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HCC in MASLD: radiological appearance, diagnosis and treatment

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Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) and its inflammatory form, metabolic dysfunction-associated steatohepatitis (MASH), are emerging as leading causes of hepatocellular carcinoma (HCC) development. This has important implications for evaluating patients with these conditions, including the potential for early diagnosis through screening techniques. Imaging techniques for the noninvasive diagnosis of HCC in the context of MASLD also present unique considerations. Notably, HCC development in patients without cirrhosis is more frequent in MASLD compared to other chronic liver disease etiologies. Moreover, the presence of liver steatosis, a common feature in MASLD patients, can modify the radiological appearance of the liver, giving HCC in MASLD/MASH uncommon imaging characteristics. Additionally, certain histological subtypes, particularly the steatohepatitic HCC, are more prevalent in MASLD/MASH, which may influence both diagnostic strategies and therapeutic decisions in these patients. This review article focuses on the radiological characteristics of HCC developed in patients with MASLD/MASH. It specifically addresses the roles of screening and surveillance, the radiological features of HCC in MASLD/MASH, the histological subtypes associated with these conditions, and the impact of imaging on treatment decisions. Finally, a brief summary of future directions and the role of new technologies in HCC diagnosis within the context of MASLD is provided.

Keywords: Hepatocellular carcinoma, MASLD, NAFLD, steatosis

INTRODUCTION

Hepatocellular carcinoma (HCC) is the sixth most common cancer and the fourth most common cause of cancer-related deaths[1]. Most cases of HCCs develop in the context of chronic liver disease, primarily at the stage of cirrhosis; alcohol, hepatitis B virus (HBV), and hepatitis C virus (HCV) are the most common causes. In the past decades, the incidence of metabolic dysfunction-associated steatotic liver disease (MASLD), previously called non-alcoholic fatty liver disease (NAFLD), has increased worldwide. The current prevalence of MASLD is around 30% of the global population[2], and up to 20% of patients with MASLD can develop liver inflammation and cellular death (metabolic dysfunction-associated steatohepatitis - MASH, previously known as non-alcoholic steatohepatitis - NASH) and can eventually progress to fibrosis/cirrhosis. This progression explains the increased risk of HCC development in these patients. Moreover, up to around one-fourth of MASH-related HCC can occur in the absence of liver cirrhosis[3-5].

Therefore, MASLD/MASH is becoming one of the leading causes of HCC development. This has several implications for evaluating patients with these diseases, including the possibility of early diagnosis through screening techniques and the unique radiological appearance of HCC in the context of MASLD.

This review article focuses on the radiological characteristics of HCC in patients with MASLD/NAFLD. Specifically, it discusses the role of screening and surveillance, the radiological appearance of HCC in MASLD/MASH, specific histological subtypes associated with MASLD/MASH, and the impact of imaging on treatment decisions.

SCREENING AND SURVEILLANCE OF HCC IN MASLD AND MASH

According to the American Association for the Study of Liver Disease (AASLD) and the European Association for the Study of the Liver (EASL), HCC screening is recommended in at-risk individuals, including patients with cirrhosis from any etiology and patients with HBV chronic hepatitis without cirrhosis[6,7] by abdominal semiannual ultrasound (US). According to AASLD (but not EASL), semiannual US is also associated with serum alpha-fetoprotein (AFP) dosage.

However, several specific issues must be considered in patients with MASLD. Although most of the data supporting the rationale for HCC screening in patients with cirrhosis are mainly based on studies including patients with viral hepatitis, the risk of HCC development in MASLD/MASH-related cirrhosis is high enough (although lower than other etiologies) to warrant active surveillance. Indeed, the annual incidence of HCC in patients with MASLD-related cirrhosis is likely between 1%-2%[8].

As previously stated, although the exact estimation is controversial, up to around one-fourth of MASH-related HCC can occur in the absence of cirrhosis[3], which is higher compared to other etiologies of chronic liver disease. While the incidence of HCC in non-advanced MASLD (without advanced fibrosis) patients is generally too low to justify universal surveillance, determining whether these patients should still undergo screening remains a dilemma. Considering that a screening test must maintain a satisfactory cost-benefit ratio, accurate stratification of patients with MASLD without cirrhosis but with an increased risk of developing a malignant lesion should be sought. Improved patient stratification can be obtained by selecting patients with advanced histologically proven fibrosis (F3), increased biological test values such as FIB-4 score, and by developing simple multivariable scores, which are promising in this setting[8].

Moreover, overweight and obesity are common in MASLD, and these factors may limit the efficacy of US examinations as a screening test for detecting HCC. A study from Samoylova *et al.* reported a decreased sensitivity of US in patients with MASH (NASH) compared to other etiologies (0.59 *vs.* 0.84) and in patients with body mass index (BMI) ≥ 30 kg/m^2 (0.76 *vs.* 0.87 for BMI < 30 kg/m^2)[9]. Although cross-sectional imaging, including computed tomography (CT) and magnetic resonance imaging (MRI), could be considered alternatives for these patients, neither CT nor MRI is ideally suited for screening purposes. The use of ionizing radiation in CT, the length of examinations, the high costs, and the limited availability of MRI restrict their applicability for screening.

In this setting, an abbreviated MRI (AMRI) protocol could be considered a valuable alternative as a screening test. The concept of the AMRI is to select a few sets of sequences to maximize the sensitivity of the examination while reducing time and costs. Several combinations have been proposed in the literature, including non-enhanced AMRI (based on T1, T2, and diffusion-weighted sequences), dynamic AMRI (including dynamic contrast-enhanced multiphase imaging sequences) and hepatobiliary AMRI (including hepatobiliary phase after hepatospecific contrast agent injection and T2 sequences with or without diffusion-weighted sequences)[10]; depending on the selected AMRI protocol, up to 15-20 min of MRI can be saved per examination. While most of the literature data on AMRI are based on retrospective series, the multicenter cohort study by Kim *et al.*, including 208 participants during 30 months of follow-up, showed that non-enhanced AMRI had marginally higher sensitivity than the biannual US for HCC detection (71.0% *vs.* 45.2% ; $P = 0.077$)[11]; therefore, alternating both modalities every 6 months could be the optimal surveillance strategy. A meta-analysis from Gupta *et al.* showed that US had lower sensitivity than AMRI (53% *vs.* 82%) and that the different AMRI protocols had similar diagnostic performance[12].

Nevertheless, few data are available when considering only patients with MASLD. A prospective study including 54 patients who had an US and hepatobiliary AMRI, suggested that the use of AMRI could improve the visualization of the liver parenchyma, thus potentially increasing the detection of HCC[13], while a recent retrospective analysis including 75 patients with MASLD showed that AMRI had an excellent diagnostic performance for HCC detection[14]. Nevertheless, the significant limitations of these studies include the very small sample size. Overall, AMRI is the subject of many studies. Although many show a superiority of MRI over US, some biases must be considered. Additionally, as for patients with MASLD, very few data are available. Moreover, general limitations of MRI also apply to AMRI protocols, including the lower availability of MR scans compared to US, and the diameter of the MR bore that could limit feasibility in morbidly obese patients.

To summarize, while patients with MASLD-related cirrhosis are considered for HCC screening similarly to patients with cirrhosis from other etiologies, the necessity of screening patients with MASLD/MASH without cirrhosis remains unclear. However, there is a need for better stratification to identify the most at-risk patients[6].

In this context, a multiparametric approach that includes elastography techniques and serum-based scores (such as the GALAD score, derived from gender, age, AFP-L3, AFP, and des-gamma-carboxyprothrombin) could assist in identifying this subgroup of patients with a higher risk of HCC[15,16].

RADIOLOGICAL DIAGNOSIS OF HCC IN MASLD PATIENTS

A critical (and often overlooked) element is that the noninvasive diagnosis of HCC can be obtained only in patients who are considered at high risk of developing HCC[17,18]. The definition of high-risk patients is therefore necessary to maintain high specificity in diagnosis. Indeed, several lesions may mimic HCC

appearance in patients at low or without risk factors. The accuracy of a diagnostic test (e.g., imaging) is affected by the pre-test probability of the disease. Therefore, in a population without sufficient high pre-test probability of having HCC, typical imaging features could be observed in other non-HCC lesions (including both benign and malignant lesions), which would cause an unacceptable number of false-positive results with a reduced specificity for HCC diagnosis.

For instance, the CT/MRI and contrast-enhanced ultrasound (CEUS) Liver Imaging Reporting and Data System (LI-RADS) algorithms can only be applied to patients ≥ 18 years old with cirrhosis, chronic hepatitis B (regardless of the presence of cirrhosis), or with a prior or current history of HCC[19]. The LI-RADS diagnostic algorithm is used to assign categories to focal liver lesions based on imaging appearance, reflecting the likelihood of HCC. Categories range from LR-1 (definitely benign) to LR-5 (definitely HCC), with LR-M indicating a high likelihood of malignancy but not specific for HCC, and LR-TIV (tumor in vein) that is applied in case of intravascular tumor growth.

LI-RADS diagnostic categories cannot be applied to patients without these risk factors, nor in patients with congenital hepatic fibrosis, cirrhosis due to vascular disorders, or in the pediatric population. According to the EASL guidelines, a noninvasive imaging diagnosis of HCC can only be applied to patients with cirrhosis. A direct consequence is that the noninvasive diagnosis of HCC cannot be made in MASLD/NAFLD patients without cirrhosis, and a biopsy is indicated. Indeed, despite an unequivocally increased risk of HCC in patients with MASLD without cirrhosis, the pre-test probability in these populations has not yet been precisely established.

Data regarding the performance of the noninvasive diagnosis in MASLD patients without cirrhosis are scarce because the vast majority of studies addressing the performance of the noninvasive diagnosis of HCC adhere to the definition of high-risk populations. Ludwig *et al.* specifically focused on the performance and reliability of the LI-RADS for distinguishing HCC from non-HCC primary liver carcinomas in patients who did not meet strict LI-RADS high-risk criteria[20]. They included 131 patients, of whom 25 (19%) had steatosis without fibrosis, 10 (7%) with steatosis and fibrosis, 8 (6%) with MASH/NASH but without fibrosis, and 33 (25%) with MASH/NASH and fibrosis. In the entire cohort, the specificity of LR-5 as a predictor of HCC was 97%-100%, and the combination of LR-5 or LR-TIV as a predictor of HCC did not change the specificity. However, the authors did not provide the result for the subgroup of MASLD patients. The same group published another study focusing on non-HCC malignancies[21]. They suggested that non-HCC malignancies were more likely to mimic HCCs on CT and MRI in patients without LI-RADS-defined HCC risk factors than in the LI-RADS target population. However, here again, no subgroup analysis in MASLD patients was provided. Kim *et al.* also focused on patients without LI-RADS-defined HCC risk factors, but no MASLD patient was included[22].

IMAGING FEATURES OF HCC IN MASLD PATIENTS

Imaging appearance in patients with MASLD without liver cirrhosis

Evidence suggests that the imaging appearance of HCC developed in patients with cirrhosis related to metabolic disease is similar to other etiologies (see above). However, knowledge of imaging presentations of HCC in patients with MASLD without cirrhosis is limited. The main reason is that very few studies, including a small series of patients, have described the clinical, pathological, and imaging features of HCC developed in the liver without cirrhosis[23-26].

Interestingly, these studies consistently reported that the main imaging features of HCC are present in most patients. However, those studies did not differentiate HCC developed in patients with advanced fibrosis

from those with non-fibrotic liver and did not specifically separate simple steatosis from MASH or MASLD from other possible causes of liver disease.

Overall, most of the HCCs developed in MASLD patients without cirrhosis present as solitary lesions or as a dominant mass with satellite nodules [Figure 1], while infiltrating forms are anecdotal[24,27-29]. The vast majority of HCCs present with non-rim arterial phase hyperenhancement (APHE) and non-peripheral washout. No evidence suggests any differences between patients with and without cirrhosis, except for larger tumor size in patients without cirrhosis, probably due to surveillance programs that patients with advanced chronic liver disease are encouraged to follow.

In a systematic review and meta-analysis conducted by Park *et al.*, including five studies with 170 patients with MASLD and 193 HCCs, the pooled rate of APHE was 94.0% [95% confidence interval (CI) 89.1%-96.7%], which was the most common major feature[30]. Moreover, the pooled rates of non-peripheral washout and enhancing capsule were 72.7% (95%CI: 63.3%-80.4%) and 57.5% (95%CI: 45.1%-69.1%), respectively. The proportions of these three major radiological features did not show a significant difference between MASLD and MASH patients ($P \geq 0.21$). When comparing MRI and CT, similar pooled rates for APHE (94.3% *vs.* 93.4%, $P = 0.82$) and washout (70.4% *vs.* 77.2%, $P = 0.38$) were observed; nevertheless, MRI presented a higher pooled rate of enhancing capsule (67.1% *vs.* 44.7%, $P = 0.02$)[30]. A study by Cannella *et al.* also showed that MRI can better depict an enhancing capsule[31].

Influence of hepatic steatosis

The detection and characterization of focal liver lesions are modified by steatosis as the tumor behavior is compared to the adjacent liver. Liver steatosis is characterized by decreased liver attenuation on CT and reduced liver signal intensity on fat-suppressed or saturated, and opposed-phase T1-weighted MRI sequences. This has two main consequences. First, it may lead to underestimating the tumor burden, particularly with CT [Figure 2]. Moreover, the presence of steatosis can also make the characterization of the lesion more difficult by modifying the normal tumor to liver contrast, leading to consequent changes in radiological findings. MRI is the most appropriate imaging examination to address this limitation, as the signal from the fat can be analyzed and suppressed with dedicated sequences. Thompson *et al.* assessed the effect of hepatic steatosis on major features of HCC at MRI in patients with MASLD. They reported that for every 1% increase in hepatic fat fraction in liver without cirrhosis, the odds of absent portal phase washout [Figure 3] and enhancing capsule appearance increased by 18% and 22%, respectively[32]. A summary of each imaging modality application and limitation in patients with MASLD is provided in Table 1.

HCC HISTOLOGICAL SUBTYPES: ASSOCIATION WITH MASLD/MASH AND IMPACT ON IMAGING

The 2019 World Health Organization (WHO) classification of Digestive System Tumors classifies HCC into "not otherwise specified" (NOS)-HCC, accounting for about 65% of all HCCs, and 8 different histopathological subtypes based on their histopathological, molecular, and clinical peculiarities, constituting the remaining 35% of HCCs[33]. Among them, the two most common subtypes are the macrotrabecular-massive HCC (about 5% of HCCs) and the steatohepatitic (SH)-HCC (about 5%-20% of HCCs)[33]. Macrotrabecular-massive HCC is characterized by aggressive clinico-radiological features and poor prognosis after resection, but this subtype is rarely seen in patients with MASLD, being more commonly observed in patients with hepatitis B infection[34]. SH-HCC has been initially described in HCV patients, but its association with metabolic syndrome and MASLD is now well-established[33]. On pathology, SH-HCC is characterized by a SH component that combines microscopic features resembling steatohepatitis, including intracellular steatosis, ballooning, Mallory-Denk bodies, lobular inflammation,

Table 1. Potential applications and limitations of imaging modalities in patients with MASLD-related HCC

Imaging modality	Role in patients at high risk for HCC	Potential applications and advantages in MASLD-HCC	General limitations	Limitations in MASLD-HCC
US	HCC Screening (abdominal semiannual ultrasound) Assessment of fibrosis	Potential screening in selected higher-risk patients	Operator experience Lower sensitivity compared to CT/MRI	Decreased sensitivity in nodule detection in steatotic and obese patients
CT	Characterization of indeterminate nodules on US/noninvasive HCC diagnosis	Large gantry diameter for morbidly obese patients	Radiation exposure	Imaging appearance of HCC modified by steatosis Impaired nodule detection due to steatosis
MRI	Characterization of indeterminate nodules on US/noninvasive HCC diagnosis Assessment of steatosis and fibrosis	Limited influence of steatosis on nodule detection and characterization	Higher costs and examination time Low availability of MRI scans compared to US	Bore diameter limitations for morbidly obese patients
AMRI	Potential screening strategy alternatively or in combination with US	Reduces time and acquisition costs	Low availability of MRI scans compared to US	Limited literature data Bore diameter limitations for morbidly obese patients

AMRI: Abbreviated magnetic resonance imaging; HCC: hepatocellular carcinoma; MASLD: metabolic dysfunction-associated steatotic liver disease; MRI: magnetic resonance imaging; CT: computed tomography; US: ultrasound.

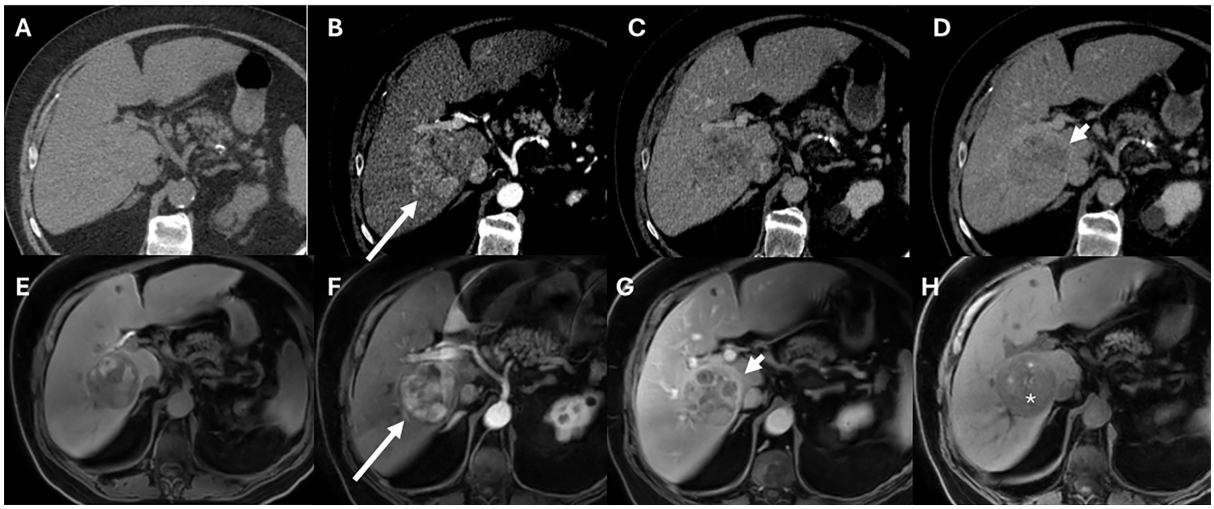

Figure 1. CT (A-D) and MRI (E and F) appearance of a histologically proven hepatocellular carcinoma in a 69-year-old patient with metabolic dysfunction steatotic liver disease and without liver cirrhosis. The tumor is isoattenuating (A) to the liver on unenhanced CT image (A). It shows non-rim APHE during the late HAP (B - arrow) and non-peripheral washout during the PVP (C) and LVP (D). The lesion is heterogeneous and hypointense on unenhanced fat-saturated T1 gradient echo image (E). After gadoxetic acid injection, the lesion shows non-rim APHE during HAP (F - arrow), washout during PVP (G), and a hypointense appearance on the hepatobiliary phase (H - asterisk). Note the presence of an enhancing capsule (small arrows) best depicted on LVP on CT (D) and PVP on MRI (G). CT: Computed tomography; MRI: magnetic resonance imaging; APHE: arterial phase hyperenhancement; HAP: hepatic arterial phase; PVP: portal venous phase; LVP: late venous phase.

and pericellular fibrosis[35,36]. The diagnosis relies on depicting this SH component on ≥ 50% of the total viable tumor surface on pathology. A less than 50% component will classify the tumor as classic HCC (non-otherwise specified HCC) with a SH component.

Clinically, SH-HCC has been linked to a higher frequency of obesity, diabetes mellitus, hyperlipidemia, and steatosis in the background liver parenchyma[37,38]. The prognostic impact of the SH-HC is still under investigation. While this subtype was initially described with a better prognosis, current studies have reported that the overall survival and recurrence-free survival of SH-HCC are not significantly different

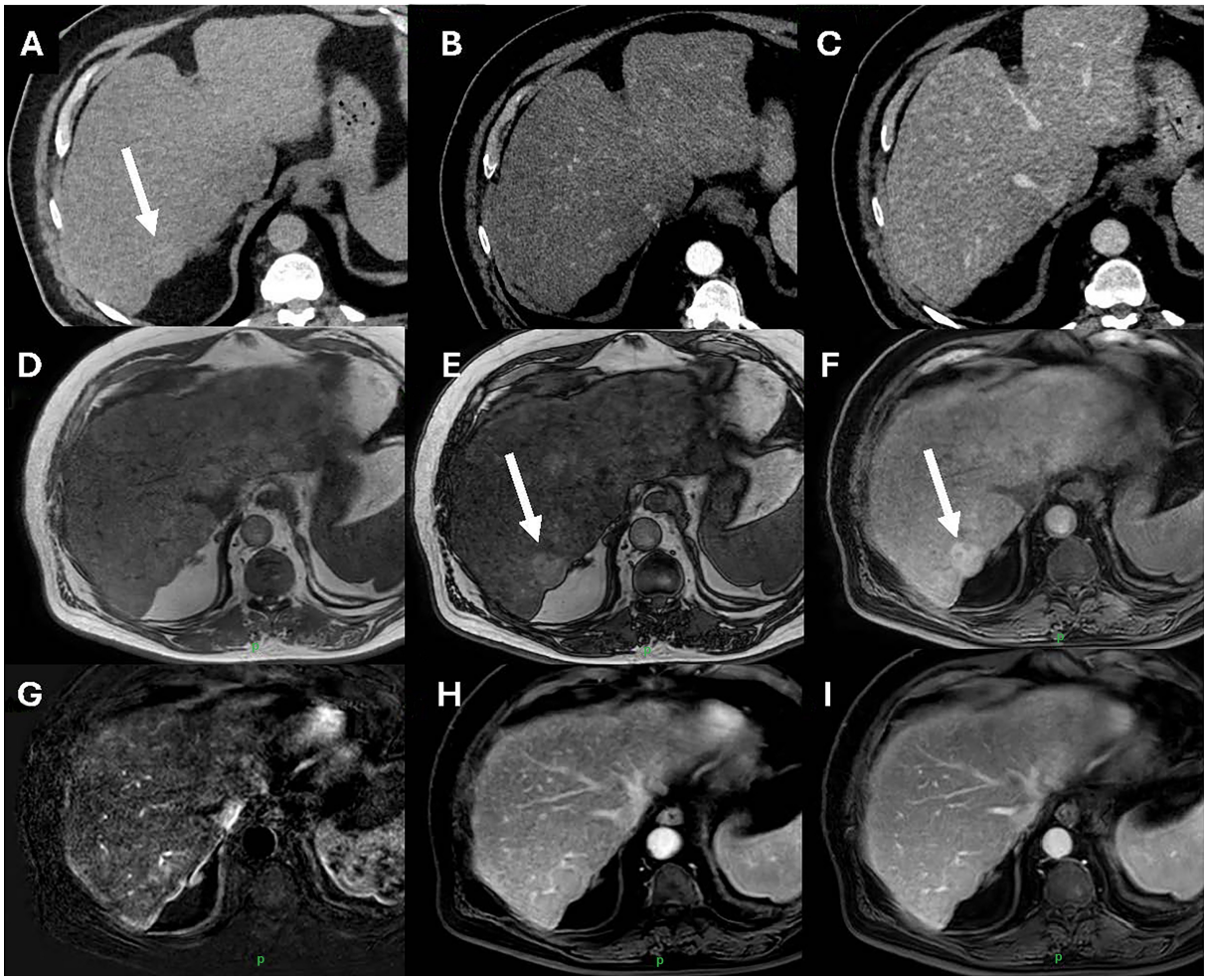

Figure 2. Influence of hepatic steatosis on hepatocellular carcinoma visibility in a 71-year-old male with metabolic dysfunction steatotic liver disease. The nodule in segment VII of the liver is slightly visible and hyperattenuating compared to the background liver on unenhanced (A - arrow) CT image, while it is not visible (iso attenuating appearance) on contrast-enhanced CT images obtained during hepatic arterial (B) and portal venous phase (C). Note the intense signal drop of the background liver on MR out-of-phase T1 image (E) compared to T1 in-phase image (D) consistent with severe hepatic steatosis, which causes the relative hyperintensity of the nodule to the background liver on out-of-phase image due to fat sparing (E - arrow). The nodule is also visible as hyperintense on unenhanced T1 fat-suppressed image (F), while it is isointense and difficult to depict on gadolinium-enhanced fat-suppressed T1 images obtained during arterial (subtraction image - G), portal (H), and late venous phase (I). CT: Computed tomography; MR: magnetic resonance.

from those of non-SH-HCC after surgical resection, with a 5-year survival rate of 77%[36].

There are still few radiological descriptions of SH-HCC. SH-HCCs are usually small in size and classically develop in a background of hepatic steatosis; therefore, tumors may be difficult to distinguish from the surrounding liver parenchyma in patients with severe hepatic steatosis.

On imaging, SH-HCC more commonly appears as a single lesion with a smaller size (median of 25-30 mm) compared to non-SH-HCC[39-41]. Major imaging features of SH-HCC overlap with those of other HCC subtypes, with a similar frequency of non-rim APHE and washout[39-41]. When applying the LI-RADS algorithm in high-risk patients, SH-HCC is classified as LR-5 observation in 70%-80% and 72%-88% of cases on CT and MRI, respectively[39,40]. Macrovascular invasion is rare in SH-HCC, being reported in less than 5% of lesions[31-33], and the majority of tumors show hypointensity in the hepatobiliary phase on MRI. A typical

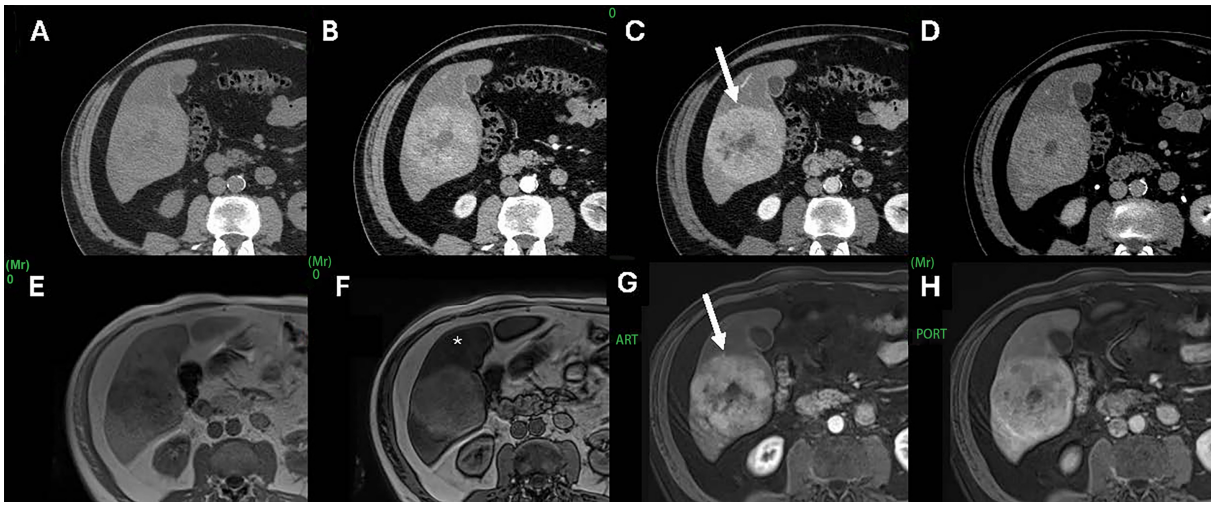

Figure 3. Absence of washout of HCC developed on a steatotic liver in a 65-year-old male. Unenhanced (A) and enhanced CT images obtained during HAP (B), PVP (C), and LVP (D) images show a large HCC in the right liver lobe. The HCC is slightly hyperattenuating to the background liver (steatotic); it shows non-rim arterial phase hyperenhancement on HAP but no washout nor enhancing capsule in PVP (C) and LVP (D). Note the intense drop of the signal of the background liver on MR out-of-phase T1 image (F - asterisk) compared to the T1 in-phase image (E), consistent with severe hepatic steatosis. On gadolinium-enhanced fat-suppressed T1 images, the nodule shows non-rim arterial phase hyperenhancement (G - arrow) but no washout on PVP (H). Conversely to CT, an enhancing capsule is depicted on MRI on PVP (H). HCC: Hepatocellular carcinoma; CT: computed tomography; HAP: hepatic arterial phase; PVP: portal venous phase; LVP: late venous phase; MR: magnetic resonance; MRI: magnetic resonance imaging.

example of SH HCC is presented in Figure 4.

Fat in mass is a common imaging feature of SH-HCC, reported in 33% of cases on CT and 54%-88% on MRI[39-43]. This is seen as a diffuse or focal low attenuation on CT and intralesional signal loss on opposed-phase T1-weighted MR images [Figure 5]. However, the presence of fat in mass alone is insufficient to reliably predict the SH-HCC subtype because this feature can also be depicted in other HCC subtypes or other fat-containing liver lesions.

Indeed, fat in mass can be observed on imaging in up to one-third of NOS-HCC and other rarer subtypes, including (rarely) the aggressive macrotrabecular-massive HCC[39-41]. The distribution and amount of intratumoral fat can also provide clues for identifying SH-HCC. The presence of homogeneous and diffuse fat in mass was more frequently reported in SH-HCC, while non-SH-HCC more commonly presented with focal fat in mass[43,44]. Park *et al.* demonstrated that SH-HCC had more commonly > 50% intratumoral steatosis detected by visual comparison of in-phase and opposed-phase T1-weighted MRI sequences[44]. A recent study by Faure *et al.* suggested that the SH-HCC subtype could be diagnosed with 97% specificity in liver observations without mosaic architecture on MRI in patients with MASH/NASH[45]. Further studies are needed to explore the potential of quantitative imaging, particularly MRI with proton density fat fraction, for identifying SH-HCC in patients with MASLD.

TREATMENT DECISIONS IN PATIENTS WITH HCC DEVELOPED ON MASLD/MASH

Treatment options for HCC include surgical, locoregional, and systemic therapies. In patients with MASLD-HCC, the proportion of patients who receive liver transplant (LT) is about 3.9%, who receive resection is about 33.6%, and who receive ablation is about 12.0%[46]. Patients with MASLD-related HCC are less likely to undergo LT and are more likely to undergo liver resection than patients with HCC due to other causes[46]. This is likely related to several factors, including the higher proportion of HCC cases developing

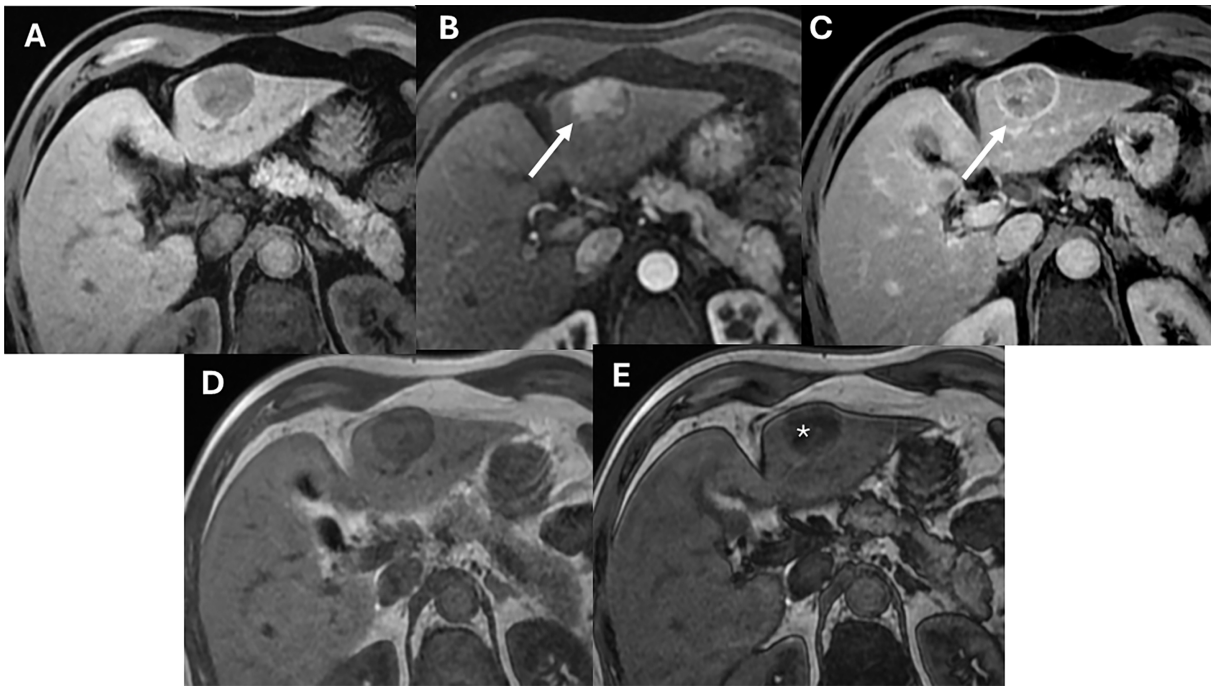

Figure 4. MRI appearance of SH-HCC developed in a 67-year-old patient with metabolic dysfunction-associated steatohepatitis. Unenhanced fat-suppressed T1 image shows a 30 mm nodule in the left liver lobe (A). Gadolinium-enhanced fat-suppressed T1 images obtained during the hepatic arterial phase (B) and late venous phase (C) show that the lesion has a non-rim arterial phase hyperenhancement (B - arrow), washout, and enhancing capsule (C - arrow). The nodule shows a diffuse drop of the signal intensity on T1 out-of-phase image (E - asterisk) compared to the T1 in-phase image (D), consistent with a fat in mass appearance. MRI: Magnetic resonance imaging; SH-HCC: steatohepatitic hepatocellular carcinoma.

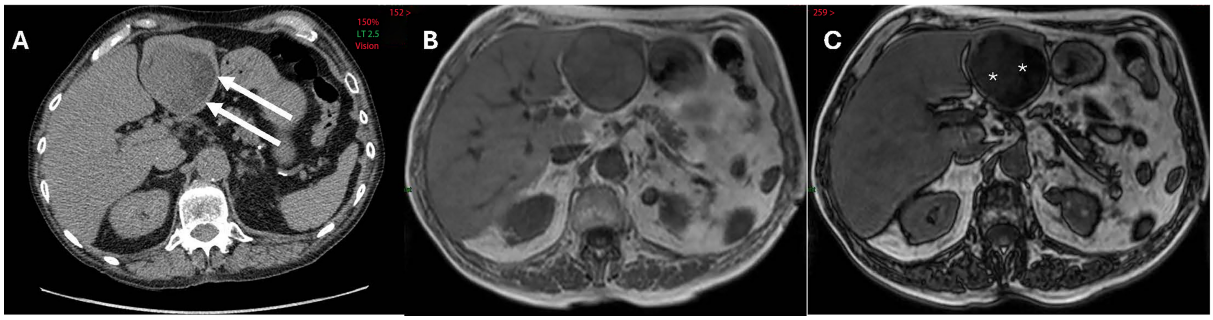

Figure 5. Imaging appearance of "fat in mass" in hepatocellular carcinoma of the left liver lobe. Unenhanced CT (A) shows a heterogeneous hypoattenuating appearance of the left portion of the lesion (A - arrows), which is hypoattenuating compared to the liver and consistent with intra-tumoral fat. The lesion is isointense to the liver on MRI inphase T1 image (B), and MRI T1 outofphase image (C) shows a diffuse drop of the signal intensity within the lesion(C - asterisks). CT: Computed tomography; MRI: magnetic resonance imaging.

without cirrhosis, the older age, and the higher BMI, as well as the higher proportion of associated cardiovascular disease, which can contraindicate LT.

The Barcelona Liver Clinic Cancer (BCLC) is the most commonly used staging system for guiding treatment decisions in HCC and is recommended by the AASLD[7] and EASL[6]. The latest update of BCLC staging for HCC has been published in 2022[47]. Imaging plays a pivotal role in staging HCC in patients with MASLD. In patients with cirrhosis, LI-RADS can be used for diagnosis[48]; however, noninvasive diagnosis is

not possible in patients with MASLD-HCC without cirrhosis. For staging purposes, radiologists must report the number of lesions and involved liver segments, regional adenopathy, vascular tumor invasion, and metastases. A complete CT/MRI report enables the proper treatment decision to be made for the patient.

In patients with unifocal HCC ≤ 2 cm and preserved liver function (i.e., BCLC stage 0), curative-intent thermal ablation is possible (radiofrequency ablation or microwave ablation). Thermal ablation is an efficient treatment in HCC patients with MASLD and achieves similar long-term oncological outcomes (e.g., tumor recurrence and overall survival) compared to other etiologies[49].

In patients with BCLC stage 0/A who are potential candidates for LT or in cases of larger unique lesions, liver resection is indicated, as in these patients, there is a preserved liver synthesis function in the absence of clinically significant portal hypertension. Surgical resection offers a curative-intent treatment for patients with single localized lesions; however, patients with MASLD may have comorbidities related to metabolic syndrome that may potentially worsen the perioperative risk profiles. Indeed, some studies reported that patients with MASLD-HCC who undergo resection have higher intraoperative blood loss, more postoperative complications, and longer lengths of stay compared to non-MASLD patients[50,51]. However, a meta-analysis by Chin *et al.*[52], which pooled 5,579 patients across nine studies, demonstrated that patients with MASLD-HCC have long-term survival benefits with aggressive curative therapy, including improved overall survival and disease-free survival.

MASLD is the most rapidly growing cause of HCC among US patients listed for LT, with a 7.7-fold increase in the time frame from 2002 to 2016[53]. LT is the curative-intent option for patients who are not eligible for resection (e.g., due to liver dysfunction or multinodular disease) but meet the transplantability criteria[54], the most used being the Milan criteria (one lesion < 5 cm or from 2 to 3 lesions between 3 and 5 cm). In addition, the 2022 BCLC edition indicates that LT may be an option in a subgroup of BCLC-B patients with multinodular HCC who might be eligible for transplantation in case of successful downstaging by transarterial chemoembolization. The overall survival of patients with MASLD-HCC who undergo LT seems similar to or slightly lower than that of patients with HCC from other causes[55-57].

In patients in the BCLC stage B with diffuse, infiltrative, and extensive bilobar liver involvement and patients in the BCLC stage C, the BCLC 2022 indicates systemic therapy. In particular, the combination of Atezolizumab with Bevacizumab or Durvalumbab-Tremelimumab is currently considered first-line treatment in these patients. The efficacy and safety of systemic therapy in patients with MASLD-HCC is largely unknown[58], with some preliminary evidence that immune checkpoint inhibitors may be less effective in MASLD-HCC compared with viral HCC[59], which needs to be further confirmed.

The BCLC staging system, as well as the EASL and AASLD guidelines, have historically been based on patients with viral hepatitis and do not recommend the selection of a specific treatment pathway according to the etiology of underlying chronic liver disease. However, major differences exist in the clinical characteristics of patients with MASLD-HCC. First, a lower proportion of patients with MASLD-related HCC undergo surveillance for HCC before cancer diagnosis compared to patients with HCC from other causes (32.8% *vs.* 55.7%, respectively)[46]. Because there is no surveillance program for MASLD patients without cirrhosis, individuals with MASLD-related HCC are more likely to be older, have a higher BMI, poorer performance status, larger tumors at diagnosis, and are less likely to present with established cirrhosis or clinically significant portal hypertension compared to those with HCC from other causes, such as viral hepatitis[49,56,60,61]. However, BCLC staging does not account for a specific algorithmic approach to HCC developed in patients without cirrhosis. To date, a systematic review and meta-analysis by Tan *et al.*

demonstrated a lack of significant differences in treatment allocation between patients with MASLD-related HCC and those with HCC due to other causes[46]. The study found similar survival (hazard ratio of 1.05) but longer disease-free survival for patients with MASLD-related HCC. In addition, several retrospective analyses and meta-analyses have shown better outcomes in patients with MASLD-HCC who undergo liver resection compared to those with HCC from other causes, particularly in the absence of cirrhosis[50,55,62]. Collectively, all data available for MASLD-HCC indicate particular challenges and issues unique to MASLD-HCC. On the one hand, the BCLC algorithm may be too conservative to indicate liver resection in patients with MASLD-HCC; conversely, the indication of LT or systemic therapy may need further refinement and research in patients with MASLD-HCC[58].

FUTURE DIRECTIONS AND ARTIFICIAL INTELLIGENCE

In recent years, the development of artificial intelligence (AI) and the application of new technologies in the field of radiology have opened new scenarios for diagnosing, managing, and treating patients. These techniques include machine learning, artificial neural networks, and conventional neural network approaches. In the setting of HCC, these technologies can be applied to all imaging techniques, extracting imaging-related features (radiomics) and, eventually, integrating them with non-radiological data and biomarkers with three main objectives: reducing diagnostic variability, optimizing costs, and improving data analysis[63].

For example, the optimization of patient screening according to the increased risk of the development of HCC is a major challenge, especially in patients with MASLD, in which HCC diagnosis is often late. Machine learning models developed on standard medical biomarkers can be used to predict the risk of HCC development to achieve an early diagnosis[64,65]. AI models can also enhance lesion characterization or predict HCC response to treatment, including curative or palliative ones[66]. The development of AI models is rapidly advancing across all fields of medicine, including hepatology. These approaches extend beyond imaging; "omics" methods have been created to integrate various types of data, from genomics to biological and clinical information[67,68]. Building multiscale models that employ a multimodal approach is essential to developing algorithms that can be effectively incorporated into clinical routines.

Despite the continuing and unrelenting number of publications, the application of AI for HCC has yet to significantly impact clinical practice. This is related to the fact that these techniques are often limited by a lack of standardization and reduced large-scale applicability. That notwithstanding, it is highly likely that we will see a radical change in the approach to the noninvasive diagnosis of HCC in the coming years.

PRACTICAL SUMMARY

Patients with MASLD-related cirrhosis should undergo screening similar to those with cirrhosis from other causes.

AMRI may be a useful alternative screening tool, helping to overcome some of the limitations associated with US.

The imaging appearance of HCC in patients with MASLD-related cirrhosis is similar to HCC arising from other etiologies.

In MASLD patients, HCC frequently presents as solitary lesions or a dominant mass with satellite nodules, exhibiting classic HCC features such as non-rim APHE, non-peripheral washout, and an enhancing capsule.

Liver steatosis may reduce imaging accuracy for detecting and characterizing liver nodules.

MASLD patients have a higher prevalence of the SH-HCC subtype, which is typically small, displays typical major imaging features including non-rim APHE, non-peripheral washout, and an enhancing capsule, often accompanied by a diffuse fat in mass appearance, and lacks tumor venous invasion.

The HCC treatment algorithm should be adapted to better address the specifics of MASLD-related HCC and MASLD patients.

AI is rapidly advancing in hepatology, integrating diverse data types, including imaging. Despite growing research, its impact on HCC clinical practice is limited by standardization and scalability issues, though significant changes in noninvasive diagnosis are expected soon.

CONCLUSION

Considering the increasing prevalence of MASLD, developing and optimizing an effective screening and surveillance program for HCC is essential. This can be achieved through the improved selection of high-risk patients and the eventual implementation of dedicated screening programs utilizing the AMRI protocol. Given the radiological characteristics of HCC in patients with MASLD, it is crucial to apply noninvasive diagnostic criteria accurately to ensure correct diagnoses. Furthermore, stratifying HCC according to histological subtype can enhance therapeutic decision making, with SH-HCC being the most prevalent specific HCC subtype associated with MASLD.

DECLARATIONS

Authors' contributions

Equally participated in all stages of manuscript production, design, figures, writing and review of the final version: Dioguardi Burgio M, Cannella R, Vernuccio F, Ronot M, Vilgrain V

Availability of data and materials

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Conflicts of interest

Cannella R disclosures: research collaboration with Siemens Healthineers; support for attending meetings from Bracco and Bayer. The other authors declare that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Oh JH, Jun DW. The latest global burden of liver cancer: a past and present threat. *Clin Mol Hepatol.* 2023;29:355-7. DOI PubMed PMC
2. Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology.* 2023;77:1335-47. DOI PubMed PMC
3. Singal AG, Lampertico P, Nahon P. Epidemiology and surveillance for hepatocellular carcinoma: new trends. *J Hepatol.* 2020;72:250-61. DOI PubMed PMC
4. Dyson J, Jaques B, Chattopadyhay D, et al. Hepatocellular cancer: the impact of obesity, type 2 diabetes and a multidisciplinary team. *J Hepatol.* 2014;60:110-7. DOI PubMed
5. Mittal S, El-Serag HB, Sada YH, et al. Hepatocellular carcinoma in the absence of cirrhosis in United States veterans is associated with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol.* 2016;14:124-31.e1. DOI PubMed PMC
6. Association for the Study of the Liver. EASL clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol.* 2018;69:182-236. DOI PubMed
7. Singal AG, Llovet JM, Yarchoan M, et al. AASLD practice guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. *Hepatology.* 2023;78:1922-65. DOI PubMed PMC
8. Singal AG, El-Serag HB. Rational HCC screening approaches for patients with NAFLD. *J Hepatol.* 2022;76:195-201. DOI PubMed PMC
9. Samoylova ML, Mehta N, Roberts JP, Yao FY. Predictors of ultrasound failure to detect hepatocellular carcinoma. *Liver Transpl.* 2018;24:1171-7. DOI PubMed
10. An JY, Peña MA, Cunha GM, et al. Abbreviated MRI for hepatocellular carcinoma screening and surveillance. *Radiographics.* 2020;40:1916-31. DOI PubMed PMC
11. Kim DH, Yoon JH, Choi MH, et al. Comparison of non-contrast abbreviated MRI and ultrasound as surveillance modalities for HCC. *J Hepatol.* 2024;81:461-70. DOI PubMed
12. Gupta P, Soundararajan R, Patel A, Kumar-M P, Sharma V, Kalra N. Abbreviated MRI for hepatocellular carcinoma screening: a systematic review and meta-analysis. *J Hepatol.* 2021;75:108-19. DOI PubMed
13. Huang DQ, Fowler KJ, Liau J, et al. Comparative efficacy of an optimal exam between ultrasound versus abbreviated MRI for HCC screening in NAFLD cirrhosis: a prospective study. *Aliment Pharmacol Ther.* 2022;55:820-7. DOI PubMed PMC
14. Soundararajan R, Pooja AB, Gupta P, et al. Diagnostic performance of abbreviated MRI for HCC detection in patients with non-alcoholic fatty liver disease. *J Clin Exp Hepatol.* 2024;14:101276. DOI PubMed PMC
15. Best J, Bechmann LP, Sowa JP, et al. GALAD score detects early hepatocellular carcinoma in an international cohort of patients with nonalcoholic steatohepatitis. *Clin Gastroenterol Hepatol.* 2020;18:728-35.e4. DOI PubMed
16. Cerrito L, Mignini I, Ainora ME, Mosoni C, Gasbarrini A, Zocco MA. Hepatocellular carcinoma in patients with nonalcoholic fatty liver disease: the prognostic role of liver stiffness measurement. *Cancers.* 2023;15:637. DOI PubMed PMC
17. Cannella R, Dioguardi Burgio M, Sartoris R, Gregory J, Vilgrain V, Ronot M. Adherence to LI-RADS and EASL high-risk population criteria: a systematic review. *Hepatology.* 2023;77:1958-67. DOI PubMed
18. Cannella R, Zins M, Brancatelli G. ESR Essentials: diagnosis of hepatocellular carcinoma-practice recommendations by ESGAR. *Eur Radiol.* 2024;34:2127-39. DOI PubMed PMC
19. CT/MRI LI-RADS® v2018 CORE. Available from: https://www.acr.org/-/media/ACR/Files/RADS/LI-RADS/LI-RADS-2018-Core.pdf. [Last accessed on 18 Dec 2024].
20. Ludwig DR, Fraum TJ, Cannella R, et al. Expanding the liver imaging reporting and data system (LI-RADS) v2018 diagnostic population: performance and reliability of LI-RADS for distinguishing hepatocellular carcinoma (HCC) from non-HCC primary liver carcinoma in patients who do not meet strict LI-RADS high-risk criteria. *HPB.* 2019;21:1697-706. DOI PubMed
21. Fraum TJ, Cannella R, Ludwig DR, et al. Assessment of primary liver carcinomas other than hepatocellular carcinoma (HCC) with LI-RADS v2018: comparison of the LI-RADS target population to patients without LI-RADS-defined HCC risk factors. *Eur Radiol.* 2020;30:996-1007. DOI PubMed
22. Kim DH, Choi SH, Kim DW, et al. Combined hepatocellular-cholangiocarcinoma: magnetic resonance imaging features and prognosis according to risk factors for hepatocellular carcinoma. *J Magn Reson Imaging.* 2021;53:1803-12. DOI PubMed
23. Desai A, Sandhu S, Lai JP, Sandhu DS. Hepatocellular carcinoma in non-cirrhotic liver: a comprehensive review. *World J Hepatol.* 2019;11:1-18. DOI PubMed PMC
24. Di Martino M, Saba L, Bosco S, et al. Hepatocellular carcinoma (HCC) in non-cirrhotic liver: clinical, radiological and pathological findings. *Eur Radiol.* 2014;24:1446-54. DOI PubMed
25. Gaddikeri S, McNeeley MF, Wang CL, et al. Hepatocellular carcinoma in the noncirrhotic liver. *AJR Am J Roentgenol.* 2014;203:W34-47. DOI PubMed
26. Mamone G, Di Piazza A, Carollo V, et al. Imaging of primary malignant tumors in non-cirrhotic liver. *Diagn Interv Imaging.* 2020;101:519-35. DOI PubMed
27. Winston CB, Schwartz LH, Fong Y, Blumgart LH, Panicek DM. Hepatocellular carcinoma: MR imaging findings in cirrhotic livers and noncirrhotic livers. *Radiology.* 1999;210:75-9. DOI PubMed
28. Lafitte M, Laurent V, Soyer P, et al. MDCT features of hepatocellular carcinoma (HCC) in non-cirrhotic liver. *Diagn Interv Imaging.* 2016;97:355-60. DOI PubMed

29. Brancatelli G, Federle MP, Grazioli L, Carr BI. Hepatocellular carcinoma in noncirrhotic liver: CT, clinical, and pathologic findings in 39 U.S. residents. *Radiology.* 2002;222:89-94. DOI PubMed
30. Park EJ, Son JH, Choi SH. Imaging features of hepatocellular carcinoma in nonalcoholic fatty liver disease and nonalcoholic steatohepatitis: a systematic review and meta-analysis. *Abdom Radiol.* 2022;47:2089-98. DOI PubMed
31. Cannella R, Ronot M, Sartoris R, et al. Enhancing capsule in hepatocellular carcinoma: intra-individual comparison between CT and MRI with extracellular contrast agent. *Diagn Interv Imaging.* 2021;102:735-42. DOI PubMed
32. Thompson SM, Garg I, Ehman EC, et al. Non-alcoholic fatty liver disease-associated hepatocellular carcinoma: effect of hepatic steatosis on major hepatocellular carcinoma features at MRI. *Br J Radiol.* 2018;91:20180345. DOI PubMed PMC
33. WHO Classification of Tumours Editorial Board. Digestive system tumours. Available from: https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours/Digestive-System-Tumours-2019. [Last accessed on 18 Dec 2024].
34. Mulé S, Galletto Pregliasco A, Tenenhaus A, et al. Multiphase liver MRI for identifying the macrotrabecular-massive subtype of hepatocellular carcinoma. *Radiology.* 2020;295:562-71. DOI PubMed
35. Salomao M, Yu WM, Brown RS Jr, Emond JC, Lefkowitch JH. Steatohepatitic hepatocellular carcinoma (SH-HCC): a distinctive histological variant of HCC in hepatitis C virus-related cirrhosis with associated NAFLD/NASH. *Am J Surg Pathol.* 2010;34:1630-6. DOI PubMed
36. Trapani L, Beaufrère A, Hobeika C, et al. Pathological overview of steatohepatitic hepatocellular carcinoma in a surgical series. *Histopathology.* 2023;83:526-37. DOI PubMed
37. Yamaoka K, Saitoh S, Kinowaki K, et al. Clinicopathological assessment of steatohepatitic hepatocellular carcinoma. *Clin Res Hepatol Gastroenterol.* 2022;46:101799. DOI PubMed
38. Jain D, Nayak NC, Kumaran V, Saigal S. Steatohepatitic hepatocellular carcinoma, a morphologic indicator of associated metabolic risk factors: a study from India. *Arch Pathol Lab Med.* 2013;137:961-6. DOI PubMed
39. Cannella R, Dioguardi Burgio M, Beaufrère A, et al. Imaging features of histological subtypes of hepatocellular carcinoma: implication for LI-RADS. *JHEP Rep.* 2021;3:100380. DOI PubMed PMC
40. Mulé S, Serhal A, Pregliasco AG, et al. MRI features associated with HCC histologic subtypes: a western American and European bicenter study. *Eur Radiol.* 2023;33:1342-52. DOI PubMed
41. Auer TA, Halskov S, Fehrenbach U, et al. Gd-EOB MRI for HCC subtype differentiation in a western population according to the 5(th) edition of the World Health Organization classification. *Eur Radiol.* 2023;33:6902-15. DOI PubMed PMC
42. Inui S, Kondo H, Tanahashi Y, et al. Steatohepatitic hepatocellular carcinoma: imaging findings with clinicopathological correlation. *Clin Radiol.* 2021;76:160.e15-25. DOI PubMed
43. Chen K, Xu Y, Dong Y, et al. Contrast-enhanced imaging features and clinicopathological investigation of steatohepatitic hepatocellular carcinoma. *Diagnostics.* 2023;13:1337. DOI PubMed PMC
44. Park JH, Park YN, Kim MJ, et al. Steatotic hepatocellular carcinoma: association of MRI findings to underlying liver disease and clinicopathological characteristics. *Liver Int.* 2023;43:1332-44. DOI PubMed
45. Faure A, Dioguardi Burgio M, Cannella R, et al. Imaging and prognostic characterization of fat-containing hepatocellular carcinoma subtypes. *Radiol Med.* 2024;129:687-701. DOI PubMed
46. Tan DJH, Ng CH, Lin SY, et al. Clinical characteristics, surveillance, treatment allocation, and outcomes of non-alcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis. *Lancet Oncol.* 2022;23:521-30. DOI PubMed PMC
47. Reig M, Forner A, Rimola J, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. *J Hepatol.* 2022;76:681-93. DOI PubMed PMC
48. American College of Radiology™. Liver imaging reporting & data system (LI-RADS®). Available from: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/LI-RADS. [Last accessed on 18 Dec 2024].
49. Nguyen N, Rode A, Trillaud H, et al. Percutaneous radiofrequency ablation for hepatocellular carcinoma developed on non-alcoholic fatty liver disease. *Liver Int.* 2022;42:905-17. DOI PubMed
50. Koh YX, Tan HJ, Liew YX, et al. Liver resection for nonalcoholic fatty liver disease-associated hepatocellular carcinoma. *J Am Coll Surg.* 2019;229:467-78.e1. DOI PubMed
51. Cauchy F, Zalinski S, Dokmak S, et al. Surgical treatment of hepatocellular carcinoma associated with the metabolic syndrome. *Br J Surg.* 2013;100:113-21. DOI PubMed
52. Chin KM, Prieto M, Cheong CK, et al. Outcomes after curative therapy for hepatocellular carcinoma in patients with non-alcoholic fatty liver disease: a meta-analysis and review of current literature. *HPB.* 2021;23:1164-74. DOI PubMed
53. Younossi Z, Stepanova M, Ong JP, et al; Global Nonalcoholic Steatohepatitis Council. Nonalcoholic steatohepatitis is the fastest growing cause of hepatocellular carcinoma in liver transplant candidates. *Clin Gastroenterol Hepatol* 2019;17:748-55.e3. DOI PubMed
54. Burgio M, Garzelli L, Cannella R, Ronot M, Vilgrain V. Hepatocellular carcinoma: optimal radiological evaluation before liver transplantation. *Life.* 2023;13:2267. DOI PubMed PMC
55. Wong CR, Njei B, Nguyen MH, Nguyen A, Lim JK. Survival after treatment with curative intent for hepatocellular carcinoma among patients with vs without non-alcoholic fatty liver disease. *Aliment Pharmacol Ther.* 2017;46:1061-9. DOI PubMed
56. Reddy SK, Steel JL, Chen HW, et al. Outcomes of curative treatment for hepatocellular cancer in nonalcoholic steatohepatitis versus hepatitis C and alcoholic liver disease. *Hepatology.* 2012;55:1809-19. DOI PubMed
57. Haldar D, Kern B, Hodson J, et al; European Liver and Intestine Transplant Association (ELITA). Outcomes of liver transplantation

for non-alcoholic steatohepatitis: a European liver transplant registry study. *J Hepatol* 2019;71:313-22. DOI PubMed PMC

58. Foerster F, Gairing SJ, Müller L, Galle PR. NAFLD-driven HCC: safety and efficacy of current and emerging treatment options. *J Hepatol.* 2022;76:446-57. DOI PubMed
59. Pfister D, Núñez NG, Pinyol R, et al. NASH limits anti-tumour surveillance in immunotherapy-treated HCC. *Nature.* 2021;592:450-6. DOI PubMed PMC
60. Pal Chaudhary S, Reyes S, Chase ML, et al. Resection of NAFLD/NASH-related hepatocellular carcinoma (HCC): clinical features and outcomes compared with HCC due to other etiologies. *Oncologist.* 2023;28:341-50. DOI PubMed PMC
61. Younossi ZM, Otgonsuren M, Henry L, et al. Association of nonalcoholic fatty liver disease (NAFLD) with hepatocellular carcinoma (HCC) in the United States from 2004 to 2009. *Hepatology.* 2015;62:1723-30. DOI PubMed
62. Molinari M, Kaltenmeier C, Samra PB, et al. Hepatic resection for hepatocellular carcinoma in nonalcoholic fatty liver disease: a systematic review and meta-analysis of 7226 patients. *Ann Surg Open.* 2021;2:e065. DOI PubMed PMC
63. Koh B, Danpanichkul P, Wang M, Tan DJH, Ng CH. Application of artificial intelligence in the diagnosis of hepatocellular carcinoma. *egastro.* 2023;1:e100002. DOI
64. Okanoue T, Yamaguchi K, Shima T, et al. Artificial intelligence/neural network system that accurately diagnoses hepatocellular carcinoma in nonalcoholic steatohepatitis. *Hepatol Res.* 2023;53:1213-23. DOI PubMed
65. Sarkar S, Alurwar A, Ly C, et al. A machine learning model to predict risk for hepatocellular carcinoma in patients with metabolic dysfunction-associated steatotic liver disease. *Gastro Hep Adv.* 2024;3:498-505. DOI PubMed PMC
66. Kawka M, Dawidziuk A, Jiao LR, Gall TMH. Artificial intelligence in the detection, characterisation and prediction of hepatocellular carcinoma: a narrative review. *Transl Gastroenterol Hepatol.* 2022;7:41. DOI PubMed PMC
67. Ghosh S, Zhao X, Alim M, Brudno M, Bhat M. Artificial intelligence applied to 'omics data in liver disease: towards a personalised approach for diagnosis, prognosis and treatment. *Gut.* 2025;74:295-311. DOI PubMed
68. Martinino A, Aloulou M, Chatterjee S, et al. Artificial intelligence in the diagnosis of hepatocellular carcinoma: a systematic review. *J Clin Med.* 2022;11:6368. DOI PubMed PMC