

Is Transient Elastography a Valid Screening Method for Esophageal Varices?

Gastroesophageal varices are a common complication of cirrhosis and are present in approximately 50% of patients with cirrhosis.^[1] Acute gastroesophageal variceal hemorrhage is a severe complication of cirrhosis or portal hypertension associated with high mortality.^[1-3] Although mortality of gastroesophageal variceal hemorrhage has decreased in the past three decades, it remains the most common lethal complication of cirrhosis^[1] with an overall mortality of approximately 15–20% per episode.^[3]

The gold standard for the diagnosis of varices is esophagogastroduodenoscopy (EGD). Guidelines recommend that EGD should be performed once the diagnosis of cirrhosis is established.^[1,4,5] Identifying varices provides the opportunity for primary prophylaxis with a nonselective beta-blocker or esophageal variceal ligation, thereby significantly lowering the risk of hemorrhage.^[1,6]

In this issue of the Journal, Qu *et al.* performed a meta-analysis to assess the diagnostic accuracy of transient elastography (TE) as an alternative to EGD for the prediction of esophageal varices in patients with cirrhosis.^[7] The search strategy employed a limited number of keywords. It could be significantly improved by identifying and adding all appropriate index terminology (for example Medical Subject Headings (MeSH) and Emtree) and synonymous terms, thereby potentially identifying additional articles that meet the inclusion criteria.^[8] The authors did not adequately describe their system of solving disagreements between the two reviewers who evaluated the papers for inclusion, exclusion, and data extraction. Furthermore, the authors did not report a Kappa value for agreement between the two reviewing authors.

Twenty studies (2530 patients) comparing TE and EGD were included in the final meta-analysis. The pooled sensitivity, specificity, positive, and negative likelihood ratios and diagnostic odds ratio were 0.84 (95% confidence interval (CI): 0.79–0.87), 0.68 (95% CI: 0.61–0.73), 2.58 (95% CI: 2.15–3.10), 0.24 (95% CI: 0.19–0.32), and 10.60 (95% CI: 7.20–15.62), respectively. They concluded that TE could serve as an effective noninvasive screening tool with a good sensitivity and a moderate specificity for the prediction of esophageal varices.

The heterogeneity between included studies was large and significant ($Q = 28.884$, $P = 0.000$, $I^2 = 93.08$, 95% CI: 86.90–99.25). The authors' subgroup analyses did not find a source for the heterogeneity. However, we can postulate potential reasons. First, the cut-off value for the Area Under the Receiver Operating Characteristic (AUROC) curve in the various trials ranged from 12.0 kPa to 29.7 kPa. This is a large range and would dramatically vary the sensitivity and specificity in each trial. In addition to likely contributing to the heterogeneity, nonagreement on a cutoff value also limits its applicability for clinicians. Because of the life-threatening nature of variceal hemorrhage, one would want a sensitivity of a screening modality to approach 100%. The studies with the highest sensitivities had cutoff values close to the authors' cutoff value for cirrhosis (12 kPa). This would be consistent with current guidelines suggesting that all patients diagnosed with cirrhosis should undergo EGD to screen for esophageal varices.^[1] Second, TE values to diagnose cirrhosis vary according to etiology. Therefore, it is conceivable that TE values for significant portal hypertension leading to esophageal varices also may vary, and using a single cutoff value (as each trial did) may add to the heterogeneity. Interestingly, when the authors analyzed the heterogeneity of trials that included only patients with hepatitis C cirrhosis, there was no heterogeneity between trials. Third, most of the trials included analyzed a small number of patients.

This meta-analysis analyzed the use of TE used alone to screen for esophageal varices. Combining TE values with other readily available information may further improve specificity and sensitivity. The Baveno VI criteria for screening of esophageal varices in cirrhosis recommend that patients with a liver stiffness <20 kPa and with a platelet count >150,000 have a very low risk of having varices requiring treatment, and can avoid screening endoscopy (1b; A).^[9] There is emerging evidence suggesting that this is a viable alternative to EGD screening.

It is also important to note that not all varices are secondary to cirrhosis. Other patients at risk for the development of varices without having cirrhosis include those with hepatitis C and bridging fibrosis; primary biliary cirrhosis (PBC); and splenic vein thrombosis (they may develop gastric varices).^[11]

Esophageal varices are also not the only type of gastrointestinal varices that are worrisome for variceal bleeding. EGD also screens for gastric and duodenal varices, which is outside the scope of the current meta-analysis.

The size of the esophageal varices (large as opposed to small) is a risk factor for variceal hemorrhage.^[1,2] The present meta-analysis pooled the results of ten studies that evaluated TE vs EGD for the detection of large esophageal varices. The cutoff value for AUROC ranged from 14.6 to 38.2 kPa between the 10 trials. The pooled sensitivity was 0.84 (95% CI: 0.80–0.88), whereas the pooled specificity was 0.72 (95% CI: 0.65–0.79). The Positive and Negative Likelihood Ratios (PLR and NLR) were 3.02 (95% CI: 2.33–3.90) and 0.22 (95% CI: 0.17–0.29), respectively. The Diagnostic Odds Ratio (DOR) was 13.65 (95% CI: 8.65–21.53) and the AUROC was 0.85 (95% CI: 0.81–0.88). The heterogeneity remained high ($Q = 4.817$, $P = 0.045$, $I^2 = 58.48$), but disappeared when analyzing the trials that included only patients with hepatitis C. Size is an important risk factor for variceal hemorrhage, however, it is certainly not the only important risk factor. The variceal appearance on endoscopy for “red signs” as well as the location of varices are also important.^[1,2] Signs such as red wale marks (longitudinal streaks on varices), cherry-red spots (discrete red flat spots on varices), hemato-cystic spots (discrete, red, raised spots), and diffuse erythema can be observed on endoscopy, however, would not be readily evident with an alternative screening tool such as TE. Ascites is also an important risk factor for variceal hemorrhage^[1,2] and would make TE difficult to perform.

In conclusion, screening for esophageal varices with EGD is currently recommended in all patients who are diagnosed with cirrhosis. The results of this meta-analysis will likely not change that recommendation. EGD is the gold standard for variceal screening, providing both a diagnosis and potential prophylactic therapy. Modalities such as TE or capsule endoscopy provide adjunct information currently, however, they may have a larger role in screening for esophageal varices in the future.

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