

Liver Transient Elastography Combined to Platelet Count (Baveno VI) Predict High Esophageal Varices in Black African Patient with Compensated Hepatitis B Related Cirrhosis

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Abstract

Aim: To assess the predictive value of the Baveno VI criteria for the diagnosis of large esophageal varices (EV) in Black African patient with compensated hepatitis B related cirrhosis. **Methods:** We carried out a cross-sectional study from January 2 to July 3 (2016), in Department of Gastroenterology at University Hospitals of Cocody (CHUC) and Yopougon (CHUY). All the black African patients included were more than 15 years old and their liver elasticity score (LES) was carried out at Yopougon University Hospital. Hepatitis B related cirrhosis was defined by LES \geq 11 kPa (FibroScan® (Echosens, France)) with positive HBs antigen (HBsAg) and anti HBc antibody. All the patients with hepatitis B related cirrhosis performed a gastroscopy at Cocody University Hospital and esophageal varices were ranked according to *société française d'endoscopie digestive* (SFED) classification. Data analysis was performed by SPSS model 20.0 statistics software (SPSS Inc., Chicago, IL, United States). Diagnostic performance of LES < 20 kPa and platelet count > 150,000/mm³ (Baveno VI criteria) for the diagnosis of large EV by gastroscopy was studied (area under the ROC curve, specificity (Sp), sensitivity (Se), positive predictive value (PPV) and negative predictive value (NPV). **Results:** During the study period, 720 patients achieved liver FibroScan® at CHUY. Of these, 60 respondents to our inclusion criteria were prospectively included in our study. Twelve (20%) of these 60 patients met the Baveno VI criteria. EV

were present in 40% of cases (n = 24) with 6.7% (n = 4), 15% (n = 9) and 18.3% (n = 11) of grade 1, 2 and 3, respectively. (66.7% (n = 40) without EV or with small EV) and 33.3% (n = 20) with large EV. The Baveno VI criteria had a Se, Sp, PPV and NPV of 100%, 41.6%, 30% and 100% respectively for the diagnosis of large EV. The area under the ROC curve of a platelet count greater than 150,000/mm³, a liver elasticity score of less than 20 kPa and combination of both were respectively 0.763 [0.645 - 0.880; P = 0.272]; 0.588 [0.436 - 0.739; P = 0.01] and 0.650 [0.513 - 0.787 P = 0.005]. **Conclusion:** The combination of liver elasticity score < 20 kPa and a blood platelet count > 150,000/mm³, allowed the exclusion of large esophageal varices at gastroscopy with a 100 % NPV in Black African patients with compensated hepatitis B related cirrhosis.

Keywords

Cirrhosis, Esophageal Varice-Fibroscan®-Baveno, Negative Predictive Value, Africa

1. Introduction

Upper gastrointestinal bleeding secondary to rupture of esophageal varices (EV) in a patient with cirrhosis is fatal in more than 15% cases [1] [2] [3]. Primary prevention of this hemorrhage is based on the screening of these EV by gastroscopy. Several authors study non-invasive criteria to exclude the presence of EV at gastroscopy [4]-[11]. The Baveno VI conference experts suggested not to perform gastroscopy in a patient with compensated hepatitis B related cirrhosis if there are both: a liver elasticity score < 20 kPa and a blood platelet count > 150,000 constituents by mm³ [12] [13]. These criteria have been studied in several studies to assess their relevance [14] [15] [16] [17]. None of these studies, as far as we know, has been carried out in a black African population with hepatitis B related cirrhosis. The aim of our study was to assess the predictive value of the Baveno VI criteria for the diagnosis of large esophageal varices in patients with compensated hepatitis B related cirrhosis.

2. Patients and Method

2.1. Sample Population

We carried out a cross-sectional study from January 2 to July 31 (2016) in department of gastroenterology at University Hospitals of Cocody (CHUC) and Yopougon (CHUY). We included all the patients older than 15 years, irrespective of gender, in whom hepatitis B related cirrhosis was previously diagnosed, based on a liver elasticity score. Liver elasticity threshold for the diagnosis of cirrhosis was respectively 11 kPa [18]. Patients with at least one of the following criteria were not included: acute ethylic intoxication during the four (4) weeks before FibroScan® test, regular alcohol intake higher than 20 g per day, splenec-

tomised ones, transaminases greater than 5-fold normal, liver tumor or portal thrombosis or significant ascites or dilatation of hepatic veins on ultrasound.

2.2. Method

In each of these patients, the following variables were gathered using a pre-established survey form: anamnestics data (age, sex, treatments in progress or received (diuretics, antiviral B and/or C treatment and alcohol), clinics data (splenomegaly, ascites, hepatic encephalopathy, jaundice), biologicals data (transaminases, blood platelets, Prothrombin, albuminemia). We established Child-Pugh-Turcotte score (Class A, B and C) [19].

All the gastroscopies were carried out at Cocody University Hospital (CHUC) by two physicians (gastroenterologist) with more than 15 years of seniority in digestive endoscopy. Esophageal varices were ranked according to *Société Française d'Endoscopie Digestive* classification (grade 1, 2 and 3) [20]. Gastroscopy also looked for the presence of red signs on the varices, for gastric varices and for portal hypertension gastropathy.

All the liver elasticity measurements were performed at Yopougon University Hospital (CHUY) by two experienced gastroenterologists. The device used was the FibroScan® (Echosens, France). The results of FibroScan® data were expressed in kPa using a medium-size probe (M). The patient was lying on his back, his right hand raised behind his head. The doctor applied a water-based gel on the skin at the level of the liver, then takes measurements on the right side. The probe was placed in the intercostal space, perpendicularly to the skin. A minimum of 2 or 3 hours fasting was required of the patient before the test. The test consists of 10 successive measurements. The validation criteria of the measurements were: a success rate of about 60%, IQR < 1 and a rate of variability <30% of the median value.

2.3. Statistical Analyses

Data analysis was performed by SPSS model 20.0 statistics software (SPSS Inc., Chicago, IL, United States). Variables by category were presented in percentage form, the ones which are continuous by their median, standard deviation and stretch (minimum maximum). The patients were separated into two groups according to the results of the gastroscopy. Those having grade 2 or 3 varices were classified into group II (large varices) and those having grade 1 varices or not having varices were classified into group I (small varices). Comparison between these two groups was performed by the chi-square test for the variables by category and the ANOVA test for the ones which are continuous. Diagnosis performance of the liver elasticity score (LES) < 20 kPa and platelet count > 150,000/mm³ for the diagnosis of large EV by gastroscopy was assessed with the following parameters: specificity (Sp), sensitivity (Se), positive and negative predictive value (PPV) and (NPV), positive (LR+) and negative likelihood ratio (LR-).

2.4. Ethical Clearance

A double oral informed consent was obtained: the one of the patient before his inclusion and the one of the attending physician.

3. Results

During the study period, 720 patients performed a liver FibroScan® at the CHUY. Of these, 60 respondents to our inclusion criteria were prospectively included in our study. Twelve (20%) of these 60 patients met the Baveno VI criteria. All the patients performed a gastroscopy which found EV in 40% of cases ($n = 24$), with 6.7% ($n = 4$), 15% ($n = 9$) and 18.3% ($n = 11$) of grade 1, 2 and 3 respectively. Patients were classified into 2 categories according to the size of their EV: 66.7% ($n = 40$) of patients with small or no EV (group I) and 33.3% ($n = 20$) with large EV (group II). None of the patients with large varices met the Baveno VI criteria. The characteristics of the two groups are shown in **Table 1**. There was no difference between them in age, sex, transaminases and median liver elasticity score. Patients with no large EV had no red sign and no gastric varices. Child-Pugh scores of patients with large EV were significantly higher than the ones of those who did not have EV ($P < 0.001$). None of the patients with platelet count $> 150,000/\text{mm}^3$ had large EV (**Table 1**). **Table 2** shows the diagnostic performance of these two criteria. In application of the Baveno VI score, respectively 20% and 46.7% of gastroscopies would have been needless and useless (**Table 3**).

4. Discussion

Our prospective study carried out exclusively in black African patients with hepatitis B related cirrhosis shows that in these patients, Baveno VI criteria allowed to exclude the presence of large EV at gastroscopy with a 100% NPV. Comparable results (NPV 98%) have been reported by Maurice *et al.* but in a hepatitis C related cirrhosis predominantly [15]. The prevalence of EV was 40% in our sample comparable to that reported from a sample of 1250 patients by Augustin *et al.* [14]. By applying the Baveno criteria, 20% of gastroscopies would have been avoided, no significant varices would have been detected, proportions also reported by Augustin *et al.* but with a lower percentage of unnecessary gastroscopy (38% versus 46.7%) [14].

To our knowledge, it is the only study carried out in patients with only hepatitis B related cirrhosis on the Baveno VI criteria. Our results suggest that in these patients when diagnosing compensated cirrhosis, gastroscopy screening for EV could be postponed. This alternative is interesting in Ivory Coast because few hospitals have technical platform and digestive endoscopy staff. However, there is no clear consensus on the periodicity of this non-invasive evaluation [15]. In addition, when interpreting these criteria, it is essential, as pointed out by several authors, to respect scrupulously FibroScan® conditions and contraindications to avoid misclassification of patients [16] [17]. The diagnosis of cirrhosis based on

Table 1. Cirrhotic patients' characteristics according to the size of varices.

Variables	Small varice n = 40	High varice n = 20	P value
Sex ratio	2.3	5.7	0.172
Age median in years \pm SD	49 \pm 13.3	48.5 \pm 12	0.720
BMI median in kg/m ² \pm SD	22.6 \pm 3.4	22.1 \pm 2.8	0.108
ASAT in UI/l \pm SD	43.5 \pm 42.6	47.5 \pm 188.9	0.264
ALAT in UI/l \pm SD	35 \pm 31.5	46.5 \pm 150.8	0.184
Platelets/mm ³ \pm SD	157500 \pm 106639	59500 \pm 30201	<0.0001
Platelets > 150,000/mm ³	21 (52.5%)	0	<0.0001
Child Pugh score < 0.0001			
A	33 (82.5%)	7 (35%)	
B	7 (17.5%)	13 (65%)	
Median of SLE (kPa) \pm SD	20.7 \pm 13.4	25.9 \pm 18.6	0.062
SLE < 20 kPa	19 (47.5%)	6 (30%)	0.269
SLE < 20 kPa and platelets > 150,000/mm ³	12 (30%)	0	
Grade of EV			
1	4 (10%)	-	
2	-	9 (45%)	
3	-	11 (55%)	
Other endoscopic sign			
Red sign in EV	0 (0%)	9 (45%)	<0.0001
PHG	1 (2.5%)	6 (30%)	0.004
Gastric varices	0 (0%)	1 (5%)	0.333

SD = standard deviation; BMI = body mass index; ASAT = aspartat amino transferase ALAT = alanine amino transferase; EV = esophageal varice; PHG= portal hypertensive gastropathy; SLE = liver elastography score.

Table 2. Predictive negative value of the platelet count and score of the liver elastography to exclude large esophageal varices.

Criteria	PPV	NPV	Se	Sp	RV+	RV-
Platelet > 150,000/mm ³	51.3%	100 %	100 %	52.5 %	2.10	0
SLE < 20 kPa	33.3 %	60 %	70 %	30 %	1	1
Platelet count > 150,000/mm ³ and SLE < 20 kPa	41.6%	100%	100%	30%	1.42	0

SLE = Score of Liver Elastography; PPV = Predictive Positive Value; PNV = Predictive Negative Value; Se = Sensitivity; Sp = Specificity.

Table 3. Diagnostic performance of the Baveno VI criteria to screen for large esophageal varices.

Variables	Number	Percentage
Large varices non diagnosed	0	0
Needless gastroscopies	12/60	20 %
Useless gastroscopies	28 /60	46.7 %

FibroScan® of the liver, notwithstanding the problems of sampling fluctuation, is difficult to currently implement in Ivory Coast because there is only one device for the whole country. On the other hand, the poor PPV of these Baveno criteria in our study as in others does not allow to base the diagnosis of significant EVs nor to start a preventive treatment of these [12]-[17]. A blood platelet count > 150,000/mm³ also had a 100% NPV to exclude large EVs. It is an easy test to obtain especially in our environment with lack of FibroScan®. The use of platelet count as a non-invasive marker for portal hypertension is the subject of many studies [9] [21]. The platelet count appears as an independent predictive factor for the diagnosis of large varice in cirrhotic patients. A retrospective Moroccan study showed that a platelet count of less than 100,000/mm³ was correlated with the presence of EVs but not that of large EVs in viral cirrhosis [9]. Another Egyptian study, like our work showed that a normal platelet level was correlated with the absence of large EVs [21]. The advantage of the combination is that a normal level of platelets is found in any healthy individual but a liver elasticity score greater than 11 kPa immediately suggests cirrhosis. On the other hand, liver elasticity score at 20 kPa alone had a lower NPV to exclude the diagnosis of large EV in our work. This result is in contradiction with the one reported by Maurice *et al.* where the NPV of the LES was higher than platelets count [1]. Unlike the sample of this work, in ours, we found that the platelet count and the median LES were respectively statistically significant and not significant between patients with EV and those who did not have EVs. Hua *et al.*, like our results, observed a lack of difference between the LES between these two groups [22] in opposition to those of Sharma *et al.* [23]. Other authors have studied these two criteria with different cut-offs. Ding *et al.* also reported a 100% NPV when LES > 25 kPa and platelets count < 100,000/mm³ [24]. Augustin *et al.* also observed similar results, but at a higher threshold [25]. This was in contradiction to the one reported by Pas *et al.* In their work, liver elasticity score was higher than platelet counts to predict the presence of large EV [26]. One limitation of this study is the use of elastometric criteria (>14 kPa) for the diagnosis of cirrhosis as we know the value used was not validated in the black African population. Liver FibroScan® values were set up from a study in black Africa comparing FibroScan® performance for the diagnosis of hepatitis B related cirrhosis compared to the result of liver histology. This study showed that at the threshold of 11 kPa the LES had a Se and a Sp of 71% and 88% for the diagnosis of fibrosis F4 [18]. Another limitation of our work is to have assessed only the prediction of large EVs. Although they are responsible for nearly 80% - 90% of the upper gastrointestinal hemorrhages, others lesions of portal hypertension, though rare, may be responsible. These are small EVs with red signs or occurring on severe cirrhosis, portal hypertensive gastropathy and gastric varices. They would also require measures to prevent hemorrhage [11]. In our work none of patients without large EV had gastric varices not red signs on EV. And on the other hand there was no patient with a Child Pugh C score in patient with small varice.

5. Conclusion

The combination of liver elasticity score <20 kPa in association with a count of platelet >150,000/mm³ could allow to exclude the presence of large esophageal varices at gastroscopy with a 100% NPV in hepatitis B related cirrhosis. These parameters could allow us to identify patients who could be delayed gastroscopy screening for large EVs, knowing that those patients do not have EVs. Prospective internal and external validation on large samples is necessary to confirm these cut-off values.

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