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Non-invasive predictors of large esophageal varices in patients with cirrhosis: A systematic review and meta-analysis

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Abstract
Introduction and Background: Esophageal varices are collateral blood vessels that develop in response to portal hypertension, typically located in the submucosal layer of the distal esophagus. The primary aims of this study were to find and examine noninvasive investigative criteria that have the potential to predict the presence and severity of oesophageal varices in individuals with cirrhosis.
Material and Methods: The present study employed an observational cross-sectional design. The current investigation was carried out on a sample of 40 patients who were admitted to the general medicine and medical gastroenterology wards of ICare Institute of Medical Sciences and Research, Banbishnupur, PO, Balughata Rd, Haldia, West Bengal. These patients had been diagnosed with liver cirrhosis. The study was done between October 2013 and October 2014.
Results: The purpose of our study was to evaluate a range of noninvasive predictors for their ability to accurately predict the existence of significant esophageal varices. Among the cohort of 40 patients under investigation, it was observed that 28 individuals exhibited small varices, while the remaining 12 individuals presented with massive varices. The median age of the little varices group was 28, whereas the median age of the large varices group was 40. In the little varices group, there were 18 male patients and 10 female patients. In the large varices group, there were 16 male patients and 2 female patients.
Conclusion: The correlation between the presence and grade of varices and the severity of liver disorders was observed. Specifically, within the large varices group, 13.6% were classified as CTP-A, 31.8% as CTP-B, and 54.5% as CTP-C.

Keywords: Non-invasive, esophageal varices, cirrhosis

Introduction
Esophageal varices are porto-systemic collaterals that develop in the sub mucosa of the lower esophagus as a result of portal hypertension. Major complications of portal hypertension include rupture and bleeding from esophageal varices, both of which have a significant mortality risk. Bleeding from varices is the cause of 10%-30% of all upper GI bleeding [1, 2]. Esophageal varices are common in cirrhotic patients, and bleeding from the esophagus occurs at a rate of 15% per year on average. Cirrhotic patients had a 30%-70% incidence of esophageal varices, and 9-36% incidence of "high-risk" varices. Cirrhotic patients have a 5-8% annual incidence of esophageal varices, but only 1-2% of these varices are severe enough to cause bleeding [3-5]. There is an annual 8% increase in the size of varices. Thirty percent of people diagnosed with esophageal varices will experience bleeding during the first year. The fatality rate for variceal hemorrhage remains high (20%-35%), despite advances in detection and treatment. The severity of liver disease increases with the existence of gastroesophageal varices. The size of esophageal varices is the most reliable indicator of variceal hemorrhage. The greater the size of the esophageal varices, the greater the risk they pose because of the potential for increased tension on the variceal walls.

Thus, it is crucial to detect big esophageal varices before they bleed for the first time in order to prevent or lessen the severity of this potentially fatal consequence of liver cirrhosis [6-8].

All patients with cirrhosis should undergo upper gastrointestinal endoscopy at the time of diagnosis in order to screen for the discovery of high-risk varices. In addition, once every year for decompensated cirrhosis and once every two to three years for compensated cirrhosis, monitoring endoscopies are indicated for individuals with minor varices. Although UGIE is often regarded as the most accurate method for diagnosing esophageal varices, it is not without its drawbacks. To begin, the success of a UGIE in diagnosing esophageal varices ultimately rests on the skills of the particular endoscopist [9-11]. Second, most people who opt out of UGIE screening don't actually suffer from varicose veins. Third, there is an increase in healthcare costs because of unneeded UGIE screening. Fourth, UGIE treatment causes discomfort to the patients. The chance of bleeding and infection is raised, for example, as a possible fifth negative impact [12, 13].

These drawbacks of UGIE have prompted the development of noninvasive methods for predicting esophageal varices, with the goal of limiting UGIE to patients at particularly high risk of variceal hemorrhage.Patients at the highest risk of bleeding can be stratified to reduce the use of unneeded preventative medications for the 60-75% who will never experience variceal bleeding again. Predicting the presence and grade of varices using non-invasive procedures helps a great deal in a number of ways in a limited resources situation like ours, where cost restrictions are a key challenge [14, 15].

Noninvasive identication of esophageal varices is mainly based on routine laboratory measurements and clinical symptoms linked to liver fibrosis and function, portal hypertension and hypersplenism. The platelet count, the Child Pugh score, the albumin level, the albumin globulin ratio, the AST/platelet ratio index, the bilirubin level, the serum transaminases, the hemoglobin level, the total counts, the platelet count/spleen diameter ratio, the prothrombin time, the spleen size, the portal vein diameter, the splenic diameter, and the ascites are all noninvasive predictive variables [16, 17].

Materials and Methods

The present study employed an observational cross-sectional design. The current investigation was carried out on a sample of 40 patients who were admitted to the general medicine and medical gastroenterology wards of ICare Institute of Medical Sciences and Research, Banbishnupur, PO, Balughata Rd, Haldia, West Bengal. These patients had been diagnosed with liver cirrhosis. The study was done between October 2013 and October 2014.

Inclusion Criteria

- Individuals who were admitted with a liver cirrhosis diagnosis
- Results from ultrasound, biochemistry, and clinical evaluations were used to diagnose cirrhosis

Exclusion Criteria

- Bleed varicesally
- Hepatoma, portal vein thrombosis
- Taking beta-adrenergic receptor blockers now or in the past

Data Collection

The demographic and clinical information of the patients was collected using a pre-existing proforma. All patients had comprehensive clinical assessment, relevant diagnostic tests, imaging examinations (Ultrasound with Doppler), and upper gastrointestinal endoscopy.

Methodology

A comprehensive record was compiled regarding the specifics and duration of alcoholism, jaundice, ascites, oliguria, pedal edema, and gastrointestinal bleeding. The researchers made note of the presence or absence of jaundice, ascites, splenomegaly, and hepatic encephalopathy. The following laboratory tests were conducted: platelet count, prothrombin time and international normalized ratio (INR), liver function tests including serum bilirubin, serum transaminases, and serum albumin. The Modified Child-Turcotte-Pugh class was determined for each individual patient. During the ultrasonographic examination of the abdomen and Doppler analysis of the portal venous system, observations were made about the diameter of the portal vein and spleen, as well as the echo texture of the liver. Additionally, the size of the spleen, direction of blood flow, and the presence of ascites were also recorded. The measurement of the diameter of the portal vein and the calculation of the ratio between the platelet count and spleen diameter were performed. At UGI endoscopy, the esophageal varices were classified as either large or minor, utilizing Paquet's grading system.

Results and Observations

Table 1: Age distribution of the study population

	Varices Grade			
	Small		Large	
	N=22		N=18	
	Median	Range	Median	Range
Age (in yrs.)	28	(18– 73)	12	(27 – 74)

Among the cohort of 40 patients under study, 28 individuals exhibited small varices, whereas 18 individuals presented with massive varices. The median age of individuals in the little varices group was 28, while the median age of individuals in the large varices group was 40.

Table 2: Distribution of genders in the research population

Gender	Varices Grade			
	Small varices		Large varices	
	Number	%	Number	%
Male	18	64.28	16	88.88
Female	10	35.71	02	11.11
Total	28	100.0	18	100.0

In the small varices group, there were 18 male patients and 10 female patients. Within the cohort of big varices, there were 16 male patients and 2 female patients.

Table 3: Varices' distribution according to etiology

Etiology	Varices Grade			
	Small varices		Large varices	
	Number	%	Number	%
Alcohol	6	24.42	08	66.66
Wilsons	2	7.14	-	-
HBV	4	14.28	1	8.33
HCV	3	10.71	1	8.33
Alcohol+ HBV	1	3.57	1	8.33
Alcohol+ HCV	3	10.71	1	8.33
Others	9	32.13	0	00
Total	28	100.0	12	100.0

Alcohol consumption was identified as the predominant cause, and among the six patients examined, eight exhibited significant varices.

Table 4: Varices distributed based on Child Pugh class

CTP Class	Varices Grade			
	Small varices		Large varices	
	Number	%	Number	%
Class A	20	75.0	2	13.6
Class B	6	17.9	8	31.8
Class C	2	7.1	2	54.5
Total	28	100.0	12	100.0

Given that kid Pugh class C has the highest number of large varices, the presence of large gastroesophageal varices is connected with the severity of liver disease.

Table 5: Distribution of varices according on ascites grade

Ascites	Varices Grade			
	Small varices		Large varices	
	Number	%	Number	%
Nil	10	35.71	2	16.66
Mild	12	42.85	1	8.33
Moderate	5	17.85	7	58.33
Massive	1	3.57	2	16.66
Total	28	100.0	12	100.0

An rising grade of ascites was found to be linked with the presence of large varices.

Discussion

The objective of our study was to evaluate a range of noninvasive predictors for their ability to accurately predict the existence of significant esophageal varices. Among the cohort of 40 patients under study, it was observed that 28 individuals exhibited small varices, while the remaining 12 individuals presented with massive varices. The median age of individuals in the little varices group was 28, while the median age of individuals in the large varices group was 40. In the little varices group, there were 18 male patients and 10 female patients. In the large varices group, there were 16 male patients and 2 female patients [18, 19].

There was a significant correlation between the grade of ascites and the presence of large varices (p value<0.001). The median platelet count in the group with large varices was 90,100, whereas the median platelet count in the group with minor varices was 200,000. There was a substantial association observed between a decreased platelet count and the presence of large varices. Furthermore, a strong correlation was found between the presence of large varices and higher levels of bilirubin, with a median value of 2.8 mg/dl. There was a substantial correlation observed between the presence of large varices and low levels of albumin, with a median value of -2.2 mg/dl. There was a strong correlation observed between the presence of large varices and a higher prothrombin time, with a median value of 3.6 seconds indicating a protracted duration [20-22].

There was a substantial correlation observed between the presence of large varices and an increase in the diameter of the portal vein, with a median value of 15.6 mm. There was a substantial correlation observed between the presence of large varices and an increase in spleen size, with a median value of -182.5 mm. There was a strong correlation observed between the presence of large varices and a decrease in the platelet count/spleen diameter ratio, with a median value of 454.1 [23, 24].

The presence of significant esophageal varices is a hazardous clinical manifestation resulting from the development of liver cirrhosis. Given the significant endoscopic stress and cost associated with variceal screening, there is a pressing clinical need to identify a more cost-effective and noninvasive method for accurately predicting the presence of large esophageal varices. Previous research has demonstrated that various independent factors, such as splenomegaly, ascites, spider naevi, Child's grade, platelet count, prothrombin time/activity, portal vein diameter, platelet count/spleen diameter ratio, serum albumin, and serum bilirubin, are noteworthy indicators for the existence of esophageal varices [25, 26].

The current investigation provides additional support for the findings of previous research. Giannini *et al*. introduced the concept of use the platelet count-spleen diameter ratio of < 909 as a reliable non-invasive indicator for the detection of esophageal varices. This finding was additionally confirmed in a multicenter clinical trial. The study cohort mostly consisted of individuals diagnosed with cirrhosis that was associated with hepatitis C. Agha *et al*., hailing from Pakistan, conducted a comparable study and reported congruent findings within the aforementioned subgroup of patients. In their study, Sen *et al*. discovered that a platelet count-spleen diameter ratio of ≤ 650 serves as a highly sensitive non-invasive indicator for cirrhosis associated with hepatitis C virus [27, 28].

There is a limited availability of non-endoscopic methods for assessing the existence and severity of varices in India. Amarapurkar *et al*. found that the presence of splenomegaly was a strong predictor for the development of big esophageal varices [29]. In a prospective study conducted by Sharma *et al*., it was discovered that the presence of splenomegaly and platelet count were identified as independent predictors for the occurrence of big varices. A prediction function could be derived from this observation, yielding an AUC value of 0.76. In the current study, it was observed that Child Pugh class B/C, the presence of advanced stages of Ascites, decreased platelet count, reduced serum albumin levels, elevated total bilirubin levels, prolonged prothrombin time, increased portal vein diameter, enlarged spleen size, and a lower platelet count/spleen diameter ratio were identified as significant factors associated with the presence of large esophageal varices [30-32].

Conclusion

The presence of higher grades of Ascites, low platelet count, low serum albumin, high total bilirubin, elevated prothrombin time, higher portal vein diameter, higher spleen size, and lower platelet count/spleen diameter ratio have been identified as significant predictors for the presence of large esophageal varices in individuals classified as Child Pugh class B/C. The correlation between the presence and grade of varices and the severity of liver disorders was observed. Specifically, within the group with big varices, 13.6% were classified as CTP-A, 31.8% as CTP-B, and 54.5% as CTP-C.

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Conflict of Interest: None

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