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Magnetic Resonance Imaging-Based Surveillance of Hepatocellular Carcinoma: Current Status and Future Perspectives

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Abstract

Purpose of Review We aimed to introduce various magnetic resonance imaging (MRI)-based hepatocellular carcinoma (HCC) surveillance strategies in high-risk patients from technical to clinical viewpoints and provide guidance on selecting patients who would benefit from MRI-based surveillance.

Recent Findings MRI has recently gained attention as an HCC surveillance tool due to its superior sensitivity in detecting early-stage HCC over ultrasonography (US). However, complete-sequence contrast-enhanced liver MRI has limitations of long scan time and high cost. Abbreviated MRI (AMRI) utilizes only the essential sequences for detecting HCC and has gained popularity for reduced scan time and cost while maintaining high diagnostic performance. Three AMRI protocols have been proposed, including hepatobiliary-phase, dynamic contrast-enhanced, and non-enhanced AMRI. Herein, technical details, result interpretation, performances based on previous work, ongoing trials, and current issues regarding each MRI protocol are discussed. For maximum benefits of MRI-based surveillance, a risk-stratified approach should be undertaken to select the target population, simultaneously considering cost-effectiveness. MRI-based HCC surveillance can be beneficial for populations whose US examination has inadequate quality. Evidence of cost-effectiveness of MRI-based surveillance for high-risk patients is growing.

Summary MRI-based surveillance, particularly using AMRI, shows promise as a sensitive and cost-effective approach for early detection of HCC. Tailored approaches that take into account the patient's HCC risk and the quality of ultrasonographic images can optimize the benefits of MRI-based surveillance. Further research is needed to assess the cost-effectiveness of MRI-based surveillance strategies.

Keywords Hepatocellular carcinoma · Liver · Surveillance · Magnetic resonance imaging

Introduction

Hepatocellular carcinoma (HCC), the most common form of primary liver cancer, is a highly lethal malignancy and the third leading cause of cancer-related deaths worldwide [1, 2]. The number of new cases of liver cancer per year is predicted to increase by 55% between 2020 and 2040. Further, 1.4 million people are predicted to be diagnosed with liver cancer, and 1.3 million people are predicted to die from liver cancer in 2040 globally (56.4% more than that in 2020) [3].

The prognosis of patients with HCC is extremely poor, with a 5-year survival rate below 20% [4, 5], contributing to high premature mortality. It largely depends on the tumor stage, and curative treatments are available only for patients whose cancer is diagnosed at an early stage [4, 5]. Even for patients with early HCC, the chance of curative local ablation, such as radiofrequency ablation (RFA), the most

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cost-effective treatment for HCC [6], is often limited to very-early-stage disease (single lesion < 2 cm) [7–9], which highlights the importance of surveillance to detect HCCs at the very early stage.

Currently, biannual ultrasonography (US) is generally recommended for the surveillance of patients at risk to detect HCC at an early stage based on serum α-fetoprotein levels [10–12]. However, studies have identified that the sensitivity of US in detecting very early-stage HCC is only approximately 18–30% in patients with cirrhosis [13–16]. This low sensitivity of US for detecting very early or early HCC can be attributed to a poor sonic window caused by structural distortion of the cirrhotic liver and poor lesion conspicuity in the background of coarse liver echotexture. Approximately 20–30% of US scans are classified as inadequate for HCC surveillance in patients with cirrhosis [17, 18]. The effectiveness of HCC detection using US is further constrained in patients with obesity and steatohepatitis [19, 20].

These limitations of US highlight the requirement of novel surveillance strategies for a selected group of patients. Thus, the recently updated international guidelines allow the use of alternative imaging tools, such as contrast-enhanced US, computed tomography (CT), or magnetic resonance imaging (MRI), for HCC surveillance in patients with a high probability of having an inadequate US report [10–12]. Among these surveillance tools, MRI is the most promising tool owing to its superior diagnostic performance and lack of radiation exposure, but MRI surveillance is limited by its higher cost compared to that of US. Nonetheless, the cost-effectiveness of cancer screening programs greatly relies on the incidence of cancer and sensitivity of the screening test [21]. Therefore, using an expensive but highly sensitive test (e.g., MRI) for cancer screening may be justified in a population with a high risk of cancer [22–24].

In this review, we introduce MRI as an emerging imaging surveillance tool for HCC. We provide an overview of technical details, interpretation of results, performances based on previous work, introduction of ongoing trials, and current issues regarding various MRI-based surveillance strategies. Additionally, we summarize the results of cost-effectiveness studies on MRI-based surveillance and provide guidance on how to select patients for an MRI surveillance program.

Types of MRI for HCC Surveillance

For HCC surveillance, several MRI protocols can be introduced, which can be classified as complete MRI and abbreviated MRI (AMRI). Complete MRI is a conventional form of liver MRI used for the evaluation and diagnosis of focal hepatic lesion in daily clinical practice. It is commonly composed of approximately ten MRI sequences, usually enhanced with intravenous contrast agents. Despite excellent diagnostic performance, it requires long acquisition time and high cost, which mitigate its practicality in a surveillance setting. AMRI has been proposed as an alternative surveillance tool. It is a shortened version of complete MRI and includes only two or three essential imaging sequences focusing on detection rather than characterization of newly appeared focal hepatic lesions.

Complete MRI

Complete MRI typically includes T1-weighted dual gradient-echo in- and out-of-phase imaging (dual gradient echo imaging), diffusion-weighed imaging (DWI), T2-weighted imaging (T2WI) with various echo times, and dynamic contrast-enhanced T1-weighted imaging. Each imaging sequence serves a unique purpose in detecting and characterizing focal hepatic lesions in complete MRI. Table 1 summarizes the major role of each imaging sequence comprising complete liver MRI. Figure 1 shows a representative example of typical HCC.

In complete MRI, intravenous contrast media are crucial for detecting and characterizing focal hepatic lesions. Two types of intravenous gadolinium-based contrast media are available in liver MRI: liver-specific contrast media and extracellular contrast media (ECCM). Gadoxetic acid (Eovist® or Primovist®, Bayer) is a widely used liver-specific contrast medium that offers both hemodynamic and functional information of focal hepatic lesions and the hepatobiliary system. It is taken up by the functioning hepatocytes and excreted into the biliary system. Thus, approximately 20 min after injection, the hepatobiliary-phase (HBP) image is obtained. On HBP imaging, most focal liver lesions, including HCC, appear hypointense compared to the strongly enhancing liver parenchyma, thereby providing high lesion detectability. HBP imaging is considered the most sensitive MRI sequence for detecting HCC [25, 26]. However, HBP imaging is also the primary factor causing the lengthy scanning time required for complete gadoxetic acid-enhanced MRI, as patients should wait in the MRI machine for 20 min after contrast agent administration. In contrast, ECCM distributes only in the extracellular space, similar to CT contrast media, thereby providing only the hemodynamic information of the focal lesion.

Complete liver MRI using gadoxetic acid or ECCM has demonstrated excellent performance in HCC surveillance for high-risk patients [13, 27]. In a study comparing US and complete gadoxetic acid-enhanced MRI [13••], of 423 high-risk patients with cirrhosis, 48 HCCs were diagnosed in 43 patients during 1057 screening rounds using paired US and MRI at 6-month intervals. Most (97.7%) patients with HCC had a very early or an early-stage disease according to the Barcelona Clinic Liver Cancer staging system [28]. In this study, the sensitivity of MRI (86.0%) was significantly higher than that of US (27.9%; $P < 0.001$) for detecting

Table 1 Role of each imaging sequence in complete liver MRI

	T1WI IP/OP	DWI	T2WI	T1WI DCE	HBP imaging
Major function	· Lesion characterization	· Lesion detection	· Lesion characterization	· Lesion characterization	· Lesion detection
Details	· Assessment of fat and iron contents in the liver and focal liver lesions	· Detection of focal hepatic lesions	· Identification of definitely benign lesions showing bright SI*	· Assessment of hemodynamic information of focal liver lesions · Assessment of imaging hallmarks of HCC	· Detection of focal hepatic lesions · Assessment of liver function
Appearance of HCC	· Mostly hypointense · Signal drop in OP images in fat-containing HCC	· High SI on high *b*-value DWI (restricted diffusion)	· Mild to moderately high SI	· Arterial-phase hyperenhancement and washout appearance	· Typically hypointense (may be hyperintense in rare cases)

*Definitely benign lesion, including typical hepatic cyst and hemangioma

DCE, dynamic contrast-enhancement; *DWI*, diffusion-weighted imaging; *HBP*, hepatobiliary-phase; *HCC*, hepatocellular carcinoma; *IP/OP*, in-phase/opposed phase; *SI*, signal intensity; *T1WI*, T1-weighted imaging; *T2WI*, T2-weighted imaging

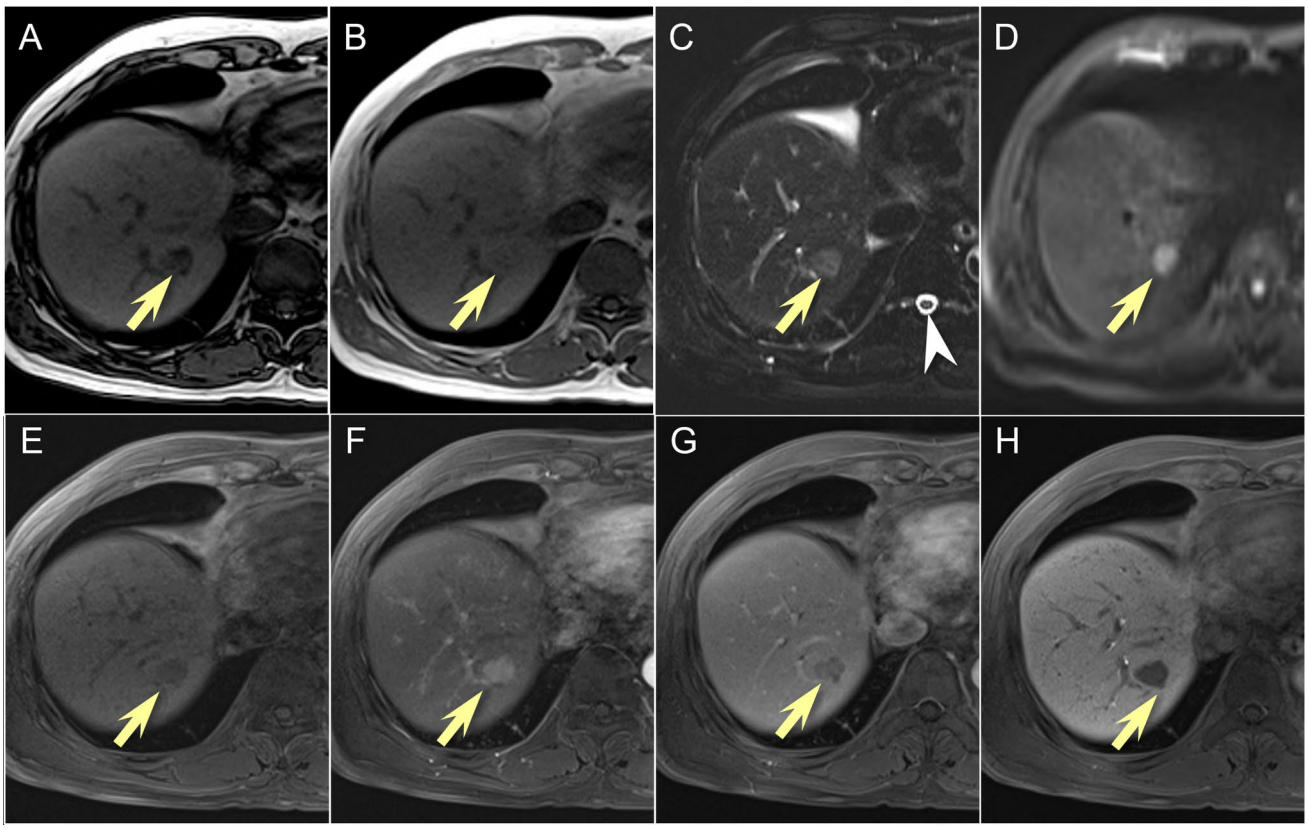

Fig. 1 Typical appearance of hepatocellular carcinoma (HCC) in complete gadoxetic acid-enhanced liver MRI. In a 55-year-old man with hepatitis B-associated liver cirrhosis, a 1.6-cm HCC is seen in segment VII of the liver (arrows). In the T1-weighted opposed-phase image (**A**), the HCC exhibits a signal drop compared to that in the T1-weighted in-phase image (**B**), suggesting the presence of intralesional fat. **C** In the fat-saturated T2-weighted image (**C**), the HCC appears only mildly hyperintense, whereas the cerebrospinal fluid in the spinal canal exhibits a much brighter signal intensity (arrowhead). In the diffusion-weighted image (**D**) with a *b*-value of 900 s/mm^2, the HCC exhibits restricted diffusion. In the dynamic contrast-enhanced T1-weighted images (**E**–**G**), the HCC exhibits hypointensity in the precontrast image (**E**), arterial-phase hyperenhancement (**F**), and washout appearance in the portal venous phase (**G**), which are typical imaging findings of HCC. In the hepatobiliary-phase image (**H**), the HCC appears markedly hypointense and is well-discriminated from the adjacent hyperintense liver parenchyma

HCC. The false-positive rate was considerably lower for MRI (3.0%) than that for US (5.6%; $P = 0.004$). This study highlighted the superior performance of complete gadoxetic acid-enhanced MRI over US in detecting early HCCs in high-risk patients with cirrhosis, which can lead to a higher probability of curative treatment and improved patient survival. Another study on complete MRI using ECCM [27] demonstrated its high surveillance performance. In this study, 294 patients with liver cirrhosis underwent annual liver MRI using ECCM for HCC surveillance between 2008 and 2017, and 35 HCCs were diagnosed. MRI showed a sensitivity of 83.3% and specificity of 95.4% in detecting early-stage HCC.

Despite the high diagnostic performance of complete MRI, long acquisition time and high cost limit its widespread use in the surveillance setting. The issue of cost-effectiveness of MRI-based surveillance will be discussed later in this article.

AMRI

Currently, three AMRI protocols have been proposed: gadoxetic acid-enhanced MRI with HBP imaging (HBP-AMRI), dynamic contrast-enhanced MRI using ECCM (DCE-AMRI), and non-enhanced MRI (NE-AMRI; Table 2).

HBP-AMRI Using Gadoxetic Acid

The imaging sequences of HBP-AMRI include HBP imaging, DWI, and T2WI. HBP-AMRI focuses on the detection rather than characterization of a focal lesion and reduces scan time by omitting dynamic contrast-enhanced imaging. HBP imaging [25, 26] and DWI [29–32] play a critical role in detecting HCC, as these two sequences are the most sensitive for finding focal hepatic lesions. T2WI is essential for excluding common benign lesions (such as hemangiomas or cysts) that may mimic HCC on HBP imaging or DWI.

The workflow can be simplified by administering gadoxetic acid in the waiting area. Patients can enter the MRI examination room 15–20 min after the injection to begin scanning. The image acquisition time of HBP-AMRI is less than 15 min, including the set-up time [33–35]. The most time-consuming sequence in this type of AMRI is DWI, whose acquisition time is several minutes depending on the number of *b*-values [36]. However, with the advancement of imaging techniques and application of simultaneous multi-slice [37–39] or deep learning, the examination time may soon become shorter.

Each HBP-AMRI examination can be reported as "negative," "subthreshold," or "positive." An examination with liver observation(s) ≥ 10 mm and not definitely benign (i.e., diffusion restriction or mild to moderate T2 hyperintensity or HBP hypointensity) or with a thrombus in a vein should be considered as "positive" and requires recall tests (Table 3; Fig. 2). The quality of HBP images should also be assessed and reported, as it can impact the lesion conspicuity [40, 41]. Standardized reporting and image quality classification for liver observations detected on HBP-AMRI are recommended and described in detail elsewhere [42].

Table 2 Summary of AMRI approaches for HCC surveillance

	HBP-AMRI	DCE-AMRI	NE-AMRI
Sequences	HBP, DWI, T2WI	Pre- and post-contrast T1WI (AP, PVP, DP/TP)	DWI, T2WI, optional T1W IP/OP
Scan time*	<15 min	<15 min	<15 min
Strength	· Highest sensitivity among AMRI approaches	· No requirement of a recall test after positive results · Evaluation of vascular thrombus	· Most time- and cost-saving · No contrast agent-related issues
Weakness	· Relatively high false-positives · Additional recall tests required after a positive result · Quality of HBP imaging influenced by liver function · Potential harms related to the contrast agent	· Narrow time window for the arterial phase · No evaluable ancillary imaging features on T2WI or DWI · Potential harms related to the contrast agent	· Heavily dependent on DWI for lesion detection, which is prone to artifacts · Additional recall tests required after positive results

*Reported values from the literature including the set-up time (i.e., room turnover, installation, calibration, sequence preparation, and intravenous line placement if required).

AMRI, abbreviated magnetic resonance imaging; *AP*, arterial phase; *DCE*, dynamic contrast-enhanced; *DP*, delayed phase; *DWI*, diffusion-weighted imaging; *HBP*, hepatobiliary-phase; *IP/OP*, in/opposed phase; *NE*, non-enhanced; *PVP*, portal venous phase; *TP*, transitional phase; *T1W*, T1-weighted; *T2WI*, T2-weighted imaging

Table 3 Positive criteria and recall strategy of each AMRI strategy

	HBP-AMRI	DCE-AMRI	NE-AMRI
Positive criteria	· Observation(s) ≥10 mm, not definitely benign* · Changes in imaging characteristics† or threshold growth‡ of previous subthreshold observation(s) · Thrombus in a vein	· Observation(s) ≥10 mm, showing arterial-phase hyperenhancement with washout appearance	· Observation(s) ≥10 mm, not definitely benign* · Changes in imaging characteristics† or threshold growth‡ of previous subthreshold observation(s) · Thrombus in a vein
Recall strategy for positive observation	· Dynamic CT or MRI (only dynamic enhanced images required)§	· Not required in the case of definite HCC · Second-look HBP-AMRI or NE-AMRI may be considered to increase sensitivity	· Dynamic CT or MRI (only dynamic enhanced images required)§

*The term "not definitely benign" refers to diffusion restriction, mild to moderate T2 hyperintensity, or HBP hypointensity

†Any new appearance of not-definitely-benign characteristics

‡Size increase by ≥50% in ≤6 months

§In the case of MRI, T2-weighted imaging, diffusion-weighted imaging, and HBP imaging may be omitted. For the MRI contrast agent, extracellular contrast media would be preferred over gadoxetic acid

AMRI, abbreviated magnetic resonance imaging; *CT*, computed tomography; *DCE*, dynamic contrast-enhanced; *HBP*, hepatobiliary-phase; *NE*, non-enhanced

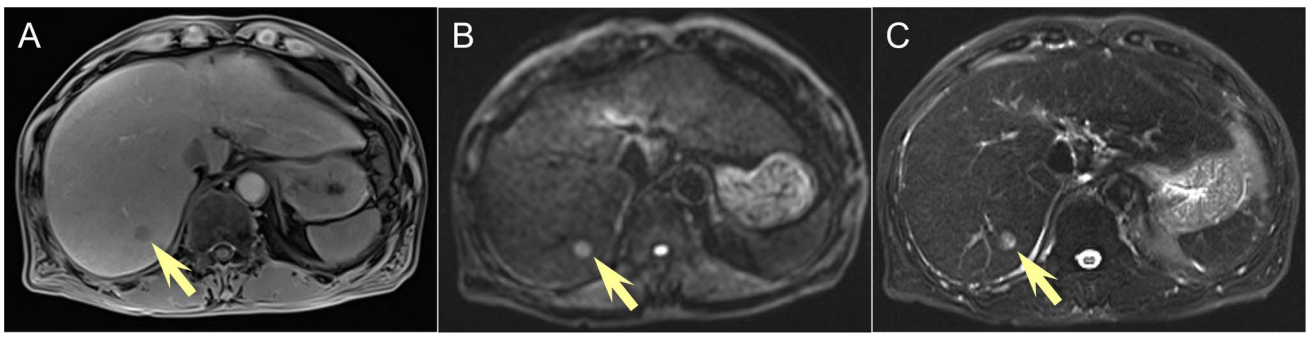

Fig. 2 Positive finding on hepatobiliary-phase abbreviated magnetic resonance imaging (HBP-AMRI). In a 56-year-old man with hepatitis B-associated liver cirrhosis, HBP imaging (**A**) shows a 1.2-cm hypointense observation in liver segment VII (arrow). This lesion shows restricted diffusion on diffusion-weighted imaging (**B**, *b*-value = 900 s/mm^2, arrow) and mildly high signal intensity on T2-weighted imaging (**C**, arrow), which are positive findings on surveillance. Complete gadoxetic acid-enhanced MRI confirmed the diagnosis of hepatocellular carcinoma (not shown)

To date, five retrospective studies [33, 34, 43–45] have evaluated the performance of HBP-AMRI in a surveillance setting for at-risk patients with no history of HCC (Table 4). The reported per-patient sensitivity ranged from 80.8 to 92.0%, while the specificity ranged from 91.0 to 95.6%. According to a recent meta-analysis by Gupta et al. [50], the pooled sensitivity and specificity of HBP-AMRI from the six studies in surveillance or diagnostic settings [33, 34, 43, 44, 51, 52] were 86% and 94%, respectively. Although no prospective study has been published, a randomized clinical trial is underway in Korea (KCT0007417, https://trialsearch.who.int/Trial2.aspx?TrialID=KCT0007417) to prove the clinical feasibility of HBP-AMRI over US.

Several issues are associated with using HBP-AMRI for HCC surveillance. First, the incidence of false-positive results may be relatively high on HBP imaging. HBP hypointensity can be observed in "any" focal hepatic lesion with a reduced expression of the organic anion–transporting polypeptide transporter [53]. As a result, not only HCC but also precancerous lesions can show HBP hypointensity [53–55]. Discriminating the malignant HBP hypointense lesions from precancerous HBP hypointese lesions may not always be possible in the absence of hemodynamic information. The impact of relatively low specificity resulting from false-positives should be considered when implementing HBP-AMRI as an HCC surveillance tool [56]. Second, recall tests are always necessary if a "positive" observation is detected on HBP-AMRI, as the vascular profiles of lesions essential for the HCC diagnosis cannot be evaluated with HBP-AMRI alone. Recall imaging tests should include

Table 4 Summary of published AMRI studies on HCC surveillance settings

Study	Year	Study design	Country	Sample size	M/C Etiology (%)	LC (prevalence, %)	HCC (prevalence, %)	Sens (%)	Spec (%)	Detected HCC size (cm)	Sequences
HBP-AMRI											
Marks et al. [43]	2015	R	USA	298	HCV (51.0)	NR	16.4	83.7	93.2	1.0–1.9: 28.6%, ≥2.0: 71.4%	HBP, DWI, T2WI
Tillman et al. [44]	2018	R	USA	79	HBV (41.8)	64.6	16.5	85.2	NR	Median, 2.1 (range, 1.1–10)	HBP, T2WI
Brunsing et al. [33]	2019	R	USA	141	HCV (42.6)	92.9	8.5	92.0	91.0	Range, 1.1–4.3	HBP, DWI, T2WI
Vietti Violi et al. [34]	2020	R	USA	237	HCV (25.7)	87.3	5.5	80.8	94.9	Mean, 3.4 (range, 1–12)	HBP, DWI, T2WI
Park et al. [45•]	2021	R	Korea	382	HBV (72.3)	100.0	11.3	86.0	95.6	Mean, 1.6	HBP, DWI, T2WI
NE-AMRI											
Vietti Violi et al. [34]	2020	R	USA	237	HCV (25.7)	87.3	5.5	61.5	95.5	Mean, 3.4 (range, 1–12)	DWI, T2WI
Park et al. [46]	2020	R	Korea	382	HBV (72.3)	100.0	11.3	79.1	97.9	Mean, 1.6	DWI, T2WI
Ahmed et al. [47]	2020	P	Egypt	41	HCV (100.0)	100.0	24.3	100.0	100.0	NR	DWI, T2WI
Sutherland et al. [48]	2017	P	Australia	192	HBV (56.0)	NR	3.0	83.0	98.0	Range, 0.8–3.1	DWI
MAGNUS-HCC [49]	2020	P	Korea	161	HBV (72.3)	100.0	19.3	71.0	NR	NR	DWI, T2WI, T1W IP/OP

AMRI, abbreviated magnetic resonance imaging; *DWI*, diffusion-weighted imaging; *HCC*, hepatocellular carcinoma; *HBP*, hepatobiliary-phase; *IP/OP*, in/opposed phases; *LC*, liver cirrhosis; *M/C*, most common; *NE*, non-enhanced; *NR*, not reported; *P*, prospective; *R*, retrospective; *Sens*, sensitivity; *Spec*, specificity

dynamic contrast-enhancement phases. Both dynamic contrast-enhanced CT and MRI can serve as confirmatory tests. Park et al. [57] suggested that dynamic CT can be used as a diagnostic test for hepatic nodules detected on HBP-AMRI. When MRI is used, imaging sequences that have been evaluated on HBP-AMRI are not necessarily repeated; instead, only dynamic contrast-enhanced sequences are sufficient for the characterization of the nodules. Regarding the choice of the intravenous contrast agent for confirmatory MRI, ECCM is preferred over gadoxetic acid to more reliably assess arterial-phase hyperenhancement [58–62]. Table 3 shows the recommended recall strategy. Another issue with HBP-AMRI is that the quality of HBP imaging is considerably influenced by liver function, which may lead to poor hepatic enhancement during HBP imaging and hinder the detection of HCC in patients with decompensated cirrhosis [40, 41] (Fig. 3). Finally, concern is growing about the potential risks associated with gadolinium-based contrast agents, such as nephrogenic systemic fibrosis and gadolinium retention in human tissue [63, 64]. Considering the repetitive nature of surveillance tests, this issue cannot be easily disregarded.

Dynamic Contrast-Enhanced (DCE)-AMRI Using ECCM

DCE-AMRI is composed of unenhanced and post-contrast T1WI scans in the arterial, portal venous, and delayed phases acquired after administrating ECCM (Fig. 4). DCE-AMRI can shorten the scan time by omitting other sequences, such as DWI or T2WI. The image acquisition time for DCE-AMRI is approximately <15 min, including the set-up time [34, 65]. The major advantage of this strategy is that it can demonstrate the major features essential for a definitive diagnosis of HCC. If the lesion clearly shows the imaging hallmark of HCC [12, 66], the diagnosis with DCE-AMRI can be made without further recall tests. DCE-AMRI also offers the advantage of detecting and characterizing vascular thrombi, which could be missed on HBP-MRI or NE-MRI.

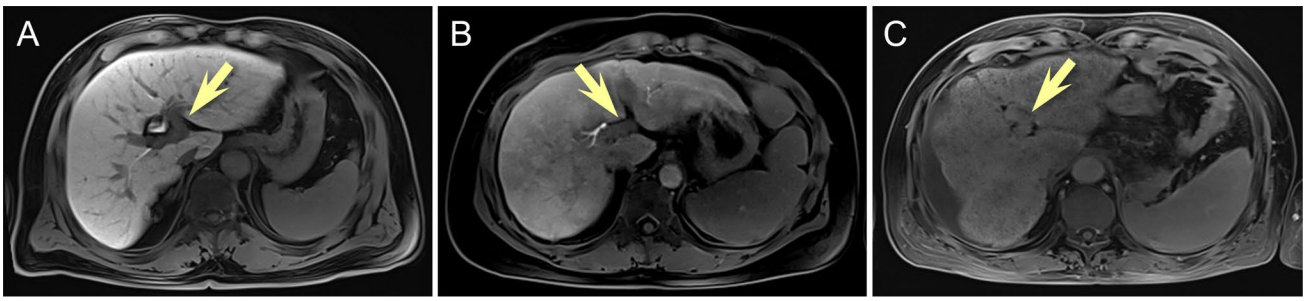

Fig. 3 Different qualities of hepatobiliary-phase (HBP) imaging based on liver function. As liver function declines, the uptake of gadoxetic acid by hepatocytes decreases, resulting in a low quality of the HBP image. In the case of poor quality of the HBP image in which the liver-to-lesion contrast is considerably reduced, the high sensitivity advantage of the HBP image cannot be utilized. **A** Adequate image quality of HBP imaging: The liver signal intensity (SI) is considerably higher than that of the vessel (arrow), and the liver texture is only mildly heterogeneous. This level of HBP imaging quality is unlikely to obscure liver lesions < 1.0 cm. **B** Intermediate image quality of HBP imaging: The liver SI is slightly higher than that of the vessel (arrow) and moderately heterogeneous. With this level of HBP imaging quality, the sensitivity to detect liver lesions <1.0 cm is likely to be reduced. **C** Inadequate image quality of HBP imaging: The liver SI is the same as or even lower than that of the vessels (as noted by the extrahepatic portal vein indicated by the arrow). With this level of HBP imaging quality, the sensitivity to detect liver lesions ≥1.0 cm is likely to be reduced

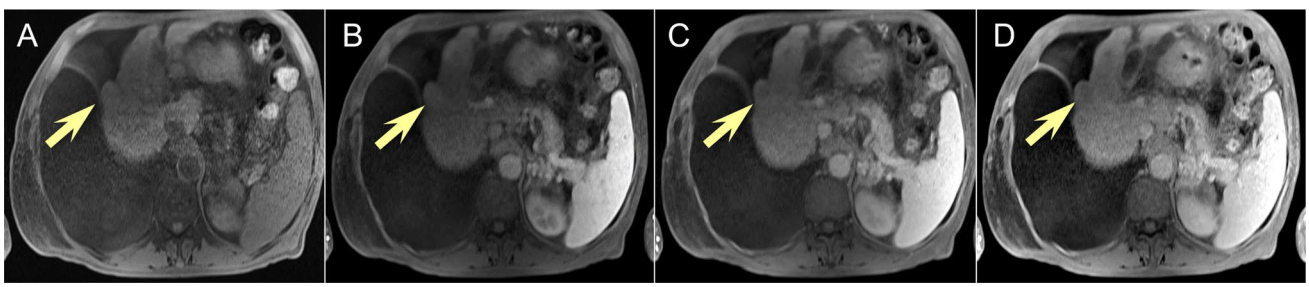

Fig. 4 Positive dynamic contrast-enhanced abbreviated magnetic resonance imaging (DCE-AMRI) using extracellular contrast media. In a 62-year-old man with alcoholic liver cirrhosis, the precontrast T1-weighted (**A**) and arterial-phase (**B**) images demonstrate a 2.0-cm lesion with arterial-phase hyperenhancement in liver segment IV (arrows). The portal venous (**C**) and delayed (**D**) phase images show washout appearance of the lesion (arrows), meeting the criteria for definite hepatocellular carcinoma

Studies on the performance of DCE-AMRI are scarce, particularly in the surveillance setting. Since 2017, two retrospective studies [65, 67] have investigated the value of DCE-AMRI in detecting HCC in the diagnostic setting. Lee et al. [65] evaluated the differences in Liver Imaging Reporting and Data System (LI-RADS) categorization between DCE-AMRI and complete MRI using ECCM and showed only 5% changes in the LI-RADS categorization. This study did not evaluate the diagnostic performance of DCE-AMRI. Khatri et al. [67] reported a high per-patient sensitivity of 92.1% and specificity of 88.6%, but the high incidence of HCC in the study (32.6%) suggests that this study was done in a diagnostic setting. The performance of DCE-AMRI in the surveillance setting requires to be further validated prospectively. A prospective study to prove the clinical feasibility of DCE-AMRI over US in Korea (NCT03731923) is ongoing.

If the lesion meets the imaging criteria for definite HCC on DCE-AMRI, no further confirmatory test is required. For probable HCC (i.e., LI-RADS category 4) or indeterminate observations (i.e., LI-RADS category 3) [12, 66] on DCE-AMRI, further diagnostic tests for these lesions may vary based on regional differences in the clinical practice [12, 68, 69]. It should be tailored through multidisciplinary discussions for each patient. In the surveillance setting wherein the sensitivity is prioritized over specificity, a second-look recall HBP-AMRI or NE-AMRI may be used for the follow-up examination to increase the sensitivity [70]. If specificity is valued more than sensitivity, such as in the diagnostic setting, further management is likely to adhere to the LI-RADS recommendations [69].

Optimal arterial-phase imaging is essential in DCE-AMRI, as lesion characterization relies primarily on the presence of arterial-phase hyperenhancement. Obtaining optimal arterial-phase imaging can be challenging because of its narrow time window. Furthermore, the absence of additional sequences, such as DWI and T2WI, makes it impossible to apply ancillary features favoring HCC or malignancy and is likely to reduce the sensitivity. Similar to HBP-AMRI, DCE-AMRI cannot be free from gadolinium-related issues.

Non-enhanced AMRI

NE-AMRI is the simplest AMRI strategy. It includes DWI and T2WI with optional T1-weighted in/opposed imaging (dual-echo imaging; Fig. 5). Unlike contrast-enhanced AMRI protocols, NE-AMRI does not require intravenous contrast injections and is free from the costs and concerns related to gadolinium use.

As mentioned earlier, DWI has shown excellent performance in detecting hepatic malignancy [29–32, 46]. As NE-AMRI relies vastly on DWI for lesion detection, high-quality DWI images are crucial. The role of T2WI in HBP-AMRI is to increase specificity by excluding common benign lesions rather than to detect the lesion as well as to detect focal hepatic lesions.

Similar to the two aforementioned AMRI types, NE-AMRI has demonstrated acceptable performance for HCC surveillance. In a recent clinical trial (MAGNUS-HCC, NCT02551250) [49], the diagnostic performance

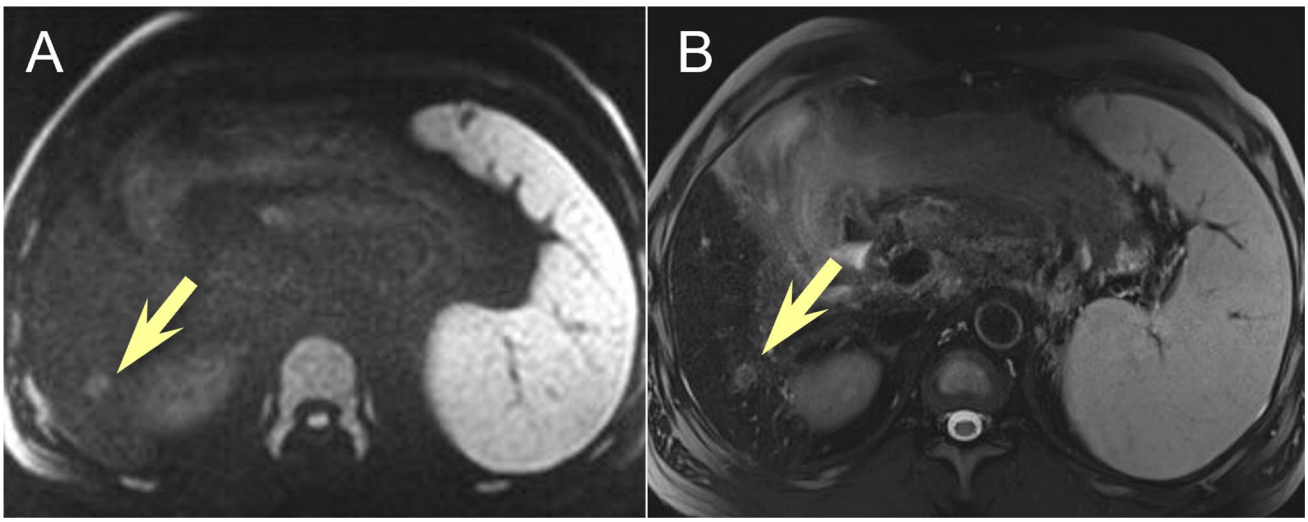

Fig. 5 Positive non-enhanced abbreviated magnetic resonance imaging (NE-AMRI). A 49-year-old man with alcoholic liver cirrhosis. The diffusion-weighted (**A**, *b*-value = 900 s/mm^2) and T2-weighted (**B**) images demonstrate a 1.0-cm hyperintense nodule in liver segment VI (arrows). On complete gadoxetic acid-enhanced MRI, hepatocellular carcinoma was confirmed (not shown)

of annual NE-AMRI and semiannual US in patients with cirrhosis was compared, and the per-patient sensitivity of annual NE-AMRI was 71.0%, higher than the 45.2% sensitivity of semiannual US. In this study, a method of alternating US and NE-AMRI every 6 months was simulated, and this method showed a sensitivity of 83.9%, suggesting that alternating between US and NE-AMRI may be a good approach. Several retrospective studies [34, 46–48] have evaluated the performance of NE-AMRI in the surveillance setting. The sensitivity and specificity were 61.5–100% and 95.5–100%, respectively. One study comparing NE-AMRI (T2WI plus DWI) and US in the surveillance setting [46] showed significantly higher per-examination sensitivity of NE-AMRI (79.1%) compared with that of US (27.9%) as well as significantly higher specificity compared with that of US (97.9% vs. 94.5%). An ongoing randomized clinical trial from France (FASTRAK study; NCT05095714) is comparing the performance of NE-AMRI and US as surveillance tools in patients at a high risk of HCC (>3% per year). Another ongoing prospective multicenter study from Korea (NCT02551250) is comparing the effectiveness of NE-AMRI and dynamic CT as post-treatment surveillance tools in patients who received curative treatment for HCC and have remained recurrence-free for 2 years thereafter.

An issue with NE-AMRI is its relatively low sensitivity. The reported sensitivity of NE-AMRI ranges from 61.5 to 100%, while that of HBP-AMRI ranges from 80.8 to 92.0% [34, 46–48]. For example, in Vietti et al.'s study [34], the sensitivity of HBP-AMRI was 80.8%, while that of NE-AMRI was 61.5%, highlighting the importance of HBP imaging to increase sensitivity. However, in the same study, the specificity of NE-AMRI (95.5%) was slightly higher than that of HBP-AMRI (94.9%). The specificity of NE-AMRI ranged from 95.5 to 100.0%, higher than that of HBP-AMRI, from 91.0 to 95.6%. In addition, similar to HBP-AMRI, a recall test is necessary for those with a positive result on NE-AMRI. Finally, NE-AMRI heavily depends on DWI for lesion detection, which is prone to artifacts, such as susceptibility artifacts.

Cost-Effectiveness of MRI-Based Surveillance

Evidence is mounting to support risk-stratified HCC surveillance strategies, with more sensitive tests, such as MRI, being reserved for patients at a high risk [13, 16, 23, 24, 46, 49]. The incidence of HCC and sensitivity of the surveillance test are the strongest determinants of the cost-effectiveness of HCC surveillance tests. Paradoxically, the sensitivity of US is particularly impaired in patients at the highest risk of developing HCC because of the nodular cirrhotic liver. In contrast, the higher detection rates of very-early-stage HCC by MRI allows more patients to receive curative treatments, particularly RFA, which is a standard treatment option for very-early-stage HCC due to its less invasive nature and low cost. In line with these results, several cost-effectiveness studies demonstrated that a higher incidence of HCC ensures cost-effectiveness of MRI surveillance for HCC [22–24].

According to Goossens et al. [23], implementing risk-stratified surveillance using MRI for high- and intermediate-risk patients was more cost-effective than un-stratified surveillance using universal semiannual US. Kim et al. [24•] demonstrated that complete gadoxetic acid-enhanced MRI is a cost-effective surveillance option in high-risk patients with an annual HCC incidence rate of ≥1.81%. These two studies have demonstrated that implementing risk-stratified MRI-based HCC surveillance for high-risk patients is not only cost-effective but also superior to the currently recommended non-stratified US-based surveillance for all at-risk patients. However, for patients with a low or medium HCC risk, US remains the preferred option. Further research is required to define the indications and target populations for MRI-based HCC surveillance, using the cost-effectiveness analysis as a basis. With the advancement of MRI techniques, such as deep learning, the scan time for MRI is expected to decrease in the near future, which would further improve the cost-effectiveness of MRI-based HCC surveillance.

Patient Selection for MRI-Based Surveillance

Considering the limited availability and high costs of MRI compared with those of US, implementing MRI-based surveillance for all target populations would not be practical for HCC surveillance. Instead, it should be selectively applied to those who would benefit more from MRI than from US. The original rationale behind MRI-based HCC surveillance was to offer an alternative for populations with suboptimal ultrasonographic image quality. For instance, approximately 20–30% of ultrasonographic examinations in patients with liver cirrhosis are classified as inadequate for HCC surveillance [17, 18], which implies that MRI-based surveillance would be beneficial for this population. Additionally, previous ultrasonographic examinations can help predict the quality of subsequent examinations. A study evaluating three rounds of HCC surveillance found that the image quality of the first ultrasonographic examination remained unchanged in most cases (83.3–92.2%) throughout the follow-up rounds [45]. Thus, in patients with a poor visualization score on previous US, MRI-based surveillance should be considered.

Previous studies that supported MRI-based HCC surveillance primarily involved patients with advanced liver

cirrhosis, as evidenced by their higher annual incidence (6.4–8.5 per 100 patient-years) [34, 41, 45, 46, 49] and prevalence (3.0–24.3%) [27, 33, 34, 41, 44–49] of HCC compared to the average risk of surveillance populations [71, 72]. In surveillance populations in which obesity or non-alcoholic steatohepatitis are increasingly prevalent [18, 73], the sensitivity of US can be further deteriorated because of the limited penetration of the sonic beam. A recent study showed that the sensitivity of US was only 21% in patients with body mass index (BMI) ≥ 30 kg/m^2 compared to 77% in those with BMI < 30 kg/m^2 [19]. Therefore, patients with obesity or advanced liver cirrhosis are likely to benefit from MRI-based surveillance than from US-based surveillance.

Conclusions

As a result of efforts to overcome limitations of US for HCC surveillance, particularly for detecting HCC at an earlier stage, evidence of the clinical feasibility of MRI is rapidly accumulating. Complete MRI has shown excellent surveillance performance but has limitations of a long scan time and high cost. Three AMRI protocols with reduced sequences have been proposed, i.e., HBP-AMRI, DCE-AMRI, and NE-AMRI, each with unique benefits and drawbacks. All three AMRI techniques have demonstrated acceptable performance in detecting HCC, although evidence from prospective studies in a true surveillance setting remains insufficient. MRI-based HCC surveillance is cost-effective for high-risk patients rather than for low- or medium-risk patients. MRI-based HCC surveillance is also useful for patients whose ultrasonographic image quality is unsatisfactory. Risk-stratified MRI-based HCC surveillance should be considered for patients who have a high risk of developing HCC.

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Data Availability Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

Compliance with Ethical Standards

Ethical Approval Not applicable.

Conflict of Interest Y.S.L. received grant from Gilead Sciences, has been a consultant for AbbVie, Assembly Biosciences, GlaxoSmithKline, Gilead Sciences, Janssen, Olix Pharmaceuticals, Roche, Vaccitech, and Vir Biotechnology, and received speaker fees from AbbVie, Gilead Sciences, and Vaccitech. The remaining authors have no financial disclosures.

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- • Of importance
- •• Of major importance

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