

INPLASY

INPLASY202660137

doi: 10.37766/inplasy2026.6.0137

Received: 29 June 2026

Published: 29 June 2026

Corresponding author:

Xu Zhang

dr.xu_zhang@qq.com

Author Affiliation:

Hangzhou Xixi Hospital.

Diagnostic accuracy of quantitative electroencephalography for detection of minimal/covert hepatic encephalopathy in cirrhotic patients: a systematic review and meta-analysis

Zhang, X.

ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202660137

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 June 2026 and was last updated on 29 June 2026.

INTRODUCTION

Review question / Objective To determine the pooled diagnostic accuracy (sensitivity, specificity, and area under the SROC curve) of quantitative EEG spectral analysis for detecting minimal/covert hepatic encephalopathy in adult patients with cirrhosis, using neuropsychological testing or clinical criteria as the reference standard.

Condition being studied Minimal hepatic encephalopathy (MHE), also referred to as covert hepatic encephalopathy (CHE) when combined with West-Haven grade I HE, is the mildest form of hepatic encephalopathy occurring in patients with cirrhosis. It is characterised by subtle cognitive deficits—including impairments in attention, psychomotor speed, executive function, and visuospatial ability—that are not detectable on routine clinical examination but are evident on specialised neuropsychological testing. The condition is caused by the failure of the liver to clear gut-derived neurotoxins (primarily ammonia), leading to astrocyte swelling, low-grade cerebral

oedema, and alterations in neuronal oscillatory activity that can be detected by EEG.

METHODS

Participant or population Adult patients (aged 18 years or older) with cirrhosis of any aetiology (viral hepatitis, alcohol-related, metabolic dysfunction-associated steatotic liver disease, autoimmune, cryptogenic, etc.), regardless of Child-Pugh class or MELD score.

Intervention Quantitative electroencephalography (qEEG) spectral analysis, also termed spectral EEG, with quantitative parameters including mean dominant frequency (MDF), relative power in delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), and beta (13-30 Hz) frequency bands, or derived indices such as the theta/alpha ratio, alpha suppression index, or SEDACA-derived spectral components.

Comparator Neuropsychological testing as the reference standard: Psychometric Hepatic Encephalopathy Score (PHES), Number

Connection Test A/B (NCT-A, NCT-B), Digit Symbol Test (DST), and/or West-Haven clinical grading criteria (grade 0 = no HE vs. grade ≥ 1 = MHE/grade I HE).

Study designs to be included Cross-sectional diagnostic accuracy studies and cohort studies (prospective or retrospective) that report sufficient data to construct 2x2 contingency tables (true positives, false positives, false negatives, true negatives).

Eligibility criteria Inclusion: (1) adult cirrhotic patients; (2) qEEG spectral analysis with quantitative parameters as the index test; (3) neuropsychological testing or West-Haven criteria as reference standard; (4) sufficient data for 2x2 table construction; (5) original peer-reviewed studies. Exclusion: (1) qualitative/visual EEG only; (2) exclusively overt HE (West-Haven ≥ 2) or acute liver failure; (3) conference abstracts, reviews, case reports; (4) duplicate cohorts.

Information sources Electronic databases: PubMed/MEDLINE, EMBASE (Elsevier), Cochrane Library (CENTRAL), China National Knowledge Infrastructure (CNKI), and Wanfang Data. Additional sources: manual screening of reference lists of included studies and relevant narrative reviews. Grey literature will not be systematically searched.

Main outcome(s) Primary outcomes: pooled sensitivity and pooled specificity of qEEG for diagnosis of MHE/CHE, with 95% confidence intervals. Secondary outcomes: area under the summary receiver operating characteristic curve (SROC-AUC); Q* point on the SROC curve; pooled positive and negative likelihood ratios (LR+, LR-); pooled diagnostic odds ratio (DOR).

Quality assessment / Risk of bias analysis The methodological quality of included studies will be assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool, which evaluates four domains: patient selection, index test, reference standard, and flow and timing. Each domain will be rated as "low risk," "high risk," or "unclear risk" of bias. Applicability concerns will be assessed using the same domains. Two reviewers will independently perform the assessment.

Strategy of data synthesis Sensitivity and specificity will be logit-transformed and pooled using the DerSimonian-Laird random-effects model. The Moses-Shapiro-Littenberg (MSL) method will be used to construct the summary

receiver operating characteristic (SROC) curve. The area under the SROC curve (AUC) will be estimated using the weighted log diagnostic odds ratio approach. Heterogeneity will be quantified using the I^2 statistic (low: 75%). Pooled positive and negative likelihood ratios will be calculated. A Fagan diagram will illustrate the clinical utility of qEEG. Publication bias will be assessed using Deeks' funnel plot asymmetry test ($p < 0.10$ considered significant). Statistical analyses will be performed using Python 3.11.

Subgroup analysis Pre-specified subgroup analyses: (1) by type of reference standard (PHES vs. NCT-based tests vs. combined criteria); (2) by qEEG theta-power diagnostic threshold (low $\leq 22.7\%$ vs. high $> 22.7\%$); (3) by geographic region (European vs. Asian studies). If sufficient data are available, subgroup analysis by cirrhosis aetiology and Child-Pugh class distribution will also be performed.

Sensitivity analysis Sensitivity analyses will be performed by: (1) excluding studies judged to be at high or unclear risk of bias on QUADAS-2 assessment; (2) excluding studies with outlying diagnostic odds ratios (DOR) that may unduly influence pooled estimates; (3) restricting the analysis to studies using PHES as the sole reference standard to assess the impact of reference standard heterogeneity.

Country(ies) involved China.

Keywords hepatic encephalopathy; minimal hepatic encephalopathy; quantitative EEG; spectral analysis; diagnostic accuracy; meta-analysis; systematic review; cirrhosis.

Contributions of each author

Author 1 - Xu Zhang.

Email: dr.xu_zhang@qq.com