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HEPATOBILIARY-PANCREAS

# The diagnostic performance of gadoxetic acid disodium-enhanced magnetic resonance imaging and contrast-enhanced multi-detector computed tomography in detecting hepatocellular carcinoma: a meta-analysis of eight prospective studies

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## Abstract

**Aim** The purpose of this study was to determine the relative diagnostic benefit of gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)–enhanced magnetic resonance imaging (MRI) over contrast-enhanced multi-detector computed tomography (CEMDCT) for the detection of hepatocellular carcinoma (HCC).

**Methods** Two investigators searched multiple databases from inception to January 8, 2019, for studies comparing Gd-EOB-DTPA-enhanced MRI with CEMDCT in adults suspected of HCC. Two reviewers independently selected studies and extracted data.

**Results** Eight studies were included enrolling 498 patients. MRI showed significantly higher sensitivity than CT (0.85 vs. 0.68). There was no significant difference in the specificity of MRI and CT (0.94 vs. 0.93). The negative likelihood ratio and positive likelihood ratio of MRI and CT were not significantly different (0.16 vs. 0.15 and 14.7 vs. 11.2, respectively). The summary receiver operating characteristics (SROC) of MRI was higher than that of CT at 0.96 vs. 0.91. In the subgroup analysis with a lesion diameter below 2 cm, the sensitivity of MRI was significantly higher than that of CT (0.79 vs. 0.46).

**Conclusion** Gd-EOB-DTPA-enhanced MRI showed higher sensitivity and overall diagnostic accuracy than CEMDCT especially for hepatocellular carcinoma lesions smaller than 2 cm.

## Key Points

- *Gd-EOB-DTPA-enhanced MRI can detect small lesions of hepatocellular carcinoma.*
- *Gd-EOB-DTPA-enhanced MRI showed higher sensitivity and overall diagnostic accuracy than CEMDCT in patients with hepatocellular carcinoma.*
- *Eight prospective studies showed that Gd-EOB-DTPA-enhanced MRI provides greater diagnostic confidence.*

**Keywords** Hepatocellular carcinoma · Gadoxetic acid disodium · Magnetic resonance imaging · Tomography, X-ray computed · Meta-analysis

## Abbreviations

| | |
|---|---|
| CEMDCT | Contrast-enhanced multi-detector computed tomography |
| DCE | Dynamic contrast enhanced |
| FN | False negative |
| FP | False positive |
| Gd-EOB-DTPA | Gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid |
| HCC | Hepatocellular carcinoma |
| MRI | Magnetic resonance imaging |
| TN | True negative |
| TP | True positive |

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## Introduction

Hepatocellular carcinoma (HCC) can be accurately diagnosed by gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) or contrast-enhanced multi-detector computed tomography (CEMDCT) without a pathological diagnosis [1]. However, different imaging methods can give different results. Detecting small HCC is important because it can change the pre-surgical Barcelona staging of some patients by detecting potential small HCC lesions. Therefore, the diagnosis of small intra-hepatic lesions as early as possible prior to surgery is important. It is also important to accurately detect small lesions to be excised during surgery to reduce tumor recurrence and increase the overall survival [2].

Contrast-enhanced CT is a common radiological detection method for the diagnosis of HCC, but it often fails to detect small lesions in the liver. Gd-EOB-DTPA is a liver-specific contrast agent that not only shows the characteristics of extracellular contrast agents (dynamic stage) but also demonstrates those with liver-specific contrast agents (static stage). It is excreted from the body through the kidney or biliary system and is conductive to the detection and qualitative diagnosis of lesions [3].

Many studies have suggested that Gd-EOB-DTPA DCE-MRI is an effective method for the detection of small intra-hepatic lesions that cannot be diagnosed using CEMDCT, and DCE-MRI is a superior technique to CEMDCT for the detection of small intra-hepatic lesions [2, 4–10]. However, there are also some reports that Gd-EOB-MRI was not significantly superior to MDCT in detecting the sensitivity of HCC [11].

Gd-EOB-DTPA-enhanced MRI is superior to MDCT and MRI enhancement using other contrast agents for the detection and qualitative diagnosis of liver lesions [12]. However, it is uncertain whether MRI can replace CT as the preferred examination for patients who are suspected to have HCC.

**Table 1** Literature search strategy

| Step no. | Query |
|---|---|
| #1 | "Tomography, X-Ray Computed/methods"[Mesh][a] |
| #2 | "computed tomography" OR CT |
| #3 | "Magnetic Resonance Imaging"[Mesh] |
| #4 | "Magnetic Resonance" OR MR |
| #5 | "Carcinoma, Hepatocellular"[Mesh] |
| #6 | "hepatocellular carcinoma" OR HCC |
| #7 | "Gadolinium DTPA"[Mesh] |
| #8 | Gd-EOB-DTPA OR "gadoxetate disodium" OR "gadoxetic acid" |
| #9 | #1 OR #2 |
| #10 | #3 OR #4 |
| #11 | #5 OR #6 |
| #12 | #7 OR #8 |
| #13 | #9 AND #10 AND #11 AND #12 AND (English[Language]) |

[a] Medical subject headings

There is also no consensus on whether additional Gd-EOB-DTPA DCE-MRI is necessary for patients with HCC who have been diagnosed by MDCT. While a number of systematic reviews and meta-analyses have examined the performance of CT and/or MRI in the diagnosis of HCC [9, 13–19], the results of these meta-analyses have been inconsistent. All of these meta-analyses included retrospective studies but no subgroup analysis of the prospective studies. Our goal here was to compare the accuracy of Gd-EOB-DTPA, DCE-MRI, and CEMDCT in the diagnosis of HCC through this meta-analysis. All of these included prospective studies. In these studies, each patient received MRI and CT examinations successively.

## Materials and methods

### Literature search

Two independent investigators (J.L. and J.W.) conducted a systematic literature search in PubMed, EMBASE, and Cochrane Library to identify relevant articles published before January 8, 2019. We limited the language to English. The detailed search strategy and query terms are shown in Table 1.

### Study selection

The titles, abstracts, and full texts of the original articles were independently reviewed by the two investigators mentioned above to determine whether they were eligible for further quantitative analyses. Disagreements were harmonized by consensus. If consensus could not be reached, a third reviewer was consulted. The inclusion criteria were as follows: (1) The article investigated the diagnostic accuracy of Gd-EOB-DTPA-MRI and MDCT for HCC; (2) There were more than 30 cases; (3) The reference standard for HCC diagnosis was based on the following: (a) pathologic proof obtained after liver explant, resection, and/or biopsy and (b) imaging follow-up; (4) The original data are available to calculate the true-positive (TP) value, false-positive (FP) value, false-negative (FN) value, and true-negative (TN) value; (5) The article was a prospective original research; and (6) The article was in English.

The exclusion criteria included the following: (1) letters, systemic evaluation, review literature, comments, or animal models; (2) retrospective study; (3) the patient had only an MRI or only a CT; (4) multiple reports were published for the same study population, in which case only the most detailed and/or most recent publication was included; and (5) conference abstracts or non-English language papers.

## Data extraction

The following variables were extracted from each study: demographics including primary author, country of study, and year of publication and baseline characteristics of the patient including the number of patients, lesion number, age, and lesion size. The index tests (MRI vs. CT) were also extracted including TP, FP, FN, and TN.

## Imaging follow-up

For undiagnosed lesions, benign lesions were diagnosed when there was no significant change in lesions after at least 6 months of follow-up by imaging (MRI and/or CT). In dynamic monitoring, previously undiagnosed or newly diagnosed lesions were diagnosed as HCC lesions if they met the non-invasive diagnostic criteria.

## Quality assessment

The quality of all studies was evaluated using a quality assessment of diagnostic accuracy studies-2 (QUADAS-2) tool. The quality of the primary diagnostic studies was assessed through estimation of risk of bias for four domains that discuss patient selection, index test, reference standard, and flow of patients through the study and timing of the index tests and reference standard (flow and timing); each domain can be divided into three risk assessments, i.e., high, medium, and low [20].

## Statistical analysis

Forest plots of sensitivity and specificity and SROC curve were constructed using Review Manager (RevMan) (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The homogeneity test was constructed, and the sensitivity, specificity, and their 95% confidence intervals (CIs) were derived using Stata version 15.1 for Mac (64-bit Intel) (Stata, College Station, TX, USA).

Subgroup analysis was conducted according to the diameter of the lesion. This included subgroup 2 with lesions less than 2 cm and subgroup 3 with lesion diameters greater than 2 cm. Subgroup 1 was a study with high heterogeneity and was extracted from the eight overall studies. Subgroup 4 was an article with high

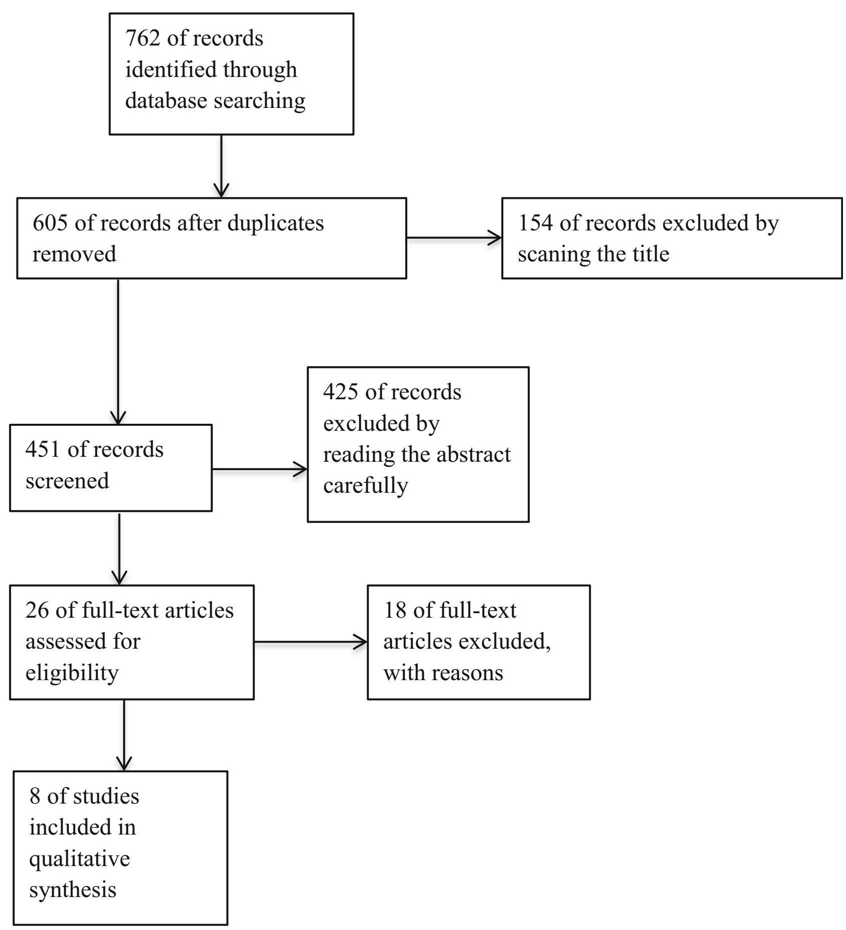



**Fig. 1** The process of study selection

heterogeneity that was extracted from four studies with lesion less than 2 cm diameters.

## Update

When we wrote the paper, Yoon's article that was published in advance on August 13, 2018, was officially published in February 2019. Therefore, we used the latter date.

## Results

The keywords and databases led to 762 potential literature citations; 154 duplicate articles were excluded. Next, after extensively reading the title and the abstract, 581 additional reports were excluded. Of these, 26 articles were selected for full-text review. A total of 18 articles were excluded after a full-paper review. The eight studies [5–7, 21–24] were finally included in the current meta-analysis. Four of them offered comparative analyses of tumors with diameters less than 2 cm. Figure 1 shows the details of the study selection process. The overall risk of bias in the eight studies is shown in Fig. 2.

### Study characteristics

The important characteristics of the studies are presented in Table 2. All studies provided information on a per-lesion basis. These studies collectively included 498 patients with 502 HCC lesions. The results of the eight reports are detailed in Table 3.

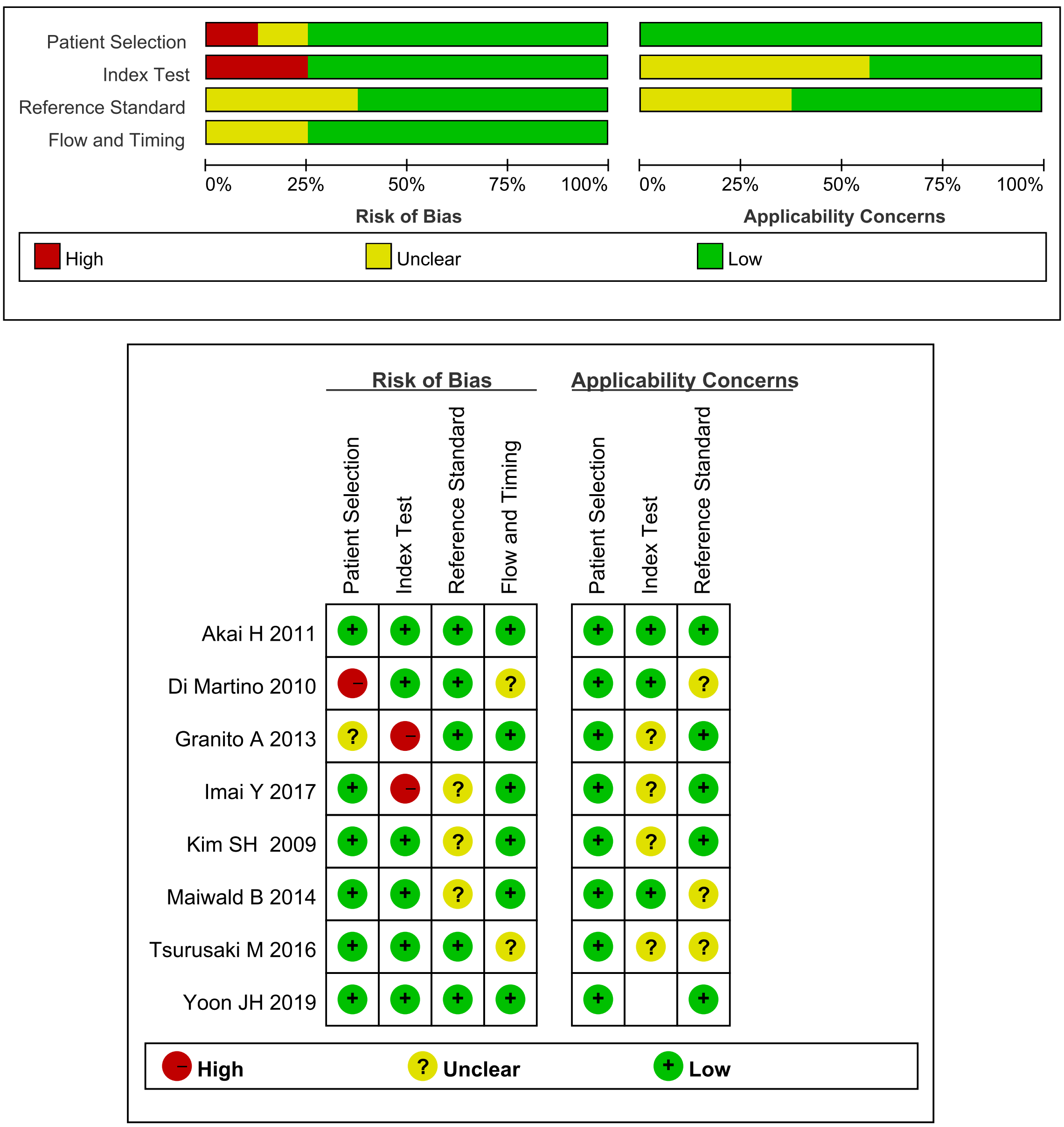



**Fig. 2** Methodological quality of the studies (QUADAS-2 results)

**Table 2** Characteristics of the included studies

| Author | Year | Patients | Lesions | HCC lesions | Lesion size (cm) | Male:female | Patient age | Gold standard | Follow-up imaging | Equipment | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | MRI | CT |
| Kim SH | 2009 | 62 | 132 | 83 | 2.9 (0.5–10.5) | 57:8 | 55 (31–67) | P(E) | > 6 months | 3.0 T | 16/40/64 |
| Di Martino | 2010 | 58 | 109 | 87 | 1.8 (0.3–7.0) | 39:19 | 63 (35–84) | P(E/B)/I | 220 days (90–370) | 1.5 T | 64 |
| Akai H | 2011 | 34 | 97 | 52 | 2.6 (0.4–15.2) | 27:7 | 65 (48–78) | P(E) | > 6 months | 1.5 | 64 |
| Granito A | 2013 | 33 | 48 | 38 | 1.8 (1.0–3.0) | 58:8 | 70 (48–74) | P(E)/I | 24 months (22–28) | 1.5 | 16 |
| Maiwald B | 2014 | 50 | 71 | 71 | 3.3 | 42:8 | 60.6 (29–84) | P(E/B)/I | 6 months | 3.0 T | 64 |
| Tsurusaki M | 2016 | 54 | 125 | 83 | 2.7 (0.5–14) | 39:15 | 63 (35–84) | P(E)/I | 12 months (12–31) | 3.0 T | 64 |
| Imai Y | 2017 | 97 | 66 | 66 | 0.9 (0.5–2.0) | 64:33 | 73 ± 9 (45–92) | P(E)/I | 385 days (86–1141) | 1.5 T/3.0 T | 64 |
| Yoon JH | 2019 | 110 | 131 | 80 | < 2 cm ($n$ = 124); > 2 cm ($n$ = 7) | 85:25 | 65.8 + 10.2 (34–89) | P(E/B) | > 6 months | 1.5 T/3.0 T | 64 |

*P*, pathology; *E*, explant; *B*, biopsy; *I*, imaging follow-up; *HCC*, hepatocellular carcinoma; *MRI*, magnetic resonance imaging; *CT*, computed tomography

## Heterogeneity test

The homogeneity test of the sensitivity and specificity of MRI and CT demonstrated significant heterogeneity ($I^2 = 83.51\%$ and $I^2 = 58.77\%$, $I^2 = 93.05\%$ and $I^2 = 69.93\%$, respectively). Due to the high heterogeneity of the eight studies, we used a method that removed them one-by-one and found that after excluding one study (Yoon 2019), the remaining seven studies showed no heterogeneity in sensitivity for MRI ($I^2 = 5.28\%$, $p = 0.39$). The sensitivity of CT still had significant heterogeneity ($I^2 = 79.62\%$). The specificity for MRI and CT showed significant heterogeneity ($I^2 = 51.68\%$, $p = 0.05$ and $I^2 = 54.56\%$, $p = 0.04$).

The sensitivity and specificity of MRI and CT were also highly heterogeneous in subgroups with tumor diameters below 2 cm ($I^2 = 77.32\%$ and $I^2 = 80.12\%$, $I^2 = 84.59\%$ and $I^2 = 35.78\%$, respectively). The heterogeneity comes mainly from the previous article. The sensitivity of MRI and CT had no significant heterogeneity after exclusion of an article.

## Evaluation of publication bias

Deek's funnel plot asymmetry test suggested that the study had no publication bias ($p = 0.23$).

## Diagnostic accuracy

The forest plots for sensitivities and specificities of MRI and CT are shown in Fig. 3, and the area under the curve (AUC) of summary receiver operating characteristics (SROC) for MRI and CT are shown in Fig. 4. Table 4 compares the diagnostic accuracy of MRI and CT in the diagnosis of HCC.

(Overall analysis) The difference in diagnostic performance was revealed by paired SROC curves between the two methods of eight studies: The area under the curve of MRI was larger than that of CT. The pooled sensitivities of MRI were significantly higher than that of CT. Likelihood ratio tests showed that there is a significant difference between the pooled sensitivities of the two tests ($p < 0.05$). The pooled specificities were similarly high ($p > 0.05$). The summarized NLRs were smaller than 1.00, and the summarized PLR of both tests were larger than 1.00 indicating informative results of both tests.

Subgroup 1 had pooled sensitivities, specificity, NLR, PLR, DOR, and AUC of MRI that were similar to the eight studies. Subgroup 2 compared the diagnostic performance of MRI and CT via subgroup tumor size. The sensitivities of both tests decreased as the diameter of lesion decreased for lesions < 2 cm. However, the sensitivity of CT was still lower than that of MRI ($p < 0.05$). The two are similar in specificity (more than 90%). Subgroup 3 had a small number of lesions: The differences in sensitivity and specificity were greater in

**Table 3** Various indicators of included literature

| Author | Year | Child-Pugh class (A/B/C) | The time interval of MRI and CT | Nation | Enrollment patients | Non-invasivediagnosis |
|---|---|---|---|---|---|---|
| Kim SH | 2009 | Unavailable | < 4 weeks | Korea | January 2007 to January 2008 | Ar |
| Di Martino M | 2010 | 30/21/7 | > 4 weeks | Italy | Consecutive 21 months (February 2007 to October 2008) | L |
| Akai H | 2011 | Unavailable | > 2 weeks | Japan | Consecutive patients (July 2008 to February 2009) | L |
| Granito A | 2013 | 28/5/0 | > 1 week | Italy | Consecutive 59 months (December 2008 to October 2013) | Ar |
| Maiwald B | 2014 | 27/16/7 | > 1 week | Germany | Unavailable | L |
| Tsurusaki M | 2016 | 53/1/0 | < 4 weeks | Japan | Nonconsecutive patients | An |
| Imai Y | 2017 | 80/17/0 | 2.2 days (0–30 days) | Ikeda | November 2010 to December 2012 | Ar |
| Yoon JH | 2019 | 99/11/0 | 13 days (0–30 days) | Korea | December 2009 to July 2012 | Ar |

*MRI*, magnetic resonance imaging; *CT*, computed tomography; *Ar*, arterial hyperenhancement/washout in the venous phase; *L*, LIRADS-4 plus LIRADS-5; *An*, any two of the five following criteria: (a) clearly visible hyperenhancement during the arterial phase, (b) hypoattenuation or hypointensity compared with the surrounding liver during portal venous or equilibrium phases (i.e., washout), (c) peripheral rim enhancement during the equilibrium phase (fibrous capsule), (d) infiltration of adjacent vessels, and (e) hypointensity during the delayed hepatobiliary phase

different studies. Subgroup 4 had pooled sensitivities, specificity, and AUC for MRI that were similar to the four studies.

## Discussion

Although there are many meta-analyses on the diagnosis of HCC via MRI and CT, none focused exclusively on prospective studies. Meanwhile, their conclusions remain controversial. Most meta-analyses indicated that MRI was superior to CT for the diagnosis of hepatocellular carcinoma [9, 13–18], but a recent meta-analysis suggested that the differences in pooled diagnostic performance are insufficient to definitively recommend MRI over CT [19]. We conducted this meta-analysis on the diagnosis of HCC by both methods, and all included reports were prospective. To the best of our knowledge, this is the first meta-analysis on HCC diagnosis using MRI with Gd-EOB-DTPA and CT where all studies were prospective.

Our results revealed that specificity of MRI with Gd-EOB-DTPA and CT in diagnosing HCC was similarly high (above 0.90 in both overall analysis and subgroup analysis). This was the same even in subgroup analyses of tumors smaller than 2 cm. In the eight studies we included, the sensitivity of MRI was significantly better than that of CT, and there was no significant difference in specificity between the two. This is similar to previous studies [15, 18, 19]. However, the sensitivity and specificity of these studies are very heterogeneous. Studies of heterogeneity are critical to understanding the possible factors affecting estimation accuracy and whether it is appropriate to evaluate a combination of different studies. We examined these studies by culling the literature individually. After excluding an article by Yoon, the remaining seven articles showed no heterogeneity in MRI sensitivity. The pooled sensitivities of MRI for the seven studies were similar to those of the eight studies (0.87 vs. 0.85). The pooled sensitivities of CT for the seven studies had a major improvement relative to the eight studies as a whole (0.75 vs. 0.69). The MRI sensitivity is still better than that of CT. The reason for the heterogeneity might be that the majority (124/131) of lesions contained in this article were smaller than 2 cm. Even so, the results of this article suggested that the sensitivity of MRI was higher than that of CT ($p < 0.05$).

CT was less sensitive to tumors smaller than 2 cm in diameter, but the sensitivity of CT still had significant heterogeneity in the seven articles. The recent meta-analysis published in *Hepatology* also showed that the sensitivity of MRI was higher than that of CT while maintaining similar specificity [20]. However, due to the high heterogeneity, the authors concluded that there was insufficient reason to recommend MRI over CT. We found that the reports they included were unfocused with poor subgroup analysis. Liu et al [9] found that Gd-EOB-DTPA-enhanced MRI demonstrated higher sensitivity and overall diagnostic accuracy than MDCT up to 2 cm.

All of these eight studies were single site. The sensitivity of MRI was better than CT in the diagnosis of HCC even for lesions smaller than 2 cm. The summary results also suggested the same thing. These eight studies (except for one [25]) reported that seven lesions were found by CT combined with contrast-enhanced ultrasound but not by MRI. All other studies showed that lesions found by CT could be found by MRI, while some lesions found by MRI could not be found by CT. More studies have further verified that Gd-EOB-DTPA DCE-MRI has obvious advantages in sensitivity and accuracy for the diagnosis of HCC compared with MDCT [2, 4, 7, 8, 14–16, 21, 26, 27]. Some studies recommend that Gd-EOB-DTPA-enhanced MRI be the first-choice imaging method for the detection of HCC and therapeutic decisions [23].

Four studies provided diagnostic analyses with tumor diameters less than 2 cm, and we conducted subgroup analysis on

**Fig. 3** Forest plots showing the sensitivity and specificity with corresponding 95% confidence intervals (CIs) for the diagnosis of HCC by MRI and CT in each study. The overall analysis included eight articles. Subgroup 1 excluded an article with high heterogeneity from eight articles. Subgroup 2 focused on the literature containing tumors smaller than 2 cm in diameter. Subgroup 3 used the literature containing tumors larger than 2 cm in diameter. Subgroup 4 excluded an article with high heterogeneity from subgroup 2

**Over all CT**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Akai H 2011 | 41 | 3 | 11 | 18 | 0.79 [0.65, 0.89] | 0.86 [0.64, 0.97] |
| Di Martino 2010 | 60 | 5 | 18 | 17 | 0.77 [0.66, 0.86] | 0.77 [0.55, 0.92] |
| Granito A 2013 | 22 | 0 | 16 | 10 | 0.58 [0.41, 0.74] | 1.00 [0.69, 1.00] |
| Imai Y 2017 | 25 | 4 | 23 | 45 | 0.52 [0.37, 0.67] | 0.92 [0.80, 0.98] |
| Kim SH 2009 | 74 | 3 | 9 | 46 | 0.89 [0.80, 0.95] | 0.94 [0.83, 0.99] |
| Maiwald B 2014 | 22 | 6 | 4 | 18 | 0.85 [0.65, 0.96] | 0.75 [0.53, 0.90] |
| Tsurusaki M 2016 | 58 | 2 | 25 | 40 | 0.70 [0.59, 0.79] | 0.95 [0.84, 0.99] |
| Yoon JH 2019 | 20 | 1 | 65 | 45 | 0.24 [0.15, 0.34] | 0.98 [0.88, 1.00] |

**Subgroup 1 MRI**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Akai H 2011 | 45 | 4 | 7 | 41 | 0.87 [0.74, 0.94] | 0.91 [0.79, 0.98] |
| Di Martino 2010 | 74 | 1 | 13 | 21 | 0.85 [0.76, 0.92] | 0.95 [0.77, 1.00] |
| Granito A 2013 | 30 | 0 | 8 | 10 | 0.79 [0.63, 0.90] | 1.00 [0.69, 1.00] |
| Imai Y 2017 | 41 | 3 | 7 | 46 | 0.85 [0.72, 0.94] | 0.94 [0.83, 0.99] |
| Kim SH 2009 | 77 | 2 | 6 | 47 | 0.93 [0.85, 0.97] | 0.96 [0.86, 1.00] |
| Maiwald B 2014 | 24 | 6 | 2 | 18 | 0.92 [0.75, 0.99] | 0.75 [0.53, 0.90] |
| Tsurusaki M 2016 | 69 | 2 | 14 | 40 | 0.83 [0.73, 0.90] | 0.95 [0.84, 0.99] |

**Subgroup 1 CT**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Akai H 2011 | 41 | 3 | 11 | 18 | 0.79 [0.65, 0.89] | 0.86 [0.64, 0.97] |
| Di Martino 2010 | 60 | 5 | 18 | 17 | 0.77 [0.66, 0.86] | 0.77 [0.55, 0.92] |
| Granito A 2013 | 22 | 0 | 16 | 10 | 0.58 [0.41, 0.74] | 1.00 [0.69, 1.00] |
| Imai Y 2017 | 25 | 4 | 23 | 45 | 0.52 [0.37, 0.67] | 0.92 [0.80, 0.98] |
| Kim SH 2009 | 74 | 3 | 9 | 46 | 0.89 [0.80, 0.95] | 0.94 [0.83, 0.99] |
| Maiwald B 2014 | 22 | 6 | 4 | 18 | 0.85 [0.65, 0.96] | 0.75 [0.53, 0.90] |
| Tsurusaki M 2016 | 58 | 2 | 25 | 40 | 0.70 [0.59, 0.79] | 0.95 [0.84, 0.99] |

**Subgroup 2 MRI**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Di Martino 2010 | 47 | 2 | 8 | 18 | 0.85 [0.73, 0.94] | 0.90 [0.68, 0.99] |
| Granito A 2013 | 16 | 3 | 5 | 4 | 0.76 [0.53, 0.92] | 0.57 [0.18, 0.90] |
| Imai Y 2017 | 41 | 0 | 7 | 46 | 0.85 [0.72, 0.94] | 1.00 [0.92, 1.00] |
| Yoon JH 2019 | 50 | 1 | 30 | 43 | 0.63 [0.51, 0.73] | 0.98 [0.88, 1.00] |

**Subgroup 2 CT**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Di Martino 2010 | 33 | 3 | 22 | 17 | 0.60 [0.46, 0.73] | 0.85 [0.62, 0.97] |
| Granito A 2013 | 11 | 0 | 10 | 3 | 0.52 [0.30, 0.74] | 1.00 [0.29, 1.00] |
| Imai Y 2017 | 25 | 4 | 23 | 45 | 0.52 [0.37, 0.67] | 0.92 [0.80, 0.98] |
| Yoon JH 2019 | 20 | 1 | 60 | 43 | 0.25 [0.16, 0.36] | 0.98 [0.88, 1.00] |

**Subgroup 3 MRI**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Di Martino 2010 | 27 | 0 | 5 | 3 | 0.84 [0.67, 0.95] | 1.00 [0.29, 1.00] |
| Granito A 2013 | 14 | 0 | 3 | 2 | 0.82 [0.57, 0.96] | 1.00 [0.16, 1.00] |
| Yoon JH 2019 | 0 | 0 | 5 | 2 | 0.00 [0.00, 0.52] | 1.00 [0.16, 1.00] |

**Subgroup 3 CT**

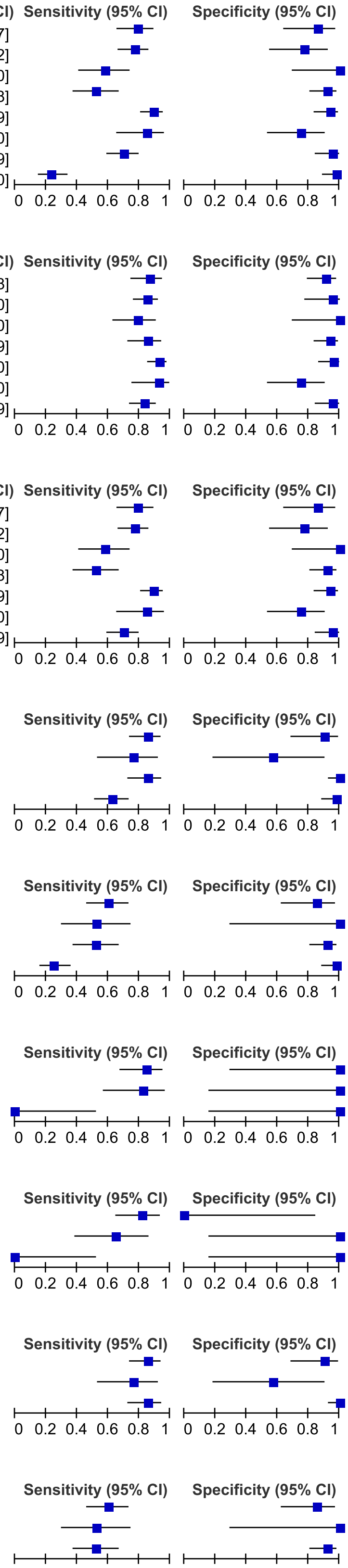
| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Di Martino 2010 | 27 | 2 | 6 | 0 | 0.82 [0.65, 0.93] | 0.00 [0.00, 0.84] |
| Granito A 2013 | 11 | 0 | 6 | 2 | 0.65 [0.38, 0.86] | 1.00 [0.16, 1.00] |
| Yoon JH 2019 | 0 | 0 | 5 | 2 | 0.00 [0.00, 0.52] | 1.00 [0.16, 1.00] |

**Subgroup 4 MRI**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Di Martino 2010 | 47 | 2 | 8 | 18 | 0.85 [0.73, 0.94] | 0.90 [0.68, 0.99] |
| Granito A 2013 | 16 | 3 | 5 | 4 | 0.76 [0.53, 0.92] | 0.57 [0.18, 0.90] |
| Imai Y 2017 | 41 | 0 | 7 | 46 | 0.85 [0.72, 0.94] | 1.00 [0.92, 1.00] |

**Subgroup 4 CT**

| Study | TP | FP | FN | TN | Sensitivity (95% CI) | Specificity (95% CI) |
|---|---|---|---|---|---|---|
| Di Martino 2010 | 33 | 3 | 22 | 17 | 0.60 [0.46, 0.73] | 0.85 [0.62, 0.97] |
| Granito A 2013 | 11 | 0 | 10 | 3 | 0.52 [0.30, 0.74] | 1.00 [0.29, 1.00] |
| Imai Y 2017 | 25 | 4 | 23 | 45 | 0.52 [0.37, 0.67] | 0.92 [0.80, 0.98] |



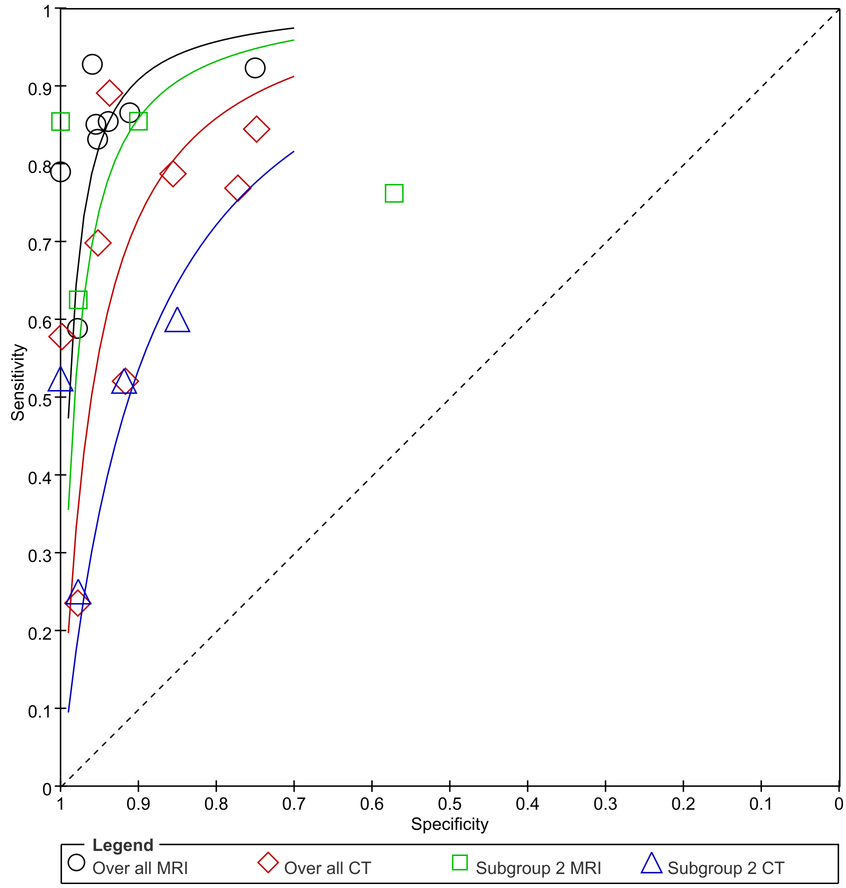



**Fig. 4** Summary receiver operating characteristic curves (SROC) of MRI and CT. A line connects the pair of points representing the tests of MRI and CT from each study. Overall analysis included all eight studies. Subgroup 2 used four studies with lesions smaller than 2 cm

these systems. Our results suggest that the sensitivity of MRI and CT decreased with decreasing tumor diameter, but the sensitivity of MRI was still significantly higher than that of CT similar to previous reports [2, 9, 15, 28]. However, the specificity of MRI and CT was the same as before and still similar and higher than 90%. Even in this subgroup analysis with tumor diameters below 2 cm, the heterogeneity remained high, and the main source was the Yoon article. The results showed that the sensitivity of MRI and CT in their article was significantly lower than those of other three studies. The sensitivity of MRI in this study was even close to that of CT in the other three studies. This might be because Imai and Granito combined their sample with contrast-enhanced ultrasound for the examination. However, there were five HCC lesions larger than 2 cm in diameter that were not diagnosed by MRI and CT in the Yoon article. There might have been other factors at play.

Some studies have shown that Gd-EOB-DTPA DCE-MRI is superior to MDCT in the diagnosis and detection of small HCC, and several reports have verified that Gd-EOB-DTPA DCE-MRI can improve the detection of early-stage HCC lesions less than 2 cm [2, 4–7, 12, 29]. Gd-EOB-DTPA DCE-MRI can detect additional HCC lesions in patients with HCC who have been diagnosed by MDCT to improve these patients prognosis [2]. In terms of economic benefits, several studies have shown

**Table 4** Comparison of the diagnostic accuracy in the detection of HCC of MRI and CT

| | Methods | Sensitivity (95% CI) | Specificity (95% CI) | AUC (95% CI) | NLR (95% CI) | PLR (95% CI) | DOR (95% CI) |
|---|---|---|---|---|---|---|---|
| Overall | MRI | 0.85 (0.77–0.90) | 0.94 (0.88–0.97) | 0.96 (0.94–0.97) | 0.16 (0.11–0.25) | 13.8 (7.5–25.2) | 84 (46–154) |
| | CT | 0. 68(0.51–0.81) | 0.92 (0.84–0.96) | 0.91 (0.88–0.93) | 0.35 (0.23–0.55) | 8.0 (4.6–13.9) | 23 (11–46) |
| Subgroup 1 | MRI | 0.87 (083–0.90) | 0.93 (0.87–0.96) | 0.92 (0.89–0.94) | 0.15 (0.11–0.19) | 11.7 (6.5–21.1) | 81 (41–160) |
| | CT | 0.73 (0.62–0.82) | 0.90 (0.83–0.94) | 0.90 (0.87–0.93) | 0.30 (0.21–0.43) | 7.1 (4.1–12.2) | 24 (11–49) |
| Subgroup 2 | MRI | 0.79 (0.67–0.87) | 0.92 (0.77–0.97) | 0.90 (0.87–0.93) | 0.23 (0.15–0.36) | 9.7 (3.4–27.6) | 42 (14–126) |
| | CT | 0.46 (0.32–0.61) | 0.93 (0.83–0.97) | 0.82 (0.78–0.85) | 0.58 (0.45–0.74) | 6.8 (3.0–15.3) | 12 (5–27) |

*AUC*, the area under the curve of summary receiver operating characteristics; *NLR*, negative likelihood ratio; *PLR*, positive likelihood ratio; *DOR*, diagnostic odds ratio; *95% CI*, 95% confidence intervals; *MRI*, magnetic resonance imaging; *CT*, computed tomography that Gd-EOB-DTPA DCE-MRI could reduce health care expenditures associated with HCC by reduced utilization of confirmatory diagnostic procedures and unnecessary treatments [30, 31]. Therefore, MRI is recommended as the preferred examination method for patients with suspected HCC.

## Conclusions and limitations

Gd-EOB-DTPA DCE-MRI is more sensitive than MDCT in the diagnosis of HCC—especially for lesions smaller than 2 cm. All studies included in this meta-analysis were prospective, but there is high heterogeneity in these studies due to various inconsistencies such as different tumor diameters and different properties of CT and MRI. Importantly, most of these studies were not stratified analysis, and more prospective studies on stratification are needed.

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## Compliance with ethical standards

**Guarantor** The scientific guarantor of this publication is Songqing He.

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**Statistics and biometry** One of the authors has significant statistical expertise.

**Informed consent** Written informed consent was not required for this study because it is a meta-analysis.

**Ethical approval** Institutional Review Board approval was not required because it is a meta-analysis.

**Methodology**
• prospective
• multicenter study

## References

1. Manini MA, Sangiovanni A, Fornari F et al (2014) Clinical and economical impact of 2010 AASLD guidelines for the diagnosis of hepatocellular carcinoma. J Hepatol 60(5):995–1001
2. Kim HD, Lim YS, Han S et al (2015) Evaluation of early-stage hepatocellular carcinoma by magnetic resonance imaging with gadoxetic acid detects additional lesions and increases overall survival. Gastroenterology. 148(7):1371–1382
3. Pascolo L, Cupelli F, Anelli PL et al (1999) Molecular mechanisms for the hepatic uptake of magnetic resonance imaging contrast agents. Biochem Biophys Res Commun 257(3):746–752
4. Yoo SH, Choi JY, Jang JW et al (2013) Gd-EOB-DTPA-enhanced MRI is better than MDCT in decision making of curative treatment for hepatocellular carcinoma. Ann Surg Oncol 20(9):2893–2900
5. Granito A, Galassi M, Piscaglia F et al (2013) Impact of gadoxetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance on the non-invasive diagnosis of small hepatocellular carcinoma: a prospective study. Aliment Pharmacol Ther 37(3):355–363
6. Yoon JH, Lee JM, Lee YJ, Lee KB, Han JK (2019) Added value of sequentially performed gadoxetic acid-enhanced liver MRI for the diagnosis of small (10-19 mm) or atypical hepatic observations at contrast-enhanced CT: a prospective comparison. J Magn Reson Imaging 49(2):574–587
7. Di Martino M, Marin D, Guerrisi A et al (2010) Intraindividual comparison of gadoxetate disodium-enhanced MR imaging and 64-section multidetector CT in the detection of hepatocellular carcinoma in patients with cirrhosis. Radiology. 256(3):806–816
8. Li J, Li X, Weng J et al (2018) Gd-EOB-DTPA dynamic contrast-enhanced magnetic resonance imaging is more effective than enhanced 64-slice CT for the detection of small lesions in patients with hepatocellular carcinoma. Medicine (Baltimore) 97(52):e13964
9. Liu X, Jiang H, Chen J, Zhou Y, Huang Z, Song B (2017) Gadoxetic acid disodium-enhanced magnetic resonance imaging outperformed multidetector computed tomography in diagnosing small hepatocellular carcinoma: a meta-analysis. Liver Transpl 23(12):1505–1518
10. Kim BR, Lee JM, Lee DH et al (2017) Diagnostic performance of gadoxetic acid-enhanced liver MR imaging versus multidetector CT in the detection of dysplastic nodules and early hepatocellular carcinoma. Radiology. 285(1):134–146
11. Joo I, Lee JM, Lee DH, Ahn SJ, Lee ES, Han JK (2017) Liver imaging reporting and data system v2014 categorization of hepatocellular carcinoma on gadoxetic acid-enhanced MRI: comparison with multiphasic multidetector computed tomography. J Magn Reson Imaging 45(3):731–740
12. Inoue T, Kudo M, Komuta M et al (2012) Assessment of Gd-EOB-DTPA-enhanced MRI for HCC and dysplastic nodules and comparison of detection sensitivity versus MDCT. J Gastroenterol 47(9):1036–1047
13. Chen L, Zhang L, Bao J et al (2013) Comparison of MRI with liverspecific contrast agents and multidetector row CT for the detection of hepatocellular carcinoma: a meta-analysis of 15 direct comparative studies. Gut. 62(10):1520–1521
14. Hanna RF, Miloushev VZ, Tang A et al (2016) Comparative 13-year meta-analysis of the sensitivity and positive predictive value of ultrasound, CT, and MRI for detecting hepatocellular carcinoma. Abdom Radiol (NY) 41(1):71–90
15. Duncan JK, Ma N, Vreugdenburg TD, Cameron AL, Maddern G (2017) Gadoxetic acid-enhanced MRI for the characterization of hepatocellular carcinoma: a systematic review and meta-analysis. J Magn Reson Imaging 45(1):281–290
16. Lee YJ, Lee JM, Lee JS et al (2015) Hepatocellular carcinoma: diagnostic performance of multidetector CT and MR imaging-a systematic review and meta-analysis. Radiology. 275(1):97–109
17. Ye F, Liu J, Ouyang H (2015) Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance imaging and multidetector-row computed tomography for the diagnosis of hepatocellular carcinoma: a systematic review and meta-analysis. Medicine (Baltimore) 94(32):e1157

18. Guo J, Seo Y, Ren S et al (2016) Diagnostic performance of contrast-enhanced multidetector computed tomography and gadoxetic acid disodium-enhanced magnetic resonance imaging in detecting hepatocellular carcinoma: direct comparison and a meta-analysis. Abdom Radiol (NY) 41(10):1960–1972
19. Roberts LR, Sirlin CB, Zaiem F et al (2018) Imaging for the diagnosis of hepatocellular carcinoma: a systematic review and meta-analysis. Hepatology. 67(1):401–421
20. Whiting PF, Rutjes AW, Westwood ME et al (2011) QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 155(8):529–536
21. Kim SH, Lee J, Kim MJ et al (2009) Gadoxetic acid-enhanced MRI versus triple-phase MDCT for the preoperative detection of hepatocellular carcinoma. AJR Am J Roentgenol 192(6):1675–1681
22. Akai H, Kiryu S, Matsuda I et al (2011) Detection of hepatocellular carcinoma by Gd-EOB-DTPA-enhanced liver MRI: comparison with triple phase 64 detector row helical CT. Eur J Radiol 80(2): 310–315
23. Maiwald B, Lobsien D, Kahn T, Stumpp P (2014) Is 3-Tesla Gd-EOB-DTPA-enhanced MRI with diffusion-weighted imaging superior to 64-slice contrast-enhanced CT for the diagnosis of hepatocellular carcinoma? PLoS One 9(11):e111935
24. Tsurusaki M, Sofue K, Isoda H, Okada M, Kitajima K, Murakami T (2016) Comparison of gadoxetic acid-enhanced magnetic resonance imaging and contrast-enhanced computed tomography with histopathological examinations for the identification of hepatocellular carcinoma: a multicenter phase III study. J Gastroenterol 51(1):71–79
25. Imai Y, Katayama K, Hori M et al (2017) Prospective comparison of Gd-EOB-DTPA-enhanced MRI with dynamic CT for detecting recurrence of HCC after radiofrequency ablation. Liver Cancer 6(4):349–359
26. Ahn SS, Kim MJ, Lim JS, Hong HS, Chung YE, Choi JY (2010) Added value of gadoxetic acid-enhanced hepatobiliary phase MR imaging in the diagnosis of hepatocellular carcinoma. Radiology. 255(2):459–466
27. Huppertz A, Balzer T, Blakeborough A et al (2004) Improved detection of focal liver lesions at MR imaging: multicenter comparison of gadoxetic acid-enhanced MR images with intraoperative findings. Radiology. 230(1):266–275
28. Imbriaco M, De Luca S, Coppola M et al (2017) Diagnostic accuracy of Gd-EOB-DTPA for detection hepatocellular carcinoma (HCC): a comparative study with dynamic contrast enhanced magnetic resonance imaging (MRI) and dynamic contrast enhanced computed tomography (CT). Pol J Radiol 82:50–57
29. Hwang J, Kim SH, Lee MW, Lee JY (2012) Small (</= 2 cm) hepatocellular carcinoma in patients with chronic liver disease: comparison of gadoxetic acid-enhanced 3.0 T MRI and multiphasic 64-multirow detector CT. Br J Radiol 85(1015):e314–e322
30. Nishie A, Goshima S, Haradome H et al (2017) Cost-effectiveness of EOB-MRI for hepatocellular carcinoma in Japan. Clin Ther 39(4):738–750 e734
31. He X, Wu J, Holtorf AP et al (2018) Health economic assessment of Gd-EOB-DTPA MRI versus ECCM-MRI and multi-detector CT for diagnosis of hepatocellular carcinoma in China. PLoS One 13(1):e0191095


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