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EVALUATION OF EVENDO SCORE FOR IDENTIFYING HIGH-RISK ESOPHAGEAL VARICES

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ABSTRACT

Liver cirrhosis can cause life-threatening esophageal varices (EV), which cause upper gastrointestinal bleeding. High-risk varices must be identified in cirrhotic patients to prevent severe bleeding and death. Cirrhosis may benefit from EVendo Score for high-risk varices. This study examined the diagnostic accuracy of EVendo Score in predicting high-risk esophageal varices using upper GI endoscopy as the gold standard.

METHODOLOGY

This cross-sectional study was conducted from March 2024 to August 2024 in the Outpatient Gastroenterology Department of Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU), Larkana. The sample of 175 patients were included through non-probability purposive sampling after taking an informed consent. This study included both male and female patients aged 18–60 years with the diagnosis of liver cirrhosis. The data were statistically analyzed by using SPSS v. 26.0. The receiver operating characteristic (ROC) curve was created, and area under the curve (AUC) was also reported.

RESULTS

The study participants were divided into two groups with esophageal varices (n=74) and those without esophageal varices (n=101). Mean age was slightly higher in the group without esophageal varices (49.46 ± 9.55 vs. 47.39 ± 11.24). In gender distribution the proportion of males was documented as slightly higher in both groups (66.2% in varices group vs. 62.4% in no varices group). The area under the curve (AUC) was noted as 0.849 (95% CI: 0.786–0.912). The optimal cutoff value was found to be ≥ 1.50, with a sensitivity of 98.6% and a specificity of 95.0%.

CONCLUSION

The E/Vendo score is found to be a simple and useful non-invasive tool to diagnose high-risk esophago-gastric varices in cirrhotic patients. It offers a high degree of combined sensitivity and specificity at ideal cut-offs which is important for clinical utility. At very high cutoff values, this is reduced, which means that its use should be limited to thresholds that allow for proper prediction.

Keywords: *Baveno VI Criteria, Cirrhosis, Esophageal Varices, EVendo Score, High Risk Varices*

INTRODUCTION

Cirrhosis of liver (COL) is chronic inflammation of the liver, diffuse hepatic parenchymal inflammation, and replacement of normal hepatic parenchyma by regenerative nodules [1]. Data from the Global Burden of Disease for 2017 showed an estimated 112 million cases of compensated cirrhosis and 10.6 million cases of decompensated cirrhosis worldwide [2]. Cirrhosis leads to numerous complications which includes variceal bleeding, hepatic encephalopathy ascites, hepatorenal syndrome and infections [3].

Variceal hemorrhage remains a complex complication of decompensated liver disease and is associated with death in 20–40% of patients [4]. In clinically significant portal hypertension–defined as hepatic venous pressure gradient of ≥ 10mmHg developed gastroesophageal varices in liver cirrhosis [5]. Gastroesophageal varices (GOV) have a direct correlation with the severity of liver cirrhosis, and prevalence rates of 30–40% and of 85% in compensated and decompensated liver disease (DCLD) respectively have been reported [6,7].

The gold standard for the diagnosis of esophageal varices is the upper GI endoscopy, it is invasive, expensive and time consuming limiting its clinical use in countries where health resources suffer [8]. The consensus statement with Baveno VI of 2015 recommends for the prediction of high-risk esophageal varices in individuals with compensated liver disease the use of non-invasive markers. Thus, numerous non-invasive tests and resources have been established to forecast esophageal varices among cirrhotic patients, but controversy surrounding their actual effectiveness exists [9]. Various studies have explored the predictive accuracy of a new marker EVendo score to identify patients at high risk for EV.

Jan et al conducted a study to assess the diagnostic ability of EVendo score for high-risk esophageal varices. The 17.3% rate of high-risk varices they found in their study. At the cut-off value of >8, however, they demonstrated that EVendo Score had 87.23% sensitivity, 83.56% specificity and 84.19% diagnostic accuracy for the diagnosis of high-risk EV [10]. Similarly, Yang et al, described the ongoing assessment of diagnostic performance of EVendo score for the diagnosis of high-risk EV. The prevalence of high-risk EV in their study was 33.3%, and they reported 97.4% sensitivity and 41.0% specificity to diagnose high-risk EV [11]. A study by Yasmeh et al was also conducted to evaluate the diagnostic value of EVendo score for the diagnosis of high-risk EV and they reported a 26.4% prevalence of high-risk EV in the study. Sensitivity and specificity of high-risk EV diagnosis were 95.7% and 33.7%, respectively, using the EVendo score [12]. In literature, it is shown that patients with high-risk for adverse outcomes due to variceal bleeding and EV do exist among compensated and decompensated cirrhosis and EVEndo score can be precise in high-risk EV in such population either variceal bleeding associated [12-14].While most of non-invasive tools used for esophageal varies have showed accuracy in predicting variceal hemorrhage, limited tools are available to predict presence of high-risk EV before bleeding catastrophe. Besides, tools such as Baveno VI consensus criteria require liver stiffness measurement, which is not available in most healthcare facilities in developing countries like Pakistan. This study was designed to determine the utility of EVendo score in cirrhotic patients, which is non-invasive, readily available and cost-efficient. Findings of this study will help gastroenterologists in identifying patients who will most likely benefit from upper GI endoscopy, thus avoiding unnecessary endoscopy procedures and reducing burden on healthcare resources.

METHODOLOGY

This cross-sectional study was conducted from March 2024 to August 2024 in the Outpatient Gastroenterology Department of Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU), Larkana. A sample size of 175 patients was recruited using non-probability purposive sampling. Patients aged 18–60 years of both genders, diagnosed with liver cirrhosis based on clinical findings (reduced liver size, irregular nodular surface, or stigmata of chronic liver disease such as clubbing, splenomegaly, edema, or ascites) and ultrasonographic findings (shrunken nodular liver with irregular margins and increased echotexture), were included in the study. Cirrhotic patients with a Child-Turcotte-Pugh score of 5–6 were classified as having compensated cirrhosis. Patients previously diagnosed with esophageal varices, those with a history of upper GI endoscopy, presenting with acute variceal bleeding or acute hepatitis, diagnosed with non-cirrhotic

portal hypertension, or with a history of anticoagulant use in the past four weeks or a bleeding disorder, as well as pregnant females, were excluded from the study.

Patients were assessed for baseline demographic and clinical information and entered into the predefined form following receipt of a thorough explanation of the study and signed written informed consent. Investigation including complete blood count (CBC), liver function tests, renal function tests, coagulation profiles, abdominal ultrasound and record of values of hemoglobin, platelets, AST, BUN, INR and presence of ascites. EVendo score for each patient was determined by the scores obtained from the formula: [(9.5 × INR) + (AST/35)] / [(Platelets/150) + (BUN/ 20) + (Hemoglobin/ 15)] + 1 (if ascites was present). High-risk esophageal varices were defined as an EVendo score > 8. French Classification System for classification of esophageal varices performed by a gastroenterologist with > 5 years post-fellowship experience under sedation for upper GI endoscopy. High-risk esophageal varices were graded as II (tortuous varices involving less than one-third of the esophageal lumen) or Grade III (tortuous, confluent varices involving more than one-third of the esophageal lumen).

The analysis of data will be conducted using SPSS version 26.0. Descriptive statistics were used to calculate the demographic and baseline data of the patients. The receiver operating characteristic (ROC) curve was generated, and the area under the curve (AUC) was reported, along with optimal cut-off settings for the sensitivity and specificity of EVendo Score in predicting high-risk esophageal varices.

RESULTS

Table I represents a comparison of demographic, clinical, and laboratory characteristics between participants with esophageal varices (n=74) and those without esophageal varices (n=101). Mean age was slightly higher in the group without esophageal varices (49.46 ± 9.55 vs. 47.39 ± 11.24 years; p=0.201). Proportion of males was slightly higher in both groups (66.2% in varices group vs. 62.4% in no varices group; p=0.601). The majority of participants were in Class A (70.3% for varices vs. 67.3% for no varices), with minimal representation in Class C (8.1% vs. 5.9%; p=0.670). Higher prevalence of ascites was noted in the varices group (31.1% vs. 19.8%; p=0.087).

The varices group had a significantly higher rate of encephalopathy (14.9% vs. 5.0%; p = 0.025). The laboratory results (ALT, AST, albumin, bilirubin, alkaline phosphatase, hemoglobin and platelets) were identical between groups with no significant difference (P > 0.05).

ROC curve (Figure I) depicting the diagnostic performance between the E/Vendo score for prediction of esophageal varices in cirrhosis of the liver. Results showed an area under the curve (AUC) of 0.849, which is a very good discrimination between variceal and non-variceal patients. The concave, especially in the upper-left node, specifies the strong sensitivity and specificality at optimal cutoff points.

The diagnostic metrics for E/Vendo score are summarized in Table II. The E/Vendo score could accurately predict esophageal varices, with AUC 0.849 (95% CI: 0.786–0.912). The optimal cutoff value was found to be ≥ 1.50, with a sensitivity of 98.6% (i.e. the score correctly identified 98.6% of patients with varices) and a specificity of 95.0% (i.e. the score correctly excluded 95.0% of patients without varices). A positive likelihood ratio was noted as 19.72, which indicates that model has high effectiveness in diagnosing positive esophageal varices patients as positive when they truly have the condition. Conversely a negative likelihood ratio was found to be 0.01 indicates that model has high effectiveness in diagnosing negative esophageal varices patients as negative when they do not have the condition. The p-value of 0.01, further supports that the model is statistically significant.

As indicated in table III, the E/Vendo score at various cutoff points provided sensitivity and specificity. At a cutoff of 1.50, sensitivity is 98.6% and specificity is 95.0%, thereby providing the best tradeoff between those patients both with and without esophageal varices. At a cutoff of 2.50, sensitivity is slightly reduced to 95.9%, and specificity is reduced to 79.2%. Higher cutoff values (>3.50) that greatly decrease sensitivity (>0.75) render the score ineffective for esophageal varices detection, similar to lower specificity (<0.67) that limits its diagnostic utility. At a cut-off of 11.00 the sensitivity and specificity is both 0,

which means that there is no diagnostic utility using this threshold.

Table I: Baseline Characteristics of Study Participants (n=175)				
Variables		**Esophageal Varices**		**P-Value**
		Yes, (n=74)	**No**, (n=101)	
Age in years, Mean ± SD		49.46 ± 9.55	47.39 ± 11.24	0.201
Gender	Male, *n* (%)	49 (66.2)	63 (62.4)	0.601
	Female, *n* (%)	25 (33.8)	38 (37.6)	
Child Pugh Class	A, *n* (%)	52 (70.3)	68 (67.3)	0.670
	B, *n* (%)	16 (21.6)	27 (26.7)	
	C, *n* (%)	6 (8.1)	6 (5.9)	
Complications of Cirrhosis	Ascites, *n* (%)	23 (31.1)	20 (19.8)	0.087
	Encephalopathy, *n* (%)	11 (14.9)	5 (5.0)	0.025
ALT in IU/L, Mean ± SD		45.74 ± 22.32	50.71 ± 21.72	0.141
AST in IU/L, Mean ± SD		57.19 ± 20.58	57.33 ± 19.11	0.964
Serum Albumin in g/dl, Mean ± SD		3.59 ± 0.60	3.53 ± 0.58	0.509
GGT in IU/L, Mean ± SD		68.73 ± 28.87	76.50 ± 29.83	0.086
Total Bilirubin in mg/dl, Mean ± SD		1.16 ± 0.36	1.23 ± 0.35	0.209
BUN in mg/dl, Mean ± SD		15.92 ± 6.36	16.23 ± 5.99	0.743
Alkaline Phosphatase in IU/l, Mean ± SD		180.51 ± 83.56	185.12 ± 83.48	0.719
Hemoglobin in g/dl, Mean ± SD		11.68 ± 1.89	11.62 ± 1.95	0.861
Platelets in 10^9/L, Mean ± SD		147.57 ± 44.12	148.66 ± 45.53	0.874
EVendo score, Mean ± SD		7.89 ± 2.09	4.71 ± 2.29	0.0001

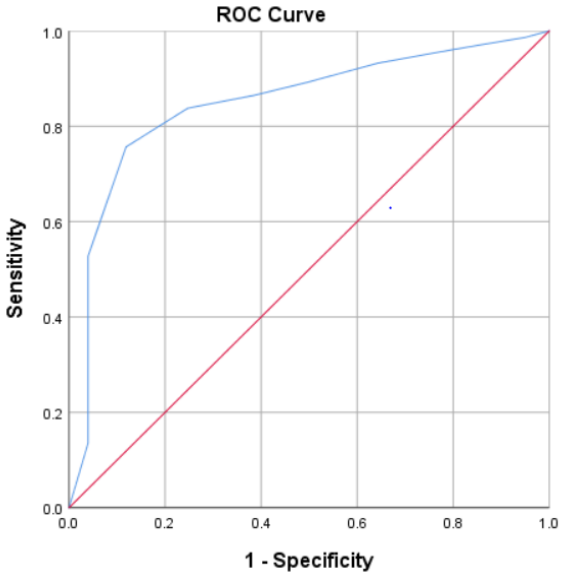

Table II: Predictive Value of EVendo Score for Esophageal Varices in Liver Cirrhosis (n=175)	
Area under the curve (AUC)	0.849
Std. Error	0.032
95% Confidence Interval	0.786----0.912
P-Value	0.0001
Cut off value	≥1.50
Sensitivity	98.6%
Specificity	95.0%
Positive Likelihood Ratio	19.72
Negative Likelihood Ratio	0.01

Table III: Coordinates of the Curve (n=175)		
Cut Off Values	**Sensitivity**	**Specificity**
.00	1.000	1.000
1.50	.986	.950
2.50	.959	.792
3.50	.932	.644
4.50	.892	.495
5.50	.865	.386
6.50	.838	.248
7.50	.757	.119
8.50	.527	.040
9.50	.135	.040
11.00	.000	.000

DISCUSSION

The EVendo score is a valuable scoring system to identify high risk of esophageal varices in patients with cirrhosis. It is used in providing a comprehensive risk assessment based on the integration of clinical parameters such as the Child-Pugh score, laboratory markers such as platelet count and prothrombin time and imaging findings. This may help to further inform management of screening and prophylactic therapy, such as beta-blockers or endoscopic interventions, in high-risk cases. The EVendo score showed an area under the curve (AUC) of 0.849 in our study, with a cutoff value of ≥1.50 providing a high sensitivity (98.6%) and a good specificity (95.0%). These results are consistent with previous studies such as that of Jan et al. who found a high diagnostic accuracy with an AUC of 0.93, sensitivity 94.92% and specificity 80.52% with a cutoff value >7.3 [10], and Alswat et al. who found moderate sensitivity and specificity with lower cutoffs [6]. These results underline their usefulness of the EVendo score to determine the presence and degree of esophageal varices, its accuracy and reproducibility need to be validated for other populations as well.

Recent studies focus on the increasing value of predictive tools, such as the EVendo score, to identify liver disease patients with particularly high-risk varices. Ramakrishnan et al. Artificial intelligence (AI) has a potential value in improving variceal detection and stratifying bleeding risk and its combination with various scoring systems including the EVendo score in improving accuracy and thereby reducing unnecessary invasive procedures has also been outlined [15]. Similarly, Malik et al. emphasized how machine learning models could be utilized to improve early detection and clinical management [16]. Kotwal et al. presented a new esophageal varices prediction score in patients with compensated chronic liver disease, thus reinforcing the importance of non-invasive markers [17]. Sharaf and Li also proposed new methods to enhance predictive performances with clinical score integration and radiomics algorithms, which are complementary and develop entirely disparate characterizations in comparison to the EVendo score [18], [19]. Results from the two advances above suggest that integration of imaging, AI and clinical parameters can provide higher predictive power and may allow a better stratification of cirrhotic patients followed by a timely intervention on the basis of the EVendo score.

Chittajallu et al. discussing prospective models for its use in hepatocellular carcinoma (HCC) reporting its eligibility in HCC for the detection of high-risk varices in advanced liver disease [20].

There's a lot to like about the EVendo score, but it has its limitations. Although a single-center evaluation, it may, in addition, not reflect the study population in advanced disease stages, or previously diagnosed endoscopically and therefore underrepresented the utility of its use [6]. Its implementation across different healthcare settings and populations needs to be validated by multicenter studies. With an established system, such as the Baveno VI criteria, for comparison the score of the EVendo will be continually refined for precision. The clinical relevance and cost-effectiveness of our algorithm could be improved by adding long-term follow-up and progressive imaging techniques such as transient elastography. Finally, although the EVendo score demonstrates high potential as a moving-forward, non-invasive diagnostic tool, more work is required to ascertain its fitness-for-purpose in the real-world and how best to maximise outcomes for patients with cirrhosis.

CONCLUSION

The E/Vendo score is found to be a simple and useful non-invasive tool to diagnose high-risk esophago-gastric varices in cirrhotic patients. It offers a high degree of combined sensitivity and specificity at ideal cut-offs which is important for clinical utility. At very high cutoff values, this is reduced, which means that its use should be limited to thresholds that allow for proper prediction.

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