Clin Schizophr Relat Psychoses
Volume 15:S6, 2021
Doi: 10.3371/CSRP.CVAA.16.0821

Clinical Schizophrenia & Related Psychoses

Research Article

Hybrid Open Access

Advanced Imaging Techniques of the Magnetic Resonance in Characterization of Hepatocellular Carcinoma Type: A Systematic Review and Meta-Analysis

Vahid Changizi[1], Ahmed Jasim Abbas[1*], Hayder Jasim Taher[1], Hayder Suhail Najim[1], Hedayat Allah Saroush[2], Zaid Hadi Hammoodi[3], Afraa Jasim farhood[3] and Mohannad Ahmed Sahib[1]

[1]*Department of Radiology and Radiotherapy, Tehran University of Medical Sciences, Tehran, Iran*

[2]*Department of Diagnostic and Interventional Radiology, Baghdad Medical City, Baghdad, Iran*

[3]*Department of Radiologists, Ministry of Health, Babylon, Iraq*

Abstract

Introduction: Conflicting results have been reported between the use of conventional protocol MRI and advanced protocol MRI to avoid unnecessary histopathology when Magnetic Resonance Imaging (MRI) is used for the diagnosis of Hepatocellular Carcinoma (HCC). Therefore, we aimed to compare the diagnostic performance of conventional MRI and advanced technique MRI to avoid unnecessary histopathology.

Methods: Original studies reporting the diagnostic performance of MRI for the diagnosis of HCC published between January 2010 and February 2021 were identified in Literature search. A systematic literature search using PubMed(https://pubmed.ncbi.nlm.nih.gov), Embase (https://www.embase.com), Web of Science (https://apps.webofknowledge. com), PROQUEST, SEMANTIC SCHOLAR Google Scholar and Cochrane Library databases (https://wwwcochranelibrary. com) were performed independently by two radiologists to identify articles published prior to June 2021.

Results: A total of 3,757 HCCs and 3,682 benign liver lesions from 35 studies were included. The overall sensitivity and specificity of the diagnostic performance of conventional MRI was 0.81 (0.77-0.94) 0.78 (0.84-0.92) and Advance MRI 0.93 (0.83-0.89), 0.86 (0.79-0.96) respectively

Conclusion: The present meta-analysis suggests that Advance MRI may increase the sensitivity, and specificity for the diagnosis of HCCs.

Keywords: Diffusion weighted image • Apparent Diffusion Coefficient • Perfusion weighted image • Meta-analysis

Introduction

Hepatocellular Carcinoma (HCC) is the most common primary malignancy of the liver [1]. HCC is the fifth most common type of cancer and the second leading cause of cancer-related death worldwide [2]. Approximately 70%-90% of HCCs are developed on the background of established liver cirrhosis or advanced fibrosis. Hepatitis B Virus (HBV) and/or Hepatitis C Virus (HCV) infection, alcohol, and Nonalcoholic Aatty Liver Disease (NAFLD) are the most predominant risk factors for HCC worldwide [3]. A tremendous development of new imaging techniques has taken place during these last year's [4]. Maximizing accuracy of imaging in the context of HCC is paramount in avoiding unnecessary histopathology, which may result in post-procedural complications up to 6.4%, and mortality up to 0.1% [5]. Noninvasive imaging modalities, including Ultrasound (US), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), have played pivotal roles in assessing HCC in recent decades [6]. Several clinical practice guidelines, the application of US is limited in obese patients and patients with very cirrhotic heterogeneous livers. In addition, the performance of US is usually deteriorated for deep, sub diaphragmatic, multiple, and treated lesions. In general, US is less accurate for diagnosing HCC than MRI [7]. Therefore, US is not yet recommended as the first-line diagnostic tool for HCC, according to current guidelines [6]. Multiphasic dynamic Computed Tomography (CT) is useful in the evaluation of nodular lesions in the cirrhotic liver [8]. Arterial phase imaging is most useful for the detection of HCC as its predominant blood supply is from the hepatic artery [9]. However, it is less sensitive for the detection of small HCC and for dysplastic nodules which appear isodense to the liver parenchyma due to their predominant blood supply from the portal vein [10]. CT arterio-portography and CT hepatic arteriography are more sensitive for the detection of HCC but the false positive rate is high due to benign hyper vascular lesions like arterioportal shunts [11]. Nowadays, magnetic resonance plays a key role in management of liver lesions, using a radiation-free technique and a safe contrast agent profile [12]. Magnetic Resonance Imaging (MRI) provides valuable imaging information for the preoperative and postoperative evaluation of HCC [13]. DWI is a functional MRI technique that allows quantitative measurements of proton diffusion in tissues [14]. HCC and other malignancies are usually characterized by increased cellularity and, thus, have restricted water proton diffusion [6]. Therefore, most HCCs are observed as a hyper intense lesion on high b value DWI with low Apparent Diffusion Coefficient (ADC) value on quantitative maps compared with background liver [15]. HCC and other malignancies are usually characterized by increased cellularity and, thus have restricted [16]. Perfusion weighted image Dynamic Contrast-Enhanced (DCEMRI) enables quantification of the vascular characteristics of tissue and tumor [17]. DCE-MRI requires IV injection of a gadolinium-based contrast agent and uses high-temporal images that capture changes in MR Signal Intensity (SI) as a function of time. Tracer kinetic modeling based on DCE-MRI has been used to detect liver fibrosis and cirrhosis and to assess tumor angiogenesis [18].

Materials and Methods

This systematic review and meta-analysis was performed in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [19].

***Corresponding Author:** Ahmed Jasim Abbas, Department of Radiology and Radiotherapy, Tehran University of Medical Sciences, Tehran, Iran; Email: ahmedalmansoory5540@gmail.com*

Received date: 26 July, 2021; **Accepted date:** 09 August, 2021; **Published date:** 16 August, 2021

Literature search

A systematic literature search using PubMed(https://pubmed.ncbi.nlm.nih.gov), Embase (https://www.embase.com), Web of Science (https://apps.webofknowledge com), SEMANTIC SCHOLAR, Google Scholar, PROQUEST, and Cochrane Library databases (https://www cochranelibrary.com) were performed independently by tow radiologists to identify articles published prior to June 2021, using the key words 'hepatocellular carcinoma', 'liver cancer', 'liver cell carcinoma', 'magnetic resonance imaging' 'diffusion magnetic resonance imaging', Meta-analysis • Systematic review susceptibility weighted image SWI. Related citations in eligible articles were also assessed for inclusion. The search was limited to English-language studies on human subjects. The time period for the studies was limited from January 1, 2010 to February 6, 2021. The detailed search strategy is described in supplementary Figure 1.

The ethical approval for this study was obtained from Tehran University of medical sciences ethical committee in our institution IR.TUMS.SPH.REC.1399.324 during 14 Mars 2021. The study included (35) articles studied consecutive with HCC. In our study, Embase, MEDLINE, PubMed, the Cochrane library, Elsevier, Springer and free journals were searched using the search queries: HCC , conventional MRI, Locally Advance MRI, diffusion weighted imaging DWI, perfusion MRI , IVIM and SWI. Only original articles that performed during the years 2010 to 2020 presented in English language that relevant to our objectives were considered for inclusion. We searched more in databases using function of Related Articles in PubMed and browsed the scholar.google.com using same terns. Also we searched the references of all retrieved articles manually for relevant related articles. Then we compared the retrieved articles and accepted recent publication for the overlapping patients 'series. Furthermore, we assessed for potential eligibility by screening for relevance on title and reading the abstracts first and then full text article and then start to apply agreed upon inclusion and exclusion criteria.

Inclusion and exclusion criteria

Studies meeting the following criteria were included: (a) population: Patients at high risk for HCC [1,2,5]; (b) index test: liver MRI with conventional protocol or advanced protocol; (c) reference standard: HCC histopathology and clinical diagnosis such as imaging follow-up or laboratory markers; Studies meeting any of the following criteria were excluded: (a) studies not reporting sufficient data to clearly establish outcomes; (b) studies for which it was not possible to obtain separate outcomes using with conventional protocol or advanced protocol; (c) studies with hepatic lesions previously treated with systemic therapy; (d) studies with case–control designs; (e) studies with partially overlapping cohorts; (f) case reports or series including fewer than ten patients; and (g) protocols, conference abstracts, reviews, guidelines, books, letters, editorials, and errata.

Data extraction and quality assessment

The following data were extracted from each eligible study: (a) Study characteristics: Authors, year of publication, institution, country, duration, and study design (prospective vs. retrospective); (b) patient characteristics: number of patients, sex, age, underlying liver disease, (c) lesion characteristics: lesion number, lesion size,; (d) MRI techniques: magnetic field, MRI protocol, (e) reference standard; The methodological quality of the selected studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool [11]. The risk of bias and applicability of each eligible study were assessed according to the four different domains of patient selection, index test, reference standard, and flow and timing. Studies without a high risk of bias in any domain were considered to have a low-to-moderate overall risk of bias. Likewise, studies without a high concern for applicability in any domain were considered to have a low-to-moderate overall concern for applicability. The data extraction and quality assessment were independently conducted by the two reviewers, with any disagreements being resolved by discussion with the third reviewer.

The two radiologists reviewed all 2380 abstracts after duplication removal and subsequently the full text of the 120 articles was obtained if the following inclusion criteria was fulfilled: 1) Included the diagnostic accuracy of conventional MRI only or with advance protocol for HCC; 2) constituted original research rather than a meta-analysis, a review article, case report or case series; 3) published in English; and 4) results are from humans and not animals 5) included both MRI with conventional protocol and advanced protocol 6) included sufficient data, with>20 patients to calculate True Positive (TP), False Positive (FP), False Negative (FN) and True Negative (TN) for constructing a 2 × 2 contingency table; and 7) patients at high risk for HCC using pathological analysis (surgical resection, explant and/or biopsy) or imaging from follow-up according to the guidelines for standardization of liver imaging, diagnosis, classification and reporting of hepatocellular carcinoma. In addition, articles from the same institution, which included an overlap period of patient recruitment, were considered to have an overlapping population. In these cases, the study, which had the larger number of HCCs cases, was included.

If there were disagreements between the two investigators, the consensus amongst the two radiologists was used to resolve the disagreement. Disagreements were resolved following discussions between the two investigators, until at least own of the investigators reached the same conclusion. A total of 85 studies were excluded according to the following exclusion criteria:1) They were not relevant to the present meta-analysis if they fit one of the followings conditions: Cancer type includes malignant cancer other than HCC, such as cholangiocarcinoma, hepatoepidermoid carcinoma and metastatic cancer; diagnosis of HCC using a combination of multiple imaging modalities;2) they evaluated previously treated HCCs; 3) the sensitivity and specificity was not evaluated; 4) there was a lack of sufficient data to construct a 2 × 2 contingency table; and vi) there was study population overlap. A total of 35 studies were included for analysis. In addition, the reference list of these 35 studies was reviewed.

Results

Study selection. A flow chart following the Preferred Reporting Items for Systematic Reviews and Meta-analysis principles was used to demonstrate the selection procedure (Figure 1).

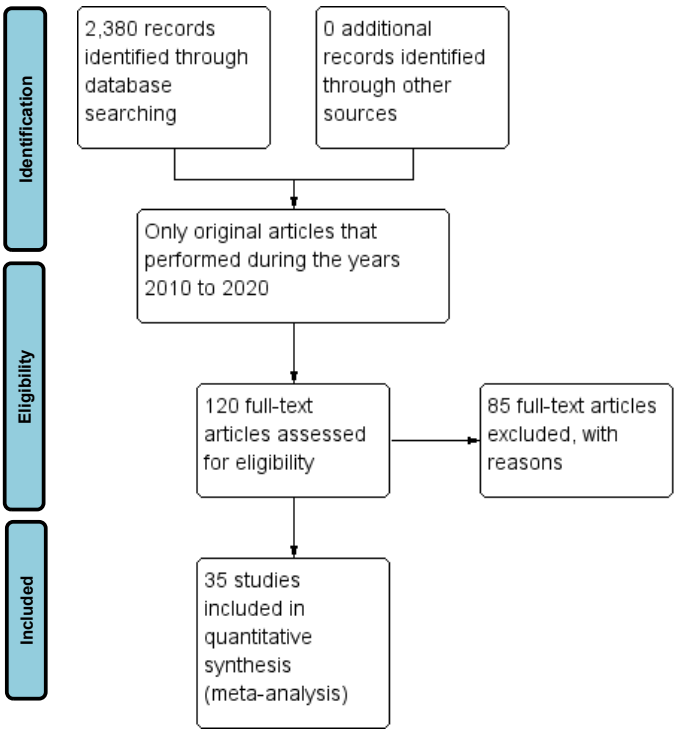

Figure 1. Flow chart of post-therapy assessment participants.

A total of 2,380 articles were initially identified. There was a total of 2,260 articles remaining following the removal of duplicates and a further 120 articles were excluded, following screening of the abstract. Amongst the remaining 85 studies, a total of 35 studies were included in the Meta analysis using the inclusion criteria.

Summary of included studies

The summarized characteristics and the diagnostic performance of conventional MRI and Advance MRI for the included 35 studies are shown in Tables 1 and 2, respectively. A total of 3,757 HCCs with a diameter 2 cm and 3,682 benign liver lesions, with a diameter 2 cm was included in the meta analysis. The DWI, HCC, MRI and were all calculated on a per lesion basis. Of the included studies, 27 originated from Asia, 7 from Europe and one from USA. In addition, 23 of the studies were retrospective, and 12 were prospective. The reference standard for the diagnosis of HCC included pathological analysis (surgical resection, explant and/or biopsy) and imaging from follow-up. MR imaging field strength was 3 T and 1.5 T.

Quality assessment and publication bias: Figure 2 demonstrates the overall evaluation for the quality of the included studies using QUADAS.2. The quality of the index test was high (90%, 9/35 studies); however, patient selection had a low score (70%, 7/35 studies), which could be due to a lack of avoidance of a case control design or the inappropriate exclusions during patient selection.

This also increased concerns regarding the applicability of patient selection. For all the 35 included studies, some of them used pathological finding as the only reference standard to diagnose HCC. For the others, Histopathology was used as a reference standard for patients when pathology analysis was not available. Liver transplantation (n¼10), surgical resection (n¼26), or fine needle aspiration biopsy (n¼55). Of the 91 nodules, 60 nodules were pathologically confirmed as WD-HCCs and 31 nodules were confirmed as HGDNs.

Therefore, the concerns of bias for applicability of reference standards was low for studies using imaging follow up as one of the reference standards for patients when pathology was not used. The risk of bias for flow and timing was high for 1 study since the interval between MRI scan and the pathological analysis exceeded 117 days for some of the patients, and was unclear for 2 studies for the lack of information regarding the time interval between MRI scan and the references standard (Figure 3 and Table 3).

Heterogeneity between studies the 35 included studies demonstrated significant heterogeneity with P<0.00001 using X2 test. The heterogeneity for the sensitivity (I2 of 93) was higher compared with that for specificity (I2 of 93). In addition, there was no threshold effect found (correlation,.0.46; proportion of heterogeneity due to threshold effect, (0.46), (P=0.65).

Synthesis of general diagnostic

Figure 4 demonstrates the forest plots of sensitivity and specificity, Tables 4-6 comparison of the diagnostic performance of conventional MRI, The pooled sensitivity and specificity were 0.81 (95% CI, 0.77-0.94) and

0.78 (95% CI, 0.84-0.92), respectively, +Advance MRI. The pooled sensitivity and specificity were 0.93 (95% CI, 0.83-0.89) and 0.86 (95% CI, 0.79-0.96), respectively. The positive and negative likelihood ratio was 0.02 (95% CI, 0.06-0.09), respectively.

SROC, The confidence region (smaller circle with dash line) represents the ellipsoid 95% confidence region in SROC space for the summary point estimate of diagnostic performance. SROC, summary receiver operating characteristics curve; AUC, area under the curve; SPEC, Specificity; SENS, Sensitivity (Figure 5).

Sensitivity was significantly higher for studies not using hepatobiliary phase compared with those using hepatobiliary phase (P<0.001). Specificity was significantly higher for studies using a 3 T magnetic field compared with those using 1.5 T magnetic field (P=0.03). There were no significant differences in either the sensitivity or in specificity for the remaining study characteristics (all P>0.05) (Figure 6).

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state. The positive actual state is 0.

The test result variable(s): Interpretation has at least one tie between the positive actual state group and the negative actual state group. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values. Diagonal segments are produced by ties.

Table 1. Summary of the patients cohorts and characteristics of MRI protocols for the included studies.

S.no	Author	Year	Country	No of Patients	No. lesions of HCC	Reference Standard	MRI field, T	MRI sequence with HBPI and without 0
1.	Shankarin Shiva	2016	India	20	22	Fine needle aspiration	3.0	0
2.	Zixing Huang, Yi Wei	2019	China	115	135	Histopathology	3.0	0
3.	Heon-Ju kwon	2015	Korea	230	222	Histopathology	1.5	1
4.	Sungmin Woo	2013	South Korea	40	42	Histopathology	3.0	0
5.	Vincenza Granata	2016	Italy	34	62	Biopsy	1.5	0
6.	Yong-Sheng Xu	2019	China	51	51	Histopathology	3.0	0
7.	Guang-Zhi Wang	2020	China	128	128	Histopathology	3.0	0
8.	Shao-Cheng Zhu	2018	China	62	62	Histopathology	3.0	0
9.	Likun Cao	2019	China	74	74	Histopathology	3.0	0
10.	Tomohisa Moriya	2017	Japan	53	56	Surgery	3.0	1
11.	Jinkun Zhao	2017	China	318	211	Hepatic resection surgery	1.5	0
12.	Jiyoung Hwang	2014	Korea	63	113	Explant	3.0	0
13.	Yanyan Zhang	2020	China	91	91	WD-HCCs	3.0	0
14.	Jie Chen	2019	China	115	121	Surgery	3.0	1
15.	Seunghee Han	2018	Korea	175	175	HCC (KLCSG-NCC)	3.0	0
16.	Yi Kyung Kim	2013	Korea	135	136	Histopathological and biopsy	3.0	0
17.	Matteo Renzulli	2018	Italy	228	420	Histology	1.5	1
18.	Yingmei Jia Yingmei Jia	2019	China	151	114	Surgery or biopsy	3.0	0
19.	Juan Peng	2020	China	65	55	Surgery	3.0	0
20.	Hina Gu	2018	Pakistan	85	48	Histopathology	1.5	0
21.	Cecilia Besa	2016	USA	174	80	Histopathology	1.5	1
22.	Rita Golfieri	2011	Italy	127	62	Histopathology	1.5	1

23.	Bedriye Koyuncu Sokmena	2019	Turkey	29	42	Histopathologically	1.5	0
24.	Dong Ik Cha	2020	Korea	122	122	Histopathology	3.0	0
25.	Ah Yeong Kim	2012	Korea	189	240	Histopathology	3.0	0
26.	A Koa	2019	Korea	117	89	Histopathology	3.0	0
27.	Michele Di Martino	2019	Italy	40	93	Histopathology	1.5	1
28.	Michele Di Martino	2016	Italy	52	71	Histopathology	3.0	1
29.	Suwannee Surattanasophon	2014	Thailand	45	101	Histopathology	3.0	1
30.	Zhi-bo Hou	2021	China	40	44	Histopathology	3.0	0
31.	Heno-Ju Know	2014	Korea	230	210	Histopathology	1.5	0
32.	Ruo-kun Li	2012	China	58	65	Histopathology	3.0	0
33.	Ruo-kun Li	2015	China	68	89	Histopathology	3.0	1
34	Meng zhou	2021	China	60	62	Histopathology	3.0	1
35.	Ijin Joo	2018	Korea	288	292	Histopathology	3.0,1.5	1

Table 2. Summary of the diagnostic performance of conventional MRI + Advance MRI.

S.no	Author ,Year	Study Period	MRI Interpretation	Study Type	Primary HCC Eatology	Size of HCCs, cm	Less than 2 cm=0 more than 2 cm=1
1.	Shiva Shankarin, 2016	Period of 18 months	A prospective study	Conventional MRI	HCV (NASH)	3 cm to 17 cm	1
2.	Zixing, YiWei and Huang, 2019	January 2016 and April 2017	Prospective	Advance MRI	Hepatitis B virus 26	7.04 ± 3.67 cm, 5.80 ± 3.95 cm	1
3.	Heon – Ju kwon, 2015	November 2009 and June 2011	Retrospective Study	Conventional MRI	Hepatitis B	0.5 cm to 2 cm	1
4.	Sungmin Woo, 2013	August 2010 to May 2012	Retrospective Study	Advance MRI	NA	4.7 cm ± 3.4, 1.2-16.3 cm	1
5.	Vincenza Granata, 2016	From August 2014 to February 2016	A retrospective Study	Advance MRI	Hepatitis C Virus 14 patients hepatitis B virus	12 mm to 20 mm	0
6.	Yong – Sheng Xu, 2019	Between December 2015 to June 2018	A retrospective Study	Conventional MRI	Hepatitis B	6 mm to 118 mm	1
7.	Guang – Zhi Wang, 2020	From December 2015 to January 2017	Prospective study	Advance MRI	Hepatitis B HBV (+) hepatitis	3.0 cm to 18.0 cm	1
8.	Shao- Cheng Zhu, 2018	Between March 2016 to May 2017	A retrospective Study	Advance MRI	Hepatitis B	-	1
9.	Likun Cao, 2019	From September 2015 to January 2017	Prospective study	Advance MRI	Hepatitis B	5.80 ± 2.68	1
10.	Tomohisa Moriya, 2017	3 months before surgery	Retrospective Study	Conventional MRI	Hepatitis B Hepatitis C	NA	-
11.	Jinkun Zhao, 2017	January 2011 and January 2015	Retrospective Study	Conventional MRI	Hepatitis	1.5 cm to 21.0 cm	1
12.	Jiyoung Hwang, 2014	From April 2008 to October 2013	Retrospective Study	Conventional MRI	Hepatitis B and C	Mean 2.0 cm+1.3 cm	0
13.	Yanyan Zhang, 2020	From January 2012 to April 2018	Retrospective Study	Conventional MRI	NA	30 mm	1
14.	Jie Chen, 2019	August 2015 to September 2018	Retrospective Study	Conventional MRI	Hepatitis B, virus B and hepatitis C	6.36(1.5, 12.73)	1
15.	Seunghee Han, 2018	From January 2012 to August 2015	Study retrospective	Conventional MRI	Hepatitis B Hepatitis C	Bigger than	0
16.	Yi Kyung Kim, 2013	December 10 and May 2012	Retrospective Study	Conventional MRI	HBV/HCV	0.6 cm to 2.0 cm	1
17.	Matteo Renzulli, 2018	From 18 June 2013 to 1 December 2015	A Prospective Study	Conventional MRI	HCV	11 mm to 150 mm	1
18.	Yingmei Jia Ying mei Jia, 2019	March 2013 and November 2016	Study retrospectively	Advance MRI	NA	NA	-
19.	Juan Peng, 2020	-	Prospective Study	Advance MRI	NA	NA	-
20.	Hina Gul, 2018	From July 2015 to June 2017	This cross-sectional Validation study	Conventional MRI	NA	(≤ 2 cm)	0
21.	Cecilia Besa, 2016	1/1/2011 to 31/12/2011	Retrospective	Conventional MRI	HCV/NASH	11 mm to 20 mm	0
22.	Rita Golfieri, 2011	May 2008 and October 2009	Prospective study	Conventional MRI	HBV/HCV	(<1 cm and 1 cm to 2 cm>)	0
23.	Bedriye Koyuncu Sokmena, 2019	Between January 2015 and October 2016	Study retrospective	Advance MRI	Hepatitis B Hepatitis C	NA	-
24.	Dong Ik Cha, 2020	Between November 2016 and September 2018	Prospective	Conventional MRI	HBV/HCV	2.1 (0.6-5.0)	1

25.	Ah Yeong Kim, 2012	Between October 2009 and February 2011	Retrospective study	Conventional MRI	Hepatitis B	(3.0 cm)	1
26.	A. Koa, 2019	Between October 2009 and January 2016	Retrospective study	Conventional MRI	Hepatitis B	Mean size 14 ± 3.4	1
27.	Michele Di Martino, 2019	Between December 2011 and April 2012	Retrospective study	Conventional MRI	HCV/HBV Cryptogenic HCV+HBV	5 mm to 20 mm	0
28.	Michele Di Martino, 2016	Between January 2014 and July 2015	Prospectively	Conventional MRI	Dynamic	(5 mm to 20 mm; median 15 mm)	0
29.	Suwannee Surattanasophon, 2014	Between January 2012 and November 2013	Retrospective study	Conventional MRI	C Hepatitis C	2.06 cm	1
30.	Zhi-bo Hou, 2021	NA	Retrospective study	Advance MRI	NA	0.7 cm to 2.8 cm	1
31.	Heon-Ju Kwon, 2014	Between November 2009 and June 2011	Retrospective Study	Conventional MRI	NA	(0.5 cm to 2 cm)	0
32.	Ruo-kun Li, 2012	Between March and August 2010	Preoperative	Advance MRI	Hepatitis B	(4.1 cm to 63.4 cm)	1
33.	Ruo-kun Li, 2015	From March 2010 to August 2012	Preoperative	Advance MRI	Hepatitis B Hepatitis C	NA	-
34.	Meng Zhou, 2021	Hospital from October 2018 to October 2019	Retrospective Study	Conventional MRI	HBV 29	<3 cm	1
35.	Ijin Joo, 2018	Between September 2012 and May 13	Retrospective Study	Conventional MRI	Chronic hepatitis image analyses	NA	-

Figure 2. Quality assessment of the included studies using the Quality Assessment of Diagnostic Accuracy Studies. The red bar indicates high risk of bias; the yellow bar indicates unclear risk of bias; and the green bar indicates low risk of bias. In the lower part, details of quality assessment were shown. Green circle with '+' indicates low risk of bias or low concern for applicability; yellow circle with '?' indicates unclear risk of bias or unclear concern for applicability; red circle with '-' indicates high risk of bias or low concern for applicability. Funnel plot of comparison.

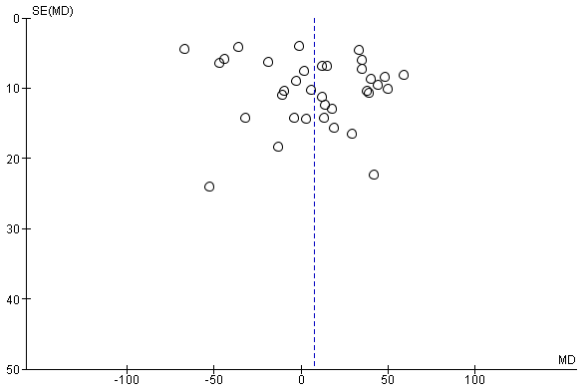

Figure 3. Deeks' funnel plot for assessment of publication bias. Potential publication exists if the calculated P<0.05.

Table 3. Subgroup analysis and meta regression.

Characteristic	No. of studies	Pooled sensitivity (CI)	P-value	Pooled specificity (CI)	P-value
MRI field strength, T			0.87		0.51
3.0	25	0.83 (0.79-0.91)		0.92 (0.77-0.95)	
1.5	10	0.91 (0.88-0.97)		0.80 (0.79-0.89)	
Country of origin			0.36		0.79
Asia	27	0.79 (0.81-0.95)		0.83 (0.88-0.92)	
Europe	7	0.88 (0.86-0.90)		0.81 (0.82-0.94)	
USA	1	0.91 (0.90-0.97)		0.87 (0.89-0.97)	
Study design			0.64		0.91
Prospective	11	0.90 (0.72-0.89)		0.79 (0.84-0.91)	
Retrospective	24	0.84 (0.77-0.99)		0.85 (0.80-0.93)	
Hepatobiliary phase imaging			0.21		0.84
Yes	21	0.77 (0.85-0.92)		0.84 (0.78-0.89)	
No	14	0.86 (0.80-0.94)		0.81 (0.88-0.98)	

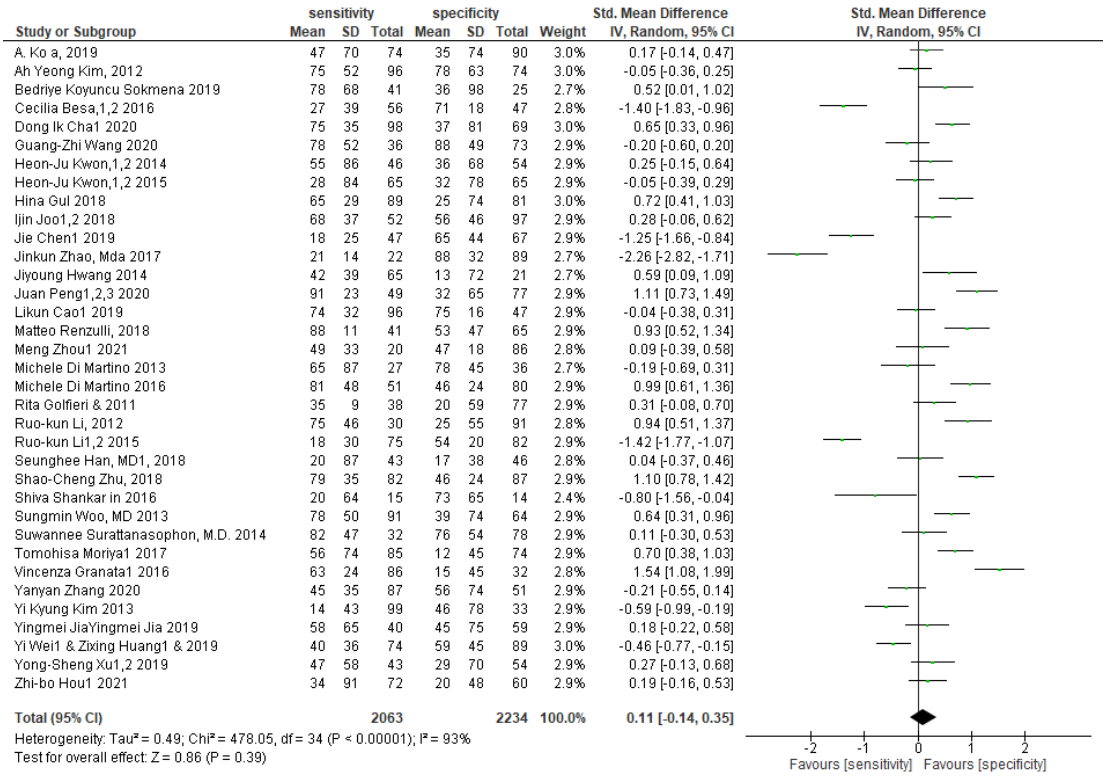

Figure 4. Forest plots of sensitivity and specificity.

Table 4. Comparison of the diagnostic performance of conventional MRI+Advance MRI.

Diagnostic methods	Pooled sensitivity (CI)	P-value	Pooled specificity (CI)	P-value
Conventional MRI	0.81 (0.77-0.94)	0.72	0.78 (0.84-0.92)	0.89
Advance MRI	0.93 (0.83-0.89)		0.86 (0.79-0.96)	

Table 5. Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.

Sequence	Valid N (list wise)
Positive	23
Negative	12
Missing	1

Table 6. Test Result Variable (s): Interpretation.

Positive if greater than or equal to	Sensitivity	1-Specificity
-1.00-	1.000	1.000
.50	.348	.250
2.00	.000	.000

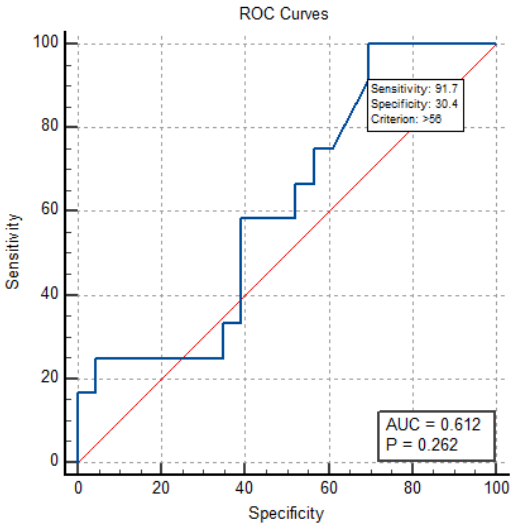

Figure 5. Sensitivity was significantly higher for studies not using hepatobiliary phase compared with those using hepatobiliary phase (P<0.001). Specificity was significantly higher for studies using a 3 T magnetic field compared with those using 1.5 T magnetic field (P=0.03). There were no significant differences in either the sensitivity or in specificity for the remaining study characteristics (all P>0.05).

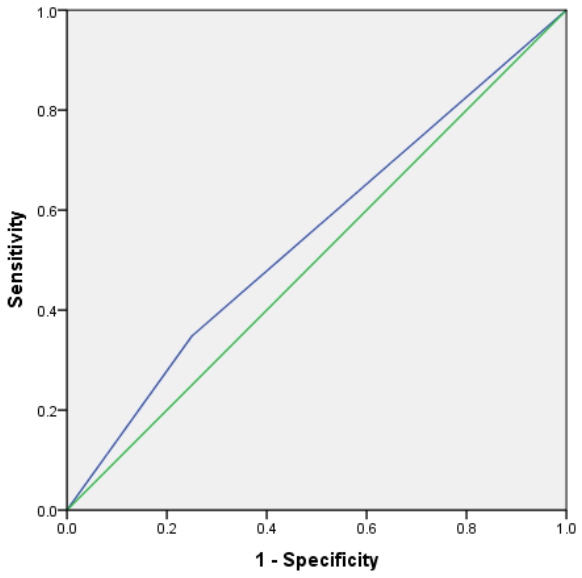

Figure 6. Diagonal segments are produced by ties.

Discussion

The aim of the present meta-analysis was to assess the diagnostic performance of advance MRI combined with conventional MRI for the diagnosis of HCC lesions. The results suggested that advance MRI with conventional MRI had a high sensitivity of 0.93 (0.83-0.89), and specificity of 0.86 (0.79-0.96). The meta-regression analysis revealed that the heterogeneity of Sensitivity was significantly higher for studies not using hepatobiliary phase compared with those using hepatobiliary phase (P<0.001). Specificity was significantly higher for studies using a 3T magnetic field compared with those using 1.5 T magnetic field (P=0.03). There were no significant differences in either the sensitivity or in specificity for the remaining study characteristics (all P>0.05). However, a threshold effect was not identified. Non-contrast enhanced Ultrasonography (US) is a common choice for HCC screening in patients who with chronic liver disease, as it is cost-effective [20]. However, there is low sensitivity when compared with that in contrast- enhanced Computer Tomography (CT) and MRI [21]. Contrast-enhanced US has emerged as a promising method to diagnose small HCCs however, additional studies are required to confirm its clinical value [20,22]. Multiple meta-analyses have found that contrast-enhanced MRI out performs contrast enhanced CT in the diagnosis of HCCs with higher sensitivity and overall accuracy [23]. Previous meta-analysis indicated that contrast-enhanced MRI had moderately high sensitivity and high specificity in the diagnosis of small HCC [24]. However, gadolinium contrast cannot be used in patients with chronic renal failure due to risk of nephrogenic systemic fibrosis and in those with history allergy to gadolinium [25]. This creates a need for imaging sequences without the use of gadolinium which can be used for diagnosing HCC in patients with contraindication for gadolinium [26]. In DCEMR, hepatic lesions, which show arterial phase enhancement without venous washout such as dysplastic nodules, and arterio- portal shunts are often encountered which hoften posea diagnostic difficulty indiscriminating HCC from these pseudo-enhancing lesions [27].

The present meta-analysis suggested that Advance MRI combined with conventional MRI increased the sensitivity and specificity in the diagnosis of HCC. However, the prognosis is poor when HCC is diag- nosed at an advanced stage. Hence, diagnosing HCC at an early stage is very important. ADC has been used to diagnose benign and malignant hepatic lesions [28].

An increasing number of studies have suggested that ADC is more accurate in grading smaller HCCs [29], and for monitoring early treatment responses of HCC to radiofrequency ablation (39).

In the 35 studies included in the present meta-analysis, one of them study Zhi-bo Hou et al. used a predetermined threshold SWI with DWI value to diagnose small HCC was found Conventional MRI, sen, spes, accuracy 81.24 83.71 80.34 and he found SWI+ DWI increase sens, spes accuracy 91.26 93.55 91.47 respectively.

Conclusion

The present meta-analysis suggests that Advance MRI may increase the sensitivity, and specificity for the diagnosis of HCCs. The aim of the present meta-analysis was to assess the diagnostic performance of advance MRI combined with conventional MRI for the diagnosis of HCC lesions. The results suggested that advance MRI with conventional MRI had a high sensitivity of 0.93 (0.83-0.89), and specificity of 0.86 (0.79-0.96).

References

1. Dominguez-Molina, Ronald Jahir, and Jose Pinto-Llerena.“Experience with Sorafenib in Patients with Advanced Hepatocellular Carcinoma Treated at the National Cancer Institute of Panama (Sorafen Study).”Markers 7 (2021): 13.
2. Zhang, Tong, Yi Wei, Xiaopeng He, and Yuan Yuan, et al.“Prediction of Remnant Liver Regeneration After Right Hepatectomy in Patients with Hepatocellular Carcinoma Using Preoperative CT Texture Analysis and Clinical Features.” Contrast Media Mol Imaging 10 (2021): 1-2.
3. Lam, Laurent, Hélène Fontaine, Marc Bourliere, and Clovis Lusivika-Nzinga, et al. “Predictive Factors for Hepatocellular Carcinoma in Chronic Hepatitis B Using Structural Equation Modeling: A Prospective Cohort Study.” Clin Res Hepatol Gastroenterol 5 (2021): 101713.
4. Mosaad, Mariam E, Abd El-Aziz, M Amany, and Walid R Abdelaziz, et al.“Role of Diffusion Weighted MRI in Assessment of Hyper Vascular Hepatic Tumors.”Egypt J Hospital Med 72 (2018): 4772-4779.
5. Gastrectomy, Sleeve, A Rottenstreich, J Shufanieh, and G Kleinstern, et al.“26th International Congress of the European Association for Endoscopic Surgery (EAES), London, United Kingdom, 30 May–1 June 2018: Oral Presentations.”Surg Endosc 32 (2018): 430-S482.
6. Jiang, Han-Yu, Jie Chen, Chun-Chao Xia, and Li-Kun Cao, et al.“Noninvasive Imaging of Hepatocellular Carcinoma: From Diagnosis to Prognosis.” World J Gastroenterol 24 (2018): 2348.
7. Lupsor-Platon, Monica, Teodora Serban, Alexandra Iulia Silion, and George Razvan Tirpe, et al.“Performance of Ultrasound Techniques and the Potential of Artificial Intelligence in the Evaluation of Hepatocellular Carcinoma and Non-Alcoholic Fatty Liver Disease.”Cancers 13 (2021): 790.
8. Waseem, Nazeeha, Kainat Saleem, Umair Waqas, and Aroosh Akhtar, et al.“Evaluation of Liver Leisons on Biphasic Computed Tomography (ct) Scan-an Observational Study.” Tomography 5 (2020): 1-2.
9. Poddar, Nishant, Boris Avezbakiyev, Zili He, and Ming Jiang, et al.“Hepatocellular Carcinoma Presenting as an Incidental Isolated Malignant Portal Vein Thrombosis.”J Gastrointest Cancer 43 (2012): 486-489.
10. Digumarthy, Subba R, Dushyant V Sahani, and Sanjay Saini.“MRI in Detection of Hepato Cellular Carcinoma (HCC).”Cancer Imaging 5 (2005): 20.
11. Tanimoto, Akihiro, Go Wakabayashi, Hiroshi Shinmoto, and Seishi Nakatsuka, et al.“Super Paramagnetic Iron Oxide-Enhanced MR Imaging for Focal Hepatic Lesions: A Comparison with CT During Arterioporto Graphy Plus CT During Hepatic Arteriography.”J Gastroenterol 40 (2005): 371-380.
12. Yilmaz, A, J Bauersachs, F Bengel, and R Büchel, et al.“Diagnosis and Treatment of Cardiac Amyloidosis: Position Statement of the German Cardiac Society (DGK).” Clin Res Cardiol 110 (2021):1-28.
13. Yu, Qian, Shan Huang, Ting-Ting Xu, and Yuan-Cheng et al. "Measuring Brown Fat Using MRI and Implications in the Metabolic Syndrome." J Magn Reson Imaging 12 (2020).
14. Pham, Trang T, Gary P Liney, Karen Wong, and Michael B Barton.“Functional MRI for Quantitative Treatment Response Prediction in Locally Advanced Rectal Cancer.” Br J Radiol 90 (2017): 20151078.
15. Cannella, Roberto, Riccardo Sartoris, Jules Grégory, and Lorenzo Garzelli, et al.“Quantitative Magnetic Resonance Imaging for Focal Liver Lesions: Bridging the Gap Between Research and Clinical Practice.”Br J Radiol 94 (2021): 20210220.
16. Stocker, Daniel, Stefanie Hectors, Octavia Bane, and Naik Vietti-Violi, et al.“Dynamic Contrast-Enhanced MRI Perfusion Quantification in Hepatocellular Carcinoma: Comparison of Gadoxetate Disodium and Gadobenate Dimeglumine.”Eur Radiol 27 (2021): 1-10.
17. Callewaert, Bram, Elizabeth AV Jones, Uwe Himmelreich, and Willy Gsell.“Non-Invasive Evaluation of Cerebral Microvasculature Using Pre-Clinical MRI: Principles, Advantages and Limitations." Diagnostics 11 (2021): 926.
18. Liberati, Alessandro, Douglas G Altman, Jennifer Tetzlaff, and Cynthia Mulrow, et al.“The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies that Evaluate Health Care Interventions: Explanation and Eaboration.”J Clin Epidemiol 62 (2009): e1-e34.
19. Lan, Hailong, Guisen Lin, and Weizhi Zhong.“A Meta-Analysis of the Added Value of Diffusion Weighted Imaging in Combination with Contrast-Enhanced Magnetic Resonance Imaging for the Diagnosis of Small Hepatocellular Carcinoma Lesser or Equal to 2 cm.” Oncol Lett 20 (2020): 2739-2748.
20. Vogel, Dechen W Tshering, Bernhard Kiss, Johannes T Heverhagen, and Katarina Benackova, et al.“Prospective Comparison of Contrast-Enhanced Ultrasound and Magnetic Resonance Imaging to Computer Tomography for the Evaluation of Complex Cystic Renal Lesions.”Urology 154 (2021): 320-325.
21. Park, Seong Ho, and Kyunghwa Han.“Methodologic Guide for Evaluating Clinical Performance and Effect of Artificial Intelligence Technology for Medical Diagnosis and Prediction.”Radiology 286 (2018): 800-809.

22. Semaan, Sahar, Naik Vietti Violi, Sara Lewis, and Manjil Chatterji, et al."Hepatocellular Carcinoma Detection in Liver Cirrhosis: Diagnostic Performance of Contrast-Enhanced CT vs. MRI with Extracellular Contrast vs. Gadoxetic Acid." Eur Radiol 30 (2020): 1020-1030.
23. Liu, Xijiao, Hanyu Jiang, Jie Chen, and You Zhou, et al."Gadoxetic Acid Disodium–Enhanced Magnetic Resonance Imaging Outperformed Multidetector Computed Tomography in Diagnosing Small Hepatocellular Carcinoma: A Meta-Analysis." Liver Transpl 23 (2017): 1505-1518.
24. Alabousi, Mostafa, and Matthew S Davenport."Use of Intravenous Gadolinium-Based Contrast Media in Patients with Kidney Disease and the Risk of Nephrogenic Systemic Fibrosis: Radiology In Training." Radiology 23 (2021): 210044.
25. Donadon, Matteo, Ezio Lanza, Bruno Branciforte, and Riccardo Muglia, et al."Hepatic Uptake Index in the Hepatobiliary Phase of Gadolinium Ethoxybenzyl Diethyl Enetriamine Penta Acetic Acid–Enhanced Magnetic Resonance Imaging Estimates Functional Liver Reserve and Predicts Post-Hepatectomy Liver Failure."Surgery 168 (2020): 419-425.
26. Xu, Peng-Ju, Fu-Hua Yan, Jian-Hua Wang, and Jiang Lin, et al. "Added Value of Breath Hold Diffusion-Weighted MRI in Detection of Small Hepatocellular Carcinoma Lesions Compared with Dynamic Contrast-Enhanced MRI Alone Using Receiver Operating Characteristic Curve Analysis." J Magn Reson Imaging 29 (2009): 341-349.
27. Guo, Meng, Hailing Zhang, Jianming Zheng, and Yangfang Liu. "Glypican-3: A New Target for Diagnosis and Treatment of Hepatocellular Carcinoma."J Cancer 11 (2020): 2008.
28. Ameli, Sanaz, Mohammadreza Shaghaghi, Mounes Aliyari Ghasabeh, and Pallavi Pandey, et al."Does the Change in Volumetric Functional MR Metrics Post-TACE Predict Histopathologic Grading of Hepatocellular Carcinoma?."Eur Radiol 30 (2020): 6709-6720.
29. Hou, Zhi-bo, Fei Zhao, Bin Zhang, and Chun-zhu Zhang."Study on Clinical Application of Susceptibility Weighted Imaging Combined with Diffusion Weighted Imaging in Patients with Liver Cirrhosis Complicated with Small Hepatocellular Carcinoma."Pak J Med Sci 37 (2021): 800.

How to cite this article: Changizi, Vahid, Ahmed Jasim Abbas, Hayder Jasim Taher and Hayder Suhail Najim, et al. "Advanced Imaging Techniques of the Magnetic Resonance in Characterization of Hepatocellular Carcinoma Type: A Systematic Review and Meta Analysis." *Clin Schizophr Relat Psychoses* 15S(2021). Doi: 10.3371/CSRP.CVAA.16.0821.