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Original Research Article

A Study on Noninvasive Predictors of OGD Scopy Confirmed Esophageal Varices in Cirrhosis in a Tertiary Care Hospital in Chengalpattu

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Abstract:

Background: In this study we wanted to determine and assess non-invasive indicators as potential esophageal varices predictors.

Methods: The Government Chengalpattu Medical College and Hospital's internal medicine wards recorded the admission of 55 patients with cirrhosis of the liver for a year as part of a prospective, observational study based in the hospital. The study was approved by the institutional ethics committee and the participants provided written informed consent. SPSS software was used to analyse the data once it was entered into Microsoft Excel.

Results: In the group with no or few variations, 72% belonged to CTP class A, 20% to CTP class B, and 7% to CTP class C. 19% of the big varices group belonged to the CTP-class A group, 31% to the CTP-class B group, and 50% to the CTP-class C group. Large varices were positively connected with liver disease severity ($p < 0.001$), with the highest percentage of large varices found in Child Pugh class C; those with moderate to severe ascites had massive varices, whereas those with minor or no varices had either mild or no ascites. Varices were substantially correlated with an increasing ascites grade when the p-value was less than 0.001. The mean number of platelets in the minor varices group was 2,00,000, while the large varices group had a median of 96,300. Less than 0.001 was the p-value. Thus, there was a strong correlation between big varices and low platelet counts. Significant correlations were seen between large variances and rising total bilirubin levels (median value 3.1 (0.2-10.2), $p = 0.04$) and falling serum albumin levels (median value 2.2 (1.6-3.9), $p = 0.048$). There was no significant correlation (p value -0.096) between increasing varices' size and elevated prothrombin levels. Large varices showed a significant correlation ($p <0.001$) with increasing portal vein width, with a median value of 15.75 mm. There was a strong correlation ($p <0.001$) between the size of the spleen and the size of the varices. Large varices also showed a strong correlation ($p < 0.001$) with lower platelet count and spleen diameter ratio values, with a median value of 503.

Conclusion: In a setting with limited resources and high costs, non-invasive predictors can be used to identify the presence and grade of varices, eliminating the need for invasive upper GI endoscopies.

Keywords: Noninvasive Predictors, Esophageal, Cirrhosis.

Introduction

Esophageal varices are chronic complications of cirrhosis that arise as porto-systemic collaterals, mainly in the lower esophageal submucosa due to portal hypertension. Esophageal varices that burst or bleed are major consequences of portal hypertension and carry a significant mortality risk. Varices are responsible for 10–30% of upper gastrointestinal haemorrhage cases. Most cirrhotic patients will develop esophageal varices at some point in their lifespan (5 to 15% each year), with the annual rate being 5 to 15%. Esophageal varices are more common in patients with cirrhosis (30% to 70% of cases), and 9-36% of cases are classified as "high-risk" varices. Esophageal varices occur in cirrhotic patients at a rate of 5-8% annually, but only 1-2% of these varices are dangerous for bleeding. At a rate of 8% every year, little varices develop into big varices. Thirty percent of patients with esophageal varices will bleed during the first year after diagnosis. The mortality rate from variceal haemorrhage remains

high (20%–35%) even with advancements in diagnosis and therapy. Gastroesophageal varices are associated with a higher severity of liver disease. The most important marker of variceal haemorrhage is the size of the esophageal varices. Larger varices may put more strain on the variceal walls, making esophageal varices more dangerous the more of them there are. Big esophageal varices must be identified before they bleed in order to prevent or minimise this potentially catastrophic side effect of liver cirrhosis.

It was recommended to perform repeated screening endoscopies at specific intervals to monitor the development of portal hypertensive gastropathy and esophageal varices and to detect them early. However, due to the procedure's invasiveness and cost-effectiveness, that strategy had certain drawbacks. According to one study, the use of screening endoscopy to guide therapy adds large costs with just a minor increase in effectiveness, making empiric-blocker therapy for the primary prevention of variceal haemorrhage a more cost-effective method. Spiegel & Associates (2003). [1]

Owing to these problems, noninvasive techniques have been developed to predict esophageal varices, with the goal of restricting the use of UGIE to patients who have a high risk of variceal haemorrhage. Stratification can be used to precisely identify the patients who are most at risk of bleeding, thereby attempting to decrease the 60–75% of patients who will never experience variceal bleeding again. Noninvasive methods for predicting the presence and grade of varices are very useful in environments with limited resources, such as ours, where financial constraints are a major concern. Esophageal varices are usually found without surgery, such as through routine lab tests and clinical signs of liver function and fibrosis, like portal hypertension. [2] Platelet count, Child Turcott-Pugh scoring, serum albumin level, APRI, serum bilirubin level, serum transaminases, haemoglobin level, total count, platelet count/spleen diameter ratio, PT, spleen size, PV diameter, splenic diameter, spider angiomata, etc. are some of the noninvasive predictive variables. Owing to the commonalities among these noninvasive techniques, it is possible to anticipate esophageal varices with minimal patient burden, at low expense, and with excellent consistency. To improve the sensitivity and specificity of vector prediction, multiple predictive models with various permutations of the factors indicated above are provided. Therefore, it is necessary to find clinical characteristics that can reliably predict large esophageal varices and assist in identifying patients who are more vulnerable. The aim of this study was to determine and assess noninvasive indicators as potential esophageal varices predictors.

Materials & Methods

The Government Chengalpattu Medical College and Hospital's internal medicine wards recorded the admission of 55 patients with cirrhosis of the liver for a year as part of a prospective, observational study based in the hospital. The study was approved by the institutional ethics committee and the participants provided written informed consent. The study included people who had liver cirrhosis as determined by clinical, biochemical, and radiographic means. Individuals who had a history of bleeding, had esophageal varices sclerosis or band ligation, a hepatoma, a portal vein thrombosis, or were being treated with beta-adrenergic receptor blockers now or in the past were excluded from the study.

A thorough clinical examination, relevant blood investigations, imaging examinations (ultrasound with Doppler), and upper gastrointestinal endoscopy were performed on each patient. SPSS software was used to analyse the data once it was entered into Microsoft Excel.

Results

Of the 55 patients, 26 had severe varices (grades III–IV) and 29 had mild (grades I–II) or no varices at all. Patients in the large varices group had a median age of 48 (23–70); in the small varices group, the median age was 49 (17–71). There were 17 men and 12 women in the small varices group, and 20 men and 6 women in the large varices group. (Table 1).

Table 1: Demographic Distribution

	Varices Grade			
	Small (Grades I-II) and No Varices		**Large Varices (Grades III-IV)**	
	n = 29		**n =2 6**	
	Median	**Range**	**Median**	**Range**
Age	49	(17 -71)	48	(23 -70)
Age Distribution				
	Varices Grade			
	Small (Grades I-II) and No Varices		**Large Varices (Grades III-IV)**	
	No.	**%**	**No.**	**%**
Male	17	58.6	20	76.9
Female	12	41.4	6	23.1
Total	29	100.0	26	100.0
Sex Distribution				

In the minor varices group, the most prevalent aetiologies were alcohol and HBV. Within the big varices group, alcohol use was the most prevalent cause. Nine of the sixteen patients with alcoholism had significant varices. In general, the most frequent cause of varices in patients is alcohol. In the tiny varices group, the CTP-class A group included 72% of the group, the CTP-class B group 20%, and the CTP-class C group 7%. Within the group of significant varices, 19% belonged to CTP class A, 31% to CTP class B, and 50% to CTP class C. Large varices were positively connected with liver disease severity; the highest percentage of large varices was found in Child Pugh class C ($p < 0.001$). Individuals with little or no varices had either mild or no ascites, while those with big varices had ascites that ranged from moderate to severe ($p < 0.001$). Large varices were therefore substantially correlated with an increasing ascites grade. (Table 2)

Table 2

Etiology	**Varices Grade**			
	Small (Grades I-II) and No Varices		**Large Varices (Grades III-IV)**	
	No.	**%**	**No.**	**%**
Alcohol	7	24.1	9	34.6
HBV	7	24.1	3	11.5
HCV	-	-	2	7.7
Alcohol +HBV	2	6.9	2	7.7
Alcohol +HCV	2	6.9	3	11.5
Others	11	37.9	7	26.9
Total	29	100.0	26	100.0
P - Value	0.442			
Distribution of Varices Based on Etiology				
CTP Class	**Varices Grade**			
	Small (Grades I-II) and No Varices		**Large Varices (Grades III-IV)**	
	No.	**%**	**No.**	**%**
Class A	21	72.4	5	19.2
Class B	6	20.7	8	30.8
Class C	2	6.9	13	50.0
Total	29	100.0	26	100.0
P - Value	<0.001*			
Distribution of Varices According to Child Pugh Class				
*-- Means Significant				
Ascites	**Varices Grade**			
	Small (Grades I-II) and No Varices		**Large Varices (Grades III-IV)**	
	No.	**%**	**No.**	**%**
Nil	10	34.5	3	11.5
Mild	14	48.3	3	11.5
Moderate	4	13.8	12	46.2
Massive	1	3.4	8	30.8
Total	29	100.0	26	100.0
P - Value	<0.001*			
Distribution of Varices According to Grade of Ascites				
*-- Means Significant				

A low platelet count was strongly linked with large varices, with the median platelet count in the small varices group being 2,00,000 and the large varices group being 96,300, $p < 0.001$.

With a median value of 3.1 (0.2-10.2) and a p-value of 0.04, large variances were substantially linked with rising total bilirubin levels. With a median value of 2.2 (1.6-3.9) and a p-value of -0.048, large varices were significantly linked with low blood albumin levels (Table 3).

Table 3

	Varices Grade			
	Small (Grades I-II) And no Varices		Large Varices (Grades III-IV)	
	n = 29		n = 26	
	Median	Range	Median	Range
Platelet Count	200000	(16700 -415000)	96300	(30000 -235000)
P-Value	<0.001*			
Correlation of Varices Grade with Platelet Count				
***-- Means Significant**				
	Varices Grade			
	Small (Grades I-II) and No Varices		Large Varices (Grades III-IV)	
	n = 29		n = 26	
	Median	Range	Median	Range
Total bilirubin (mg/dl)	1.4	(0.4 -19.8)	3.1	(0.2 -10.2)
P-Value	0.04*			
Correlation of Varices Grade with Bilirubin Levels				
***-- Means Significant**				
	Varices Grade			
	Small (Grades I-II) and No Varices		Large Varices (Grades III-IV)	
	n = 29		n = 26	
	Median	Range	Median	Range
Albumin (g/dl)	3.5	(0.4 -25.0)	2.2	(1.6 -3.9)
P-Value	0.048*			
Correlation of Varices Grade with Serum Albumin Levels				
***-- Means Significant**				

With a p-value of 0.096, the size of the varices did not significantly correlate with elevated prothrombin levels. Large varices showed a significant correlation ($p < 0.001$) with increasing portal vein width, with a median value of 15.75 mm.

Table 4

	Varices Grade			
	Small (Grades I-II) and No Varices		Large Varices (Grades III-IV)	
	n = 29		n = 26	
	Median	Range	Median	Range
Prothrombintime (Seconds Prolonged)	3.0	(0.4 -14.0)	3.4	(0.8 -12.0)
P-Value	0.096			
Correlation of Varices Grade with Prothrombin Time				
	Varices Grade			
	Small (Grades I-II) and No Varices		Large Varices (Grades III-IV)	
	n = 29		n = 26	
	Median	Range	Median	Range
Portal Vein Diameter	13.4	(8.2 -17.2)	15.75	(10.8 -22.4)
P-Value	<0.001*			
Correlation of Varices Grade with Portal Vein Diameter				
*-- Means Significant				

There was a strong correlation ($p < 0.001$) between the size of the spleen and the size of the varices. The big variances strongly correlated with lower platelet count/spleen diameter ratio values; the median value was 503, p-value < 0.001 (Table 5).

Table 5

	Varices Grade			
	Small (Grades I-II) and No Varices		Large Varices (Grades III-IV)	
	n = 29		n = 26	
	Median	Range	Median	Range
Spleen Size (mm)	145.0	(100 -280)	182.5	(140-257)
P-Value	<0.001*			
Correlation of Varices Grades with Spleen Size				

*-- Means Significant				
	Varices Grade			
	Small (Grades I-II) and No Varices		**Large Varices (Grades III-IV)**	
	n = 29		**n = 26**	
	Median	**Range**	**Median**	**Range**
Platelet Count /Spleen Diameter Ratio	1418.9	(83.5 -3346.7)	503.	(199.1 -715.0)
P-Value	<0.001*			
Correlation of Varices Grades with Platelet Count/Spleen Diameter Ratio				
*-- Means Significant				

Discussion

One of the most serious side effects of liver cirrhosis is the development of massive esophageal varices. To detemine the presence and extent of esophageal varices, upper gastrointestinal endoscopy carries a significant financial and logistical burden. Another practical issue is the patient's consent to the surgery. Therefore, for reliable esophageal varices prediction, we can employ noninvasive predictors that are as successful.

Numerous previous investigations have demonstrated the usefulness of independent, noninvasive indicators as major predictors of the existence of esophageal varices.

Large varices were correlated with high bilirubin levels, low albumin levels, prolonged prothrombin time, severe ascites, and splenomegaly in this investigation.

Patients with liver cirrhosis frequently exhibit an enlarged spleen, which is linked to an increased risk of complications from portal hypertension. In decompensated cirrhosis, the spleen diameter was substantially larger than in compensated cirrhosis. Bipolar spleen diameter >150 mm in ultrasound examination may be used as an alternate method for VE diagnosis in liver cirrhosis, according to a comprehensive study.[2] There are several known causes of splenomegaly, including tissue hyperplasia, fibrosis, and portal congestion.

One of the most frequent side effects in individuals with chronic liver disease is thrombocytopenia. Patients with cirrhosis have low platelet counts due to three main mechanisms: sequestration, accelerated destruction, and decreased creation. Portal hypertension is the first step in the sequestration process, causing the spleen to expand and sequester platelets. Thrombopoietin, a hemapoietic growth factor mostly produced in the liver, is diminished, and this is the most typical mechanism of reduced platelet formation. Additional causes include the negative effects of antiviral medicine, particularly interferon-based therapy, and viral infection, specifically HCV, which suppresses the bone marrow. Sepsis, hyperfibrinolysis, bacterial translocation, and shear stress all contribute to the accelerated destruction of platelets. [3,4]

Splenomegaly on its own was found to be a strong predictor of the development of big esophageal varices by Amarapurkar et al. [5] In a prospective research, Sharma et al. [6] found that the prevalence of large varices was independently predicted by splenomegaly and platelet count. Based on this discovery, they were able to build a prediction function with an AUC of 0.76.

Qamar et al. [7] reported different findings, concluding that a platelet count of less than 100,000/μL could not be used as a non-invasive EV predictor. On the other hand, the research conducted by Irsan Hasan and colleagues [8] discovered that a platelet count of less than 100,000/μL was linked to the existence of moderate-to-large EV.

In the current study, it was discovered that a higher incidence of large esophageal varices was correlated with a lower platelet count and splenic vein diameter. Giannini et al. 2003 proposal [9] was to use the ratio of low platelet count/spleen bipolar diameter to predict the presence of EV in cirrhotic individuals. They discovered that the platelet count by itself may not always be a reliable indicator and that the only predictor that was found to be positively correlated with the presence of EV was the platelet count/spleen bipolar diameter ratio. In order to indicate the presence of EV, the platelet count/spleen bipolar diameter ratio of 909 had a 100% NPV (Negative Predictive Value). According to a recent meta-analysis, the AUC value for any varices was 0.88 when the platelet count to spleen diameter ratio was used, with a cutoff value of 909. It is advised that patients with a ratio less than 909 undergo an EGD surgery for evaluation. [10]

A different cut-off value for the platelet count/spleen diameter ratio was employed by Abu El Makarem et al. [11] The AUC, sensitivity, and specificity were 0.84, 100%, and 86.3%, respectively, with a cut-off value of 939.7. The cut-off value of 1014 was used in a different study by Baig et al. [12] and the results showed an AUC value, sensitivity, and specificity of 0.94, 98.1%, and 86%, respectively.

A multicenter trial served as additional validation

for this. [13] Patients with cirrhosis associated with hepatitis C constituted the majority of the study population. Agha et al. [14] related investigation from Pakistan found the same things in the same patient subset. Sen et al. [15] discovered that in HCV-related cirrhosis, the platelet count-spleen diameter ratio of ≤ 650 was a sensitive non-invasive diagnostic with an AUC (Area Under the Curve) of 0.81.

In the Child Pugh class B/C study by Cherian JV et al., a low platelet count and a large spleen were found to be strong indicators of the presence of large esophageal varices. [16] Among these variables, CTP class B/C preserved one endoscopic operation for every six procedures carried out and missed less than 10% of patients with significant varices. In CTP class A, four of the forty-two patients exhibited significant varices. Each of the four patients possessed a spleen bipolar diameter > 160 mm or a platelet count < 90,000/μl.

Cirrhosis portal hypertension is also linked to spleen and splenic vein dimensions. The splenic vein becomes wider as a result of hypertension. This results in splenomegaly, or congestion of the spleen. Research has demonstrated that compared to patients with low-risk EVs or healthy controls, people with cirrhosis who have high-risk EVs have a substantially larger splenic vein diameter. [17] According to earlier research, PC/SD outperforms spleen diameter in terms of diagnostic effectiveness and is a significant predictor of EVs. [18] But in the Huixin Liang study, [19] spleen diameter and the SSL-EV prediction model produced a higher AUROC than PC/SD in EV presence prediction. This finding aligns with a prior investigation by Hong et al. [20] wherein spleen width outperformed platelets/spleen width in terms of predictive accuracy when it came to identifying EVs in patients with cirrhosis due to HBV (AUROC: 0.736 ± 0.049 vs. 0.7095 ± 0.0488).

A portal vein diameter of 1.19 cm and a spleen diameter of 11.5 cm were found to have substantial predictive value for the occurrence of oesophageal varices in the study by Halleys Kumar E et al. [21] Less sensitivity, specificity, positive and negative predictive values, and area under the curve (<0.7) were observed for other indicators in the study, such as total bilirubin and PT (Prothrombin Time).

Conclusion

In a setting with limited resources and high costs, non-invasive predictors can be used to identify the presence and grade of varices, eliminating the need for invasive upper GI endoscopies.

References

1. Spiegel BM, Targownik L, Dulai GS, Karsan HA, Gralnek IM. Endoscopic screeningfor esophageal varices in cirrhosis: Is it ever cost-effective? Hepatology 2003;37(2):366-77.
2. Binţinţan A, Chira RI, Mircea PA. Non-invasive ultrasound-based diagnosis and staging of esophageal varices in liver cirrhosis. A systematic review of the literature published in the third millenium. Med Ultrason 2013;15(2): 116-24.
3. Afdhal N, McHutchison J, Brown R, Jacobson I, Manns M, Poordad F, et al. Thrombocytopenia associated with chronic liver disease. J Hepatol 2008;48(6):1000-7.
4. Mitchell O, Feldman DM, Diakow M, Sigal SH. The pathophysiology of thrombocytopenia in chronic liver disease. Hepat Med 2016;8:39-50.
5. Amarapurkar DN, Parikh SS, Shankaran K, Chopra K, Dhawan P, Kalro RH, et al. Correlation between splenomegaly and oesophageal varices in patients with liver cirrhosis. Endoscopy 1994;26(6):563.
6. Sharma SK, Aggarwal R. Prediction of large esophageal varices in patients with cirrhosis of the liver using clinical, laboratory and imaging parameters. J Gastroenterol Hepatol 2007;22 (11):1909-15.
7. Qamar AA, Grace ND, Groszmann RJ, Garcia-Tsao G, Bosch J, Burroughs AK, et al. Platelet count is not a predictor of the presence or development of gastroesophageal varices in cirrhosis. Hepatology (Baltimore, Md) 2008;47 (1):153-9.
8. Hasan I, Sulaiman AS, Jasirwan CO, Loho IM, Zulkifly S, Sardjan J, et al. Non-invasive predictors of moderate–large esophageal varices in compensated cirrhotic patients. Journal of Gastroenterology and Hepatology Research 20 21;10(2)
9. Giannini E, Botta F, Borro P, Risso D, Romagnoli P, Fasoli A, et al. Platelet count/spleen diameter ratio: Proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut 2003;52(8):1200-5.
10. Chen R, Deng H, Ding X, Xie C, Wang W, Shen Q. Platelet count to spleen diameter ratio for the diagnosis of gastroesophageal varices in liver cirrhosis: a systematic review and meta-analysis. Gastroenterology Research and Practice 2017;2017:7407506.
11. Abu El Makarem MA, Shatat ME, Shaker Y, Aleem AA, El Sherif AM, Moaty MA, et al. Platelet count/bipolar spleen diameter ratio for the prediction of esophageal varices: The special Egyptian situation: Noninvasive prediction of esophageal varices. Hepatitis Monthly 2011; 11(4):278-84.
12. Baig WW, Nagaraja MV, Varma M, Prabhu R. Platelet count to spleen diameter ratio for the diagnosis of esophageal varices: Is it feasible? Can J Gastroenterol 2008;22(10):825-8.
13. Giannini E, Zaman A, Kreil A, Floreani A,

Dulbecco P, Testa E, et al. Platelet count/spleen diameter ratio for the noninvasive diagnosis of esophageal varices: Results of a multicenter, prospective, validation study. Am J Gastroenterol 2006;101(11):2511-9.
14. Agha A, Anwar E, Bashir K, Savarino V, Giannini EG. External validation of the Platelet count/Spleen diameter ratio for the diagnosis of esophageal varices in Hepatitis C virus-related cirrhosis. Dig Dis Sci 2009;54:654–60.
15. Sen S, Griffiths WJ. Non-invasive prediction of oesophageal varices in cirrhosis. World J Gastroenterol 2008;14(15):2454-5.
16. Cherian JV, Deepak N, Ponnusamy RP, Somasundaram A, Jayanthi V. Non-invasive predictors of esophageal varices. Saudi J Gastroenterol 2011;17(1):64-8.
17. Jamil Z, Malik M, Durrani AA. Platelet count to splenic diameter ratio and other noninvasive markers as predictors of esophageal varices in patients with liver cirrhosis. Turk J. Gastroenterol 2017;28 (5):347–52.
18. Giannini E, Botta F, Borro P, Risso D, Romagnoli P, Fasoli A, et al. Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut 2003;52(8):1200-5.
19. Liang H, Si H, Liu M, Yuan L, Ma R, Zhang G, et al. Non-invasive prediction models for esophageal varices and red signs in patients with hepatitis B virus-related liver cirrhosis. Front Mol Biosci 2022;9:930762.
20. Hong WD, Zhu QH, Huang ZM, Chen XR, Jiang ZC, Xu SH, et al. Predictors of esophageal varices in patients with HBV-related cirrhosis: a retrospective study. BMC Gastroenterol 2009;9:11.
21. Karthick M, Prabakaran PT, Rajendran K, Gowrishankar A, Kumar EH, Kannan R, et al. A study on non-endoscopic predictors of esophageal varices and portal hypertension in chronic liver disease. Int J Res Pharm Sci 2020;11(SPL)(2):228-34.