade III varices also had a low Platelet / spleen ratio with a mean of 190. This was similar to other studies and the p values were as follows: Borro, et al 0.0001 Bulat et al 0.01 Cherian et al 0.001 and Present study 0.002. However El Makarem et al¹² found the relationship as statistically insignificant. (pvalue-0.739). Bulat et al¹⁵ demonstrated a significant relation between the presence of EV and right lobe diameter/serum albumin ratio (p-value<0.01) whereas in the present study similar results were observed with significant p value of around 0.05. In the study those patients with grade-III varices had mean Fibroscan score of 62.43 and grade-II varices had a mean score of 44.77. The mean score of grade-I varices is around 38.34. The relationship with Fibroscan and EV was significant as the p value is around 0.001. The results suggest that the increased liver stiffness has a direct correlation with severity of PHT. Moreover, When Fibroscan was compared with CTP score the p value was significant 0.003. Waleed K. Al-Hamoudi et al¹⁰ showed that Fibroscan had a positive correlation when compared to the grade of EV ($\gamma=0.747$, $p<0.001$). The correlation coefficient for the present study was $r=0.523$ implying that fibroscan score had a strong positive correlation with grade of EV.

Conclusion

This study has revealed that the newer parameter transient elastography or Fibroscan is far more better predictor of presence of varices and also the size of varices when compared to other parameters. However the study has also reiterated the fact that older and often used non-invasive parameters like platelet count / spleen diameter ratio and platelet count are also much better when compared to the Right lobe diameter / albumin ratio. These parameters can be used in situations where the invasive endoscopic examination is not possible due to non-availability or contraindicated. Patients who satisfy the criteria can be started on early treatment with prophylactic beta-blocker therapy. These parameters can also be used to identify those patients who may have larger varices which needs an endoscopic intervention. This can avoid the overburden cases requiring endoscopy.

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