# **INPLASY**

INPLASY2024110104

doi: 10.37766/inplasy2024.11.0104 Received: 23 November 2024

Published: 24 November 2024

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# Value of abbreviated magnetic resonance sequence in hepatocellular carcinoma screening: A Systematic Review and Meta-analysis

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#### **ADMINISTRATIVE INFORMATION**

**Support -** Zhengzhou City collaborative innovation major project (No. 20XTZX11020).

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2024110104

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 November 2024 and was last updated on 24 November 2024.

# INTRODUCTION

Review question / Objective The purpose of this study is to explore the screening value of abbreviated magnetic resonance imaging sequences for high-risk populations of hepatocellular carcinoma. The chosen research method is diagnostic accuracy testing. The studies included according to the PICOS criteria are as follows:

Population: High-risk group for HCC.

Index test: Abbreviated magnetic resonance imaging (AMRI), which employing a limited number of sequences for offering comparable performance to conventional complete contrast-enhanced MRI (CE-MRI), while saving time and reducing costs. Reference standard: Adopt the recognized imaging and/or pathological diagnosis as the gold standard.

Outcomes: The diagnostic accuracy of AMRI protocol in HCC screening.

Exclusion criteria: (i) Studies not aimed at screening or simulated screening; (ii) studies for

which primary or original information for data analysis was not available; (iii) studies with magnetic resonance equipment field strengths below 1.5 T; (iv) repeatedly published studies.

Condition being studied Hepatocellular carcinoma (HCC) is the most common primary malignant tumor of the liver, accounting for about 75%~90% of all cases, HCC is the third leading cause of cancer-related death. Currently, most domestic and foreign guidelines use biannual ultrasound examination as the main screening method for HCC. However, the sensitivity of ultrasound screening for early liver cancer was as low as 47%. In addition, ultrasound examination is highly contingent upon the proficiency of the operator. While ultrasound is widely used for HCC screening, its diagnostic sensitivity and suboptimal visualization is limited, particularly in patients with obesity or advanced cirrhosis, reduce its effectiveness in detecting early-stage hepatocellular carcinoma, which highlighting the need for alternative methods such as MRI. However, the multiple and complex of MRI scans with complete sequences pose a significantly burden on time and cost-effectiveness, which is limited the usefulness of MRI in the screening of high-risk populations. In this situation, part of studies have attempted to use abbreviated magnetic resonance imaging (AMRI), which is desirable to be a cost-effective screening program with the aim of achieving a diagnostic performance comparable to conventional complete contrastenhanced MRI (CE-MRI). Despite the increasing interest in AMRI for HCC screening, there exist differences and inconsistencies in the reported results within the previous literature, which might influence clinical decision-making and selection. Moreover, the sample size of these published studies is relatively small, and the statistical methods of some studies lack relative scientific reliability, which makes the results lack robustness in clinical application. In addition, the current literature needs to be updated, and the quality of included studies and insufficient analysis of previous meta-analyses tend to threaten the conclusions. Therefore, in order to further clarify the diagnostic accuracy of different AMRI protocols for HCC screening, a systematic review and meta-analysis was conducted.

#### **METHODS**

## **Search strategy**

PubMed

#1 "Carcinoma, Hepatocellular"[Mesh] OR "Liver Neoplasms"[Mesh:NoExp]

#2 (liver\*[Title/Abstract] OR hepatic\*[Title/Abstract] OR Hepato\*[Title/Abstract] AND (carcinoma\*[Title/Abstract] OR cancer[Title/Abstract] OR cancers[Title/Abstract] OR tumor[Title/Abstract] OR neoplas\*[Title/Abstract] OR malignan\*[Title/Abstract])

#3 hepatocarcinoma\*[Title/Abstract] OR hepatoma\*[Title/Abstract] OR "liver carcinoma"[Title/Abstract] OR HCC[Title/Abstract] #4 #1 OR #2 OR #3

#5 "Magnetic Resonance Imaging" [Mesh]

#6 Magnetic-Resonanc\*[Title/Abstract] OR "MR"[Title/Abstract] OR "MRI"[Title/Abstract] OR "diffusion-weighted"[Title/Abstract]

#7 #5 OR #6

#8 abbreviat\*[Title/Abstract] OR surveillanc\*[Title/Abstract] OR screen\*[Title/Abstract]

#9 "mass screening"[MeSH]

#10 #8 OR #9

#11 "Sensitivity and Specificity" [Mesh]

#12 "False Negative"[Text Word] OR "False positive"[Text Word] OR "True Negative"[Text Word] OR "True positive"[Text Word] OR "PPV"[Text Word] OR

Word] OR "NPV"[Text Word] OR Sensitivit\*[Text Word] OR Specificit\*[Text Word]

#13 #11 OR #12

#14 #4 AND #7 AND #10 AND #13

#15 #14 AND ("2000/01/01"[Date - Publication]: "2024/08/10"[Date - Publication]) AND (English[Language])

#### **Embase**

#1 'liver cell carcinoma'/exp OR 'liver cancer'/de

#2 ((liver\* OR hepatic\* OR hepato\*) NEAR/6 (carcinoma\* OR cancer\* OR tumor\* OR neoplas\* OR malignan\*)):ab,ti,kw

#3 hepatocarcinoma\*:ab,ti,kw OR hepatoma\*:ab,ti,kw OR 'liver carcinoma':ab,ti,kw OR hcc:ab,ti,kw

#4 #1 OR #2 OR #3

#5 'nuclear magnetic resonance imaging'/exp OR 'mr':ti OR 'mri':ab,ti,kw

#6 'magnetic resonanc\*':ab,ti,kw OR 'diffusion-weighted':ab,ti,kw

#7 #5 OR #6

#8 abbreviat\*:ab,ti,kw OR surveillanc\*:ab,ti,kw OR screen\*:ab,ti,kw

#9 'cancer screening'/exp OR 'disease surveillance'/exp

#10 #8 OR #9

#11 'sensitivity and specificity'/de

#12 'false negative':ab,ti,kw OR 'false positive':ab,ti,kw OR 'true negative':ab,ti,kw OR 'true positive':ab,ti,kw OR 'ppv':ab,ti,kw OR 'npv':ab,ti,kw OR specificit\*:ab,ti,kw

#13 #11 OR #12

#14 #4 AND #7 AND #10 AND #13

#15 #14 AND [english]/lim AND [2000-2024]/py AND ([article]/lim OR [article in press]/lim OR [review]/lim)

#### Cochrane Library

#1 MeSH descriptor: [Carcinoma, Hepatocellular] explode all trees

#2 MeSH descriptor: [Liver Neoplasms] explode all trees

#3 ((Hepatocellular\* OR liver-cell\* OR hepatic-cell\* OR Hepato-cell\*) NEAR/6 (Cancer\* OR tumor\* OR Neoplas\* OR carcinoma\*)):ti,ab,kw

#4 (hepatocarcinoma\* OR hepatoma\* OR "liver carcinoma" OR HCC):ti,ab,kw

#5 #1 OR #2 OR #3 OR #4

#6 MeSH descriptor: [Magnetic Resonance Imaging] explode all trees

 $\mbox{\#7}$  (Magnetic-Resonanc\* OR "MR" OR "MRI" OR "diffusion-weighted"):ti,ab,kw

#8 #6 OR #7

#9 (abbreviat\* OR surveillanc\* OR screen\*):ti,ab,kw #10 MeSH descriptor: [Mass Screening] explode all trees

#11 #9 OR #10

#12 MeSH descriptor: [Sensitivity and Specificity] explode all trees

#13 ("False Negative" OR "False positive" OR "True Negative" OR "True positive" OR "PPV" OR "NPV" OR Sensitivit\* OR Specificit\*):ti,ab,kw #14 #12 OR #13 #15 #5 AND #8 AND #11 AND #14

Web of Science

#1 TS=("Carcinoma, Hepatocellular" OR "Liver Neoplasms")

#2 TS=((Hepatocellular\* OR liver-cell\* OR hepatic-cell\* OR Hepato-cell\*) NEAR/6 (Cancer\* OR tumor\* OR Neoplas\* OR carcinoma\*))

#3 TS=(hepatocarcinoma\* OR hepatoma\* OR "liver carcinoma" OR HCC)

#4 #1 OR #2 OR #3

#5 TS=("Magnetic Resonance Imaging")

#6 TS=(Magnetic-Resonanc\* OR "MR" OR "MRI" OR "diffusion-weighted")

#7 #5 OR #6

#8 TS=(abbreviat\* OR surveillanc\* OR screen\*)

#9 TS=("mass screening")

#10 #8 OR #9

#11 TS=( "Sensitivity and Specificity" OR "False Negative" OR "False positive" OR "True Negative" OR "True positive" OR "PPV" OR "NPV" OR Sensitivit\* OR Specificit\*)

#12 #4 AND #7 AND #10 AND #11.

Participant or population High-risk group for HCC (in accordance with the Chinese Clinical Oncology Society 2022 edition of the Guidelines for the Management of Primary Liver Cancer or the American National College of Radiology Liver Imaging Reporting and Data System criteria), and no previous history of other tumors or surgery.

**Intervention** Abbreviated magnetic resonance imaging (AMRI), which employing a limited number of sequences for offering comparable performance to conventional complete contrast-enhanced MRI (CE-MRI), while saving time and reducing costs, such as non-contrast MRI protocol, which does not use contrast media and using at most three sequences of T2, T1 (T1 Weighted Imaging) and DWI.

**Comparator** In this study, the accuracy of ultrasound and AMRI screening for hepatocellular carcinoma will be compared.

**Study designs to be included** Diagnostic accuracy testing.

Eligibility criteria Reference standard: Adopt the recognized imaging and/or pathological diagnosis

as the gold standard, and the imaging diagnosis standard is in accordance with the radiological hallmarks of AASLD (American Association for the Study of Liver Diseases), the Korean Liver Cancer Study Group-National Cancer Center Korea, the European Association for the Study of the Liver Clinical Practice Guidelines, the 2022 edition of the Chinese Society of Clinical Oncology Guidelines for the Treatment of Primary Liver Cancer, and the pathological diagnosis standard is in accordance with the International Liver Cancer Consensus Group standards and the 2015 edition of the Chinese Anti-Cancer Society Guidelines for Standardized Pathological Diagnosis of Primary Liver Cancer.

Exclusion criteria: (i) Studies not aimed at screening or simulated screening; (ii) studies for which primary or original information for data analysis was not available; (iii) studies with magnetic resonance equipment field strengths below 1.5 T; (iv) repeatedly published studies.

**Information sources** Medline (via PubMed), EMbase, The Cochrane Library, Web of Science, CNKI, WanFang Data, VIP databases.

Main outcome(s) The diagnostic accuracy of AMRI protocol in HCC screening. If the results are combined according to different abbreviated sequences, we divide the study data into subgroups, including non-contrast MRI (NC MRI): abbreviated sequence without hepatobiliary phase and using at most three sequences of T2, T1 and DWI; contrast enhanced hepatobiliary phase MRI (HBP MRI): abbreviated sequences including hepatobiliary specific phase and/or others.

**Quality assessment / Risk of bias analysis**Quality Assessment Tool for Diagnostic Accuracy
Studies (QUADAS-2).

Strategy of data synthesis When stata software was selected for data analysis, heterogeneity was considered if I<sup>2</sup> > 30% and P < 0.1. The combined effect size of random effect model was selected if there was heterogeneity, while the combined effect size of fixed effect model was selected if there was no heterogeneity. The pooled diagnostic efficacy indicators calculated included: pooled sensitivity, pooled specificity, pooled positive likelihood ratio(PLR), pooled negative likelihood ratio(NLR), and pooled diagnostic odd ratio (DOR), and all pooled effect measures were provided with their 95% confidence interval (CI) using a bivariate mixed-effects model for the meta-analysis of diagnostic tests, by logit transformation of true positive and false positive rates. The forest plot and summary receiver operating characteristic

(SROC) curve were drawn, and the area under the SROC curve (AUC) was calculated to compare the diagnostic efficacy of each type of abbreviated sequence scheme, and the closer the AUC was to 1.0, the higher the diagnostic efficacy of the abbreviated sequence scheme. The presence of publication bias was assessed by Deek's asymmetric regression test, P<0.05 indicated that the difference was statistically significant, suggesting publication bias. Fagan plots and the dot plot of likelihood ratio were drawn to evaluate the value of the diagnostic tests for clinical use. Analysis of sensitivity and meta-regression analysis were used to explore the sources of heterogeneity among studies, and P<0.05 suggested that covariate was the factor causing heterogeneity.

**Subgroup analysis** We divide the study data into subgroups, including non-contrast MRI (NC MRI): abbreviated sequence without hepatobiliary phase and using at most three sequences of T2, T1 and DWI; contrast enhanced hepatobiliary phase MRI (HBP MRI): abbreviated sequences including hepatobiliary specific phase and/or others.

**Sensitivity analysis** Stata software carries out sensitivity analysis to reflect the sensitivity of the article by the change of the effect size after deleting one of the articles.

# Country(ies) involved China.

**Keywords** Magnetic resonance imaging; Hepatocellular carcinoma; Screening; Abbreviated sequences; Meta-analysis.

#### Contributions of each author

Author 1 - Cong Wang.

Author 2 - Jing-hong Liang.

Author 3 - Shao-cheng Zhu.