Screening for Esophageal Varices

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Despite a major improvement in its management over the past 2 decades, the rupture of esophageal varices (EVs) remains a common and severe complication of cirrhosis with a mortality rate still reaching 20%. Screening for EVs is crucial because it provides the ability to reduce the risk of a first bleeding episode.

Who to Screen?

According to the Baveno V guidelines,¹ every patient with cirrhosis should be screened for EVs. This strategy is aimed at identifying patients with varices with a high risk of bleeding, that is, large esophageal varices (LEVs; grade II or III or a diameter > 5 mm) or varices with red signs. These high-risk patients should benefit from primary prophylaxis with beta-blockers or band ligation. All patients with portal hypertension (PHT), even those without cirrhosis (i.e., patients with conditions such as portal vein thrombosis, nodular regenerative hyperplasia, and congenital hepatic fibrosis), should be screened for EVs.

When to Screen?

Screening is indicated when cirrhosis or PHT is diagnosed. When high-risk varices are diagnosed, prophylaxis should be started, and further screening is not necessary. Otherwise, screening should be repeated every 2 to 3 year for patients without varices and every 1 to 2 year for patients with small varices. This time frame can be shortened for patients with small varices who have a high risk of variceal progression (i.e., active alcohol consumption or decompensated cirrhosis).

How to Screen?

Upper gastrointestinal endoscopy remains the gold standard technique. The advantages of endoscopy include its ability to

- Make a precise description of EVs: the location (especially the presence of gastric varices), the number, the size, and the presence of red signs.
- Assess other complications of PHT: gastropathy and antral vascular ectasia.
- Perform band ligation at the time of the diagnostic procedure.
- Assess other injuries of the upper digestive tract: ulcers and upper aerodigestive tract cancers in alcoholic patients.

Nevertheless, endoscopy has some pitfalls, including its invasiveness, discomfort (which can decrease a patient's observance), cost, and interobserver variability (which can reach 30% for small varices). Moreover, nowadays, when cirrhosis is diagnosed earlier because of noninvasive methods, more than half of procedures may be unnecessary.² Therefore, research is particularly active for developing noninvasive methods for an EV diagnosis. One must keep in mind that a screening test should

- Be highly sensitive to avoid false-negative results.
- Be repeatable.
- Have a reasonable cost.

To date, there is no validated noninvasive screening method fulfilling these criteria, and endoscopy remains the only way to screen for EVs.

Abbreviations: AUROC, area under the receiver operating characteristic curve; CT, computed tomography; EV, esophageal varix; HVPG, hepatic venous pressure gradient; LEV, large esophageal varix; PCSD, platelet count/spleen diameter; PHT, portal hypertension; ROC, receiver operating characteristic; SS, spleen stiffness; TE, transient elastography.

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The performance characteristics of different tests may not be the same for different etiologies of cirrhosis.

Lastly, for almost every study, endoscopy has been the gold standard for an EV diagnosis, despite the low interobserver variability, and this has to be considered in the interpretation of the findings. The research areas are described next.

Methods for Assessing PHT. This is reviewed by Heller and Koh in this issue of *Clinical Liver Disease*.³

The measurement of the hepatic venous pressure gradient (HVPG) is the most sensitive method for screening patients without any risk of bleeding because patients with an HVPG less than 12 mm Hg rarely bleed. However, this procedure is much more invasive than endoscopy and is restricted to expert centers; therefore, it is not an acceptable screening test.

The original study⁴ demonstrated that the platelet count/spleen diameter (PCSD) ratio was a good marker of EVs with a sensitivity of 100%. However, further validation studies, including a multicenter, prospective validation study conducted by the same team, were disappointing.⁵ A recent meta-analysis reported a good sensitivity for this test (92%).⁶

Recent data suggest that spleen stiffness (SS) could be an accurate test for predicting EVs: an American study has proven that SS measurement by magnetic resonance elastography is feasible and is related to the presence of EVs.⁷ SS measurement by transient elastography (TE) has also been shown to be a good predictor of EVs with a sensitivity of 98.1%.⁸ In that study, the performance of SS was better than the performance of any other noninvasive tests (e.g., liver TE and PCSD ratio) and did not differ from the performance of HVPG.

Methods Related to the Assessment of Fibrosis. A retrospective French study⁹ has shown that FibroTest is able to predict the presence of LEVs with a sensitivity of 92%. Those results have to be validated. TE is not a good screening test for EV detection because of the low sensitivities reported in several studies, and it should not be used for this indication.^{10,11}

Imaging Techniques. Computed tomography (CT) seems to perform well for the diagnosis of LEVs. A recent American study has reported a sensitivity of 92.5% for the discrimination of high-risk varices.¹² Interestingly, in that study, an assessment of endoscopic variability was considered. Previous studies have shown that CT has good sensitivity for detecting EVs and, in comparison with endoscopy, is better accepted by patients and is more cost-effective.¹³ Moreover, CT enables simultaneous screening for hepatocellular carcinoma, which is

TABLE 1: Performance of Alternative Tools for the Diagnosis of EVs in Patients With Cirrhosis

Test	Study	Cutoff	Diagnosis	Patients (n)	Study Type	Diagnostic Accuracy	Sensitivity (%)	Specificity (%)	Negative Predictive Value (%)	Positive Predictive Value (%)
PCSD ratio	Giannini et al. ⁴	909	EV	145	Retrospective, prospective	C index: 0.98 (0.943-0.996)	100	93	100	96
PCSD ratio	Giannini et al. ⁵	909	EV	218	Multicenter, prospective	Diagnostic accuracy: 0.86 (0.807-0.904)	91.5	67	87	76
PCSD ratio	Ying et al. ⁶	909	EV	3063	Meta-analysis	Hierarchical summary ROC: 0.95	92	87		
SS	Colecchia et al. ⁸	41.3 kPa	EV	100	Prospective	AUROC: 0.94	98.1	66		
FibroTest	Thabut et al. ⁹	0.8	LEV	99	Retrospective	AUROC: 0.77	92	21	86	44
Liver stiffness (TE)	Castera et al. ¹⁰	21.5 kPa	EV	298	Prospective	AUROC: 0.84 (0.75-0.94)	76	78	84	68
Liver stiffness (TE)	Castera et al. ¹⁰	21.5 kPa	LEV	298	Prospective	AUROC: 0.87 (0.77-0.97)	85	68	95	39
CT scan	Yu et al. ¹²	2 mm	LEV	109	Retrospective		92.5		96.5	
CT scan	Perri et al. ¹³		LEV	102	Prospective		90	50		
CT scan	Perri et al. ¹³		Gastric varices	102	Prospective		87			
Capsule endoscopy	Lu et al. ¹⁴		EV	446	Meta-analysis	Diagnostic accuracy: 0.63 ± 0.059	85.8	80.5		
Capsule endoscopy	Chavalitthamrong et al. ¹⁵		EV	65	Prospective	Diagnostic accuracy: 0.69 ± 0.054				
Capsule endoscopy	Chavalitthamrong et al. ¹⁵		Red marks	65	Prospective	Diagnostic accuracy: 0.52 ± 0.042				
Capsule endoscopy	Chavalitthamrong et al. ¹⁵		Other lesions	65	Prospective					

Abbreviations: AUROC, area under the receiver operating characteristic curve; ROC, receiver operating characteristic.

FIGURE 1. Illustrations of alternative tools for the diagnosis of EVs. (A) CT scan showing 2 EVs (cursors) that were 5 and 6 mm in diameter. Reprinted with permission from *Hepatology*.¹³ Copyright 2008, American Association for the Study of Liver Diseases. (B) Magnetic resonance elastography of the liver and spleen in a normal volunteer (upper row) and in a cirrhotic patient (lower row). Anatomic images are shown in the left column. The middle column shows wave image data for the liver and spleen, which are superimposed on the corresponding anatomic images. The resulting elastograms are shown in the right column. Reprinted with permission from *American Journal of Roentgenology*.⁷ Copyright 2009, American Roentgen Ray Society. (C) Images acquired with esophageal capsule endoscopy and showing EVs: (a) grade I EVs, (b) grade II EVs, (c) grade III EVs. Reprinted with permission from *Gastroenterology Research and Practice*.¹⁶ Copyright 2012, Hindawi Publishing Corp.

mandatory for patients with cirrhosis. The limits of CT are its low specificity and the exposure to radiation.

Like capsule endoscopy, esophageal capsule is safe and is minimally invasive for EV detection. Like endoscopy, it offers direct visualization of varices and red signs. A meta-analysis found a sensitivity of 85.8% when endoscopy was considered the gold standard.¹⁴ However, an American study described poor overall accuracy, especially for the detection of EV red marks, with insufficient interobserver agreement.¹⁵ Capsule performance may improve when physicians become more experienced in interpreting images. However, this technique is costly and is not available at every center, and these are major drawbacks for a screening technique.

The diagnostic performances of these alternative methods for EV screening are summarized in Table 1,^{4–6,8–10,12–15} and some illustrations of these methods are shown in Fig. 1.^{7,13,16}

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Summary

Despite many well-designed studies exploring alternatives to endoscopy for EV screening, we have to keep practicing and teaching endoscopy, which remains the gold standard to date. Universal endoscopic screening of patients with cirrhosis is becoming less and less cost-effective because of the earlier diagnosis of cirrhosis. Noninvasive methods that have high sensitivities and fulfill the criteria for screening tests are needed to more effectively select patients who will derive the most benefit from endoscopy. In the future, screening for EVs in patients with cirrhosis will probably rely on an à la carte strategy more than a one-fits-all strategy.

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