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# The noninvasive diagnosis of esophageal varices and its application in clinical practice

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## KEYWORDS

Cirrhosis;  
Esophageal varices;  
Portal hypertension;  
Noninvasive  
diagnosis;  
Elastometry;  
Blood markers

**Summary** Here, we review recent improvements made to different noninvasive tests used for the diagnosis of esophageal varices (EV) in the light of the recent Baveno VI recommendation and with an emphasis on clinical application. Like for fibrosis tests, these noninvasive EV tests can be classified as direct markers when they provide a visualization of EV (including all imaging procedures like endoscopy or radiology) and as indirect markers when they do not (blood markers or elastometry). Clinical descriptors expressed as percentages, especially the spared endoscopy rate and the missed high-risk esophageal varices (HREV) rate, are more eloquent in this setting than classical statistical descriptors like accuracy. Single biomarkers are insufficient, generally due to a missed HREV rate exceeding the acceptable limit of 5% indicated in the Baveno VI consensus. Thus, biomarker combinations are currently garnering the most interest. The Baveno VI recommendation states that in alcoholic and viral cirrhoses, screening endoscopy can be safely set aside for patients with liver stiffness < 20 kPa and platelets > 150 G/L. The Baveno rule's mean missed HREV rate is < 5% but its spared endoscopy rate is < 20%. New combinations or stepwise algorithms show promise but must be validated. Going forward, the Baveno rule provides a simple noninvasive method to rule out HREV in clinical practice but the need for further research continues. The noninvasive diagnosis of HREV will be significantly improved by new, simple and affordable combinations.

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**Abbreviations:** ARFI, acoustic radiation force impulse; ASPS, ARFI-spleen diameter ratio score; AUROC, area under the receiver operating characteristic; CLD, chronic liver disease; cACLD, compensated advanced chronic liver disease; CSPHT, clinically significant portal hypertension; EV, esophageal varices; EVRS, esophageal varices risk score; HREV, high risk esophageal varices; HVPG, hepatic venous-pressure gradient; LS, liver stiffness; LSPS, LSM-spleen diameter to platelet ratio score; MDCT, multidetector computed tomography; MRE, magnetic resonance elastography; NSBB, non-selective beta-blockers; PSR, platelet/spleen diameter ratio; SS, spleen stiffness; SWE, shear wave elastography; TE, transient elastography; PHT, portal hypertension; UGIE, upper gastrointestinal endoscopy; VCE, video capsule endoscopy.

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<http://dx.doi.org/10.1016/j.clinre.2017.07.006>

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Please cite this article in press as: Pateu E, et al. The noninvasive diagnosis of esophageal varices and its application in clinical practice. Clin Res Hepatol Gastroenterol (2017), <http://dx.doi.org/10.1016/j.clinre.2017.07.006>

## Introduction

One of the main consequences of liver cirrhosis is portal hypertension (PHT). This latter leads to severe complications, such as variceal bleeding, portal hypertensive enteropathy, ascites, sepsis, hepatorenal syndrome and hepatic encephalopathy. The occurrence of esophageal varices (EV) represents an independent risk factor for mortality and necessitates a significant change in the management of chronic liver disease (CLD) [1].

A hepatic venous pressure gradient (HVPG) higher than 10 mmHg defines clinically significant PHT (CSPHT) and thus implies an increased risk of EV development [2].

EV are usually classified into three, size-defined grades, which largely indicate the associated bleeding risk. Thus, high-risk esophageal varices (HREV) are defined by EV grades 2 and 3 (roughly an EV diameter  $\geq 5$  mm) as well as grade 1 when red color signs are also present. Bleeding is observed when HVPG is higher than 12 mmHg. Primary prophylaxis of variceal bleeding using non-selective beta-blockers (NSBB) or endoscopic band ligation is recommended for HREV [3]. It is therefore currently recommended to perform EV screening by upper gastrointestinal endoscopy (UGIE) at the time of cirrhosis diagnosis and every one to three years thereafter depending on initial EV grade and CLD course [2].

However, UGIE for EV screening does have inconveniences. The yearly incidence rate of EV development in cirrhosis patients is only around 7% [4] and the cumulative five-year incidence rate is 21% [5]. Also, EV screening by UGIE is limited by its cost, invasiveness, the logistics of a screening agenda and the discomfort it imposes on patients. Moreover, large interobserver variability in assessing the classification of EV makes UGIE an imperfect gold standard [6]. And finally, in a recent survey, EV screening was not applied in around half of concerned patients [7].

With the goal of circumventing these inconveniences, a number of noninvasive EV grading methods have been evaluated over the past 20 years. Recently, the Baveno VI

consensus stated that liver stiffness (LS) by transient elastography (TE)  $\geq 20$  kPa could be considered as indicative of CSPHT. Additionally, the Baveno VI recommendation states that patients with cirrhosis of viral or alcoholic etiology who have a combination of LS  $< 20$  kPa and blood platelet count  $> 150$  G/L are highly unlikely to have EV needing treatment and can therefore forego UGIE. Thus, for the first time, noninvasive tests can be used for the diagnosis of CSPHT and EV [3].

The aim of this review is to present recent improvements made to different noninvasive tests used for the diagnosis of EV in the light of the Baveno VI recommendation and with an emphasis on clinical application.

## What is known?

Considering the well-established relationship between fibrosis, PHT and EV [8], noninvasive tests for fibrosis diagnosis should also be useful tools for EV screening.

The development of noninvasive tests to diagnose cirrhosis earlier in its course also implies an earlier detection of complications such as PHT. This might be an advantage. However, the proportion of UGIE done for EV screening but that does not lead to therapeutic changes is already high with the classic attitude based on the histological or clinical diagnosis of cirrhosis. Applying the same detection rules based on the new attitude of noninvasive cirrhosis diagnosis would therefore lead to an increase of UGIE overuse (Fig. 1). To date, HREV tests have been evaluated in cirrhosis populations. The new objective is to determine, first, the most pertinent cut-offs of noninvasive fibrosis tests for HREV screening, and, second, the capacity of noninvasive tests to replace UGIE. These two steps can be united in a single pursuit: determining the cut-offs of one or several noninvasive fibrosis tests to rule HREV out and in.

This topic has been developing over more than twenty years. In the beginning, the noninvasive diagnosis of EV

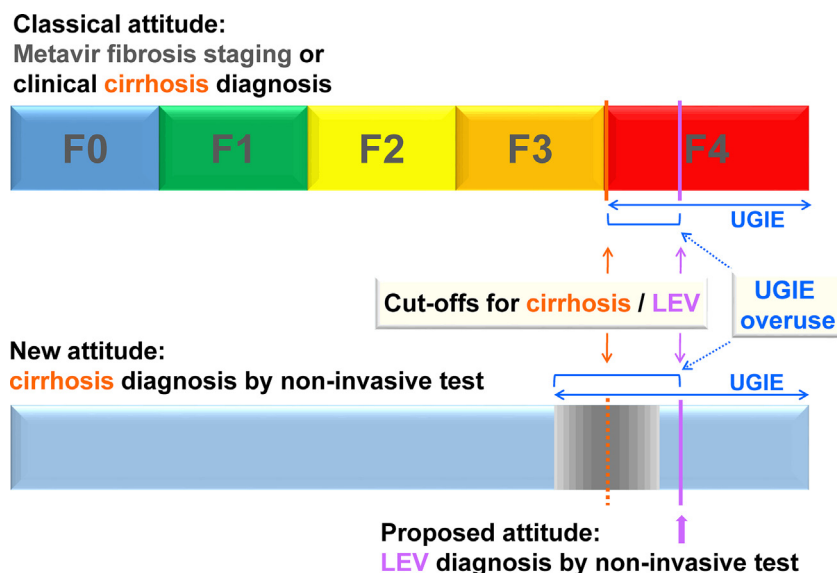


Figure 1 Risk of endoscopy (UGIE) overuse with the diagnosis of chronic liver disease by noninvasive tests for liver fibrosis.

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