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Interest of Non-Invasive Methods to Predict Esophageal Varices in Cirrhotic Patients in Togo

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Abstract

Background: upper digestive endoscopy is the best method for detecting esophageal varices, but its invasiveness and cost make it inaccessible to certain social classes. **Aim**: to evaluate the performance of non-invasive methods for the presumptive diagnosis of esophageal varices in cirrhotic patients in Togo. **Patients and method**: this was a cross-sectional descriptive and analytical retrospective data collection conducted over 2 years. It included medical records of cirrhotic patients hospitalized in the Hepato-gastroenterology who undergone transaminase assay, blood count, abdominal ultrasound and an upper GI endoscopy. **Results**: A total of 114 patients were included, 84 of them were men (sex ratio: 2.8). The mean age of patients was 48±14 years. The most frequent reason for admission was abdominal distension (86%). According to the Child-Pugh classification, cirrhosis was decompensated in 109 patients (95.6%). Esophageal varices were present in 71.1% of patients. At a cutoff value of 110 mm for spleen diameter, the sensitivity for prediction of esophageal esophageal varices was 70.4%, with an area under the ROC curve of 0.63. The areas under the ROC curve for prediction of esophageal varices were 0.27; 0.29; 0.29 respectively for platelet count, platelet/spleen diameter ratio and the [platelets^2/spleen diameter] x AST level. A low [platelets^2/spleen diameter] x AST level ratio correlated with the presence of esophageal varices at endoscopy. **Conclusion**: Spleen diameter is a performant non-invasive tool for the prediction of esophageal varices.

Keywords

Esophageal Varices, Spleen, Platelets, Togo

1. Introduction

The presence of esophageal varices in cirrhotic patients is a major complication due to the risk of bleeding with high mortality [1]. The prevalence of esophageal varices in the cirrhotic population is 60% - 80% and the risk of variceal hemorrhage at 1 year is 5% for small varices and 15% for large varices [1] [2], which justifies upper gastrointestinal (GI) endoscopy at the time of diagnosis of decompensated cirrhosis [3]. In Togo, the prevalence of esophageal varices in the cirrhotic population is 73% [4]. However, in Togo as in other developing countries, digestive endoscopy is not only unavailable in all regions and reserved for referral centers, but is also expensive for most patients [5] [6]. This has motivated the development of non-invasive methods for predicting esophageal varices, including the albumin-serum-ascites gradient, which was evaluated in Togo [7]-[13]. The aim of this study was to evaluate the performance of non-invasive methods such as platelet count, spleen diameter, platelet/spleen diameter ratio and [platelet^2/spleen diameter] × AST ratio for the presumptive diagnosis of esophageal varices in cirrhotic patients in Togo.

2. Patients and Method

This was a descriptive and analytical cross-sectional study, with retrospective data collection, involving medical records of all cirrhotic patients followed at Campus Teaching Hospital from January 1, 2019 to January 1, 2021. Included were medical records of cirrhotic patients of both sexes, aged 18 and over, including transaminase assay, blood count, abdominal ultrasound and upper GI endoscopy. Records of cirrhotic patients who had undergone endoscopic band ligation, were on beta-blocker therapy or had portal thrombosis were not included. Data collected included clinical, biological, morphological (ultrasound or abdominal CT scan) and endoscopic data. Esophageal varices were described using the 3-grade classification proposed by the Japanese Society for Portal Hypertension Research [14]. Varices were then classified as:

- Grade 1: esophageal varices fading on continuous insufflation and not confluent
- Grade 2: esophageal varices not fading on continuous insufflation, not confluent and occupying less than 1/3 of the lumen
- Grade 3: tortuous, confluent esophageal varices occupying more than 1/3 of the lumen.

2.1. Operational Definitions

- The diagnosis of cirrhosis was made on the basis of clinical, biological and morphological arguments [15] [16].
- Grade 2 and 3 esophageal varices were considered large varices.
- Spleen diameter was measured using a basic frequency probe (3.5 MHz) by an experienced radiologist. Splenomegaly was defined as a diameter greater than 120 mm.

- The platelet/spleen diameter ratio was obtained by dividing the platelet count/mm^3 by the spleen diameter (mm).
- The ratio [platelets^2/spleen diameter] × AST was obtained by squaring the number of platelets (giga/l) over the spleen diameter (mm), multiplied by the Alanine Aminotransferase (AST) value.
- Thrombocytopenia was defined as an absolute platelet count of less than 150000/mm^3.

2.2. Statistical Analysis

The data collected were cleaned and analyzed using R software version 4.3.2. Categorical variables were compared using chi-square and Fisher tests of independence. Statistical tests were considered significant when the p-value was less than or equal to 0.05. The ROC curve showed the sensitivity and specificity of the different methods. The diagonal corresponds to a classification model of a random classifier. A classifier was good and acceptable if its curve was above the diagonal. A classifier was perfect if the area under its ROC curve was 1. The closer the area under the curve was to 1, the more the classifier was considered a good classifier.

2.3. Ethical Considerations

From an ethical point of view, the hospital's management agreed to carry out the study. The questionnaire was designed to be submitted and processed by computer. Thus, each file had a unique number that identified the report in order to preserve anonymity.

3. Results

3.1. General Characteristics of the Population

During the study period, 114 cirrhotic patients were included, 84 men and 30 women, corresponding to a sex ratio of 2.8. The mean age of patients was 48 ± 14 years, with extremes of 16 and 93 years. The reason for hospitalization was abdominal distension in 86% of cases, followed by jaundice (20.2%). Physical examination revealed ascites, jaundice and splenomegaly in 96.5%, 24.6% and 0.9% of cases respectively. One hundred and nine patients, *i.e.* 95.6%, had decompensated cirrhosis, 53.2% of whom were in stage C of the Child-Pugh classification. Cirrhosis was of viral B origin in 60.5% of cases. Upper GI endoscopy revealed esophageal varices in 71.1% of patients. Varices were large in 69 patients (85.2%). Median platelet count was 120 giga/l. Median spleen diameter was 122 mm. Table 1 summarizes the clinical and paraclinical data.

3.2. Diagnostic Performance of Different Non-Invasive Methods for the Prediction of Esophageal Varices

The optimal threshold for spleen diameter was 110 mm. At this threshold value, the prediction of esophageal varices had a sensitivity of 70.4%, a specificity of 51.5%, a positive predictive value of 78.1% and a negative predictive value of

Table 1. Comparative table of patients with and without esophageal varices.

	Esophageal varices n = 81	No esophageal varices n = 33	p-value
Mean age in year (SD)	47 [38 - 54]	50 [36 - 61]	0.786
Gender, n (%)			
Male	59 (72.8)	25 (75.8)	0.748
Female	22 (27.2)	8 (24.2)	
Lifestyle, n (%)			
Alcool intake	24 (29.6)	7 (21.2)	0.36
Traditional drugs intake	19 (23.5)	19 (57.6)	<0.001
Tobacco intake	27 (33.3)	11 (33.3)	0.005
Physical examination, n (%)			
Ascites	81 (100)	29 (87.9)	0.006
Jaundice	19 (17.3)	9 (27.3)	0.668
Non-invasive methods, mean (SD)			
Platelets (giga/l)	102 [70 - 154]	160 [111 - 216]	<0.001
Spleen diameter (mm)	130 [105 - 149]	108 [92 - 133]	0.026
Platelets/spleen diameter ratio	857 [523 - 1254]	1500 [887 - 2385]	<0.001
[Platelets^2/spleen diameter ratio] × AST level	8×10^9 [2×10^9 - 27×10^9]	24×10^9 [13×10^9 - 48×10^9	<0.001
Child-Pugh score, n (%)			0.004
A	0 (0)	5 (15.2)	
B	37 (45.7)	14 (42.4)	
C	44 (54.3)	14 (42.4)	

SD: Standard Deviation.

41.5%. The area under the spleen diameter ROC curve for prediction of esophageal varices was 0.63 as shown in Figure 1. At a spleen diameter threshold of 110 mm, prediction of large varices had a sensitivity of 71%, a specificity of 33.3% and an area under the ROC curve of 0.54. Table 2 summarizes the performance indices of the different methods for predicting esophageal varices. The areas under the ROC curve for the prediction of esophageal varices were 0.27; 0.29; 0.29 for platelet count, platelet/spleen diameter ratio, and [platelets^2/spleen diameter] × AST ratio, respectively. For a threshold value of 95,000 platelets/mm^3, the platelet count had a sensitivity of 49.4% and a specificity of 87.9%.

Table 2. Performance of various non-invasive methods for diagnosing esophageal varices.

	Cutoff value	AUROC [95% CI]	Ss (%)	Sp (%)	Ppv (%)	Nvp (%)
Diagnosis of esophageal varices						
Platelet count (giga/l)	95	0.27 [0.17 - 0.38]	49.4	87.9	90.9	41.4
Spleen diameter (mm)	110	0.63 [0.51 - 0.75]	70.4	51.6	78.1	41.5
Platelets/Spleen diameter ratio	915	0.29 [0.18 - 0.39]	58	69.7	82.5	40.4
[Platelets^2/spleen diameter ratio] × AST levels	70.3×10^7	0.29 [0.19 - 0.38]	58	15.2	62.7	12.8
Diagnosis of large esophageal varices						
Spleen diameter (mm)	110	0.548	71	33.3	86	16.7

AUROC: Area Under ROC; 95% CI: 95% Confidence Intervall; Ss: Sensitivity; Sp: Specificity; Ppv: Positive predictive value; Nvp: Negative predictive value.

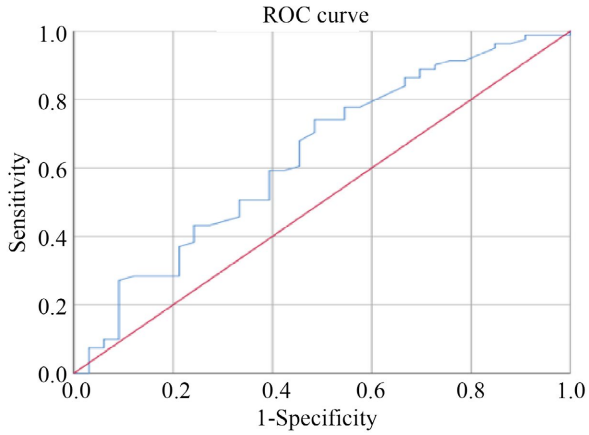

Figure 1. ROC curve of spleen diameter for prediction of esophageal varices.

4. Discussion

The main limitation of this study lies in its retrospective data collection nature, which makes it impossible to validate the results obtained. Although thrombocytopenia was associated with the presence of esophageal varices in univariate analysis ($p < 0.001$), platelet count, at a threshold of 95 giga/l was not a good predictor of the presence of esophageal varices at endoscopy (AUROC = 0.27). In the study by Mahassadi *et al.* in Côte d'Ivoire [10], platelet count was a good predictor of esophageal varices (AUROC = 0.768, Se: 80%) for a threshold value of 110.5 giga/l. According to the recommendations of Baveno VII [3], a threshold of 150 giga platelets /l can be used to identify patients at risk of bleeding complications and who should benefit from primary prophylaxis. The presence of thrombocytopenia correlates with the presence and size of esophageal varices [17] [18], justifying diagnostic endoscopy when the platelet count is below 150000/mm^3, as recommended by Baveno VII [3]. In our study, spleen diameter was an acceptable predictor of esophageal varices (AUROC = 0.63, Se: 70.4%). In line with literature data, spleen diameter is a good diagnostic parameter for esophageal varices and

was also correlated with variceal size in several studies [19]-[21]. Splenomegaly, mainly related to portal hypertension in cirrhosis, is therefore not only a good predictor of esophageal varices, but also of variceal size. In the study by Mahassadi *et al*. [11], the platelet/spleen diameter ratio was a better predictor of esophageal varices, with high sensitivity and specificity than either platelet count or spleen diameter taken in isolation. As these two parameters are good predictive markers of esophageal varices, their fusion would increase diagnostic cost-effectiveness. However, in our study, the spleen platelet/diameter ratio was not a good predictor of esophageal varices (AUROC = 0.290). This result may be explained by the size of our study population. In univariate analysis, a low [Platelet count^2/spleen diameter] × AST ratio correlated with the presence of esophageal varices ($p < 0.001$). Unlike the study by Mattos et al in Brazil [22], which found a sensitivity of 95.8% for a threshold of $3 \times 10^8/mm^3$, this ratio was not predictive of esophageal varices in our study (sensitivity 22%).

5. Conclusion

Of the four non-invasive methods for predicting esophageal varices evaluated, spleen diameter had the best diagnostic performance and is an acceptable mean of predicting esophageal varices, especially in locations where digestive endoscopy is not accessible. Upper GI endoscopy nevertheless remains the essential tool for the detection of esophageal varices with a view to appropriate prophylactic treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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