Original Article

Magnetic resonance elastography can predict the development of hepatocellular carcinoma: a meta-analysis and systematic review

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Background: Hepatocellular carcinoma (HCC) has become the third leading cause of cancer-related death worldwide, and its incidence rate is increasing. Magnetic resonance elastography (MRE) can indirectly realize the accurate non-invasive evaluation of liver reserve function in HCC patients. In this study, we aimed to evaluate the effectiveness of MRE in the diagnosis of HCC patients.

Methods: We searched globally-recognized electronic databases, such as PubMed, EMBASE, China National Knowledge Infrastructure, and Cochrane Central, for relevant literature on MRE prediction of HCC. The diagnostic performance of all studies was quantitatively summarized using a bivariate random effects model including heterogeneity analysis, receiver operating characteristic (ROC) curve, and bias determination.

Results: The diagnostic accuracy of MRE for HCC was based on 1,735 patients. The sensitivity (31–100%) was lower than the specificity (81–94%). The overall sensitivity was 64% [95% confidence interval (CI): 46–79%; I^2=92.44%], and the overall specificity was 85% (95% CI: 82–88%; I^2=67.86%). Limited publication bias was observed in this study, and the sensitivity analysis showed that the study was robust.

Discussion: The results of our meta-analysis show that MRE has moderate sensitivity and excellent specificity in the detection of HCC. MRE can be an effective diagnostic tool for HCC and can provide strong support for the selection of clinical treatment methods and prognostic judgment.

Keywords: Magnetic resonance elastography (MRE); hepatocellular carcinoma (HCC); meta-analysis.

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Introduction

Liver cancer refers to a malignant tumor of the liver, and includes both primary and secondary liver cancers (1,2). The etiology of primary liver cancer is unknown. At present, it is believed to be related to a hepatitis viral infection, aflatoxin, and some chemical carcinogens. Secondary liver cancer is caused by the metastasis of other malignant tumors to the liver (3-5).

Magnetic resonance elastography (MRE) is a new method of MR examination that inputs shear waves into the brain and detects brain tissue elasticity by phase coding (6-8). As a novel and non-invasive imaging technology, MRE is a traditional mechanical and quantitative means of palpation that is not limited by the diagnosis site, and is thus known as "image palpation" (9-11).

Studies have shown that the measurement of non-tumor liver tissue hardness by MRE can indirectly achieve accurate and non-invasive evaluation of liver reserve function in hepatocellular carcinoma (HCC) patients, which can simplify the clinical liver function evaluation procedure and provide strong support for the selection

of clinical treatment methods as well as the assessment of prognosis (12-15).

Considering the limited analysis of MRE imaging in the diagnosis of HCC, we conducted this research to determine the performance of MRE imaging in the diagnosis of HCC. This will allow for a deeper understanding of the overall diagnostic performance of MRE, enhance the imaging consistency technology, and help to improve the effectiveness of this diagnostic test as much as possible. We present the following article in accordance with the PRISMA-DTA reporting checklist (available at https://dx.doi.org/10.21037/jgo-21-196).

Methods

Literature search strategy

We retrieved relevant peer-reviewed articles published from 1990 to 2020 from the following databases: PubMed, EMBASE, Cochrane Central, and China National Knowledge Infrastructure, using the following keywords: "magnetic resonance elastography", "MRE", "liver cancer", "liver tumor", "hepatocellular carcinoma", "HCC", "liver cell carcinoma", and "hepatic cell carcinoma". No restrictions on the publication language were applied in the literature retrieval. The reference lists of retrieved articles and review articles were manually checked to identify further relevant studies that were not identified using the search strategy.

Study selection

The search strategy involved identifying potentially relevant articles, screening of identified papers based on their titles and abstracts, conducting a qualification review of the full text of potentially relevant studies, and requiring the included studies meet the following inclusion criteria:

(I) Using MRE;
(II) Patients with HCC;
(III) The full text is provided.

Based on the following exclusion criteria, we systematically excluded studies that did not meet the inclusion criteria:

(I) Research focused on other health problems;
(II) Patients receiving other diagnostic technologies;
(III) A lack of research on available data.

Data extraction and quality assessment

Two researchers carefully reviewed the full texts of all eligible studies and independently extracted relevant data, including the name of the first author, year of publication, country, sample size, study period, age and gender of patients, etc. The overall quality of the study was evaluated using the Cochrane bias risk assessment tool.

Statistical analysis

The results of classified variables were presented as a risk ratio (RR) and 95% confidence interval (CI), while the results of continuous variables were presented as a mean difference (MD) and 95% CI. The Cochrane Q-test index was used for detecting the existence of heterogeneity between the results of the primary studies and I-square index (I^2) determined the degree of the heterogeneity in meta-analysis based on I^2 value of 25%, 50%, and 75% were nominally regarded as low, moderate, and high estimates, respectively. A random effect model was used for high heterogeneity, and a fixed effect model was employed for low heterogeneity. A funnel plot was used to evaluate publication bias.

Sensitivity analysis was utilized to test the effect of each individual study on the stability of the overall results by deleting each study in turn. Stata 12.0 (StataCorp LP, College Station, TX, USA) was used for statistical analysis.

Results

Literature search

In total, the electronic search retrieved 886 potentially relevant articles. Based on a careful reading of the title and abstracts, 804 full-text papers were selected for full review. A total of 56 articles were excluded due to a lack of relevance, insufficient data, or other article types.

Finally, the meta-analysis was conducted using nine papers. Based on careful consideration of the purpose of the study, inclusion and exclusion criteria were established to guide the subsequent search process, as shown in *Figure 1*.

Characteristics of included studies

Table 1 summarizes the total number of patients. Relevant data were extracted from nine papers (16-24), including the first author's name, year of publication, country, gender distribution (male/female), sample size, age range, and

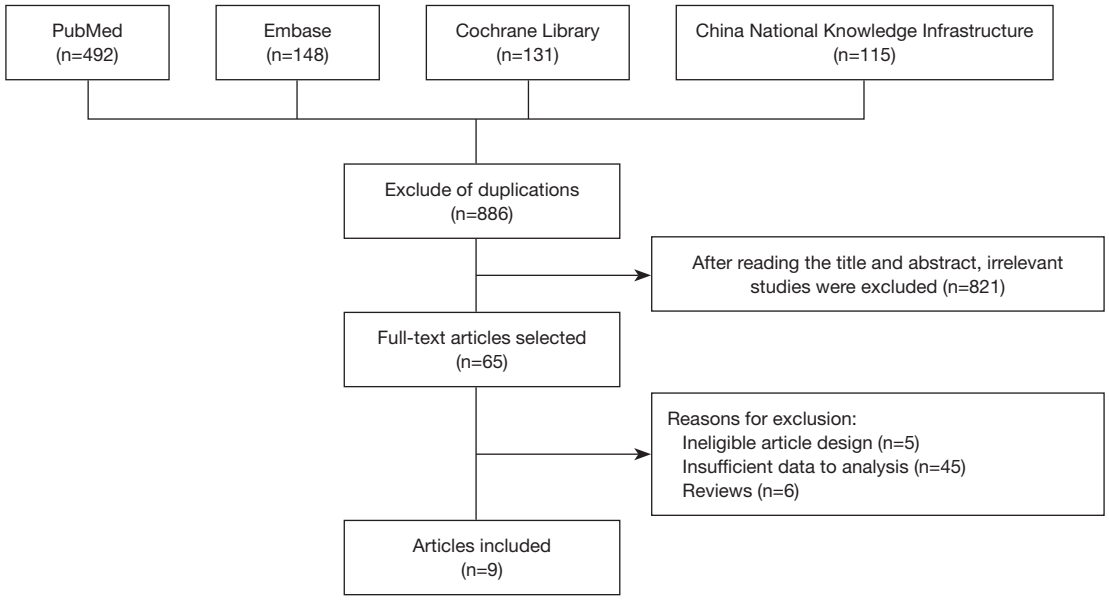

Figure 1 Research selection flowchart.

Table 1 Research characteristics of the meta-analysis

Study	Year	Language	Country	Gender distribution (female/male)	Age range (mean ± SD)	Number of patients	Years of onset
Ahn	2018	English	Korea	32/147	56.71±24.2	179	January 2012 to December 2013
Cha	2020	English	Korea	107/442	55±31	549	January 2010 to December 2014
Chou	2017	English	China	14/63	61.22±13.85	77	August 2013 to September 2015
Jang	2016	English	Korea	7/31	57.1±11.9	38	January 2009 to August 2013
Lee	2016	English	Korea	38/106	58.9±11.1	144	January 2010 to June 2013
Lee	2017	English	Korea	35/162	54.28±9.43	197	January 2011 to December 2012
Rao	2020	English	China	6/88	52±11	94	February 2016 to March 2017
Tamaki	2019	English	Korea	220/126	68.2±10	346	January 2015 to December 2017
Wei	2020	English	China	21/90	52.6±11.7	111	July 2015 to September 2018

recruitment time. A total of 1,735 patients were selected for analysis. All included studies were journal articles published between 2009 and 2018. The study sample sizes ranged from 38 to 549 patients.

Quality assessment

According to the results of the Cochrane risk of bias assessment tool, which included selection bias, detection bias, performance bias, loss bias, and reporting bias, the nine included trials exhibited no risk of bias (*Figures 2,3*).

Heterogeneity test

Assessment of heterogeneity

The nine studies included in the heterogeneity assessment showed significant heterogeneity (P=0.00), and the sensitivity (I^2=92.44%) was relatively higher than the specificity (I^2=67.86%).

Diagnostic accuracy

Nine studies with 1,735 patients were included in this meta-analysis. The sensitivity and specificity of these nine studies

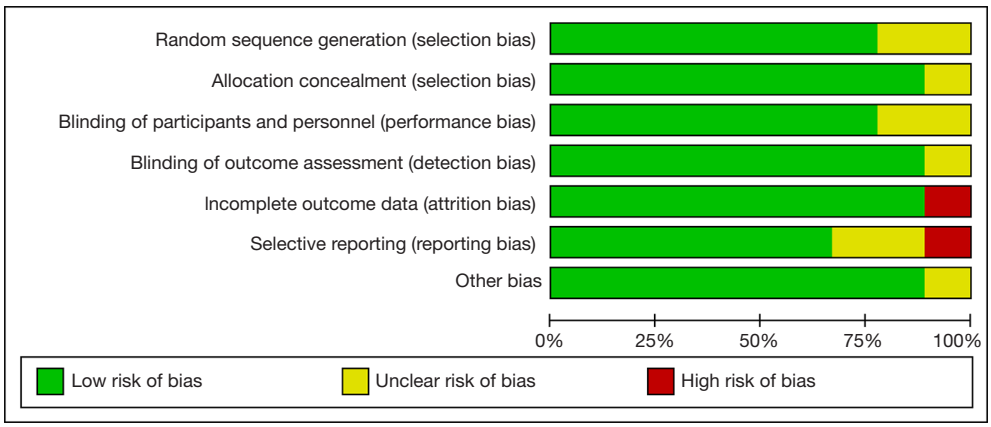

Figure 2 The risk of bias by color in the quality assessment. Red indicates a high risk of bias, yellow indicates an ambiguous risk of bias, and green indicates a low risk of bias of bias.

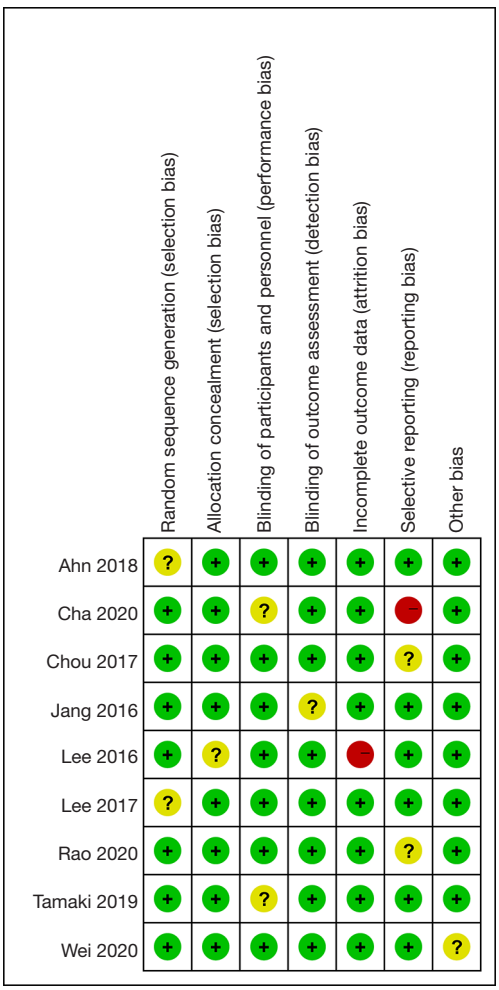

Figure 3 Quality assessment of included studies.

are shown in *Figure 4*. The variability of sensitivity (range, 31–100%) was relatively greater than that of specificity (range, 81–94%).

The diagnostic performance of MRE for HCC was estimated to have a sensitivity of 64% (95% CI: 46–79%) and a specificity of 85% (95% CI: 82–88%). *Figure 5* shows the summary ROC (relative operating characteristic) curve, which had an area under the curve of 86%.

Sensitivity analysis and publication bias

A funnel plot was used to analyze publication bias. The funnel plot contained the nine included studies. Considering the good symmetry of the funnel plot, there is limited publication bias (*Figure 6*).

Discussion

In this study, nine eligible studies were included to evaluate the effectiveness of MRE in the diagnosis of HCC. Our meta-analysis of these studies showed a moderate sensitivity of 64% and a high specificity of 85%. The sensitivity of individual studies varied widely, ranging from 31% to 100%, while the specificity ranged from 81% to 94% (25,26). Our results were consistent with the findings of Qayyum *et al.* (12).

HCC is the main type of primary liver cancer, accounting for approximately 70–90%. It is the third most common cause of cancer-related mortality worldwide. Primary

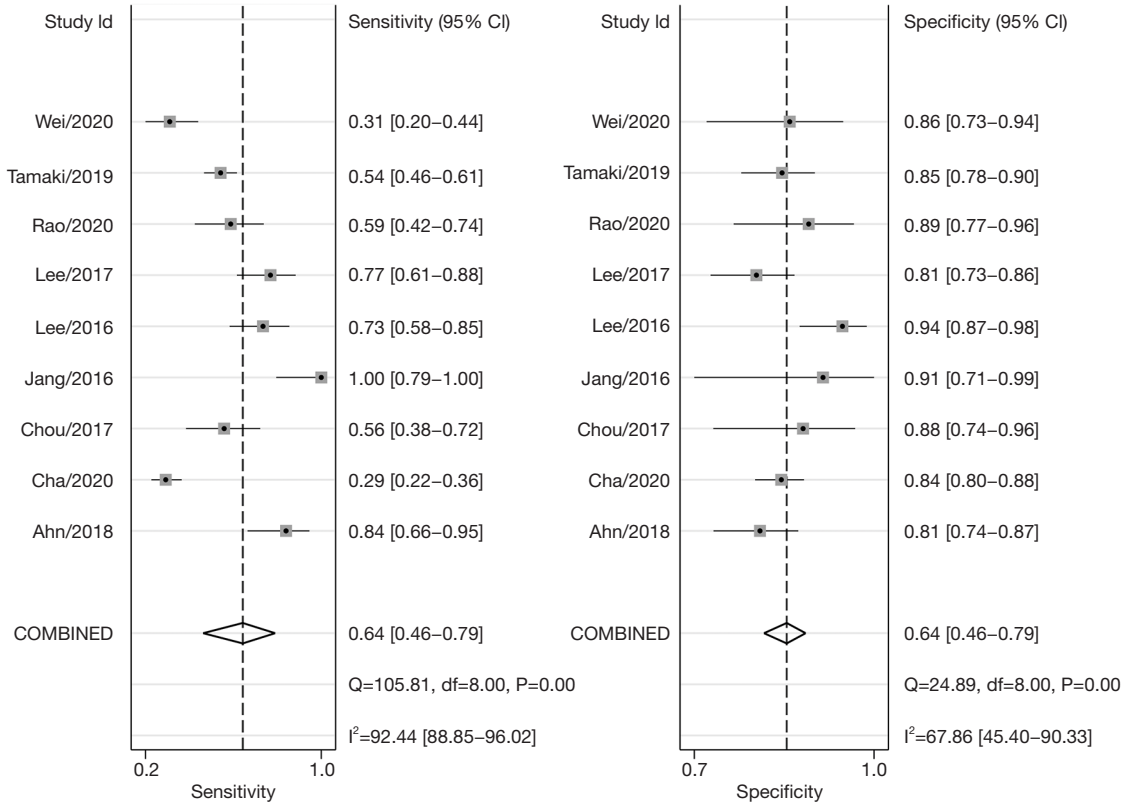

Figure 4 MRE detects the sensitivity and specificity of HCC forest plot. MRE, magnetic resonance elastography; HCC, hepatocellular carcinoma.

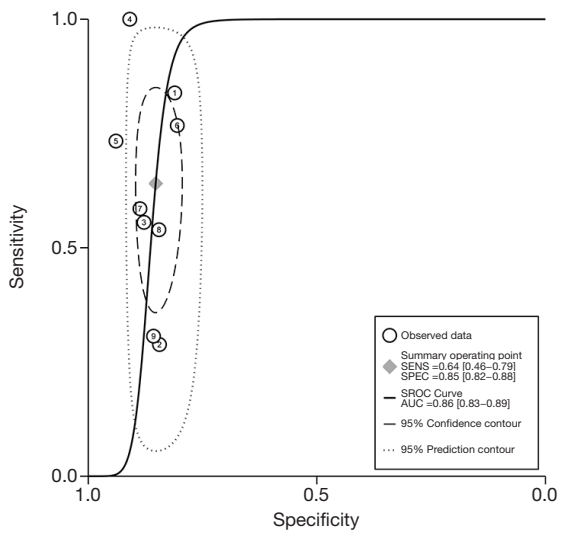

Figure 5 SROC curve of the accuracy of MRE detection of HCC. SROC, summary ROC; MRE, magnetic resonance elastography; HCC, hepatocellular carcinoma.

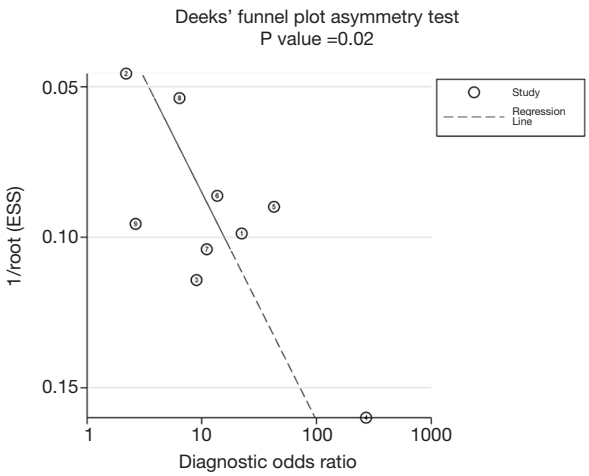

Figure 6 Funnel plot of publication bias.

liver cancer refers to a malignant tumor originating from stem cells or intrahepatic bile duct epithelial cells, and includes HCC, intrahepatic cholangiocarcinoma (ICC), and HCC-ICC mixed type. Secondary liver cancer refers to a malignant liver tumor that is caused by the metastasis of another malignant tumor, typically from the respiratory tract, gastrointestinal tract, breast, and other non-liver parts, to the liver (27-29).

MRE is a non-invasive imaging method for the quantitative detection of soft tissue elasticity and structure. In the process of MRE detection, slight mechanical vibration (between 30 and 70 Hz) propagates to the tissue under investigation through an external vibration device, and the dynamic propagation of the vibration wave in the tissue is collected by a nuclear MRI (Magnetic Resonance Imaging) (30-32). During post-processing, we can quantify the hardness and softness of the tissue according to the appearance (wavelength and amplitude) of the vibration wave in the tissue.

Clinical examination of HCC includes serum alpha-fetoprotein, circulating tumor cells, CT (computed tomography), MRI, DSA (digital subtraction angiography), liver ultrasound, pathological examination, etc. The basic principle of MRE is to use MR technology to detect the particle displacement of tissues or organs in the body under the action of an external force, and obtain the MR phase image via the motion sensitive gradient. A distribution map of elastic coefficient of each point in the tissue or organ is obtained, and the elastic mechanical parameters of the tissue or organ are used as the basis of medical diagnosis (33-37).

Malignant tumors of the liver can increase tissue elasticity, which improves the applicability of MRE in the diagnosis of liver cancer. MRE uses a unique magnetic resonance technology to distinguish the transmission and change of mechanical waves in tissue and judge the evolution of tissue elasticity. MRE has been used to evaluate the pathological changes of patients with chronic liver disease, which has the advantages of high safety, high diagnostic accuracy, and non-invasive. MRE can be used to stage liver fibrosis instead of liver biopsy (35,36).

However, there were some limitations in this study that should be noted. Firstly, the comparison of different tumor sizes was not considered, and thus, further study is needed. Secondly, the details of different stages of the tumor were not taken into account, and should be analyzed in future research. In conclusion, MRE imaging has moderate sensitivity and excellent specificity in the detection of HCC, and can be used as a recommended diagnostic technique for HCC.

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Footnote

Reporting Checklist: The authors have completed the PRISMA-DTA reporting checklist. Available at https://dx.doi.org/10.21037/jgo-21-196

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/jgo-21-196). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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