Clinical Radiology 69 (2014) e545–e552

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Diagnostic value of magnetic resonance elastography for detecting and staging of hepatic fibrosis: A meta-analysis

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ARTICLE INFORMATION

Article history:
Received 23 April 2014
Received in revised form
25 August 2014
Accepted 4 September 2014

AIM: A meta-analysis was performed to evaluate the diagnostic value of magnetic resonance elastography (MRE) in detecting and staging hepatic fibrosis.

MATERIALS AND METHODS: A systematic search of PubMed, EMBASE, Web of Science, and Cochrane Library Database up to October 2013 was undertaken to find studies on the evaluation of MRE in patients suspected of hepatic fibrosis. Data from the articles were analysed using Meta-disc 1.4 and Stata 12.0 software. The sensitivity, specificity, and area under the summary receiver operating characteristic (ROC) curve (AUROC) were pooled for all stages of hepatic fibrosis ($F \geq 1$, $F \geq 2$, $F \geq 3$, and $F = 4$). Publication bias was assessed through the Deeks' funnel plot asymmetry tests.

RESULTS: Thirteen studies comprising 989 patients met the inclusion criteria. The pooled sensitivity and specificity for $F \geq 1$, $F \geq 2$, $F \geq 3$, and $F = 4$ were 0.87 (95% CI = 0.84–0.89) and 0.92 (95% CI = 0.87–0.96), 0.87 (95% CI = 0.84–0.90) and 0.92 (95% CI = 0.89–0.95), 0.88 (95% CI = 0.85–0.91) and 0.91 (95% CI = 0.88–0.93), 0.91 (95% CI = 0.87–0.94) and 0.92 (95% CI = 0.89–0.94), respectively. The pooled AUROC for $F \geq 1$, $F \geq 2$, $F \geq 3$, and $F = 4$ were 0.9502, 0.9663, 0.9644, and 0.9768, respectively. The non-significant slope of Deeks' funnel plot asymmetry tests indicated that no significant bias was found.

CONCLUSIONS: MRE has a high diagnostic accuracy for the quantitative detection and staging of hepatic fibrosis.

Introduction

Hepatic fibrosis is a common histological process associated with a multitude of liver injuries. Viral, autoimmune, hereditary, metabolic, and toxin-mediated liver disease can result in hepatocellular dysfunction, expansion of the extracellular matrix with distortion of hepatic architecture, portal hypertension, and finally, liver cirrhosis.[1] A precise estimation of the degree of liver fibrosis is important for the prediction of prognosis, surveillance, and treatment decision in patients with chronic liver disease.[2,3]

The current clinical standard of reference for assessing hepatic fibrosis is liver biopsy,[4] and one of the widely used systems for classifying fibrosis is the METAVIR classification system, which generally divides the spectrum of liver fibrosis due to chronic hepatitis into five stages: no fibrosis (F0); portal fibrous expansion (F1); thin fibrous septa emanating from portal triads (F2); fibrous septa bridging portal triads and central veins (F3); and cirrhosis (F4). Clinically significant fibrosis is generally defined as a stage of F2 or greater.[5] However, biopsy is an invasive method,

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http://dx.doi.org/10.1016/j.crad.2014.09.001
0009-9260/

and has limitations, such as costs, possible complications, and sampling variability. It is also not an ideal approach for screening, longitudinal monitoring, or assessing therapeutic effect.[6,7] Therefore, considerable research has been conducted to find non-invasive methods for the assessment of hepatic fibrosis.[8–11]

Recently, magnetic resonance elastography (MRE) has been developed to non-invasively image the viscoelastic mechanical properties (elasticity or stiffness) of various tissues.[12] In an MRE examination, a mechanical driver device is placed in contact with the patient's body wall adjacent to the liver to generate shear waves within the abdomen at a predetermined frequency (typically between 40 and 120 Hz). MR images are acquired with a gradient-echo sequence as the waves propagate through the liver.[12] As the liver becomes stiff due to fibrosis, the resulting changes in viscoelastic properties can be measured as changes in shear stiffness by MRE.[13] An increasing number of studies have shown MRE to be an accurate method for diagnosing and staging hepatic fibrosis.[12,13]

The objective of this study was to assess the overall diagnostic value of MRE for the detection and staging of hepatic fibrosis by performing a meta-analysis with histopathology as a reference standard.

Materials and methods

Literature search and study selection

A systematic literature search of PubMed, EMBASE, Web of Science, and the Cochrane Library Database was performed to find the relevant articles assessing MRE for the diagnosis and staging of liver fibrosis published before October 2013. The following search terms were used: liver fibrosis OR hepatic fibrosis; magnetic resonance elastography OR MR elastography OR MRE. The search used free-text words and Medical Subject Headings (MESH) terms to increase the sensitivity of the search strategy. No language restriction was applied. In addition, PubMed's related articles feature was used to identify studies that had not been captured by the primary search strategy and the reference lists of enrolled studies were manually searched.

The identified studies were screened independently by L.N.S. and B.X.L., and then verified reciprocally. The inclusion criteria were as follows: (1) patients with suspected cirrhosis; (2) stiffness value of MRE as the index test; (3) histopathology as the reference test using the METAVIR staging system: F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with few septa; F3, numerous septa without cirrhosis; and F4, cirrhosis; (4) defined optimal cut-off values of stiffness value; and (5) raw data [i.e., true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) results] that could be found or calculated. The exclusion criteria were: (1) duplicate publication (based on the same primary study); (2) non-original research; (3) sample size of <20; (4) not published in English; and (5) no full text.

Data extraction and quality assessment

The data were extracted independently by L.N.S. and B.X.L. using a predefined form. The following data were extracted: (1) author; (2) year of publication; (3) total participants (i.e., patients and volunteers); (4) included participants; (5) study designation (i.e., retrospective or prospective); (6) time period between reference standard and index test; (7) mean patient age; (8) patient spectrum, and (9) TP, FN, FP, and TN results. The following imaging features were also extracted from the primary study: (1) imaging method; (2) cut-off value used; (3) MR system used; (4) magnetic field strength; and (5) wave frequency for MRE.

The methodological quality of the included studies was assessed independently by the same two investigators using the Quality Assessment of Studies of Diagnostic Accuracy (QUADAS) tool.[14] Any differences in quality assessment or data extraction were resolved by P.Y.

Statistical analysis

Data associated with the diagnostic performance of MRE were used to construct 2×2 contingency tables that included the TP, FP, TN, and FN results. The 2×2 contingency tables were extracted for the classification of F0 versus F1–F4 ($F \geq 1$), F0 and F1 versus F2–F4 ($F \geq 2$), F0–F2 versus F3 and F4 ($F \geq 3$), and F0–F3 versus F4 ($F = 4$), respectively. The pooled sensitivity, specificity, and diagnostic odds ratio (DOR) with 95% CI were obtained. Positive likelihood and negative likelihood values were derived as functions of these summary estimates, and the derived estimates of sensitivity, specificity, and respective variances were also used to construct a summary receiver operating characteristic (ROC) curve. The area under the ROC curve (AUROC) was used as an alternative global measure of test performance.[15–17] A diagnostic tool is defined to be perfect if the AUROC is 100%, excellent if the AUROC is $>$90%, and good if the AUROC is $>$80%.[17] Moreover, the mean stiffness cut-off value of each group was calculated.

The inconsistency index (I^2) was used to assess heterogeneity among the studies included in the meta-analysis. Heterogeneity was classified as moderate ($I^2 \geq 30\%$), substantial ($I^2 \geq 50\%$), or considerable ($I^2 \geq 75\%$).[18] A fixed-effects model (FEM) was utilized if homogeneity existed among different studies, whereas a random-effects model (REM) was used if heterogeneity existed. Publication bias was assessed visually by using the Deeks' funnel plot asymmetry tests, a scatter plot of the inverse square root of the effective sample size (1/ESS1/2) versus the diagnostic log odds ratio. Publication bias was considered to be present if there was a non-zero slope coefficient ($p < 0.05$).[19]

Statistical analyses were undertaken using Meta-DiSc (v. 1.4),[11] (Meta-DiSc, produced by Javier Zamora, is freeware to perform systematic review of studies by evaluation of diagnostic and screening tests) except for the Deeks' funnel plot asymmetry tests, which were undertaken using Stata version 12.0 software. $p < 0.05$ was considered statistically significant.