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MINIREVIEWS

Noninvasive scores for the prediction of esophageal varices and risk stratification in patients with cirrhosis

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Abstract

The primary purpose of variceal screening in patients with cirrhosis is to detect gastroesophageal varices at high risk of hemorrhage and implement preventative intervention(s). It was previously recommended that all patients with cirrhosis undergo initial and periodic longitudinal variceal screening *via* upper endoscopy. However, there has been growing interest and methods to identify patients with cirrhosis who may not have clinically significant portal hypertension and therefore be unlikely to have varices requiring intervention or benefit from upper endoscopy. Because the population of patients with compensated advanced chronic liver disease continues to grow, it is neither beneficial nor cost-effective to perform endoscopic variceal screening in all patients. Therefore, there is ongoing research into the development of methods to non-invasively risk stratify patients with cirrhosis for the presence of high-risk esophageal varices and effectively limit the population that undergoes endoscopic variceal screening. This is particularly important and timely in light of increasing healthcare reform and barriers to healthcare. In this review, we discuss and compare, with respect to test characteristics and clinical applicability, the available methods used to non-invasively predict the presence of esophageal varices.

Key Words: Gastroesophageal varices; Variceal screening; Advanced chronic liver disease; Cirrhosis; Non-invasive screening; Upper endoscopy

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Core Tip: Because the population of patients with compensated advanced chronic liver disease continues to grow, it is neither beneficial nor cost-effective to perform endoscopic variceal screening in all patients. Therefore, there is ongoing research into the development of methods to non-invasively risk stratify patients with cirrhosis for the presence of high risk esophageal varices and effectively limit the population that undergoes endoscopic variceal screening. These topics are reviewed in this article.

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INTRODUCTION

Variceal screening and surveillance is an important part of the management of patients with cirrhosis. The primary goal of upper endoscopy (EGD) in this context is to identify patients with gastroesophageal varices (GEV) at high risk of hemorrhage so that strategies to minimize this risk, including potential endoscopic treatments, can be implemented[1]. The previous American Association for the Study of Liver Diseases (AASLD) guidelines on the management of GEV and the Baveno consensus conference in its first five editions recommended variceal screening and periodic surveillance with EGD in all patients with cirrhosis. However, the introduction of transient elastography (TE) in clinical practice has allowed the identification of patients with early chronic liver disease manifested by advanced fibrosis, an entity that was subsequently termed compensated advanced chronic liver disease (cACLD)[2]. This population comprises a heterogeneous group of patients with varying degrees of portal hypertension (PH), ranging from no PH (hepatic venous portal gradient (HVPG) of 1-5 mm Hg) to mild or "subclinical" PH (HVPG of 5-9 mmHg) to clinically significant portal hypertension (CSPH) (defined as an HVPG of ≥ 10 mmHg)[2-4]. Above this threshold of 10 mmHg, all complications of PH, including the development of GEV and variceal hemorrhage, are more likely to occur[4-6]. Reflecting this, the prevalence of GEV ranges from 20%-40% in patients with cACLD to as high as 85% in patients with decompensated cirrhosis (who have CSPH)[3]. GEV also have a variable risk of hemorrhage: The overall rate of variceal hemorrhage is around 10%-15% per year, but this varies with both the severity of liver disease (Child class B or C) and with endoscopic features of the varices including size and the presence of high risk stigmata[3,7]. Furthermore, there are small but notable risks associated with EGD, and the costs incurred on both the patient and the healthcare system in the context of a growing chronic liver disease population is substantial[7,8].

In light of this heterogeneity, the most recent AASLD guidance statement and the 2015 Baveno VI consensus statement recommend the use of non-invasive tests to stratify patients and rule out high risk esophageal varices (HREV) in patients with cACLD[2]. The AASLD practice guidance states that patients with a liver stiffness of < 20 kPa as measured by TE and a platelet count (PC) of > 150000/mm^3 can avoid EGD but that those who do not meet these criteria, known as the Baveno VI criteria, should receive a screening EGD[3]. There are ongoing efforts to develop alternative non-invasive models using clinical, biochemical, and radiographic parameters to stratify patients for variceal screening[9]. The goal is to balance good test characteristics (< 5% of patients with HREV are missed) with ease of administration and widespread availability of testing in clinical practice[2]. This review will discuss the non-invasive methods for esophageal variceal (EV) prediction in patients with cACLD.

PLATELET COUNT TO SPLEEN DIAMETER RATIO

Because low PC and enlarged spleen size are independently suggestive of PH, their

combination into the PC to spleen diameter ratio (PC/SD) was evaluated for the prediction of EV. In the initial proof-of-concept retrospective study of 137 adult patients with confirmed EV by EGD, a PC/SD cutoff value of 909 (n/mm^3)/mm offered a net present value (NPV) of 73% and a positive predictive value (PPV) of 74%[10]. A 2012 systematic review and meta-analysis of PC/SD including 1275 adult patients with cirrhosis yielded a pooled sensitivity of 89% [95% confidence interval (CI): 87%-92%] and pooled specificity of 74% (95%CI: 70%-78%), but the pooled positive and negative likelihood ratios were only moderately helpful[11]. The largest study was a 2017 Cochrane meta-analysis including 2637 patients across 17 studies evaluating the PC/SD at a cut-off of 909 (n/mm^3)/mm demonstrated an even better sensitivity of 0.93 (95%CI: 0.83-0.97) and specificity of 0.84 (95%CI: 0.75-0.91) for the detection of varices of any size. However, it was noted that 7% of adults with any EV would be missed[12]. They therefore further evaluated the ability of the PC/SD to predict the presence of HREV [also known as varices needing treatment (VNT)], which refers to medium or large varices, varices with high risk stigmata, or small varices in Child C cirrhosis. Interestingly, the PC/SD performed worse in the prediction of HREV at a cut-off value around 909 (n/mm^3)/mm (between 897 and 921), with a sensitivity of 0.85 (95%CI: 0.72-0.93) and specificity of 0.66 (95%CI: 0.52-0.77).

While the PC/SD is advantageous in that it is easy to calculate and relies on only two data points, its test characteristics are not adequate for the prediction of EV or HREV. The authors considered that it could potentially be incorporated into a more comprehensive prediction rule[11]; however, an additional challenge with widespread use is that spleen diameter is not consistently included in ultrasound reports.

TRANSIENT ELASTOGRAPHY

Liver stiffness (LS) as measured by transient elastography (TE) performs well in the diagnosis of cirrhosis with an area under the receiver operating characteristic (AUROC) of 0.96, and at a cut-off of 17.6 kPa, the NPV and PPV for the diagnosis of cirrhosis are 92% and 91%, respectively[13]. A meta-analysis of 11 studies evaluating LS and HVPG demonstrated a significant correlation (r = 0.783, 95%CI: 0.737-0.823) and that LS also had good diagnostic performance for the assessment of CSPH, with a sensitivity of 87.5% and specificity of 85.3%[14]. A 2013 meta-analysis including 5 studies and 420 patients demonstrated that LS by TE is an accurate means of diagnosing CSPH, with an AUROC of 0.93 (95%CI: 0.90-0.95), sensitivity of 0.90 (95%CI: 0.81-0.95), and specificity of 0.79 (95%CI: 0.58-0.91)[15].

Several studies have subsequently been conducted to evaluate the accuracy of TE in the diagnosis of EV with variable findings. In a prospective study including patients with cirrhosis of multiple etiologies, a cut-off value of 27.5 kPa provided a NPV of 95% in diagnosing HREV[13]. However, subsequent meta-analyses demonstrated that LS alone is not sufficiently accurate to diagnose either EV or HREV. Based on these studies, the AUROC for TE in the diagnosis of HREV ranged from 0.78 to 0.83[15,16], and the AUROC for TE in the diagnosis of EV ranged from 0.82 (95%CI: 0.79-0.86) to 0.84 (95%CI: 0.80–0.87)[17].

It is important to note that these studies included patients with multiple and varied etiologies of chronic liver disease which contributed substantial heterogeneity[15,16] although the majority of patients across these studies had untreated viral or alcoholic cirrhosis[15]. In addition, the TE-LS cutoffs evaluated varied significantly across studies, ranging from 12.0 to 29.7 kPa for the detection of any EV and from 14.6 to 38.2 for the detection of HREV[16,17]. The optimal cutoffs for TE-LS used to stage fibrosis and diagnosis cirrhosis vary with etiology of liver disease and may be disease-specific. Therefore, this may be the case for TE in the diagnosis of EV and HREV and perhaps establishing disease-specific cut-offs would improve test characteristics. However, the sensitivity of TE in the diagnosis of EV or HREV is good but the specificity is only moderate. Therefore, it was concluded that although TE has a role in the assessment of PH, it should not be used alone in selecting patients for variceal screening[18].

COMBINATION OF LIVER STIFFNESS, SPLEEN DIAMETER, AND PLATELET COUNT

The role of LS in combination with other parameters has been evaluated. LS, SD and PC have been evaluated in various combinations for the prediction of EV. One such

score is called the liver stiffness – spleen diameter to platelet ratio (LSPS) and is calculated as follows: LS × SD/PC. LSPS is accurate in the diagnosis of CSPH with an AUROC of 0.918 (95%CI: 0.872-0.965, $P < 0.0001$)[19]. In a prospective study of patients with cirrhosis due to hepatitis B, it was found that LSPS < 3.5 has a 94.0% NPV for the prediction of HREV while LSPS > 5.5 has a PPV of 94.2. LSPS had excellent accuracy with AUROC of 0.953 and performed better in the prediction of HREV than any of the components individually and PC/SD[20]. However, a second study including patients with diverse etiologies of cirrhosis showed that LSPS < 3.21 offered a better NPV in the prediction of EV, again demonstrating heterogeneity in optimal cutoffs[19]. Furthermore, these studies suggested better performance of LSPS in Child A than Child B + C cirrhosis[20].

Another study developed an EV prediction score using multivariable analysis of the individual parameters of the LSPS which is calculated accordingly: - 4.364 + 0.538 (spleen diameter) – 0.049 (PC) – 0.044 (LS) + 0.001 (LS × PC). This score had an AUROC of 0.909 (95%CI: 0.841-0.954, $P < 0.0001$) and it performed similarly when evaluated by etiology of liver disease[19]. A third score, calculated simply by PC/$\log_{10}$ LS, was evaluated in a prospective study of 107 patients. It was found that values ≤ 122,000/μL × kPa predicted high-risk varices with 100% sensitivity and 100% NPV, which would prevent 20.6% of patients from receiving unnecessary screening endoscopy ($p = 0.003$)[21].

These studies together demonstrate that combinations of LS, SD, and PC can perform well in the diagnosis of CSPH and EV/HREV. However, despite their excellent test characteristics, these scores have not gained momentum, and one important reason for this is that calculating a score is cumbersome when applied to busy clinical practice because it requires an additional step. The Baveno VI consensus acknowledged this in favoring a method that combines data points sequentially rather than *via* a calculation.

LIVER STIFFNESS AND PLATELET COUNT: THE BAVENO VI CRITERIA

The combination of LS and PC has demonstrated high performance in the prediction of CSPH and EV, and the use of sequential clinical parameters is quick and simple to apply in clinical practice. A 2014 prospective, proof-of-concept study of 49 patients with TE-LS ≥ 13.6 kPa and EGD noted that 90% of patients with EV had a PC < 150000/mm^3 and an abnormal ultrasound suggesting a simple sequential strategy could be used to avoid EGD in low-risk patients[22]. A subsequent 2015 retrospective study of 271 patients (71 training, 200 validation) with Child Pugh A cirrhosis and LS > 13.6 kPa found that the optimal threshold for excluding HREV was the combination of LS ≤ 25 kPa and PC ≥ 100000/mm^3. This combined model had a NPV of 100% for the prediction of HREV in both the training and validation cohorts[23]. Of note, the majority of patients had hepatitis C cirrhosis and in addition, the frequency of GEV was low (10% overall) which is good in that it reflects real-life practice in compensated cirrhosis but worth noting because it does affect the model development and test characteristics[23].

Based on these findings that HREV could be excluded with a very low miss rate[22,23], the 2015 Baveno VI consensus conference recommended that surveillance endoscopy is not necessary for patients with compensated cirrhosis who have normal platelets > 150000/mm^3 and LS < 20 kPa[2]. Many studies including high-volume single center retrospective studies and meta-analyses have validated the Baveno VI recommendation in patients with different etiologies of cACLD (including hepatitis B, hepatitis C, alcohol, and non-alcoholic steatohepatitis) and variable prevalence of EV, ranging from 23% to 65%[21,24-32]. Across all of these studies, the overall missed HREV rate has been 2% or less, in keeping with the proposed < 5% threshold defined by Baveno VI. In these studies, 20% of EGDs could have been saved by applying the criteria. As is most frequently the case, the most common etiologies across these multiple studies were viral and alcohol-related cirrhosis. However, a 2018 large multi-center cross-sectional study of 790 patients with cirrhosis due to nonalcoholic fatty liver disease (NAFLD) demonstrated a HREV miss rate of 0.9% using the Baveno VI criteria[33]. A subsequent 2019 retrospective cross-sectional study evaluated Baveno VI in 227 patients with cACLD due to cholestatic liver diseases including primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC), which are mechanistically distinct in that they may have a pre-sinusoidal component of PH. Baveno VI had a 0% false negative rate in the prediction of HREV in PBC and PSC[34]. The robustness of the Baveno VI criteria in ruling out HREV led to its adoption in the AASLD practice

guidance statement[3].

EXPANDING ON THE BAVENO VI CRITERIA

Noting that the total number of EGDs avoided using the Baveno VI criteria is low relative to the prevalence of HREV, several studies have attempted to expand the Baveno VI and improve its discriminatory accuracy by adjusting the LS and PC cutoff values. Based on 2 large-scale retrospective studies, a PC > 110000/mm^3 and LS < 25 kPa was shown to potentially spare up to 40% of EGDs where the Baveno VI criteria would spare only 20% at an acceptable missed VNT rate of 1.6% (95%CI: 0.7% -3.5%)[32,35]. This came to be known as the "Expanded Baveno VI criteria" and was initially shown to maintain a similar missed VNT rate of < 5% across different subgroups including hepatitis C, alcohol, non-alcoholic steatohepatitis, and PSC/PBC[32,34,35]. However, a large-scale retrospective study in an Asian population showed that while the Expanded Baveno VI criteria spared more EGDs compared to the Baveno VI criteria (51.7% *vs* 27.6%), it missed an unacceptable number of HREV in comparison (6.8% *vs* 3.8%)[30].

Subsequently, a large meta-analysis including 30 studies and 8469 patients reproduced a similar finding, that although the Expanded Baveno VI criteria could reduce the proportion of unnecessary EGDs, it would do so at a higher rate of missed HREVs[31]. Thus, the Expanded Baveno VI criteria are not recommended. LS < 25 kPa with a PC > 125000/mm^3 was evaluated as an alternate expansion of the Baveno VI criteria and was shown to spare an additional 15% of endoscopies above the Baveno VI criteria with an acceptable missed HREV rate in a large retrospective study of 442 patients[32] but this was not subsequently validated. This same study looked at PC > 150000/mm^3 and model for end stage liver disease 6 as a method of ruling out HREV but misclassified 10% of patients[32].

Some studies have examined disease-specific cut-offs. A large-scale NAFLD patient cohort was also used to identify a NAFLD-specific LS and PC cutoff to be applied in a similar fashion and found that the best thresholds to rule out HREV were PC > 110000/mm^3 and either LS < 30 kPa with the medium-sized probe or LS < 25 kPa using the extra-large probe[33]. They demonstrated that applying these criteria in the NAFLD population would reduce the number of screening EGDs by almost half with an acceptable HREV miss rate of < 5%[33]. However, this has not subsequently been validated and an additional challenge is that LS measurements are less accurate in obese patients, in fact, TE is not technically feasible in approximately 20% of patients[36]. One retrospective study of hepatitis B-related compensated cirrhosis showed that after removing patients meeting Baveno VI criteria, the remaining patients could be further selected for absence of HREV using LS, PC, or the Lok index cutoff [- 5.56 – 0.0089 × PC (10^3/mm^3) + 1.26 × (Aspartate Transaminase/Alanine Aminotransferase) + 5.27 × International Normalized Ratio Lok] = [exp (logodds)]/[1 + exp (logodds)][27] stratified by alanine aminotransferase and total bilirubin[29]. This study is specific to hepatitis B and does not put forth a single recommendation but rather suggests that Baveno VI can be optimized further.

SPLEEN STIFFNESS MEASUREMENT

Portal hypertension leads to splenic congestion which leads to architectural changes in the splenic arteries and veins, resulting in fibrosis of the spleen and therefore, a rise in spleen stiffness. Methods for measuring spleen stiffness include shear wave elastography, TE, and acoustic radiation force impulse imaging. Of these methods, acoustic radiation force impulse imaging has been studied most frequently because this method is not limited by the presence of ascites or obesity[37]. Spleen stiffness measurement (SSM) appears to perform well in the prediction of CSPH: In a prospective study of 78 patients, SSM was able to diagnose HVPG ≥ 10 mmHg and HVPG ≥ 12 mmHg with AUROCs of 0.97 and 0.95, respectively[37]. Some studies have indicated that SSM is superior to LS in diagnosing CSPH[38-40]; however, other studies provide contrary views[41-43]. According to present literature, it is difficult to determine which metric is superior.

Several studies have explored SSM in the prediction of EV[40,44-47]. A prospective study of 135 patients demonstrated that patients with any EV had higher SSM than those with no EV (3.37 m/s *vs* 2.79 m/s, P < 0.001); and patients with HREV had an even greater difference in SSM (3.96 m/s *vs* 2.93 m/s, P < 0.001)[44]. In addition, at a

cutoff value of < 3.20 m/s, NPV for excluding HREV was 99%[44]. SSM was therefore evaluated in 2 prospective studies and demonstrated good diagnostic accuracy for prediction of any EV, with AUROC of 0.872 to 0.933 at a cutoff of 2.89-3.18 m/s, and good diagnostic accuracy for the prediction of HREV, with AUROC of 0.930–0.969 at cutoffs of 3.30 m/s[45,47]. One study demonstrated that the combination of SSM by TE at a cutoff of ≤ 46 kPa and Baveno VI criteria would have safely spared (0 HREV missed) 37.4% of EGDs compared with only 16.5% when using the Baveno VI criteria alone[24]. In these studies, SSM has demonstrated good performance across different subgroups including viral, non-viral, and Child B cirrhosis, but these subgroups all used different SSM cutoffs which complicates translation to clinical practice[45,47]. In subsequent meta-analyses, heterogeneity in the technique of obtaining SSM and in cutoffs used was a problem and as a result, diagnostic accuracy was not as high[43,46]. Furthermore, SSM is not widely available at this time and therefore this cannot be recommended on a large scale.

VIDEO CAPSULE ENDOSCOPY

Video capsule endoscopy (VCE) has been evaluated for the diagnosis of HREV. However, a Cochrane systematic review of 6 studies could not substantiate VCE as a non-invasive method of assessing for EV. The pooled sensitivity was 73.7% (95%CI: 52.4%-87.7%) and the pooled specificity was 90.5% (95%CI: 84.1%-94.4%)[48]. It was concluded that the sensitivity of VCE is not sufficient to replace EGD as a method of variceal screening in these patients. Given its higher specificity, it was recommended that it could be considered in patients who refuse or have a contraindication to EGD[49]. However, this is not likely cost-saving, not widely available, and is still a procedure requiring endoscopy staff and specialized equipment and with a certain level of procedural risk (*e.g.* capsule retention)[48,49].

EVENDO SCORE

Despite the excellent performance characteristics of LS and PC, TE is far from widely available and therefore there is interest in developing prediction scores independent of LS. With this in mind, the EVendo score was recently developed and validated in a multi-center study of 238 patients with cirrhosis. The score was developed using a machine learning algorithm to identify factors significantly associated with the presence of EVs and HREVs. The investigators then developed the EVendo score, which is calculated as follows: [(9.5 × international normalized ratio + aspartate transaminase/35)/(platelets/150 + blood urea nitrogen/20 + hemoglobin 15)] + 1 point for ascites. This score identified patients with EVs in the training set with an AUROC of 0.84 and was then validated in an independent prospective cohort with good performance (AUROC of 0.82 for EV in all patients, AUROC of 0.81 in subgroup of patients with Child-Pugh A cirrhosis). The score identified patients with HREV in the training set with an AUROC of 0.74, in the validation set with an AUROC of 0.75, and in patients with Child-Pugh A cirrhosis with an AUROC of 0.75. An EVendo score below 3.90 would have spared 30.5% patients from EGDs, missing only 2.8% of VNT and 40.0% patients with Child-Pugh A cirrhosis from EGDs, missing only 1.1% of VNT[50].

The EVendo score is advantageous in that it relies on routinely collected laboratory values, has robust performance characteristics across a broad array of liver disease etiologies, and can be readily calculated using a published on-line calculator (https://www.mdcalc.com/evendo-score-esophageal-varices). As such, it is convenient for clinical use to risk stratify and triage patients with cirrhosis who are being considered for EV screening (Figure 1). However, further validation in larger cohorts will be useful to better define its clinical utility and suitability for broader use (Tables 1 and 2).

CONCLUSION

In summary, the use of non-invasive testing to stratify cACLD patients for screening endoscopy and individualize care for PH shows promise and will continue to become more important as the cACLD population grows. However, several important caveats

Table 1 Test characteristics for noninvasive detection of esophageal varices

Non-invasive test	Sensitivity	Specificity	PPV	NPV	LR (+)	LR (-)	AUROC
PC/SD	89%-93%	74%-84%	73%	74%	3.5	0.12	
TE	84%	62%-68%			2.3-2.58	0.24-0.26	0.82-0.84
LSPS			94% (LSPS > 5.5)	94% (LSPS < 3.5)			0.882-0.953
EV prediction score							0.909
SSM	78%-94%	76%-78%		99%	3.4	0.2	0.872-0.933
EVendo	92.3%	65.9%					0.82
Capsule endoscopy	73.7%-83%	84%- 90.5%					0.90

Other noninvasive scores exist and may be used, as shown in Table 1; EVendo score selected based on it having the highest sensitivity, negative predictive value, and endoscopies saved, though it has not yet been validated outside of the United States. EV: Esophageal varices; PPV: Positive Predictive Value; NPV: Net present value; AUROC: Area under the receiver operating characteristic; PC/SD: Platelet count to spleen diameter ratio; TE: Transient elastography; LSPS: Liver stiffness–spleen diameter to platelet ratio; SSM: Spleen stiffness measurement.

Table 2 Test characteristics for noninvasive detection of high risk esophageal varices

Non-invasive test	Sensitivity	Specificity	PPV	NPV	LR (+)	LR (-)	AUROC	HREV missed	EGDs saved
PC/SD	85%	66%			3.03	0.30	0.83	7%	
TE	78%-82%	76%-77%					0.78-0.83		
PLT/$\log_{10}$LS	100% (< 122000); 86% (< 92000)			100% (< 122k); 94% (< 92k)				0	20.6%; 6.3%
Baveno VI	87%-97%	32%-41%	6%	98%-100%	1.31	0.39	0.746-0.96	< 2%	20%-27%
Expanded Baveno VI	90%	51%		92%-96%				6.8%	51%
SSM	81%-98%	52%-66%		99.4%	2.5	0.2	0.807	2%	35.8%
EVendo	100%	49.3%		100%			0.75	2.8%	30.5%
Capsule endoscopy	72%-73.7%	90.5%-91%					0.92		

Other noninvasive scores exist and may be used, as shown in Table 2; EVendo score selected based on it having the highest sensitivity, negative predictive value, and endoscopies saved, though it has not yet been validated outside of the United States. HREV: High risk esophageal varices; PPV: Positive Predictive Value; NPV: Net present value; AUROC: Area under the receiver operating characteristic; EGD: Endoscopy; PC/SD: Platelet count to spleen diameter ratio; TE: Transient elastography; PLT: Platelets; LS: Liver stiffness; SSM: Spleen stiffness measurement.

need to be kept in mind.

Non-invasive prediction of EV cannot be applied to patients with decompensated cirrhosis given the paucity of applicable data and the much higher pre-test probability of HREV. Although the AASLD guidance statement recommends that patients meeting Baveno VI criteria can safely avoid screening EGD, there is still uncertainty regarding follow-up of patients who have been ruled out for HREV. It has been suggested that these patients can be followed with annual TE and PC and undergo screening when they no longer meet the Baveno VI criteria. However, long-term follow-up studies are needed to determine whether this strategy is sufficiently accurate to identify the development of HREV in someone who was previously at low risk. There is a lack of randomized controlled trial data to inform the selection of higher-risk patients by non-invasive methods for variceal screening EGD; while prospective data exist in this regard, *e.g.* with the EVendo score[50], further clinical validation is encouraged. Finally, despite the high performance of TE, there is considerable interest in developing scores that do not require TE given that it is not widely available; moreover, its measurement can be affected by several factors including obesity, ascites, and alcohol use, which may limit its application in advanced

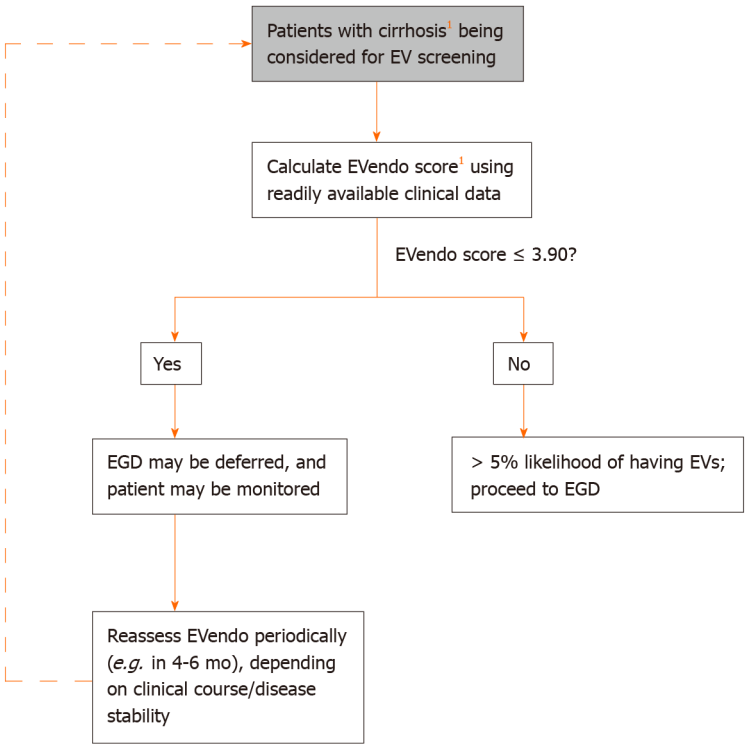

Figure 1 Proposed algorithm for noninvasive esophageal variceal assessment to risk stratify patients using the EVendo score[1]. Patients with known (biopsy-proven) or suspected cirrhosis. Excluded from the original study were patients who: (1) Had a prior upper endoscopy (EGD) for esophageal variceal screening, surveillance, or treatment; (2) Had a prior EGD that incidentally revealed esophageal varices; (3) Had noncirrhotic etiologies for portal hypertension; (4) Were on dialysis; or (5) Were on anticoagulants that would affect international normalized ratio. Online calculator and additional guidelines available here: https://www.mdcalc.com/evendo-score-esophageal-varices. [1]Other noninvasive scores exist and may be used, as shown in Tables 1 and 2; EVendo score selected and shown here based on it having the highest sensitivity, negative predictive value, and EGDs saved, though it has not yet been validated outside of the United States. EGD: Endoscopy; EV: Esophageal varices.

liver diseases[36], and it is highly operator dependent, requiring completion of 100 examinations for sufficient experience[51]. Lastly, there is uncertainty regarding when surveillance can be stopped if there is improvement in fibrosis and PH with the removal of the source of ongoing liver injury (*i.e.*, post-SVR, after abstinence from alcohol, after weight loss and metabolic improvements). Future research should be directed at these efforts and areas of uncertainty.

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