

Bedside Utility of Liaoning Score a Non-Invasive As Predictor of Esophageal Varices in Hepatitis C Associated Chronic Liver Disease in Pakistani Population

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1. Abstract

1.1. Introduction

Portal hypertension in cirrhotic patients results in the development of esophageal varices (EVs) with uncontrolled variceal bleeding accounting for approximately 50% of mortality in cirrhotic patients. Endoscopy is avoided by most of the patients due to its invasiveness. Liaoning score has been used previously in a Chinese population as a noninvasive predictor of EVs, Hence, the aim of this study was to validate the role of Liaoning score as a non-invasive predictor of esophageal varices in Pakistani population.

1.2. Methods

It was a cross-sectional study which was carried out at Sindh Institute of Urology and transplantation from 1st January 2020 to 31st December 2020. Cirrhotic patient with age > 18 years and no history of previous EGD were included in the study. Baseline laboratory investigations including ultrasound abdomen for chronic liver disease and ascites were carried out. The presence or absence of EVs was recorded on endoscopy. Liaoning score was calculated using the formula-Liaoning score: $1.205 + 1.557 \times \text{ascites}(1=\text{yes}, 0=\text{no}) - 0.008 \times \text{platelet count}$. Area under ROC was derived followed by determination of sensitivity, specificity, PPV, NPV and diagnostic accuracy of Liaoning score in predicting esophageal varices.

1.3. Results

Total number of patients included in the study were 273. Out of them, 168 (61.6%) patients were males. EV were present in 199 (72.9%) patients. Ascites was noted in 32 (11.7%) patients. On non-invasive investigations, platelet counts were significantly low-

er in the variceal group as compared to the non-variceal group

(54.4 vs 129.4, $p \leq 0.001$). High Liaoning score was found to be significantly associated with presence of esophageal varices with a p.value ≤ 0.001 . Area under ROC was is 0.78($p \leq 0.001$). At a cut off

≥ 0.55 , the sensitivity, specificity, NPV and PPV were 96.98%, 77%, 91.9% and 90.48% respectively for Liaoning score in predicting esophageal varices along with a diagnostic accuracy of 91.58%.

1.4. Conclusion

Liaoning score had an excellent diagnostic accuracy in predicting esophageal varices with good sensitivity of more than 90%. However, further studies comprising of large sample size are required to validate this non-invasive score.

2. Introduction

One of the most common etiologies resulting in portal hypertension is advanced liver disease termed as liver cirrhosis [1]. Portal hypertension results in formation of portosystemic collaterals and ascites. In cirrhotic patients, most common site of portosystemic collaterals is distal esophagus forming esophageal varices (EVs). Esophageal varices develop at a rate of 7% per year [2, 3]. Approximately, 40% of the patients with compensated and 60% with de-compensated liver disease have EVs at the time of index endoscopy [4]. Varicella bleeding is one of the most lethal complication of chronic liver disease with an increased risk of mortality and also the most common cause of gastrointestinal bleeding in cirrhotic patients [5-7].

In order to decrease the risk of varietal bleeding, early diagnosis of the varices prior to bleed is essential. Currently, endoscopy is considered a goal standard test for the detection and grading of the esophageal varices [8, 9]. According to the recent BAVENO VII

guidelines, all the patients diagnosed with liver cirrhosis should undergo surveillance endoscopy to rule out EVs and also to treat medium and large sized varices to prevent varietal bleed [10]. Performance under continuous sedation, poor availability of endoscopic units in the remote areas, high cost and invasive nature of the procedure results in avoidance of endoscopy by most of the patients [11, 12].

Recently, non-invasive scores have been proposed to have a role in detection of esophageal varices. These include platelet count, liver stiffness, ratio of platelet count to splenic diameter, splenic stiffness, AST/ALT, Child Pugh Score, P2MS, LoK score etc., [13-16]. Recently, Li Q et al., [17] developed a score 'Liaoning score' termed on the basis of the study performed in Liaoning province, China, based on simple variables, having better diagnostic accuracy as compared to the other scores in predicting EVs in liver cirrhosis.

Little work has been done previously in our country regarding the utility of this score as a non-invasive tool in the prediction of esophageal varices. This score is different from the other non-invasive scores as it can be implicated in decompensated chronic liver disease (i.e. patients with ascites) as well.

2.1. Aim

To evaluate the use of Liaoning score as a non-invasive predictor of esophageal varices in patients with liver cirrhosis.

2.2. Methods

This was a cross-sectional prospective study, which was conducted at the department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation from 1st June 2020 to 31st December 2021 after the approval from the ethical research committee of the hospital.

2.3. Inclusion criteria

Patients with either gender having age greater than 18 years and history of hepatitis C associated chronic liver disease were included in the study.

2.3.1. Liver Cirrhosis: [18]

All patients who are recently diagnosed with liver cirrhosis based on ultrasound abdomen findings of presence of at least three of the following features

- Altered echo texture of liver
- Irregular margin
- Spleen size more than 12 cm
- Portal vein diameter more than 12 mm
- Presence of fluid in abdomen on ultrasound

2.3.2. Esophageal Varices: [19]

- Esophageal varices will be diagnosed on endoscopy as presence of abnormally enlarged, tortuous or coiled shaped dilated veins within the linings of esophagus

2.4. Exclusion Criteria

- A prior history of endoscopy for EV screening, surveillance, or treatment;
- A prior history of EGD that incidentally revealed EV
- Other etiologies of chronic liver diseases i.e. hepatitis B, Alcoholic hepatitis, Non alcoholic fatty liver disease (NAFLD), Autoimmune Hepatitis
- Non-cirrhotic etiologies for portal hypertension

2.5. Data Collection Procedure

All patients presenting to outpatient departments of Hepatogastroenterology (GI-OPD), SIUT, Karachi and diagnosed with Hepatitis C associated liver cirrhosis (as per operational definition) were enrolled in this study. Informed written consent will be obtained from the participants of the study.

The baseline laboratory investigations were done for complete blood count including hemoglobin, total leucocyte count and platelets, liver function test, coagulation profile including international normalized ratio and serum albumin. The detection of HCV RNA PCR was done using ELISA (Enzyme linked Immunosorbent assay) method. All the patients then underwent abdominal ultrasound for measurement of ascites and other features of chronic liver disease which was performed by a consultant radiologist; using US machine (TOSHIBA-Apple 50 Model MCM17545TS). Each patient then underwent upper gastrointestinal endoscopy to document the presence or absence of EVs. All the data obtained was then entered in the pre-designed preform.

Liaoning score was calculated using the following formula:

Liaoning score: $1.205 + 1.557 \times \text{ascites} (1=\text{yes}, 0=\text{no}) - 0.008 \times \text{platelet count}$

2.6. Data Analysis Procedure

The data was entered and analyzed using SPSS version 20.0. The continuous variables were recorded as mean \pm S.D while categorical variables were recorded as frequency and percentages. Continuous data was analyzed using student-t test while categorical data was analyzed using chi square test. Liaoning score was calculated and area under the ROC was obtained for Liaoning score to evaluate the diagnostic performance of the score in predicting esophageal varices.

3. Results

Total number of patients included in the study were 273. Out of them, 168(61.6%) patients were males while 105(38.4%) were females. Mean age was 43.5 ± 12.5 years. The baseline characteristics are shown in (Table 1). On ultrasound abdomen, altered texture of liver was noted in 251(9.12%) patients while splenomegaly was seen in 189(69.2%), ascites in 32(11.7%) and dilated portal vein in 15(5.5%) patients respectively. 23(8.4%) patients had mild as-

cites, 9(3.3%) patients had moderate ascites while there was no ascites in 241(88.3%) patients. 180(65.9%) patients had CTP class A while 93(34.1%) had CTP class B. Mean platelet count was 74.8 ± 40.3 ($\times 10^9/L$). Mean MELD score was 10.9 ± 3.4 . Esophageal varices were present in 199(72.9%) patients. Among them, 103(37.8%) patients had grade I, 63(23.1%) had grade II and 15(5.5%) had grade III esophageal varices on index endoscopy. Mean Liaoning score was 0.79 ± 0.57 . Comparison of continuous and categorical variables in terms of esophageal varices is shown in (Table 2 and 3). On non-invasive investigations, total bilirubin ($p \leq 0.001$), Alkaline Phosphatase ($p=0.04$), Aspartate Transaminase ($p=0.008$), Alanine Transaminase ($p=0.04$), Gamma Glutamyl Transpeptidase ($p \leq 0.001$), INR ($p \leq 0.001$), MELD

score ($p \leq 0.001$) and Liaoning score was significantly higher in the patients with the presence of esophageal varices while the platelet counts ($p \leq 0.001$), serum albumin ($p=0.013$) and total leucocyte count ($p \leq 0.001$) were significantly lower in the variceal group as compared to the non-variceal group. In the studied population, male gender, CTP class A and presence of ascites were also seen to be significantly associated with the presence of esophageal varices.

Liaoning score was significantly higher in the patients with esophageal varices on endoscopy as compared to the non-variceal group (0.89 vs 0.52 , p value ≤ 0.001). Area under ROC obtained for Liaoning score was 0.78 ($p \leq 0.001$) (Figure 1). At a cut off ≥ 0.55 , the sensitivity, specificity, NPV and PPV were 96.98%, 77%, 91.9% and 90.48% respectively for Liaoning score in predicting esophageal varices along with a diagnostic accuracy of 91.58%. (Table 4)

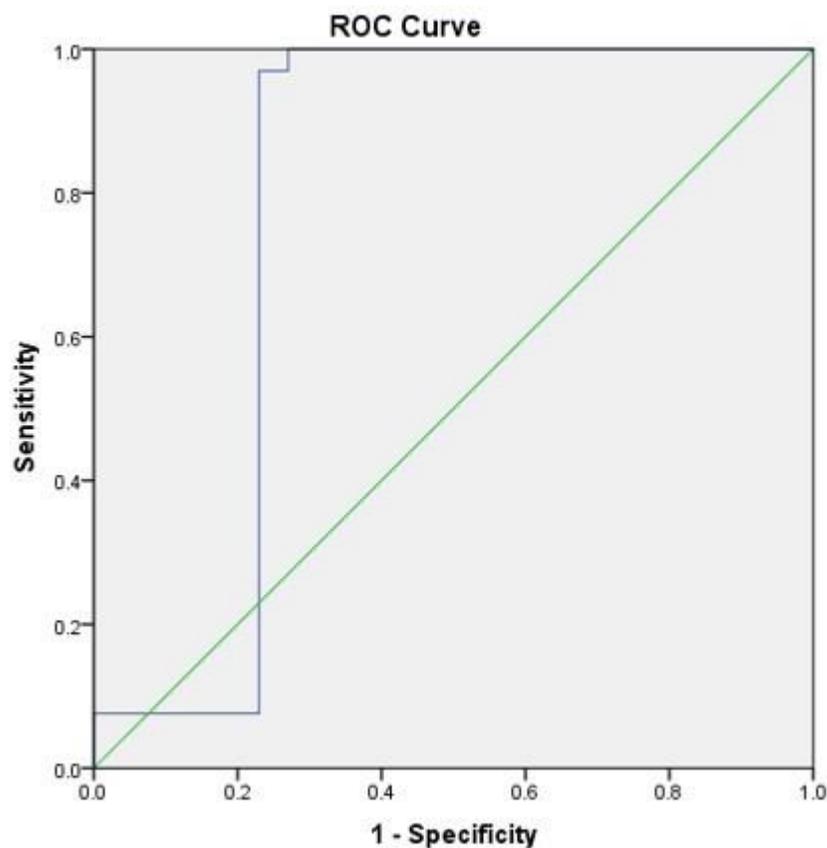


Figure 1: Area under Receiver Operating Curve (ROC) for Liaoning score in prediction of esophageal varices is 0.78 (p -value ≤ 0.001)

Table 1: Baseline characteristics of the population included in the study (n-273)

Study population		n (%)
Mean age (years±S.D)		
Gender	Male	168(61.5)
	Female	105(38.5)
Hemoglobin(g/dL)	10.8±2.1	10.8±2.1
Total Leucocyte Count(x10 ⁹ /L)	4.5±2.4	4.5±2.4
Platelet Count(x10 ⁹ /L)	74.8±40.3	74.8±40.3
Total Bilirubin(mg/dl)	1.3±0.75	1.3±0.75
Alkaline Phosphatase(IU/L)	190±187	190±187
Aspartate Transaminase(AST)(IU/L)	59±52	59±52
Alanine Transaminase(ALT)(IU/L)	45±34	45±34
Gamma Glutamyl Transpeptidase (GGT)(IU/L)	74±59	74±59
Child Turcotte Pugh Score	A	180(65.9)
	B	93(34.1)
MELD score		10.9±3.4
Esophageal varices	Present	199(72.9)
	Absent	74(27.1)
Liaoning score		0.79±0.57

Table 2: Comparison of continuous variables in terms of presence of esophageal varices

Variable	No Varices (n-74) Mean ± SD	Esophageal varices present (n-199) Mean ± SD	Mean ± SD
Age	45.6± 14.7	42.6 ± 11.4	0.089
Hemoglobin(g/dL)	11.5 ±2.01	10.1 ± 2.7	0.02
Total Leucocyte Count(x10 ⁹ /L)	6.8± 2.7	3.7 ±2.5	≤0.001
Platelet Count(x10 ⁹ /L)	129.4 ± 27.3	54.4 ± 20.4	≤0.001
Total Bilirubin(mg/dl)	0.92± 0.72	1.5 ±0.75	≤0.001
Alkaline Phosphatase(IU/L)	53±104	204± 208	0.043
Aspartate Transaminase(AST)(IU/L)	46± 23	64±59	0.008
Alanine Transaminase(ALT)(IU/L)	38±20	48±37	0.04
Gamma Glutamyl Transpeptidase(GGT)(IU/L)	65±51	98±70	≤0.001
Serum Albumin(g/dL)	3.5±0.56	3.3±0.64	0.013
International normalized ratio(INR)	1.1±0.4	1.2±0.19	≤0.001
CTP score	6.1 ± 1.1	6.2± 1.2	0.901
MELD Score	10.2±4.3	11.3 ±3.6	≤0.001
Liaoning score	0.52± 0.67	0.89± 0.5	≤0.001

Table 3: Comparison of categorical variables in terms of presence of esophageal varices

Variable		Esophageal varices present (n-199) n (%)	No Varices (n-74) n (%)	p-value
Gender	Male	115(68.4)	53(50)	≤0.001
	Female	84(31.6)	21(50)	
CTP score	A	130(56.1)	51(82.4)	≤0.001
	B	69(43.9)	23(17.6)	
Ascites	Present	15	17	0.001
	Absent	180	57	
Liaoning score	<0.55	6(94.7)	57(38.2)	≤0.001
	≥0.55	193(5.3)	17(61.8)	

Table 4: Diagnostic accuracy of Liaoning score in predicting esophageal varices

Statistics	Percentage
Sensitivity	96.98%
Specificity	77.03%
Positive Predictive Value	91.90%
Negative Predictive Value	90.48%
Diagnostic Accuracy	91.58%

4. Discussion

Liver cirrhosis leads to portal hypertension, which is most commonly manifested as esophageal varices [1]. Therefore, all clinical consensus recommend varietal screening at the time of diagnosis of liver cirrhosis [10]. This methodology will help in identifying those patients who can benefit either from non-selective beta-blockers therapy or endoscopic treatment. However, due to its cost and invasiveness, endoscopy is generally avoided by the patients [11, 12]. Currently, multiple non-invasive scores have been utilized for the prediction of esophageal varices and portal hypertension [13-16]. One of these scores include the Liaoning score that has been utilized in the Chinese population for the prediction of esophageal varices [17]. Chinese study done by Li Q et al., [20] comprised of 612 patients and had an AUROC of 0.734 in prediction of EVs. They used a cut off of 0.487 with a sensitivity, specificity, PPV, and NPV of 81.96%, 65.22%, 98.1%, and 14.3%, respectively. While in our study, we included a total of 273 patients who were HCV positive and were newly diagnosed to have cirrhosis on the basis of ultrasound abdomen. The AUROC obtained for Liaoning score was 0.78, which was slightly higher in our population as compared to that of the Chinese population with an excellent sensitivity (96.8% vs 81.96%), far better specificity (77% vs 65.22%), an excellent PPV (91.9% vs 98.1%) and NPV (90.48% vs 14.3%) respectively in predicting EVs.

Low platelet count in cirrhotic patients is likely due to hyper splenism that can be attributed to portal hypertension secondary to advanced liver fibrosis in these patients [21]. In the previous as well as in our study as well, low platelet count was significantly associated with the presence of esophageal varices (54.4 vs 129.4) ($p \leq 0.001$) but utility of platelet count alone as a marker of predictor of EVs is yet to be established as multiple other diseases can result in thrombocytopenia [22]. BAVENO VII has utilized the combination of liver stiffness and thrombocytopenia for prediction of esophageal varices in newly diagnosed cirrhotics [10].

Previously, meta-analysis has shown the utility of different bedside scores in the prediction of EVs in compensated cirrhosis [23]. However, Liaoning score is the first non-invasive bedside score for the prediction of EVs in the patients with ascites. Li et al., [20] revealed that the performance of Liaoning score was far better than the other non-invasive scores for the prediction of EVs in decompensated cirrhosis.

There are certain limitations to our study. First of all, only patients with hepatitis C associated chronic liver disease were enrolled and our sample size was low as compared to the other studies done in this regard. Secondly, we did not evaluate the utility of this score in prediction of EVs in cirrhotic patients presenting with hematemesis or Melena. Third, we did not compare the diagnostic utility of Liaoning score with other non-invasive available scores in our

population.

The strength of the study was that it was the first study that utilized the non-invasive score in the prediction of EVs in decompensated cirrhosis in our population. Secondly, it was a prospective study.

5. Conclusion

Liaoning score can be utilized for the prediction of EVs in cirrhotic patients especially those with decompensated cirrhosis. However, further studies with large sample size are required to validate the score and its comparison with other scores in predicting EVs .

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