

INPLASY PROTOCOL

To cite: He et al. Quantitative liver surface nodularity score based on imaging for assessment of early cirrhosis in patients with chronic liver disease: A protocol for systematic review and meta-analysis. Inplasy protocol 2020100096. doi: 10.37766/inplasy2020.10.0096

Received: 25 October 2020

Published: 25 October 2020

Corresponding author:
Sunfu Zhang

zsfjwk12@hotmail.com

Author Affiliation:
Department of Neurosurgery,
Chengdu Third People's
Hospital

Support: N/A.

Review Stage at time of this submission: Risk of bias assessment.

Conflicts of interest:
There are no conflicts of interest to declare for all authors.

Quantitative liver surface nodularity score based on imaging for assessment of early cirrhosis in patients with chronic liver disease: A protocol for systematic review and meta-analysis

He, Y¹; Yan, Y²; Zhang, S³.

Review question / Objective: Whether and how the quantitative liver surface nodularity(LSN) score can detect early cirrhosis in patients with chronic liver disease(CLD).
Condition being studied: Chronic liver disease(CLD) is the major cause of global healthy problem contributing to morbidity and mortality worldwide, early noninvasive detection of the CLD stage is of vital value in clinical treatment. Liver biopsy is currently considered as the reference standard for liver cirrhosis and staging of fibrosis, while the invasive nature, high cost, sampling errors, variability limit its' wide utilization. Recent studies exploring the quantitative liver surface nodularity(LSN) score for predicting early cirrhosis have shown correlation with the early stage of cirrhosis with varied diagnostic performance, further, the sample size currently is small and no clear consensus has been reached about the diagnostic accuracy of LSN. Hence, we aim to perform a systematic review and meta-analysis of the diagnostic performance of LSN score for predicting early liver cirrhosis and to further determine the cut-off value in clinical practice.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 October 2020 and was last updated on 25 October 2020 (registration number INPLASY2020100096).

INTRODUCTION

Review question / Objective: Whether and how the quantitative liver surface nodularity(LSN) score can detect early

cirrhosis in patients with chronic liver disease(CLD).

Rationale: A systematic literature search of PubMed, EMBASE, Cochrane Library

databases and Web of Science was performed to identify studies that assessed the diagnostic accuracy of quantitative LSN score in CLD patients using biopsy as reference standard. The summary receiver-operating-characteristic (ROC) and pooled sensitivity, specificity were obtained to summarize the diagnostic performance of LSN using a random-effect model. A sensitivity analysis was performed to explore the source of heterogeneity.

Condition being studied: Chronic liver disease (CLD) is the major cause of global healthy problem contributing to morbidity and mortality worldwide, early noninvasive detection of the CLD stage is of vital value in clinical treatment. Liver biopsy is currently considered as the reference standard for liver cirrhosis and staging of fibrosis, while the invasive nature, high cost, sampling errors, variability limit its' wide utilization. Recent studies exploring the quantitative liver surface nodularity (LSN) score for predicting early cirrhosis have shown correlation with the early stage of cirrhosis with varied diagnostic performance, further, the sample size currently is small and no clear consensus has been reached about the diagnostic accuracy of LSN. Hence, we aim to perform a systematic review and meta-analysis of the diagnostic performance of LSN score for predicting early liver cirrhosis and to further determine the cut-off value in clinical practice.

METHODS

Search strategy: A systematic literature search of PubMed, EMBASE, Cochrane Library databases and Web of Science was performed to identify relevant studies from database inception to 14 October 2020, using the following search terms: "liver surface nodularity", "hepatic surface nodularity", "portal hypertension", "cirrhosis", "cirrhotic" and "fibrosis". No filters were applied (i.e., language), all eligible literatures were retrieved and their reference of the initial studies were checked for additional relevant publications.

Participant or population: Patients with chronic liver disease (CLD) - 6 studies including 1327 patients were selected for this meta-analysis.

Intervention: N/A.

Comparator: N/A.

Study designs to be included: We aim to evaluate the diagnostic performance of LSN score for detecting early cirrhosis. We searched several databases to identify eligible studies using biopsy as reference standard. The summary receiver-operating-characteristic and pooled sensitivity, specificity were obtained to summarize the diagnostic performance of LSN using a random-effect model. A sensitivity analysis was performed to explore the source of heterogeneity.

Eligibility criteria: Two reviewers screened the titles and abstracts of literature independently to identify potential eligibility, then, the full texts of potentially eligible studies were reviewed for final inclusion. Researches were included according to the following criteria: (1) patients with CLD diagnosed with cirrhosis, (2) liver biopsy is considered as the reference standard, (3) liver surface nodularity measurement is conducted to evaluate liver cirrhosis, (4) studies have enough data to obtain a diagnostic 2x2 table of test performance (true positive (TP), false positive (FP), true negative (TN), and false negative (FN) diagnostic results). Exclusion criteria were as follows: (1) duplications, non-diagnostic tests, non-human trials, case reports, reviews, conference abstracts, non-original studies, irrelevant studies, (2) studies with a small sample size (patients <20), (3) studies unable to extract sufficient data for diagnostic meta-analysis.

Information sources: PubMed, EMBASE, Cochrane Library databases and Web of Science were used in this protocol.

Main outcome(s): Six articles (including 1327 patients) based on computed tomography (CT) or magnetic resonance

imaging(MRI) were retrieved. The diagnostic performance of LSN score for prediction of early cirrhosis was fairly good, with a summary sensitivity of 87%(95% confidence interval(CI):76-94%; I²=83.93) and summary specificity of 81%(95% CI:76-85%; I²=74.02), the area under the ROC curve(AUROC) was 0.86(95% CI: 0.83–0.89), and the optimal cut-off value of LSN score for diagnosing cirrhosis was 2.859. The sensitivity analysis revealed that study of Cecilia Besa et al. 2017 may attribute to the substantial heterogeneity, the corresponding values were reestimated after excluding the study, with a summary sensitivity, specificity and AUROC of 90% (95% CI:84-94%, I²=33) and 81% (95% CI:75-86%, I²=74.6) and 0.91(95% CI:0.88-0.93), respectively, which suggests that standardization is required.

Quality assessment / Risk of bias analysis:

Two independent reviewers conducted the literature search, study selection, data extraction, and quality assessment, with a third reviewer adjudicating on disagreements. The quality assessment was evaluated with the revised Quality Assessment of Diagnostic Accuracy Studies-2(QUADAS-2) tool. Each individual term was categorized as “yes” if it was reported, “no” if not reported, or “unclear” if information was not enough to reach a conclusion, and the risk of bias was comprehensively assessed for each study.

Strategy of data synthesis: The diagnostic performance of LSN score based on imaging for prediction of early cirrhosis(F4) and the optimal cut-off value were considered as outcome of this meta-analysis, of which, Stata V.15.1 (StataCorp LP, College Station, Texas) was used for statistical analysis, additionally, quality assessment was performed with Review Manager 5.3 and threshold that was obtained from Meta-Disc 1.4.

Subgroup analysis: N/A.

Sensibility analysis: A sensitivity analysis was also performed to investigate potential sources of heterogeneity by excluding each of the studies one by one and reevaluate

the remaining combined diagnostic performance to verify the robustness of the diagnostic test accuracy, and to further determine the effect of heterogeneity on the summary sensitivity and specificity of each included research. A random-effect model was used for all summary analysis.

Country(ies) involved: Mainland China.

Keywords: quantitative, liver surface nodularity, cirrhosis, systematic review, meta-analysis, protocol.

Contributions of each author:

Author 1 - Yuhao He - The author designed and drafted the manuscript.

Author 2 - Yujia Yan - The author provided statistical expertise.

Author 3 - Sunfu Zhang - The author reviewed and revised this paper.