Validation of Baveno VI and Expanded-Baveno VI Criteria for predicting gastroesophageal varices in patients with alcoholic and non- alcoholic fatty liver disease

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Abstract

Background and aims: **Baveno VI and Expanded-Baveno VI Criteria were validated to rule out high-risk esophageal varices (HRV) and to prevent unneeded endoscopies in compensated advanced chronic liver disease (cACLD) mainly related to viral hepatitis. We aim to assess these criteria to rule out low- and high-risk varices in patients with cACLD secondary to alcoholic liver disease (ALD) and non- alcoholic fatty liver disease (NAFLD).**

Methods: **Data were collected retrospectively from 2016 to 2020. Inclusion criteria were: NAFLD and /or ALD related cACLD, a liver stiffness measurement (LSM) ≥ 10 kPa and an esophagogastroduodenoscopy (EGD) within 12 months. Exclusion criteria were: use of non cardioselective β-blockers, hepatic decompensation, previous variceal bleeding, portal thrombosis, liver cancer, or liver transplant.**

Results: **One hundred and ninety-four patients were included in this study. Eighty-one patients (42%) met Baveno VI criteria and 103 (53%) met Expanded-Baveno VI criteria. Baveno VI criteria yielded a high negative predictive value (NPV ≥ 95%) for detecting HRV and varices of any size. Expanded-Baveno VI criteria yielded a high NPV ≥ 95% only for detecting HRV: the miss rate for varices of any size was 8%. Expanded-Baveno VI criteria could avoid more endoscopies than the original Baveno VI criteria to rule out HRV (53% versus 42%).**

Conclusion: **In this study, both criteria showed high NPV to rule out HRV but only original Baveno VI criteria yielded a satisfactory high NPV to rule out varices of any size. Expanded-Baveno VI criteria could avoid more endoscopies to exclude HRV.** (Acta gastroenterol. belg., **2022,** 85, **321-329**).

Keywords: esophageal varices, transient elastography, NAFLD, ALD, cACLD.

Introduction

Portal hypertension is a severe complication of advanced chronic liver disease (ACLD) responsible for the development of gastroesophageal varices (GEV). Variceal bleeding is still a major cause of morbidity and mortality (10 to 20% at 6 weeks) of cirrhosis (1-3). A primary prophylaxis by β-blockers or ligation is recommended to prevent the first variceal bleeding of high-risk varices (HRV) defined as medium-large varices or small varices with red spots (4). Therefore, the screening and surveillance of GEV remain a key point in the follow-up of cirrhotic patients. Currently, all patients with cirrhosis require surveillance with esogastroduodenoscopy (EGD). However, endoscopy is an invasive method, expensive and unpleasant for patients. In patients with compensated advanced chronic liver disease (cACLD), the prevalence of HRV is low and therefore, many of the endoscopies performed to detect HRV might be unnecessary.

Recently, the concept of clinically significant portal hypertension (CSPH) has emerged. CSPH is defined by the presence of clinical manifestations of portal hypertension such as ascites or GEV, but also, in absence of clinical signs of portal hypertension, by a hepatic venous pressure gradient (HVPG) ≥ 10mmHg. The measurement of HVPG is the gold standard method to assess the presence of CSPH (5). However, the measurement of HVPG is an invasive method and is not usually realized in clinical practice. So, over the past few years, there was a growing interest in the search of non-invasive tools able to rule out severe liver fibrosis, clinically significant portal hypertension (CSPH) and HRV (6-9).

In clinical practice, transient elastography (TE) has become one of the most widely used non-invasive method to assess liver fibrosis. A liver stiffness measurement (LSM) ≥ 10kPa is suggestive of extensive fibrosis in asymptomatic patients with known causes of chronic liver disease. TE has also allowed, in combination with other non-invasive markers, to identify patients with cACLD at risk of developing CSPH (10-11) and so, might identify patients at risk of having HRV.

In 2015, Baveno VI Consensus recommended that patients with cACLD with a LSM < 20 KPa and with platelet count >150,000 cells/L can safely avoid screening endoscopy as these criteria are associated with a very low risk of having HRV. These patients must be followed up by yearly repetition of TE and platelet count (12).

Later, Baveno VI criteria were expanded to LSM < 25kPa and platelet count >110,000 cells/L. The new Expanded-Baveno VI criteria were validated to spare more endoscopies with a minimal risk of missing HRV (13).

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Baveno VI and Expanded-Baveno VI criteria were validated to identify patients at low risk of having HRV in most of the common etiologies of cACLD, but specially in viral hepatitis (14-15). Currently, NAFLD is the most prevalent chronic liver disease worldwide (16), and, with ALD, is also the more frequent etiology of cACLD in our region (17). Therefore, it will be interesting to examine whether these criteria may be effective to identify patients at low risk of having HRV in cACLD secondary to alcoholic liver disease (ALD) and/or non- alcoholic fatty liver disease (NAFLD), and so to avoid unneeded endoscopies in those patients.

Furthermore, there is a growing interest to rule in CSPH, in asymptomatic patients with compensated ACLD. Recent data suggested that long term treatment with β-blockers could increase decompensation-free survival in asymptomatic patients with compensated ACLD and CSPH, mainly by reducing the incidence of ascites (18). Moreover, a treatment by β-blockers is not without side effects. Currently, it seems inappropriate to prescribe treatment with β-blockers in all patients with compensated ACLD and it is better to reserve this treatment to patients with GEV of any size who have certainly a CSPH. By definition, there are no gastroesophageal varices without CSPH. So, our second aim was to assess whether the Baveno VI criteria (Original and Expanded) were able to predict not only the absence of HRV, but also the absence of varices of any size.

In the present study, our primary objective was to examine whether the Baveno VI and Expanded-Baveno VI Criteria may be effective to identify patients at low risk of having HRV in NAFLD/ALD related cACLD and so, to avoid unneeded EGD. As second objective, we examine whether those criteria, in the same population, are also effective, to rule out varices of any size in order to avoid unneeded HVPG measurements and treatment by β-blockers.

Material and methods

Patients and study Design

In this cross-sectional retrospective cohort study, we reviewed all NAFLD/ALD related compensated ACLD over a 5-year period who have undergone Transient Elastography (TE), screening EGD and blood test. We started by collecting the list of patients with a TE performed between January 2016 and December 2020 at the Centres Hospitaliers de Jolimont in Belgium. Then, we selected patients (both genders, aged 18 years and over) on the basis of the following inclusion criteria: a diagnosis of ALD and/or NAFLD related cACLD, a LSM ≥ 10 kPa (confirmed by at least 8 valid measurements, with a success rate ≥ 60% and an interquartile range/median ratio – IQR/M ≤ 30%), and EGD available within 12 months of TE. Diagnosis of NAFLD required detection of steatosis on ultrasound, criteria of the metabolic syndrome and compatible abnormal laboratory liver tests with exclusion of other causes of liver disease (alcohol intake less than 20g/day for female and 30g/day for male, hepatitis B and C, autoimmune hepatitis, hereditary hemochromatosis, Wilson's disease and alpha-1 antitrypsin deficiency). Diagnosis of ALD required alcohol intake >20g/day for female and >30g/day for male and compatible abnormal laboratory liver tests with exclusion of other causes of liver disease (NAFLD, hepatitis B and C, autoimmune hepatitis, hereditary hemochromatosis, Wilson's disease and alpha-1 antitrypsin deficiency).

Our exclusion criteria were: use of non cardioselective β-blockers, a Child-Pugh score B and C, or an history of previous decompensation, of variceal bleeding, of portal thrombosis, of liver cancer, or of liver transplant.

Transient Elastography

TE was performed by gastroenterologists, specifically trained in using FibroScan® (Echosens, Paris, France). After several hours of fasting, the patient was lying in dorsal position with the right arm in maximum abduction. The probe was positioned in an intercostal space, over the right lobe of the liver, at the intersection between the middle axillary line and a transverse line at the level of the xiphoid appendix. At least 8 valid measurements were performed to calculate the median stiffness values. We excluded inadequate scans with interquartile range/median > 30% and success rate < 60%.

If patient underwent more than one TE during the study period, the latest LSM was considered.

Esophagogastroduodenoscopy

EGD were performed by experienced endoscopists to detect gastroesophageal varices. The 3-grade classification system was used to describe esophageal varices (small/medium/large). Varices were classified as no varices, low-risk varices (LRV) and high-risk varices (HRV). HRV were defined as all esophageal varices described as medium-large caliber, small caliber with red spots and any gastric varices. LRV were defined as esophageal varices of small caliber without red spots.

Clinical data and Laboratory results

The following clinical variables were recorded: age, sex, LSM, presence and type of varices, etiology of the cACLD, splenomegaly on abdominal ultrasound, hypertension (systolic blood pressure ≥ 130 mmHg), diabetes, use of statin, Body Mass Index (BMI). We collected laboratory parameters on the closest day of the LSM measurement, including platelet count, creatinine, International Normalized Ratio (INR), bilirubin, albumin and sodium. Several scores were calculated: Child-Pugh score, Model for End-Stage Liver Disease (MELD) score, original Baveno VI criteria and the Expanded-

Baveno VI criteria. Original Baveno VI criteria were defined as LSM < 20 kPa and a platelet count >150,000/mm³, while Expanded-Baveno VI criteria were defined as LSM <25 kPa and a platelet count >110,000/mm³.

Statistical Analysis

Descriptive statistics were computed for all study variables. Categorical variables were expressed as percentages, discrete variables as median [Interquartile range or IQR with the 25th–75th percentiles] and continuous variables as mean (SD) or median (IQR) according to the distribution of the observed values. Difference between "no varices", LRV and HRV were assessed using the chi-square test for categorical variables, and Kruskal-Wallis for continuous variables. Adequate post-hoc analysis was performed to differentiate statistical significance between groups by applying adjusted p-value according to Bonferroni. In Table 1, each subscript letter denotes a subset of Varices Group ("none", "LRV", "HRV") whose column proportions do not differ significantly from each other at $p<0.05$ level.

The diagnostic performance metrics, including sensitivity (Sn), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV), of Baveno VI and Expanded-Baveno VI criteria to detect either HRV or varices of any size are expressed in percentages. Sn and Sp of Baveno VI and Expanded- Baveno were compared using the Mac Nemar test as the predictive values (NPV and PPV) were compared using the relative predictive value method described by Moskowitz et al. (19) (package DTComPair). Spared gastroscopies were defined as the number of true negative (TN) among the whole cohort, or the sum of those classified as not having varices based on Baveno VI and Expanded-Baveno VI criteria among the whole cohort (TN+FN/total "Spared gastroscopy by criteria"). Missed varices were defined as the proportion of false negatives (FN) on either sum of classified as not having varices by Baveno VI and Expanded-Baveno VI criteria (FN/TN+FN: "Missed varies by criteria"). Throughout analysis, a p-value below 0.05 was considered as statistically significant. Statistical analysis was performed using R: A Language and Environment for Statistical Computing, R Core Team, Vienna, Austria, 2020, https://www.r-project.org/.

The study was approved by the local Ethics Committee of our hospital and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

Results

Study population and demographic data

From January 2016 to December 2020, 3626 TE were performed. Two thousand nine hundred and one TE were excluded because of LSM<10 KPa or inadequate scan. After excluding multiple scans on the same patients, non ALD/NAFLD related cACLD and patients without EGD within the 12 months of the TE, 249 patients met our inclusion criteria. Of these, 55 additional patients were excluded because of use of non-cardioselective β-blockers (N=9), a Child Pugh score>6 (N=23), an history of portal vein thrombosis (N=6), of liver cancer (N=6), of previous decompensation (N=6), of variceal bleeding (N=3) or of liver transplant (N=2). So, 194 patients were enrolled in the final analysis. (Fig. 1)

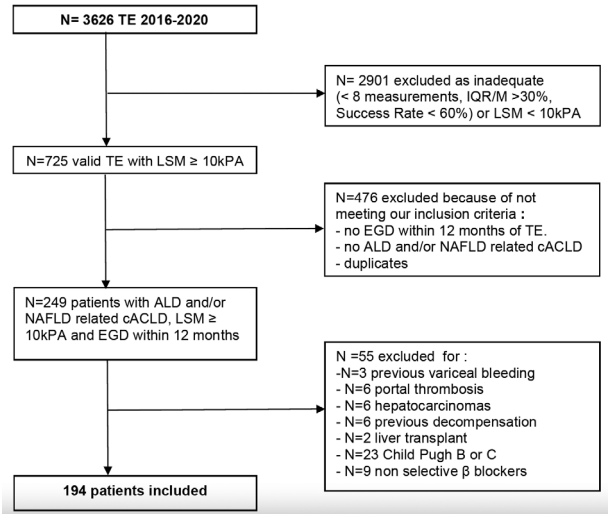

Figure 1. — 'Flow diagram of the study population'. TE, transient elastometry; IQR/M, interquartile range/median ratio; LSM, liver stiffness measurements; EGD, esophagogastroduodenoscopy; ALD, alcoholic liver disease; NAFLD, nonalcoholic fatty liver disease; cACLD, compensated advanced chronic liver disease.

The main demographic, clinical, score and laboratory data are reported in Table 1.

One hundred and forty-two patients (73%) were male and median age was 62 (IQR: 55-71). Etiologies were alcoholic steatohepatitis (ASH, N= 109, 56%), non-alcoholic steatohepatitis (NASH, N=45, 23%) or both ASH/NASH (N=40, 21%). The mean MELD score was 7.5 and most patients had a Child Pugh score A5 (n=153, 79%).

Varices were present in 39 (20%) patients among whom 16 (8%) had HRV, and 23 (12%) had LRV.

Patients with HRV had higher MELD scores ($p = 0.004$), lower platelet count ($p < 0.001$), higher bilirubin levels ($p = 0.015$) and higher INR ($p = 0.001$) than patients without varices. Those patients were also more frequently diagnosed with splenomegaly ($p <0.001$). Patients with varices of any size had higher LSM ($p <0.001$) compared to those without varices.

Baveno VI Criteria as predictor of gastro-esophageal varices (GEV)

Eighty-one patients (42%) met original Baveno VI criteria predicting the absence of HVR. Of those, 77 had no varices, 4 had LRV and 0 had HRV (Table 2).

For detecting HRV, Baveno VI criteria yielded a sensitivity (Sn) of 1.00, a specificity (Sp) of 0.46, a positive predictive value (PPV) of 0.14, and a negative

Table 1. — **General Characteristics**

	Overall, N = 194	**Oesophageal Varices**			**p-value**[2]
		None, N = 155[1]	**LRV**, N = 23[1]	**HRV**, N = 16[1]	
Gender					0.09
Female	52 (27%)	40 (26%)	10 (43%)	2 (12%)	
Male	142 (73%)	115 (74%)	13 (57%)	14 (88%)	
Age (years)	62 (55, 71)	62 (54, 71)	64 (59, 75)	68 (59, 73)	0.07
Etiologies					0.6
ALD	109 (56%)	86 (55%)	13 (57%)	10 (62%)	
ALD+NAFLD	40 (21%)	30 (19%)	7 (30%)	3 (19%)	
NAFLD	45 (23%)	39 (25%)	3 (13%)	3 (19%)	
MELD Score	7.50 (6.43, 8.47)	7.50 (6.43, 8.47)**a**	7.50 (7.50, 8.73)**a,b**	8.86 (7.50, 10.34)**b**	**0.001**
Child Pugh Score					0.08
A5	153 (79%)	126 (81%)	18 (78%)	9 (56%)	
A6	41 (21%)	29 (19%)	5 (22%)	7 (44%)	
Days Between Gastroscopy and Fibroscan	35 (9, 104)	31 (9, 94)	42 (10, 112)	68 (27, 106)	0.5
Fibroscan Value (kPa)	20 (12, 36)	17 (12, 30)**a**	32 (20, 51)**b**	48 (30, 75)**b**	**<0.001**
Platelets (cells/µL)	175,000 (136,750, 227,750)	188,000 (152,500, 233,500)**a**	160,000 (104,500, 199,000)**a,b**	105,000 (74,250, 156,000)**b**	**<0.001**
Bilirubin Levels (mg/dL)	0.60 (0.46, 0.95)	0.59 (0.44, 0.87)**a**	0.56 (0.50, 1.12)**a,b**	0.98 (0.59, 1.34)**b**	**0.02**
INR	1.10 (1.00, 1.10)	1.00 (1.00, 1.10)**a**	1.10 (1.00, 1.10)**a,b**	1.12 (1.10, 1.20)**b**	**<0.001**
Albumin (g/L)	41.8 (37.9, 44.5)	41.7 (38.3, 45.0)	42.8 (37.5, 44.1)	39.2 (34.3, 42.5)	0.2
Creatinin (mg/dL)	0.80 (0.70, 0.90)	0.80 (0.70, 0.90)	0.70 (0.70, 0.97)	0.80 (0.70, 1.02)	>0.9
Sodium (mmol/L)	140.0 (138.0, 142.0)	140.0 (138.0, 142.0)	140.0 (137.0, 141.0)	139.5 (137.0, 141.0)	0.2
Ascites	4 (2.1%)	4 (2.6%)	0 (0%)	0 (0%)	>0.9
Splenomegaly	45 (23%)	29 (19%)**a**	6 (26%)**a,b**	10 (62%)**b**	**<0.001**
Statin	70 (36%)	56 (36%)	9 (39%)	5 (31%)	0.9
Hypertension	106 (55%)	84 (54%)	15 (65%)	7 (44%)	0.4
BMI (kg/m^2)	28.0 (25.0, 32.0)	28.4 (25.0, 32.4)	27.9 (26.4, 32.3)	25.0 (21.9, 27.8)	0.09
Diabetes	65 (34%)	47 (30%)	11 (48%)	7 (44%)	0.2

[1] Statistics presented: n (%); median (IQR). [2] Statistical tests performed: Fisher's exact test; Kruskal-Wallis test; chi-square test of independence. Each script letter **(a, b)** denotes a subset of Varice Group ("none", "LRV", "HRV") whose column proportions do not differ significantly from each other at the .05 level. LRV, low-risk varices ; HRV, high-risk varices ; ALD, alcoholic liver disease ; NAFLD, nonalcoholic fatty liver disease ; BMI, body mass index.

Table 2. — **Prevalence of varices in groups generated by original Baveno VI and Expanded-Baveno VI criteria**

		Oesophageal Varices		
	Total	None	LRV	HRV
All cohort	194	155	23	16
Baveno VI criteria				
Outside Baveno VI criteria	113	78	19	16
Within Baveno VI criteria	81	77	4	0
Expanded-Baveno VI criteria				
Outside Expanded Baveno VI criteria	91	60	16	15
Within Expanded Baveno VI criteria	103	95	7	1

LRV, low-risk varices; HRV, high-risk varices. [1]Original Baveno VI criteria: within: LSM<20kPa and platelets>150x10^3 /µL; outside: LSM≥20kPa and/or platelets≤150x10^3/µL. Expanded Baveno VI criteria: within: LSM<25kPa and platelets>110x10^3 /µL; outside: LSM≥25kPa and/or platelets≤110x10^3/µL.

Table 3a. — **Performance of Baveno VI and Expanded-Baveno VI criteria for diagnosing HRV**

	Sn (%)	Sp (%)	PPV (%)	NPV (%)
Baveno VI criteria	100	46	14	100
Expanded-Baveno VI criteria	94	57	16	99
P value	0.32	<0.001	0.03	0.32

Sn, sensitivity; Sp, specificity; NPV, negative predictive value; PPV, positive predictive value; HRV, high-risk varices.

Table 3b. — **Performance of Baveno VI and Expanded-Baveno VI criteria for diagnosing all varices**

	Sn (%)	Sp (%)	PPV (%)	NPV (%)
Baveno VI criteria	90	50	31	95
Expanded-Baveno VI criteria	79	61	34	92
P value	0.045	<0.001	0.10	0.14

Sn, sensitivity ; Sp, specificity ; NPV, negative predictive value; PPV, positive predictive value.

predictive value (NPV) of 1.00. (Table 3a). For detecting all varices, these criteria yielded a sensitivity of 0.90, a specificity of 0.50, a PPV of 0.31 and a NPV of 0.95 (Table 3b).

Using Baveno VI criteria, 81 (42%) endoscopies could have been avoided, 0% of HRV would have been missed, and 5% (4/81) of varices of any size would have been missed.

The proportion of patients spared from endoscopy and with a correct diagnosis for varices screening by this non-invasive method was 42% for HRV and 40% for all varices. (Tables 4a and 4b).

Expanded-Baveno VI Criteria as predictor of gastro-esophageal varices

One hundred and three (53%) patients met Expanded-Baveno VI criteria predicting the absence of HRV. Of those, 95 had no varices, 7 had LRV and 1 had HRV (Table 2).

For detecting HRV, Expanded-Baveno VI criteria yielded a sensitivity of 0.94, a specificity of 0.57, a PPV of 0.16, and a NPV of 0.99 (Table 3a). To detect all varices, these criteria yielded a sensitivity of 0.79, a specificity of 0.61, a PPV of 0.34 and a NPV of 0.92 (Table 3b).

Using Expanded-Baveno VI criteria, 103 (53%) patients would avoid endoscopy with a miss rate of 1 % (1/103) for HRV and a miss rate of 8% (8/103) for varices of any size.

The proportion of patients spared from endoscopy and with a correct diagnosis by this non-invasive method was 53% for HRV and 49% for all varices. (Tables 4a and table 4b).

Comparison between Baveno VI and Expanded-Baveno VI criteria (Tables 3a and 3b)

Original Baveno VI and Expanded-Baveno VI criteria did significantly classify patients differently (p=0.001).

In comparison with the original Baveno VI criteria, the Expanded-Baveno VI criteria provided a significant better specificity (p<0.001) for the detection of HRV and for the detection of varices of any size. The PPV of Expanded-Baveno VI criteria was significantly better for detecting HRV (14% versus 16%, p= 0.03) but not for detecting varices of any size (31% versus 34%, p = 0.098).

Table 4a. — **Spared endoscopies and missed varices by test for HRV**

HRV	Spared endoscopies by test ((TN+FN)/Total)	Spared endoscopies with a correct diagnosis (TN/Total)	Missed varices by test (FN/(TN+FN))
Baveno VI criteria	42% (81/194)	42% (81/194)	0% (0/81)
Expanded-Baveno VI criteria	53% (103/194)	53% (102/194)	1% (1/103)

HRV, high-risk varices; TN, true negative; FN, false negative.

Table 4b. — **Spared endoscopies and missed varices by test for varices of any size**

ALL VARICES	Spared endoscopies by test ((TN+FN)/Total)	Spared endoscopies with a correct diagnosis (TN /Total)	Missed varices by test (FN/(TN+FN))
Baveno VI criteria	42% (81/194)	40% (77/194)	5% (4/81)
Expanded-Baveno VI criteria	53% (103/194)	49% (95/194)	8% (8/103)

TN, true negative; FN, false negative.

The Expanded criteria yielded statistical similar sensitivity (100% versus 94%, p= 0.32) for detection of HRV but was less performant for detection of varices of any size (90% versus 79%, p= 0.045). There were no differences for the NPV between both tests (100% versus 99 %, p=0.32 for the detection of HRV; 95% versus 92%, p = 0.14 for the detection of all varices).

Discussion

Original Baveno VI and Expanded-Baveno VI criteria were designed to rule out HRV and were validated in different studies. Nevertheless, a large part of these studies was conducted in chronic liver diseases of viral etiologies. In most available data, NAFLD/ALD related cACLD were underrepresented or absent (14-15). In this retrospective study, our main objective was to assess if Baveno VI criteria, original and expanded, were able to identify patients without HRV and so, to avoid a large number of unneeded endoscopies in NAFLD/ALD related cACLD. Our second objective was to assess if the same criteria were able to identify not only patients without HRV, but also patients without all size varices, in order to select patients at low risk of CSPH to avoid unneeded HVPG measurement and inappropriate treatment by β-blockers. Our results indicated that the Expanded-Baveno VI criteria were more efficient to identify patients at very low risk of having HRV and that the original Baveno VI criteria could efficiently identify patients with a very low risk of having all size varices.

Regarding our first aim, we found that the original Baveno VI criteria and Expanded-Baveno VI criteria could be used to rule out HRV with a high NPV of 100% and 99%, respectively. For detecting HRV, these criteria yielded a sensitivity of 100% and 94% respectively. These results are concordant with a meta-analysis by Stafylidou et al. (15). In this meta-analysis pooled sensitivity for HRV were 97% for Baveno VI and 90% for Expanded-Baveno VI criteria. Baveno VI consensus also proposed an acceptable threshold of 5% for missed varices by criteria which is not exceeded: in our study, the HRV missed rate was 0% with Baveno VI and 1% with Expanded-Baveno VI criteria. Compared to the Expanded-Baveno VI criteria, the limitation of original Baveno VI criteria is its lower specificity, resulting in a higher number of unnecessary endoscopies. We confirmed that Expanded-Baveno VI criteria works better than original Baveno VI criteria for ruling out HRV because it could spare more endoscopies (53% versus 42%) without increasing the number of missed HRV (1% versus 0%) (13). In our study, spare endoscopies with original Baveno VI and Expanded Baveno VI criteria were higher than the overall of 20% and 40% respectively, usually reported when viral hepatitis is the main etiology (13,14,20,21) but these results are concordant with available studies performed in NAFLD/ALD-related cACLD. (22-28) (Table 5). In these studies, the mean values of spare endoscopies were 29 and 58% for the original Baveno VI and the Expanded-Baveno VI criteria, respectively.

Furthermore, we also assessed these criteria to rule out varices of any size. Indeed, there is a growing interest to screen LRV. Firstly, Bhardwaj et al. suggested that carvedilol could delay the progression of small esophageal varices to HRV (29). On the other hand, PREDESCI study suggested that long term treatment with β-blockers could increase decompensation-free survival in patients with cACLD and clinically significant portal hypertension, mainly by reducing the incidence of ascites (18). By definition, patients without CSPH have no gastroesophageal varices, although, it remains possible to have a HVPG > 10mmHg and then CSHP without GEV. We thought interesting to evaluate whether these same criteria are effective to identify patients who are at low risk of having varices of any size.

In our study, we found that only the original Baveno VI criteria could be used to rule out varices of any size in NAFLD/ALD-related cACLD with a high NPV of 95%. For detecting varices of any size, the original Baveno VI criteria yielded a sensitivity of 90%. Accuracy of the Baveno VI criteria for the screening of varices of any size was assessed in several studies with a pooled sensitivity of 0.88 and specificity of 0.41 (15). The sensitivity for detecting varices of any size is lower than for HRV, but grade 1 varices without red spots are at low risk of hemorrhage and annual repetition of TE and platelet count, as recommended by the Baveno VI consensus, would counterbalance inferior accuracy in the detection of varices of any size. In our study, the threshold of 5%, proposed by Baveno VI consensus, is not exceeded for missed varices of any size. However, these results are not confirmed by all studies published on NAFLD/ALD related liver disease. The NPV of original Baveno VI criteria to rule out varices of any size is usually lower and only Galizzi et al. showed similar results (15, Table 5). Confirmation by prospective data collection should validate these observations.

However, using these Expanded-Baveno VI criteria for the detection of any size varices, the sensitivity was much lower (79%) with a NPV of 92%: 8% of varices of any size were missed, which is more than the 5% usually accepted.

Baveno VI and Expanded-Baveno VI criteria had a high NPV in contrast to poor PPV. This confirm that these criteria perform better in excluding rather than diagnosing varices.

These results suggest the key role for non-invasive markers to identify patients at low risk of having HRV who can thus avoid screening endoscopy but also to identify patients at low risk of having varices of any size, who could avoid HVPG measurement.

This study has some limitations. The retrospective design brings intrinsic biases.

Different hepatologists performed TE and different endoscopists performed EGD which could result in

Table 5. — Review of studies available in NAFLD/ALD related liver disease

Studies	Inclusion criteria	Etiologies of liver disease (%)	Patients (n)	Prevalence of HRV/ any size of varices (%)	Baveno VI criteria (spared endoscopy by test) n (%)	HRV missed by Baveno VI criteria n (%)	Any size varices missed by Baveno VI criteria n (%)	Expanded-Baveno VI criteria (spared endoscopy by test) n (%)	HRV missed by Expanded-Baveno VI criteria n (%)	Any size varices missed by Expanded-Baveno VI criteria n (%)
Bouzbib *et al.* (22)	Histology	ALD (100)	180	12/34	51 (28)	1 (2)	14 (28)	86 (48)	4 (5)	-(27)
Calès *et al.* (23)	Cirrhosis	ALD (64) NAFLD (6) Viral (26)	287	17/44	- (16,4)	0 (0)	- (13)	NA	NA	NA
Galuzzi *et al.* (24)	Histology F3: 33% F4: 67%	NAFLD (100)	21	14/29	10 (48)	0 (0)	-(4,8)	15 (71)	-(4,8)	-(9,5)
Ng *et al.* (25)	LSM > 12kPa	NAFLD (60) ALD (40)	85	8/NA	25 (29)	0 (0)	NA	NA	NA	NA
Petta *et al.* (26)	Histology or LSM>11kPA	NAFLD (100)	652 available	11,5/31,5	219 (33,5)	6 (2,7)	32 (14,6)	365 (56)	15 (4,1)	69 (19)
Siu *et al.* (27)	LSM> 14 kPa	ALD (33) NAFLD (32)	290	18/NA	45 (16)	NA	NA	NA	NA	NA
Zheng *et al.* (28)	histology or clinical data of cirrhosis	NAFLD (100)	224	NA/NA	84 (37,5)	-(1,2)	NA	127 (56,7)	-(3,15)	NA
Present study	LSM>10kPa	ALD (56) NAFLD (23) ALD/NAFLD (21)	194	8/20	81 (42)	0 (0)	4 (5)	103 (53)	1 (1)	8 (8)

HRV, high-risk varices; ALD, alcoholic liver disease; NAFLD, non alcoholic fatty liver disease; LSM, liver stiffness measurement.

interobserver variations. However, this is a real live study which reflects the usual situation in clinical practice.

Endoscopy was not performed simultaneously with the TE but with a reasonable median duration of time between TE and EGD of 35 days. We decided to use a cut off LSM value of ≥10kPa for our study, based on the Baveno VI definition to suspect patients having cACLD. This is under the usual cut off value for cirrhosis and that may increase the negative predictive value of the original and Expanded-Baveno VI criteria. However, the HRV and any size varices prevalence of 8% and 20% is consistent with other studies. In a recent meta-analysis, the prevalence of HRV ranged from 5% to 26% and the prevalence of any size varices from 15% to 72% (15).

We included TE with at least 8 valid measurements, success rate ≥ 60% and interquartile range ≤ 30%. Usually, in previous studies, 10 valid measurements were requested. However, Boursier et al. showed that liver stiffness evaluation reliability depends on IQR/M with no influence of ≥ 10 valid measurements (30,31). To increase our cohort size, we lowered the requested number of valid measurements to eight.

Conclusion

In conclusion, in this study, we showed that Expanded-Baveno VI criteria were as performant than the original criteria for excluding HRV but could avoid more unneeded endoscopies in patients with ALD/NAFLD related cACLD. By contrast, only original Baveno VI criteria yielded a satisfactorily high NPV to rule out varices of any size. Confirmation by prospective data collection should validate these observations.

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Competing interests

None.

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