International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

INPLASY202680030

doi: 10.37766/inplasy2026.8.0030

Received: 6 August 2026

Published: 6 August 2026

Multidetector computed tomography and ultrasound-based spleen stiffness measurement modalities for the diagnosis of esophageal varices in adults with liver cirrhosis

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ADMINISTRATIVE INFORMATION

Support - Xi'an Jiaotong University Second Affiliated Hospital Talent Development Special Research Fund [RC(GG)202010].

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202680030

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 August 2026 and was last updated on 6 August 2026.

INTRODUCTION

Review question / Objective PICOS framework:
Population: Adults aged 18 years or older with liver cirrhosis of any etiology, irrespective of compensation status or healthcare setting.
Index tests: MDCT-EVD, VCTE-SSM, pSWE-SSM, and 2D-SWE-SSM.
Comparator/reference standard: EGD for the diagnosis and grading of esophageal varices. Comparative analyses will include MDCT versus each SSM technique and comparisons among the three SSM techniques.
Outcomes: Sensitivity, specificity, positive and negative likelihood ratios, summary receiver operating characteristic performance, and the expected clinical consequences of selected rule-in and rule-out thresholds, including missed HREV cases and avoided endoscopic examinations.
Study design: Cross-sectional or cohort-type diagnostic test accuracy studies reporting, or allowing reconstruction of, true-positive, false-positive, false-negative, and true-negative results. Diagnostic case-control studies will be excluded.

Rationale Esophagogastroduodenoscopy remains the reference standard for detecting and grading esophageal varices, but it is invasive, resource-

intensive, and unsuitable for frequent repeated screening. Two non-invasive strategies have therefore attracted increasing clinical interest. MDCT can directly visualize esophageal and paraesophageal varices and quantify their diameter, offering an opportunity for additional variceal assessment in patients who have already undergone contrast-enhanced CT for hepatocellular carcinoma surveillance, transplantation assessment, or vascular evaluation. In contrast, spleen stiffness measurement indirectly reflects portal hypertension–related hemodynamic and structural changes and is radiation-free, rapid, and potentially suitable for repeated outpatient monitoring and pre-endoscopic triage.

Previous systematic reviews have generally evaluated CT or spleen stiffness separately, and some have combined technically distinct elastography methods. However, VCTE, pSWE, and 2D-SWE differ in wave generation, image guidance, equipment, measurement units, quality-control requirements, and positivity thresholds and should not be regarded as interchangeable. MDCT and SSM also represent different biological constructs: direct anatomical assessment of varices versus indirect assessment of portal hypertension.

A unified diagnostic test accuracy review is therefore needed to evaluate these four index tests separately, distinguish esophageal varices of any size from HREV, account for threshold heterogeneity, and separate rule-in from rule-out thresholds where clinically relevant. Such a review may clarify the appropriate clinical role of each method, quantify uncertainty, identify evidence gaps, and inform future prospective head-to-head validation studies rather than assuming that one non-invasive technique can universally replace EGD.

Condition being studied Liver cirrhosis is the end stage of many chronic liver diseases and is frequently complicated by portal hypertension. As intrahepatic vascular resistance and portal pressure increase, portosystemic collateral vessels may develop around the distal esophagus, producing esophageal varices. These varices can rupture and cause severe upper gastrointestinal bleeding, which is associated with decompensation, rebleeding, infection, organ failure, and death.

The review addresses two related target conditions. The first is esophageal varices of any size, defined as endoscopically visible submucosal varices in the esophagus, regardless of their diameter or grade. The second is high-risk esophageal varices, referring to varices associated with a clinically important risk of bleeding or a need for primary prophylaxis. Depending on the endoscopic classification used in the original study, HREV may include medium or large varices, varices exceeding a prespecified diameter, varices with red signs, small varices with red signs or in patients with Child–Pugh class C cirrhosis, or varices explicitly considered to require prophylactic treatment.

EGD is the reference standard for confirming the presence, size, morphology, and high-risk features of esophageal varices. The condition under investigation does not include isolated gastric varices, descending esophageal varices caused by superior vena cava obstruction, non-cirrhotic portal hypertension, or prognostic outcomes such as future bleeding, rebleeding, or mortality.

METHODS

Search strategy The Cochrane Library, PubMed, Embase, Scopus, and the Web of Science Core Collection were searched from database inception to May 2026. No restrictions were applied regarding language or year of publication. Separate but conceptually parallel search strategies were developed for multidetector computed tomography and ultrasound-based spleen stiffness measurement.

The search combined three main concept groups:

Population/condition: liver cirrhosis, chronic liver disease, and portal hypertension;
Index tests: computed tomography, contrast-enhanced CT, multidetector or multislice CT, CT-based variceal assessment, spleen stiffness measurement, transient elastography, VCTE, FibroScan, shear-wave elastography, pSWE, 2D-SWE, and ARFI;
Target condition: esophageal or oesophageal varices, gastroesophageal varices, high-risk varices, varices needing treatment, and high-risk esophageal varices.

Controlled vocabulary terms, where available, were combined with free-text terms, abbreviations, spelling variants, and database-specific field tags. The syntax was adapted for each database. A diagnostic-accuracy search filter was not applied in order to maximize sensitivity. The reference lists of relevant systematic reviews and all included studies were also screened for additional eligible reports.

Participant or population Adults aged 18 years or older with liver cirrhosis of any etiology, including

viral hepatitis, alcohol-related liver disease, metabolic dysfunction-associated steatotic liver disease, autoimmune liver disease, cholestatic liver disease, or other causes, irrespective of disease duration, compensation status, or healthcare setting. We excluded paediatric populations, non-cirrhotic portal hypertension, isolated portal or splenic vein thrombosis, and descending esophageal varices caused by superior vena cava obstruction.

Intervention As this is a diagnostic test accuracy review, the "interventions" are the following index tests:
Esophageal variceal diameter measured by multidetector computed tomography (MDCT-EVD);
Spleen stiffness measured by vibration-controlled transient elastography (VCTE-SSM);
Spleen stiffness measured by point shear-wave elastography (pSWE-SSM);
Spleen stiffness measured by two-dimensional shear-wave elastography (2D-SWE-SSM).
The three ultrasound-based SSM techniques were evaluated separately. Studies using different manufacturers, models, probes, measurement units, or positivity thresholds were eligible. Studies assessing only single-detector CT, liver stiffness, magnetic resonance elastography, or composite algorithms were excluded unless eligible index-test accuracy data could be extracted separately.

Comparator Esophagogastroduodenoscopy (EGD) was the reference standard for confirming and grading esophageal varices of any size and high-risk esophageal varices. Comparative analyses included MDCT-EVD versus each SSM technique and pairwise comparisons among VCTE-SSM, pSWE-SSM, and 2D-SWE-SSM. Because participant-level paired covariance data were generally unavailable, formal comparisons were primarily interpreted as between-study indirect comparisons.

Study designs to be included Prospective or retrospective cross-sectional diagnostic accuracy studies and diagnostic cohort studies were eligible. Participants had to undergo at least one eligible index test and EGD as the reference standard. Studies had to report true-positive, false-positive, false-negative, and true-negative results directly or provide sufficient information for their reconstruction. Diagnostic case-control studies were excluded.

Eligibility criteria Eligible studies had to evaluate at least one prespecified index test for detecting esophageal varices of any size or high-risk esophageal varices, using esophagogastroduodenoscopy as the reference standard, and report true-positive, false-positive, false-negative, and true-negative results or sufficient data for their reconstruction.
Studies reporting gastroesophageal or gastric varices were eligible only when data for esophageal varices could be extracted separately. Studies were excluded if they assessed only isolated gastric varices, composite varices needing treatment without separable esophageal-variceal data, single-detector CT, liver stiffness, magnetic resonance elastography, radiomics, deep-learning models, or composite algorithms without separately extractable results for an eligible index test. Prognostic outcomes such as future variceal formation, bleeding, rebleeding, or mortality were not eligible.

Information sources The Cochrane Library, PubMed, Embase, Scopus, and the Web of Science Core Collection were searched from database inception to 24 May 2026. No restrictions were applied regarding language or year of publication. Separate search strategies were developed for multidetector computed tomography and ultrasound-based spleen stiffness measurement and adapted to the syntax of each database.
The reference lists of relevant systematic reviews and all included primary studies were screened to identify additional eligible reports. The final list of included studies was also reviewed by subject experts within the author team. When a potentially eligible study reported incomplete diagnostic accuracy data, the 2×2 table was reconstructed from the published information whenever possible. The review was based on formally published full-text reports; conference abstracts, letters, and reviews were not eligible.

Main outcome(s) The primary outcomes were sensitivity and specificity, with 95% confidence intervals, for each eligible index test in detecting:
Esophageal varices of any size; and High-risk esophageal varices.
Outcomes were calculated from true-positive, false-positive, false-negative, and true-negative results for each independent cohort, index test, target condition, and eligible threshold. Clinically similar thresholds were synthesized using bivariate random-effects models, whereas studies using different thresholds or positivity criteria were synthesized using hierarchical summary receiver operating characteristic models.
No follow-up outcome was required because this was a diagnostic accuracy review. The interval between the index test and esophagogastroduodenoscopy was recorded,

assessed in the QUADAS-2 flow and timing domain, and examined in sensitivity analyses, including restriction to studies in which the interval was less than 31 days.

Quality assessment / Risk of bias analysis Two reviewers independently assessed the methodological quality of the included studies using QUADAS-2. Risk of bias was evaluated across four domains: patient selection, index test, reference standard, and flow and timing. Applicability concerns were assessed for patient selection, index test, and reference standard.
The assessment considered whether participants were enrolled consecutively or randomly, whether inappropriate exclusions were avoided, whether index-test thresholds were prespecified, whether index-test interpretation was blinded to endoscopic findings, whether EGD was an appropriate reference standard, whether endoscopists were blinded to index-test results, whether the interval between the index test and EGD was appropriate, and whether all enrolled participants were included in the analysis. Technical failures, uninterpretable results, and post hoc threshold selection were also considered.
Each domain was classified as having low, unclear, or high risk of bias or applicability concern. Assessments were conducted separately for each index test and target condition. Disagreements were resolved through discussion or, when necessary, third-party adjudication.

Strategy of data synthesis Esophageal varices of any size and high-risk esophageal varices were analysed separately. For each eligible cohort, index test, target condition, and threshold, true-positive, false-positive, false-negative, and true-negative counts were used to calculate sensitivity, specificity, positive likelihood ratios, and negative likelihood ratios with 95% confidence intervals. Paired forest plots and plots in receiver operating characteristic space were used for descriptive presentation.
For syntheses involving different thresholds or positivity criteria, hierarchical summary receiver operating characteristic models were used. Each independent cohort contributed no more than one operating point per index test and target condition to the primary all-cut-off analysis. Where multiple operating points were reported, priority was given to externally validated or prospectively specified thresholds, the study-defined primary analysis, the full analysable cohort, and the most complete result.
Bivariate random-effects models were used for exact thresholds or clinically similar threshold groups when at least three independent cohorts were available. Thresholds were considered similar only within the same target condition, index test, measurement unit, and clinical role, with an absolute relative deviation from the reference threshold of no more than 15%.
For comparative analyses, index-test type was included as a covariate in HSROC or bivariate models, and likelihood-ratio tests evaluated the overall test effect and accuracy component. Rule-in and rule-out thresholds for HREV were analysed separately. Unstable, non-convergent, or singular models were not overinterpreted. Analyses were conducted in R version 4.5.3, with two-sided $P<0.05$ considered statistically significant.

Subgroup analysis Where sufficient data were available, subgroup analyses and meta-regression were used to investigate clinical, methodological, and technical sources of heterogeneity.
Clinical factors included liver cirrhosis etiology, liver disease severity, the proportion of participants with Child–Pugh class A or C disease, prevalence of esophageal varices or high-risk esophageal varices, and geographic region. Etiology was examined as single viral etiology versus mixed or non-single viral etiologies, and geographic location as Asian versus non-Asian populations.
Methodological factors included prospective versus retrospective design, the interval between the index test and EGD, blinding of index-test interpretation, blinding of EGD interpretation, and QUADAS-2 risk-of-bias judgments. The test-to-EGD interval was examined using a 31-day threshold.
Subgroup and meta-regression analyses were performed only when the number of studies and distribution of covariates were sufficient for stable model estimation.

Sensitivity analysis Sensitivity analyses assessed the robustness of the main findings to study quality and important methodological decisions. First, studies judged to have high or unclear risk of bias in relevant QUADAS-2 domains were excluded, retaining studies with relatively low risk of bias.
Separate analyses excluded studies in which index-test interpretation was unblinded or the blinding status was unclear. Similar analyses excluded studies in which endoscopists were unblinded to index-test results or blinding was not reported.
To assess possible changes in disease status between examinations, analyses were restricted to studies in which the interval between the index test and EGD was less than 31 days. Analyses restricted to prospective studies were also conducted to examine the influence of study design.

Where relevant, studies using thresholds selected post hoc through receiver operating characteristic analysis or the Youden index were excluded. Alternative operating points from cohorts reporting multiple thresholds were assessed one at a time, and paired comparative cohorts were evaluated without treating the two test results as independent observations.
Sensitivity analyses were conducted only when sufficient studies remained to support stable estimation. When fewer than three datasets remained, models failed to converge, random-effects parameters reached boundary values, or covariate distributions were inadequate, results were summarized descriptively and unstable pooled estimates were not reported or overinterpreted.

Language restriction No language restrictions were imposed on the literature search.

Country(ies) involved China.

Keywords liver cirrhosis; esophageal varices; high-risk esophageal varices; multidetector computed tomography; spleen stiffness; diagnostic accuracy; meta-analysis.

Contributions of each author
Author 1 - Lingbo An - Conceptualized and designed the review, developed the methodology, conducted the literature search, study selection, data extraction, risk-of-bias assessment, statistical analyses and visualisation, interpreted the findings, and drafted and revised the manuscript.
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Author 3 - Zhe Wang - Independently participated in study screening and data extraction, assessed study eligibility and potentially overlapping cohorts, verified the extracted data, and reviewed the manuscript.
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