

Review Article

Elastography ultrasound for screening and early detection of esophageal varices

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ABSTRACT

Despite that esophageal varices can be effectively detected by using upper gastrointestinal tract endoscopy, the procedure is invasive and requires the integration of adequate experience and training, and it is not suitable for many patients. Accordingly, ultrasound elastography has been developed and validated by many studies in the recent literature as effective and non-invasive modalities for the early observation and diagnosis of esophageal varices and the relevant hepatic diseases. In this study, we aim to conduct a literature review to furtherly elaborate on the role and validity of elastography ultrasound to screen and early detect esophageal varices. We have discussed the diagnostic efficacy of three different types of ultrasound elastography including two-dimensional shear wave elastography, point shear wave elastography, and transient elastography in detecting and early diagnosis of esophageal varices. Transient elastography (TE) has been reported to be efficacious and the simplest technique. However, it was reported with some limitations. These limitations could be compensated by the two-dimensional shear wave elastography and the point shear wave. Nevertheless, these two modalities need high levels of experience and are not widely available. Besides, there are a few investigations that have validated the efficacy of the latter in detecting esophageal varices. Accordingly, we encourage further investigation for a future relevance.

Keywords: Elastography, Ultrasound, Radiology, Esophageal varices, Diagnosis

INTRODUCTION

Evidence from the literature shows that apparent esophageal varices can be a significant mark to successfully diagnose cases with clinically significant portal hypertension. Besides, it has been demonstrated that establishing a proper diagnosis of esophageal varices is a crucial point when managing liver cirrhosis. Furthermore, early detection of varices that need treatment is also important to enhance the prognosis and help physicians to plan early prophylactic measures to prevent any potential complications.¹⁻³ despite that esophageal varices can be effectively detected by using upper gastrointestinal tract endoscopy, the procedure is invasive and requires the integration of adequate experience and training, and it is not suitable for many patients.^{4,5} Accordingly, ultrasound elastography has been developed and validated by many studies in the recent literature as effective and non-invasive modalities to early detect and diagnose esophageal varices and the relevant liver diseases.^{4,6} Therefore, in the present study, we aim to conduct a literature review to further elaborate on the role and validity of elastography ultrasound to screen and early detect esophageal varices.

METHODS

We performed an extensive literature search of the Medline, Cochrane, and EMBASE databases on 18th June 2021 using the medical subject headings (MeSH) or a combination of all possible related terms. This was followed by the manual search for papers in Google Scholar and the reference lists of the initially included papers. Papers discussing elastography for esophageal varices were screened for relevant information. We did not pose any limits on date, language, age of participants, or publication type.

DISCUSSION

Evidence in the literature is abundantly related to the efficacy of ultrasound elastography to early detect and screen esophageal varices. Moreover, two-dimensional shear wave elastography, point shear wave elastography. Transient elastography has been well-described in the literature among studies that investigated this outcome. Transient elastography (TE) is identified as an approach of shear wave elastography and is being used widely in the assessment of hepatic and splenic stiffness measurements, with an estimated exploration volume of 3 cm², at an estimated depth under the skin of 2.5-6.5 cm.⁷ Although the modality has been well validated among various studies in the literature, it should be noted that repeated measurements for at least ten times. It should be conducted to obtain better outcomes and validity results and the findings must be according to the previously established criteria, which indicate that the median/interquartile range is $\leq 30\%$.^{8,9} Besides, it has been demonstrated that the modality cannot be successfully used for obese patients and others with ascites. Therefore, carefully interpreting the results is important in such cases for adequate

validation and favorable outcomes.⁹ With regards to the screening and identification of esophageal varices, a previous cohort study by Kazemi et al reported that the estimated cut-offs for the proper identification of any varices or varices that need treatment were 13.9, and 19.0 kPa, respectively for patients with mixed etiologies.¹⁰ In this context, another investigation by Foucher et al also estimated that the cut-off point for the proper identification and diagnosis of varices that need treatment was 27.5 kPa. Among the various studies in the literature, it appears that the cut-off points for diagnosis and detection of esophageal varices are hugely variant.¹¹ For instance, studies have estimated cut-offs that range between 6.8 and 28.0 kPa for detecting any esophageal varices (of variable sizes).^{12,13} On the other hand, the estimated cut-offs for diagnosing varices needing treatment were also variable among the different studies in the literature, with estimated values of 14 to 43 kPa.^{14,15} The wide range of results among the different studies is probably attributable to the different aims and outcomes per each study. For instance, in previous studies that aimed to investigate whether esophageal varices were present with an estimated positive predictive value of $>90\%$, the cut-offs were 15-28 kPa, while studies that focused on excluding the presence of esophageal varices with an estimated negative predictive value $>90\%$, the cut-offs were 19-48 kPa.^{10,13,15} In 2015, a report for managing portal hypertension was published by the Baveno VI consensus indicated that conducting endoscopy to diagnose esophageal varices should be conducted whenever the estimated liver stiffness measurement values were >20 kPa, and the estimated platelet counts were >150 G/L because of the reduced risk of varices needing treatment in these patients.⁴ In this context, many studies were published following these criteria to adequately and properly detect and diagnose esophageal varices.^{14,17,18} Marot et al has published a meta-analysis to estimate the cut-off point for liver stiffness measurement, which was reported to be 20 kPa for successfully predicting whether esophageal varices are present or not, with estimated negative and positive predictive values of 86%, and 43%, respectively.¹⁹ Pu et al also has published a meta-analysis that estimated that the sensitivity and specificity results were also found to be 84%, and 68%, respectively.²⁰ Therefore, it has been concluded that transient elastography should not be used alone in the screening and diagnosis of esophageal varices as a result of the hugely variable findings among the different studies in the literature, and using algorithms have been recommended instead in such situations.^{5,14,17,21}

In another context, using vibration-controlled dynamic stress has been reported with 1D-SWE, where the point shear wave elastography (pSWE) together with the two-dimensional shear wave elastography (2D-SWE) were reported to be conducted according to the ultrasound-based acoustic radiation force impulse (ARFI) technological modalities.⁷ The ARFI has been used in the pSWE to adequately initiate and develop an acoustic pulse that is characterized by short duration and high intensity and can effectively displace the liver tissues at a single specific

point.^{7,22} It has been demonstrated that such modalities can effectively visualize the liver tissues through B-Mode; an advantage that can be considered for this modality over TE, which is attributable to the implementation of the modified ultrasound probes based on the used ARFI modalities.^{7,9} Besides, it has been demonstrated that the modality can effectively be used for obese patients and those with ascites, as the modality is based on focusing on the small region of interest (ROI) instead of the body surface as the case with TE.^{7,9} However, it was also previously reported that the pSWE are more subjected to sample bias more than the other SWE methods as a result of the estimated small ROI for these approaches.⁹ To predict whether esophageal varices are present or not, Salzl et al estimated a value for the area under the curve (AUC) of 0.743, which is lower than that estimated with the TE approach, being 0.802.²³ The authors also estimated that the AUC for detecting clinically significant portal hypertension (CSPH) to be 0.855. Another prospective study in Japan also estimated similar values, with calculated AUC estimates of 0.788, 0.789, and 0.833 to detect varices needing treatment, any type of esophageal varices and CSPH, respectively.²⁴ Furthermore, another study reported that estimating the liver and splenic stiffness measurement using the pSWE was able to significantly predict whether esophageal varices were present or not, with an estimated AUC of 0.913, and 0.675, respectively. However, the sample size was a major limitation for the study outcomes, as only 21 patients suffering from low-grade esophageal varices were recruited, and the authors did not include patients with varices needing treatment.²⁵ Moreover, other studies have validated the efficacy of using spleen stiffness measurement that is based on pSWE for predicting the presence of esophageal varices.²² Studies have reported variable AUC values, that ranged between 0.580 and 0.955 for varices needing treatment and 0.578 to 0.959 for esophageal varices.^{24,26-28} In this context, a previous investigation by Takuma et al demonstrated that using spleen stiffness measurement was associated with the best diagnostic outcomes as compared to other non-invasive approaches, including spleen diameter, liver stiffness measurement and platelet counts with estimated AUC values of 0.924 and 0.944 for viral and non-viral etiologies of varices needing treatment and 0.937 and 0.923 for viral and non-viral etiologies of any esophageal varices, respectively.²⁹ Although the pSWE has more advantages over TE, it should be noted that the latter modality is a simple one and can be easily performed, while pSWE needs high levels of experience to obtain favorable outcomes.³⁰ Moreover, assessing the liver and spleen stiffness measurements based on the pSWE modalities can also be furtherly enhanced using the quality criteria.³¹ Further studies might be needed for further validation of the AUC for pSWE, in addition to investigating whether these modalities can be provided for the different healthcare settings.

Measuring multiple focal zones and using two-dimensional measurements of shear wave is achievable by

using 2D-SWE, unlike pSWE.⁷ Besides, it was previously demonstrated that real-time measurement and screening can also be achieved with this modality by displaying the images on an adjacent screen.^{9,22} Accordingly, this has been associated with improved efficacy of elastography as the clinician is now able to examine multiple tissues using a real-time modality.⁹ However, it should be noted that these modalities are not widely available and are limited to specialized healthcare centers because they usually require high levels of experience to be conducted. Moreover, evidence regarding the quality criteria for assessment of hepatic and/or splenic stiffness measurement values is not reported in the literature.²² Furthermore, many studies have validated the efficacy of 2D-SWE in the assessment of fibrosis and relevant hepatic diseases.³²⁻³⁴ However, only a few investigations have assessed whether the modality is valid for the screening and detection of esophageal varices. For instance, a previous investigation aimed to diagnose clinically significant portal hypertension by using 2D-SWE-based hepatic and splenic stiffness measurement values and found that the AUC for both modalities was 0.861 (24.6 kPa), and 0.837 (26.3 kPa), respectively.³⁵ Another study was conducted in Croatia and recruited 44 patients suffering from compensated advanced chronic liver disease to find that the estimated cut-off points to diagnose any esophageal varices were 30.3 kPa (AUC=0.790), and 19.7 kPa (AUC=0.796) for 2D-SWE-based splenic and liver stiffness measurement values, respectively.³⁶ The efficacy estimated for the modality was furtherly indicated in another investigation by Kasai et al that showed that patients with esophageal varices had a higher liver shear wave elastography than other patients without esophageal varices, with a calculated AUC of 0.807 for both.³⁷ Another large retrospective cohort investigation recruited 103 patients suffering from compensated advanced chronic liver disease to find that the estimated cut-off point for detecting any esophageal varices was 13.9 kPa, and 16.1 kPa for varices that need treatment and estimated AUC values of AUC= 0.887 and 0.880, respectively.³⁸ Another investigation also assessed the validity of using TE and 2D-SWE in detecting varices needing treatment according to the measurements of hepatic and splenic stiffness values and found that the estimated AUC values were notably low for the included population, being 0.580 and 0.600 for the spleen and liver tissues, respectively.³⁹ Accordingly, although there is sufficient evidence regarding the validity and efficacy when using 2D-SWE modalities to diagnose stiffness and tissue fibrosis, the number of studies regarding its efficacy in detecting esophageal varices is not enough, and therefore, additional investigations are still required to add to the value of the current evidence.

CONCLUSION

Transient elastography has been reported to be efficacious and the simplest technique. Nevertheless, it was reported with some limitations. These limitations could be compensated by the 1D-SWE and the 2D-SWE. However, these two modalities need high levels of experience and are

not widely available. Besides, there are a few investigations that have validated the efficacy of the latter in detecting esophageal varices. Accordingly, we encourage further investigation for a future relevance.

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