Joint Consensus Statement of the Indian National Association for Study of the Liver and Indian Radiological and Imaging Association for the Diagnosis and Imaging of Hepatocellular Carcinoma Incorporating Liver Imaging Reporting and Data System

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Hepatocellular carcinoma (HCC) is the 6th most common cancer and the second most common cause of cancer-related mortality worldwide. There are currently no universally accepted practice guidelines for the diagnosis of HCC on imaging owing to the regional differences in epidemiology, target population, diagnostic imaging modalities, and staging and transplant eligibility. Currently available regional and national guidelines include those from the American Association for the Study of Liver Disease (AASLD), the European Association for the Study of the Liver (EASL), the Asian Pacific Association for the Study of the Liver, the Japan Society of Hepatology, the Korean Liver Cancer Study Group, Hong Kong, and the National Comprehensive Cancer Network in the United States. India with its large population and a diverse health infrastructure faces challenges unique to its population in diagnosing HCC. Recently, American Association have introduced a Liver Imaging Reporting and Data System (LIRADS, version 2017, 2018) as an attempt to standardize the acquisition, interpretation, and reporting of liver lesions on imaging and hence improve the coherence between radiologists and clinicians and provide guidance for the management of HCC. The aim of the present consensus was to find a common ground in reporting and interpreting liver lesions pertaining to HCC on imaging keeping LIRADSv2018 in mind. (J Clin Exp Hepatol 2019;9:625–651)

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Abbreviations: APHE, arterial phase hyperenhancement, CT, computed tomography, HCC, hepatocellular carcinoma, LIRADS, Liver Imaging Reporting and Data System, MRCP, magnetic resonance cholangiopancreatography, MR, magnetic resonance

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Table 1 Grading of Evidence and Recommendations (Adapted From the GRADE System).

Grading of evidence	
High quality (A)	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality (B)	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low or very low quality (C)	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Any estimate of effect is uncertain.
Grading of recommendation	
Strong recommendation (1)	Warranted Factors influencing the strength of the recommendation included the quality of the evidence, presumed important patient outcomes, and cost
Weaker recommendation (2)	Variability in preferences and values or more uncertainty: more likely a weak recommendation is warranted. Recommendation is made with less certainty; higher cost or resource consumption

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

Association for the Study of the Liver,[3] the Japan Society of Hepatology,[4] the Korean Liver Cancer Study Group,[5] Hong Kong,[6] and the National Comprehensive Cancer Network[7] in the United States. India with its large population and a diverse health infrastructure faces challenges unique to its population in diagnosing HCC. Recently, American Association have introduced a Liver Imaging Reporting and Data System (LIRADS, version 2017, 2018[8,9]) as an attempt to standardize the acquisition, interpretation, and reporting of liver lesions on imaging and hence improve the coherence between radiologists and clinicians and provide guidance for the management of HCC. The aim of the present consensus was to find a common ground in reporting and interpreting liver lesions pertaining to HCC on imaging keeping LIRADSv2018 in mind.

The multidisciplinary group comprising of hepatologists and diagnostic and interventional radiologists reviewed the latest available scientific evidence and developed a set of mutually agreed best practice statements, based on various clinical and radiological parameters for the purpose of standardization.

Grading of Recommendations Assessment, Development, and Evaluation system was used for grading evidence and strength of recommendation[10] as shown in Table 1.

HCC SCREENING

The age-adjusted incidence rate of HCC in India for men ranges from 0.7 to 7.5 and for women from 0.2 to 2.2 per 100,000 persons per year.[11] Worldwide, the single largest risk factor for the development of HCC is cirrhosis of liver because of any etiology, present in 70%–90%. Paul *et al*. had estimated that during a cumulative 563 person years follow-up of cirrhotics, 9 cases of HCC were detected with an annual incidence rate of 1.6% (95% confidence interval [CI] 0.07–3.0).[12] HCCs detected when symptomatic were associated with a poor prognosis.[13]

In a randomized controlled trial (RCT) from China on 18,816 patients with hepatitis B, twice yearly ultrasound (USG) and measurement of serum alpha feto protein (AFP) concentration was compared with no surveillance. Survival of screened participants was 66% at 1 year, 53% at 3 years, and 46% at 5 years *versus* 31%, 7%, and 0%, respectively, in similar patients without screening.[14]

A systematic review of cost-effectiveness, analyzing 5 models and 2 studies, found 6 monthly USG with or without AFP to be cost-effective.[15] The INASL recommends that all patients at risk of developing HCC and who are eligible for HCC therapy are candidates for regular HCC surveillance in India.[16]

Ultrasound (US) has been found to be variably sensitive in detecting asymptomatic tumors in the context of surveillance (60–94%), and the sensitivity for detecting early stage tumors is lower (63%) as shown in a recent meta-analysis but is currently the best surveillance tool for early-stage HCC among patients with cirrhosis.[15,17] Performing US every 6 months instead of annually significantly improves the sensitivity of detecting early HCC to 70% (≥2 cm). However, it is operator dependent. Based on tumor doubling time, recent Korean study, and multicentric Italian study,[16,17] USG screening every 6 months is a reasonable strategy. A 3-monthly interval increases the likelihood of detecting small nodules of up to 10 mm but not the higher number of HCC lesions or lesions >30 mm. US Liver Imaging Reporting and Data System (LI-RADS) have proposed standardization in performing and reporting liver lesions, and this will improve the performance of US and unify management recommendations.[18]

A stringent recall policy algorithm is crucial when an abnormal finding (i.e. a newly focal hepatic nodule/mass, known focal hepatic nodule with changing echo patterns or growth) is detected during routine US screening with the aim to diagnose HCC at an early stage when curative treatment approaches can be applied. All patients found to have a nodule on USG should undergo dynamic cross-sectional imaging.

Serum AFP is the most widely tested biomarker in HCC. Unfortunately, even with the most efficient cut-off (10–20 μg/L), diagnostic sensitivity is around 60%. It does not perform well as a surveillance test because fluctuating levels may occur in any chronic HBV, HCV, not necessarily due to HCC formation. If elevated is helpful to define patients at risk.[19] A recent meta-analysis demonstrated that

at any cut-off, addition of AFP to USG does not provide any advantage in detecting early HCCs with only nonsignificant increase in pooled sensitivity from 63% to 69%.[20] Nevertheless, it is a cheap and widely available blood test, and in certain clinical situations does have a role.

Key Statements—HCC Screening

1. Surveillance for HCC can detect tumors early in the course and potentially amenable to treatment. Hence, all patients at risk of developing HCC and who are eligible for HCC treatment are the candidates for regular HCC surveillance—A1
2. Following patients should be subjected to the surveillance for HCC:
   - Patients with cirrhosis:
     - o Child-Pugh class A and B cirrhotic patient; of any etiology—A1
     - o Child-Pugh class C cirrhotic patient; of any etiology or those who are listed for liver transplantation—A1
   - Patients without cirrhosis:
     - o Patients with chronic hepatitis B: males >40 years and females >50 years—A1
     - o Patients with chronic HBV infection of any age with family history of HCC—B1
   - Patients with chronic hepatitis C and advanced fibrosis—A1
3. US abdomen for liver lesions performed every 6 months by an experienced radiologist is the recommended test of surveillance for HCC—B2
4. Serum alfa-fetoprotein has no additive role in surveillance for HCC—B2.
   *Though it is felt that this is a cheap and readily available test and may have a role in certain clinical settings.

OPTIMAL IMAGING PROTOCOL

Multiphasic computed tomography (CT) and magnetic resonance (MR) imaging with extracellular contrast agents are universally endorsed as the first-line modalities for diagnosis and staging of HCC. These examinations should include late hepatic arterial, portal venous, and at about 3–5 min, delayed phase acquisitions. Precontrast imaging is needed for MR imaging but, in order to reduce radiation dose, may be omitted during CT acquisition as there is hardly any loss of significant diagnostic information except in the patients previously treated with locoregional embolic or ablative therapies. The per-lesion sensitivity of MR imaging for nodular HCC of all sizes is 77%–100%, while that of CT is 68%–91%.[21]

Thus, while MR imaging may be preferred over CT, there is insufficient data to recommend MR imaging over CT in community or less-specialized centers.

MR imaging with hepatobiliary (HPB) agents is the most sensitive method for detection of small HCCs and of premalignant lesions likely to progress to overt HCC.[22] These agents permit acquisition of HPB phase images that provide additional information on hepatocellular function. In comparative studies, gadoxetate disodium–enhanced MR imaging had significantly higher per-lesion sensitivity and/

Key Statements: Optimal Imaging Protocol

5. Basic technical requirements as included in Table 2 for USG, Table 3 for contrast enhanced ultrasound (CEUS), Table 4 for CT, Table 5 for magnetic resonance imaging (MRI)—these are basic recommended standard agreed protocols. These requirements are must for optimal screening, detection, characterization, and follow-up of liver nodules/HCC as well as in evaluating response to treatment.
6. Dynamic CT and MRI using extracellular contrast agent should be acquired at least in late arterial, hepatic venous, and delayed phases. The acquisition of noncontrast phase is optional, except when evaluating response to locoregional therapy. A1
7. Diffusion weighted imaging (DWI) while not essential is an useful adjunct in characterization of liver lesions and evaluating response to treatment. B1
8. HPB-specific MRI if available can help in characterizing indeterminate liver lesions. B1

or overall accuracy for the diagnosis of HCC than multiphasic CT.[23–25]

Physiologic changes in intranodular blood flow that accompany carcinogenesis aided by acquisition of images before (precontrast) and dynamically after extracellular contrast agent administration permit diagnosis on dynamically acquired images. For MR imaging, three-dimensional T1-weighted sequences usually are utilized for dynamic imaging. Typically, contrast agents are administered at rates of 4–6 mL/s for CT and 2 mL/s for MR imaging followed by saline infusion (20–40 cc) to clear residual contrast material from the intravenous tubing and injected vein. For CT, 1.5–2 mL per kilogram of body weight and for MR imaging, the dose varies from 0.025 to 0.1 mmol gadolinium per kilogram.[26]

Table 2 Recommended Technical Protocol for Ultrasound (USG) Liver.

Longitudinal images	
Recommended views	Left lobe: • left of midline • at midline; include proximal abdominal aorta, celiac artery, and SMA • with IVC; include caudate lobe, MPV, and pancreatic head • with left portal vein Right lobe: • with gallbladder • with right kidney • including right hemidiaphragm and adjacent pleural space • far lateral Main portal vein; include grayscale and color Doppler Common bile duct at porta hepatis; include diameter measurement
Optional views	Color Doppler of the right and left portal veins, and hepatic veins Spectral Doppler of main portal vein to assess waveform, velocity, and flow direction
Transverse images	
Recommended views	Dome with hepatic veins; include entire right and left lobe with medial and lateral liver edges (on separate images as needed) Left lobe: • with left portal vein • falciform ligament to evaluate for the presence of patent paraumbilical vein Main portal vein bifurcation Right lobe: • with right portal vein • with main portal vein • with gallbladder • with right kidney • near liver tip
Optional views	Color Doppler view of additional vascular structures
Cine loops	
Recommended views	–
Optional views	Longitudinal and transverse cine sweeps of left and right lobes, including as much hepatic parenchyma as possible

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Acquisition of three enhanced phases are recommended: late hepatic arterial, portal venous, and delayed phase. The late arterial phase (AP) is characterized by the enhancement of the hepatic artery and its branches as well as early enhancement of the portal vein; the hepatic veins are not yet enhanced by antegrade flow. This phase coincides with peak arterial perfusion and enhancement of liver tumors, and it is critical for detection and characterization of hypervascular HCC.[27] Contrast agent bolus tracking or use of a test bolus is recommended[27,28] The portal venous phase coincides with peak parenchymal enhancement is characterized by enhancement of hepatic veins as well as portal veins and is acquired at around 60–80 s after the start of contrast agent injection.[27] The delayed phase is acquired at 3–5 min.[27] These latter phases are critical for characterizing key imaging features of HCC such as washout appearance and capsule appearance, and they help to differentiate small HCCs from small intrahepatic cholangiocarcinomas (ICCs), which typically show prolonged central enhancement (delayed phase). The portal venous and delayed phases also may be useful for measuring nodule diameter, depicting hypovascular nodules including early HCCs, and identifying vascular thrombosis. The precontrast image serves as a baseline to gauge subsequent enhancement. For observations that are hyperintense on precontrast MR images, subtraction images (postcontrast minus precontrast) may be helpful for detection of enhancement.[28]

HCC IMAGING

Liver lesions that meet strict diagnostic imaging criteria for HCC does not need to be biopsied. The diagnosis of HCC cannot be made on US alone. Multiphase CT or MRI is necessary[28] for size and venous invasion, and extrahepatic disease decides subsequent management of the patient. Biopsy is reserved for indeterminate nodules on CT or MRI, particularly nodules 1–2 cm in size.[29] There is no good evidence to show that USG screening recommendation apply to the obese patients, US is insensitive for detection of HCC in patients with hepatic steatosis as well as nodular cirrhotic livers who are undergoing surveillance.[30] Some international guidelines permit surveillance by CT or MRI, when US is limited by obesity or other factors or if the patient is at very high risk of HCC.[1–8] Patients may present with HCC, including advanced HCC (T stages T1–T4), even if US findings are negative within 1 year before diagnosis US can be unreliable in detection of HCC, and studies have shown sensitivity ranging

from 21% to 94%.[31] Additionally, many institutions in India provide multiphase CT or MRI to screen cirrhotic patients for HCC when ordered by their physicians, as long as the practice can accommodate a large volume of patients for imaging. The diagnosis of HCC on multiphase CT and MRI is made on postcontrast imaging when there is late hepatic arterial-phase hyperenhancement, venous-phase or delayed-phase washout appearance, and venous-phase or delayed-phase capsule appearance. The specificity and positive predictive value HCC is nearly 100% on CT/MRI.[32,33] For HCCs greater than 2 cm, sensitivity of MRI is 100%, and multiphase CT is 98%.[33] For HCCs less than 2 cm, sensitivity of MRI is 68%–85%, and sensitivity of CT is 61–78%[34] with a diagnostic advantage of MRI over multiphase CT in smaller nodules specially less than 1 cm.

T2-weighted sequences and DWI can be helpful in identifying liver lesions. DWI in MRI can be used for problem solving or increasing confidence when other MR sequences are equivocal.[34] Increased conspicuity of lesions on DWI increases sensitivity and justifies its routine use in MRI in detection of HCC.[34] An advantage of HPB contrast agents is that they can detect early HCC that shows relative hypoenhancement on the HPB phase when there is not yet arterial enhancement or venous-phase washout, enhancing the sensitivity and accuracy for HCC diagnosis.[35–37] HPB phase hypointensity favors a malignant or premalignant lesion rather than a low-grade dysplastic or cirrhotic nodule in studies with both hepatitis B and C patients.[35–37] Adding the HPB phase improves sensitivity of HCC detection by 5%–16% compared with MRI using the other dynamic contrast enhanced (DCE) sequences. One recent meta-analysis showed sensitivity of 91% and specificity of 95% with HPB agents.[37] Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT is not an appropriate screening test for HCC. PET/CT is also of limited utility in the diagnosis of HCC, because HCC uptake of FDG-PET is variable.[38]

In HCC patients who have already received liver directed therapy, recurrence is 6.5 times more likely in the first year after treatment than in the second year. Most commonly, the first follow-up imaging is 1 month posttreatment, followed by 3 months posttreatment.[39] This was followed by imaging every 3 months with CT or MRI for 2 years. Many centers treating HCC prefer MRI over multiphase CT because the high-density iodized oil used in transarterial chemoembolization (TACE) can make assessment for tumor recurrence difficult on CT, whereas the presence of iodized oil will not confound the assessment for tumor recurrence on MRI. Subtraction images on MRI can help diagnose new HCC or tumor recurrence in patients with previous liver directed therapy or T1 hyperintense dysplastic nodules. CEUS can be used to assess for local tumor progression and treatment planning after focal ablation of HCC lesions but is not practical for surveillance of the whole liver.[40] Also, the sensitivity of CEUS in detecting local tumor recurrence and new intrahepatic recurrence after percutaneous ablation therapy is relatively low in comparison with multiphase CT.[40] After radiofrequency ablation and percutaneous ethanol ablation, local tumor response can be evaluated with CEUS immediately after the procedure, after 1 day, after 1 month, or later. CEUS might have a role in further characterizing indeterminate nodules seen on CT/MRI or for providing target for biopsy/ablative treatments when not visible on USG.[40]

Key Statements: CT *vs* CEUS *vs* US *vs* MRI literature review including sensitivity and specificity of each modality

9. US is particularly limited for identifying HCC in patients with obesity, non alcoholic fatty liver disease (NAFLD), and nodular cirrhotic livers, which forms a significant portion of at risk population on screening. In these patient groups as well as patients who are on the liver transplant wait list, US is so limited that consideration should be made for screening for HCC with either dynamic contrast enhanced MRI (CEMRI) or multiphase CT. A1
10. Although dynamic CEMRI is preferable because of its slightly increased accuracy compared with CT, ability to detect premalignant nodules, and lack of ionizing radiation, multiphase CT scan also diagnoses HCC accurately. In a resource limited setting such as India, CT remains the essential work horse. A1
11. Given the high rate of recurrence (particularly within the first year after treatment) and insensitivity of US, multiphase CT or MRI is suggested to assess response 1 month after resection or therapy, followed by CT/MRI imaging every 3 months for at least 2 years. B1
12. Dynamic CEMRI if available is preferred over multiphasic CT scan in posttreatment surveillance of HCC because the lipiodol used in TACE can make assessment for tumor recurrence difficult on CT. B1

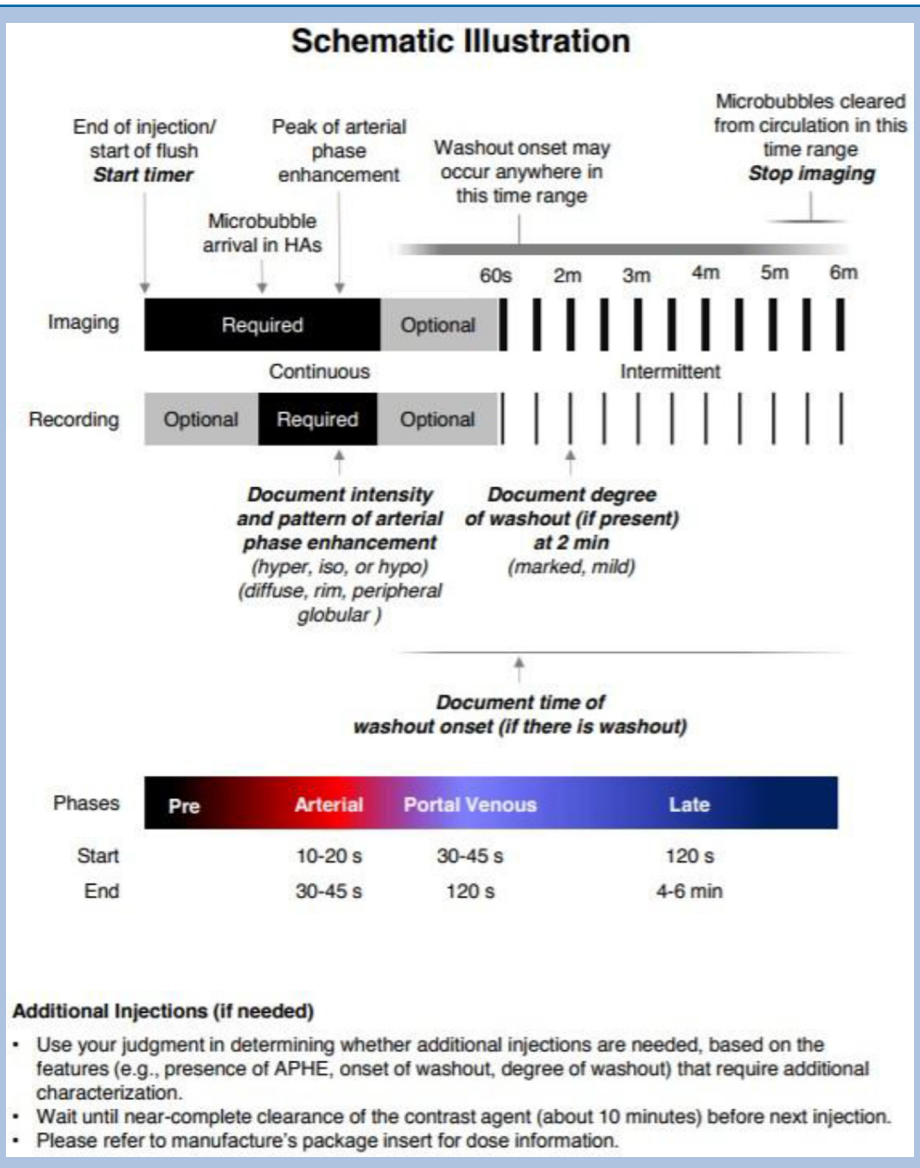
Table 3 Recommended Protocol for CEUS.

3A	
Required systems and models	• Ultrasound scanner with contrast-specific imaging capability, including dual-screen and timer display
	• Refer to contrast-specific instructions provided by scanner manufacturer
Contrast agents	• Current version of CEUS LIRADS applies to pure blood-pool agents but not to combined blood-pool/Kupffer cell agents such as Sonazoid®

Imaging—Recommended	• Precontrast—identify the following:
	  • Target nodule(s)
	  • Optimal patient position: supine, oblique, or left lateral decubitus
	  • Optimal scan plane: usually longitudinal (reduces out-of-plane resp. motion)
	  • Optimal patient breathing: quiet or suspended (neutral, inspiration, expiration)
	• Arterial phase (AP):
	  • Image continuously from contrast injection until peak AP enhancement to capture peak AP enhancement, characterize APHE, and determine presence of early washout
	• Portal venous phase (PVP) to late phase (LP)
	  • Image intermittently (every 30s) to minimize microbubble destruction until microbubbles have cleared completely from the circulation (4–6min) to detect late washout and assess its degree

Imaging—suggested	• Sweep liver in PVP or LP to identify additional nodules. These may manifest as focal hypoenhancing observations in liver
Recording—recommended and optional	• Record continuous cine loop from bubble arrival through peak APHE as a minimum requirement. Optionally the cine loop can be continued beyond the APHE peak until 60 s after injection.
	• Record static images at 60 s and with every intermittent (every ~30s) acquisition thereafter
Imaging parameters	• Use low (˂0.3) mechanical index to avoid microbubble destruction • Use default machine settings
Dual-screen imaging	• Using B-mode image for guidance, place calipers on observation on both screens simultaneously to facilitate enhancement characterization
Timing	• Begin timer after end of contrast injection, at beginning of saline flush (i.e., time 0 coincides with beginning of flush) • Record time in seconds at which washout is first detected
Injection technique	• Use ≥20 G catheter • Central venous lines and infusion ports are acceptable if safety and aseptic requirements are met • Hand inject contrast over 2–3 s, maintaining constant syringe pressure • Flush with 5–10 mL normal saline at about 2 mL/s • Repeat injection as needed, per contrast manufacturer guidelines • Do not exceed maximum total contrast dose listed in package insert
Diameter measurement	• Use B-mode (precontrast) • Use same imaging mode and plane as prior exam to assess growth

3B



APHE: arterial phase hyperenhancement; LIRADS: Liver Imaging Reporting and Data System.
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Table 4 Technical Criteria for CT.

CT	
Recommended equipment	• Multidetector CT with ≥8 detector rows
Required images	• Arterial phase (late arterial phase strongly preferred) • Portal venous phase • Delayed phase
Suggested images	• Precontrast, if patient has had locoregional treatment • Multiplanar reformations

CT: computed tomography.
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Table 5 Technical Criteria for MRI.

MRI with extracellular contrast agents or gadobenate dimeglumine	
Recommended equipment	• 1.5T or 3T • Torso phased-array coil

Required images	• Unenhanced T1-weighted OP and IP imaging
	• T2-weighted imaging (fat suppression per institutional preference)
	• Multiphase T1-weighted imaging
	  • Precontrast imaging
	  • Arterial phase (late arterial phase strongly preferred)
	  • Portal venous phase
	  • Delayed phase

Suggested or optional images	• Diffusion-weighted imaging • Subtraction imaging • Multiplanar acquisition • 1 to 3-hr hepatobiliary phase with gadobenate dimeglumine
MRI with gadoxetate disodium	
Recommended equipment	• 1.5T or 3T • Torso phased-array coil

Required images	• Unenhanced T1-weighted OP and IP imaging
	• T2-weighted imaging (fat suppression per institutional preference)
	• Multiphase T1-weighted imaging
	  • Precontrast imaging
	  • Arterial phase (late arterial phase strongly preferred)
	  • Portal venous phase
	  • Transitional phase (2–5 min after injection)
	  • Hepatobiliary phase

Suggested or optional images	• Diffusion-weighted imaging • Subtraction imaging • Multiplanar acquisition

MRI: magnetic resonance imaging.
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Table 6 List of Ancillary Features.

Ancillary features favoring malignancy	Ancillary features favoring benignity
Favoring malignancy in general, not HCC in particular • US visibility as discrete nodule • Subthreshold growth • Restricted diffusion • Mild-moderate T2 hyperintensity • Corona enhancement • Fat sparing in solid mass • Iron sparing in solid mass • Transitional phase hypointensity • Hepatobiliary phase hypointensity	• Size stability ˃ 2 years • Size reduction • Parallels blood pool • Undistorted vessels • Iron in mass, more than liver • Marked T2 hyperintensity • Hepatobiliary phase isointensity
Favoring HCC in particular • Nonenhancing 'capsule" • Nodule-in-nodule • Mosaic architecture • Blood products in mass • Fat in mass, more than adjacent liver	

US: ultrasound; HCC: hepatocellular carcinoma.
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DEFINING BENIGN NODULES AND FINDINGS IN CIRRHOTIC LIVER

The differential diagnosis of a small flash-filling hemangioma (larger hemangioma showing peripheral nodular discontinuous filling in paralleling blood pool in all the phases) from small hypervascular HCC is based on the differing enhancement patterns flash-filling hemangiomas, which demonstrate strong and homogeneous attenuation matching blood pool. Whereas in HCC enhancement during the hepatic AP is typically milder and followed by washout during the hepatic venous and delayed phases.[41] In small HCC, washout may be absent, likely because of conservation of the portal blood supply, thus making the tumor appear isoattenuating/isointense to the surrounding liver parenchyma—difficult to differentiate from a capillary hemangioma. The second scenario is when the fibrotic and scarring processes distort liver architecture, also causing a fibrotic involution of the lesion. In such cases, hemangiomas are typically hypovascular, losing features commonly observed in noncirrhotic livers, such as globular peripheral enhancement patterns and isointensity to vessels on multiphasic imaging. Hypovascular HCC is a spherical lesion, slightly hypoattenuating, and therefore recognizable, *vs* the surrounding liver in the venous phase, while fibrotic hemangiomas commonly have an irregular shape and more pronounced hypoattenuation in comparison with the surrounding liver on unenhanced and postcontrast images. Furthermore, strong hyperintensity on T2-weighted MR images is more characteristic of

Table 7 Suggested Reporting Template for HCC Reporting (LIRADS Nomenclature Suggested).

(A) Template for multiphasic CT scan abdomen		
Procedure: CT abdomen	Date	Indication Underlying liver disease, surveillance for hepatocellular carcinoma, history of treatment
Comparison: Include modality, presence/absence of contrast material on prior, and date	**Technique:** Dynamic multiphase contrast-enhanced CT imaging of the abdomen was performed [including precontrast imaging].	**Examination meeting technical recommendations?** Yes No: It is compromised by the following factor(s):
Intravenous contrast agent: [type] Volume: [] ml Rate: [] mL/sec	**Premedication/adverse events:**	
Findings: Liver: [morphology and attenuation, diffuse findings], focal hepatic observations: [for each observation, provide diameter and series/image on which it was measured, hepatic segment, major features, and change since prior; describe vascular involvement if applicable]. Benign/Indeterminate/HCC hepatic vasculature: [anatomic variants, patency], Biliary system: Extrahepatic findings: [none, splenomegaly, collaterals, ascites].[Other organs, findings, etc.]:		
Impression: Hepatic findings: [Additional liver findings as above.], Extrahepatic findings:[None]		
Recommendation		
(B) Template for dynamic contrast enhanced MRI abdomen		
Procedure: MRI Abdomen with and without contrast	Date	Indication Underlying liver disease, surveillance for hepatocellular carcinoma, history of treatment
Comparison: Include modality, presence/absence of contrast material on prior, and date	**Technique:** Precontrast and dynamic postcontrast MR imaging of the abdomen was performed. MRCP was also performed. Additional sequences may be described at institutional discretion.	**Examination meeting technical recommendations?** Yes No: It is compromised by the following factor(s):
Intravenous contrast agent: [type] Volume: [] ml Rate: [] mL/sec	**Premedication/adverse events:**	
Findings: Liver: [morphology and signal intensity, diffuse findings], **Focal hepatic observations:** [for each observation, provide diameter and series/image on which it was measured, hepatic segment, major features, and change since prior; describe vascular involvement if applicable]. Hepatic vasculature: [anatomic variants, patency], biliary system: extrahepatic findings: [none, splenomegaly, collaterals, ascites].[Other organs, findings, etc.]		
Impression: Hepatic findings: [Additional liver findings as above.], Extrahepatic findings:[None]		
Recommendation		

MRCP: magnetic resonance cholangiopancreatography; CT: computed tomography; MR: magnetic resonance; HCC: hepatocellular carcinoma; LIRADS: Liver Imaging Reporting and Data System.
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atypical hemangiomas in cirrhotic livers. Few case reports have described focal nodular hyperplasia (FNH)–like nodules in the cirrhotic liver—usually small (<2 cm).

Focal nodular hyperplasia will typically show fading to isoattenuation in the hepatic venous phase, thus showing overlapping features with hypervascular dysplastic nodules and small well-differentiated HCC.[43] These similarities in imaging create difficulties in the differential diagnosis and may lead to unnecessary treatment. Regenerative nodules, dysplastic nodules, focal nodular hyperplasia–like lesions, and about 10% of HCC can all show hyperintensity in the HPB phase. Thus, hyperintensity in HPB phase alone does not allow a specific diagnosis.[42,43]

Simple biliary cysts have similar features in cirrhotic and noncirrhotic livers: low attenuation on CT, low signal intensity on T1-weighted MR sequences, and high signal on heavily T2-weighted MR sequences, with no contrast enhancement.[44] Peribiliary cysts are cystic lesions typically found on both sides of the intrahepatic portal venous branches, as opposed to intrahepatic biliary dilatation, which is located on one side only of portal venous branches, representing cystic dilatation of the extramural glands in the periductal connective tissue and show the same imaging findings as simple cysts.[44]

When discretely visible, cirrhotic nodules have the following imaging features: diameter often less than 1 cm; similar attenuation or mildly high attenuation relative to surrounding liver parenchyma on unenhanced CT images; isointense or mildly hyperintense relative to surrounding liver parenchyma on unenhanced T1-weighted MR images; isointense or mildly hypointense relative to surrounding liver parenchyma on unenhanced T2-weighted MR images; and enhancing to a similar degree as surrounding liver in all phases after injection of extracellular contrast agents.[45]

Vascular anomalies are focal mass-like observations that often exhibit AP enhancement with early enhancement of the adjacent portal vein or hepatic vein. Arterioportal and portohepatic venous fistulas are common examples.[46] Transient hepatic intensity and attenuation differences and enhancement differences are geographic, often well-defined regions of perfusion alteration characterized by transient AP hyperenhancement (APHE) relative to background liver-visible only on APs, invisible on unenhanced images and on images from the later phases of contrast enhancement and not mass like.[46]

Hepatic fat deposition is the presence of excess lipid within hepatic parenchyma. Hepatic fat deposition can be diffuse, focal, or multifocal; MRI is more sensitive and specific than CT for the detection of hepatic fat deposition. On MRI, hepatic fat deposition may be diagnosed if the liver, in whole or in part, exhibits loss of signal intensity on T1-weighted out-of-phase compared with T1-weighted in-phase gradient-echo images or on fat-suppressed compared with non–fat-suppressed images, and on CT, it shows low attenuation in −40 HU or less on unenhanced images or 10 HU or lower than the attenuation of the spleen on unenhanced images. Fatty infiltration has no mass effect, and vessels course through the region without mass effect. Diffuse hepatic fat deposition affects a large area of the liver (entire liver, lobe, or segment) and may have a homogeneous or a heterogeneous distribution that is patchy, perivascular, subcapsular, or multisegmental.[47] Focal hepatic fat deposition affects a small area of the liver (subsegmental), usually has a geographic shape, and is often subcapsular. Less commonly, it has a rounded shape. It usually occurs in specific areas (e.g., adjacent to the porta hepatis, gallbladder fossa, falciform ligament, and ligamentum venosum). Hepatic fat sparing is lack of lipid or relative lack of lipid within a portion of otherwise fatty hepatic parenchyma.[47] It may occur around the margin of a mass or in an area with impaired portal venous perfusion, likely because this vascular alteration results in less delivery of fat to the affected hepatocytes, and it has undistorted vessels traversing the spared areas, geographic shape, and absence of mass effect.

Focal fibrosis and confluent fibrosis occur in regions of severe hepatic parenchymal damage and hepatocellular destruction sheet-like, band-like, or wedge-shaped areas, often subcapsular, of abnormal signal intensity or attenuation that often progress over time—T2 hyperintense, T1 hypointense, and hypodense on CT. They may exhibit associated retraction of the liver capsule. Progressive contrast enhancement peaks in the delayed phase after extracellular contrast administration. Fibrosis is geographic, and enhancement is homogeneous and not target-like or peripheral.[46] Pseudomass morphologic features may be seen with cirrhosis of any cause, primary sclerosing cholangitis, Budd–Chiari syndrome (BCS), chronic portal vein obstruction, or sequela of severe acute hepatitis.

Compared with surrounding fibrotic liver, the hypertrophic areas of regeneration generally have a closer to uniform appearance, lower signal intensity on T2-weighted images, higher signal intensity on T1-weighted images, similar or less enhancement during the AP, and similar or lower signal intensity or attenuation on late phase images. Because the surrounding fibrotic regions often exhibit delayed phase enhancement, the area of hypertrophy may appear relatively hypointense or hypoattenuating by comparison.[46] Temporal enhancement parallels that of the adjacent liver parenchyma.

Once the benign lesions have been diagnosed, they do not require any enhanced follow-up or biopsy, and they can be under routine surveillance.[48] In a study by Tanabe *et al*., none of the benign lesions progressed to HCC or any other malignancy during the observation period.[49] Recent systematic review and Liu *et al.* showed that diagnosis of LR1 benign lesions had 100%negative predictive value[50,51] with good interreader agreement.

Key Statements: Defining benign nodules and findings in cirrhotic liver

13. Benign lesions include cysts, hemangiomas, vascular anomalies, perfusion alterations, fat deposition or sparing, confluent fibrosis, focal fibrosis, and cirrhosis-associated nodules. Patients with these definite benign lesions having definite imaging findings can be safely kept on routine follow-up. There is no risk of conversion of these to HCC or any other malignant lesion. A1

POST CHEMOTHERAPY NODULES AND NODULES IN BUDD–CHIARI SYNDROME

Literature Review

There is not enough evidence to routinely screen patients following chemotherapy except as part of treatment algorithm for that particular cancer.[52–56] Subset of patients do develop chemotherapy-induced fatty change, hepatotoxicity, and hepatic necrosis, which can progress to cirrhosis; such cases should be dealt on a case by case basis—at present, there is not enough evidence to recommend screening in such cases.[53–56]

BCS is characterized by an obstruction of the hepatic venous outflow tract (though separate but the spectrum also includes also hepatic venoocclusive disease [HVOTO]) in the absence of right heart failure or constrictive pericarditis.

Sometimes BCS occur years after high-dose chemotherapy and hematopoietic stem cell transplantation.[57–59] In lesions with intense arterial enhancement and absence of washout in the delayed phase, dynamic MRI with HPB contrast seems to be helpful in differentiating hepatic nodules in these patients[56–58]

Majority of the hypervascular nodules might represent FNH, regenerative nodules, or FNH-like lesions, but some are similar to adenomas.[56–58] There are mainly two different types of nodular lesions that have been described with the history of impaired liver circulation: nodular regenerative hyperplasia (NRH) and large regenerative nodules (LRNs), the latter are the more FNH-like lesions In general, these nodules develop independently from liver cirrhosis, and LRNs seem to be associated with BCS and sometimes these do washout.

Some imaging features are different from those of FNH seen on normal liver, such as hyperintensity on T1-weighted and T2-weighted MR images, but they also are homogeneous, hypervascular, and the largest lesions often contain a central scar.[56–58]

In most cases, these lesions are multiple, and their size does not exceed 3 cm in diameter. Progression either by size or number is often observed.[56–58]

Patients with BCS are also at risk of HCC (11 of 97 patients in a recent cohort followed up for a mean of 5 years), suggesting that BCS patients should be monitored for HCC development. Serum alpha fetoprotein seems quite specific for HCC in this setting.[56–61]

Diagnosis is challenging at imaging, and HPB MR contrast agents are helpful. Liver biopsy is indicated in atypical cases or when significant changes occur over time. There is no evidence to date that benign regenerative nodules patients with BCS degenerate into malignancy.[56–61]

In a study by Paul *et al.*, all HVOTO with HCC patients (16/16, 100%) had underlying cirrhosis. HVOTO is a risk factor for HCC. The cumulative incidence of HCC which was 3.5% (CI 1.3–9.2%) at 10 years, 9.5% (CI 3.4–25.2%) at 15 years, and 29.5% (CI 11.4–63.6%) at 20 years. This suggests that even though the prevalence of HCC in HVOTO in South Asia is low, the cumulative incidence progressively increases over time. Degree and extent of outflow obstruction and

Key Statements: Post Chemotherapy Nodules and Nodules in Budd–Chiari Syndrome

14. Patients following high-dose chemotherapy or stem cell transplantation do develop FNH-like lesions or regenerative nodules that are often incidentally detected years after chemotherapy. There is no evidence to recommend routine screening in such cases. They should be dealt on a case-by-case basis. HPB-specific MR contrast with DWI may be helpful. B2
15. In BCS, benign regenerative nodules, NRH, and regenerative nodules are common. A1
16. BCS is a risk factor of development of hepatocellular carcinoma. B1
17. BCS patients with long-segment IVC obstruction, obstruction of both HVs and IVC, presence of cirrhosis and failure of therapeutic intervention, or recurrence of outflow tract obstruction may be the high-risk group of patients with increased propensity to develop HCC and may be screened for early detection of liver cancer. B1
18. Any nodule in BCS which shows differential enhancement to rest of the nodules, does not take up HPB contrast, and shows diffusion restriction is suspicious—biopsy should still be considered for definite diagnosis. B1

presence of advanced degree of fibrosis suggesting prolonged hepatic congestion with resultant parenchymal loss were associated with HCC. Patients with long-segment IVC obstruction, obstruction of both hepatic vein (HV) and IVC, presence of cirrhosis and failure of therapeutic intervention, or recurrence of outflow tract obstruction may be the high-risk group of patients with HVOTO to develop HCC and may be screened for early detection of liver cancer.[62]

DEFINING HCC, INFILTRATIVE HCC, SATELLITE NODULE, AND MULTIFOCAL HCC WITH LITERATURE REVIEW

APHE, sometimes termed arterial "wash-in" or arterial "hypervascularity," is defined as enhancement in the AP that unequivocally is greater than that of surrounding liver (this is however within the lesion and different from rim enhancement which is around the periphery of the lesion). Intranodular arterial supply increases during hepatocarcinogenesis when most progressed HCCs are hyperenhancing, while most cirrhotic nodules, dysplastic nodules, and early HCCs are hypoenhancing or isoenhancing in the AP. APHE in isolation is nonspecific also seen in benign perfusion alterations, small hemangiomas, small focal nodular hyperplasia–like lesions, AP shunts, some atypical cases of focal or confluent fibrosis, some atypical cirrhotic nodules and dysplastic nodules, and non-HCC malignancies such as small cholangiocarcinomas or small hypervascular metastases such as neuroendocrine tumors.

Washout defined as a visually assessed temporal reduction in enhancement relative to surrounding liver from an earlier to a later phase, resulting in portal venous or delayed phase hypoenhancement.[1–9,63–65] The mechanisms underlying washout include early venous drainage of contrast material from the tumor (true washout), progressive enhancement of background liver (because of retention of contrast material within fibrotic parenchyma), reduced intranodular portal venous blood supply, tumoral hypercellularity with corresponding reduction in extracellular volume, and intrinsic hypoattenuation/hypointensity.[66] Thus, the visually assessed temporal reduction in enhancement relative to liver may be caused by factors other than true washout, and for this reason, the term *washout appearance* is advocated by the LI-RADS.[8] Washout appearance by itself is not specific for HCC as this feature may be observed in cirrhotic nodules and dysplastic nodules, and focal areas of parenchymal distortion/enhancing fibrosis may create the perception of "washout". Recently, Liu *et al.* proposed a quantitative definition for washout based on CT attenuation values in user-defined regions of interest in lesion and adjacent liver; further studies are needed to compare the accuracy and interreader reliability for HCC diagnosis using quantitative *vs* subjective definitions of "washout.[67]"

Although the individual features are nonspecific, the combination of AP hyperenhancement and portal venous and/or delayed phase washout appearance is highly specific for HCC in patients with cirrhosis or other risk factors for HCC.[68,69] In such patients, this temporal enhancement pattern has approximately 100% specificity for HCCs 20 mm or larger and approximately 90% specificity for 10-mm to 19-mm HCC.[70]

Another imaging feature of HCC is capsule appearance, defined by peripheral rim of smooth hyperenhancement in the portal venous or delayed phase-degree of enhancement usually increases from early to later phases, and the delayed phase may be superior to the portal venous phase for identifying this feature.[70] Retrospective studies have shown that capsule appearance at CT/MR imaging correlates with the presence of a tumor capsule at pathologic examination. Some are instead surrounded by "pseudocapsules" consisting of mixed fibrous tissue and dilated sinusoids.[71] The progressive enhancement has been attributed to combination of slow flow within intracapsular vessels as well as contrast agent retention within the extravascular connective tissue of the capsule. Thus, capsule appearance is not pathognomonic for the presence of a true tumor capsule. Capsule appearance has been shown to be an important predictor of HCC,[72–74]-permitting diagnosis of HCC without definite washout appearance[74] According to two diagnostic systems, a mass 2 cm or larger with AP hyperenhancement and capsule appearance can be diagnosed definitively as HCC even in the absence of washout appearance; for 10-mm to 19-mm masses with AP hyperenhancement, both capsule appearance and washout appearance are required.[1–9]

A potential pitfall is peripheral enhancement in small ICCs, and all phases may be misinterpreted as a "capsule"; however, peripheral enhancement in ICC tends to peak in the AP and diminish in later phases, rather than progress. Another pitfall is that fibrous tissue surrounding cirrhotic nodules and dysplastic nodules may enhance on delayed phase images, generating the perception of a "capsule"; thus, radiologists should apply this feature only if the enhancing rim unequivocally is thicker or more conspicuous than the fibrous tissue surrounding background nodules.[72]

Extracapsular extension with the formation of satellite nodules, subcentimeter nodules outside the tumor margins (usually within 2 cm),[73] is seen in large progressed HCC representing intrahepatic metastases within the venous drainage area around the main tumor. They may be located within the corona enhancement area. Hence, despite their small size, they typically manifest AP hyperenhancement. The presence of satellite nodules has been recognized as predictor of recurrence and lower survival after transplantation, resection, and local ablation.[74] The sensitivity and specificity of CT or MR imaging for satellite nodules have not been extensively studied and merit further investigation.

Size refers to the largest outer-edge-to-outer-edge dimension of an observation. Size should be evaluated on the sequence, phase, or plane in which the margins are most distinct. If capsule appearance is present, the "capsule" should be included in the measurement. Size is included as a major feature since the likelihood of malignancy in a cirrhosis associated nodule is positively correlated with the size of the observation.[69–72] Threshold growth is defined as a size increase of an observation by at least 5 mm and at a sufficient rate. The size must increase by at least 50% over 6 months or by at least 100% over greater than 6 months. Alternatively, an observation that is at least 10 mm in size but was not present on an examination obtained within the previous 2 years can also be considered to meet threshold growth criteria.[8] Interval growth of nodules is a specific finding for malignancy. HCC tumor volume doubling time in the literature varies from less than 1 month to greater than a year. In general, small (less than 30 mm) HCC show shorter doubling times than large HCC.[74]

HCC has been traditionally categorized into three major types based on the Eggel growth pattern classification: nodular, massive, and diffuse. The nodular type consists of a single tumor or multiple nodular tumors with clear demarcation. The massive type consists of a large tumor with an unclear boundary that occupies most or all of a hepatic lobe. The infiltrative, or diffuse, type is characterized by the spread of minute tumor nodules throughout an entire lobe or the entire liver without a dominant nodule.[75] Infiltrative HCC is often cryptic and can masquerade as cirrhotic nodules; therefore, several authors have referred to infiltrative HCC as cirrhotomimetic-type HCC or diffuse cirrhosis; many authors believe it represents innumerable intrahepatic metastases based on observations that tumor thrombi are frequently present in large perihilar portal veins. The spread of minute tumor nodules throughout the liver is the typical pathologic macroscopic appearance of infiltrative HCC. This pattern translates as a permeative ill-defined appearance at US, CT, and MR imaging. Infiltrative HCC usually spreads over multiple hepatic segments, occupying an entire lobe or the entire liver. Moreover, multiple smaller satellite lesions are reported in up to 52% of cases.[76]

Portal vein tumor thrombosis is a common finding in patients with infiltrative HCC, often affecting both extrahepatic and intrahepatic branches, with a frequency ranging from 68% to 100%,[76] sometimes primary imaging feature. Arterial hyperenhancement and washout may be not distinct and lack HPB contrast uptake, and DWI may be discriminant. The relatively reduced conspicuity of infiltrative HCC on images obtained during the dynamic phases of enhancement likely relates to the permeative infiltrating nature of the tumor and frequent presence of portal vein thrombosis, which results in perfusion changes that can effectively conceal the tumor. Therefore, the tumor may be more visible among the surrounding liver parenchyma on diffusion-weighted, T1-weighted, and T2-weighted MR images than on dynamic contrast-enhanced images.[75]

Key Statements: Defining HCC, Infiltrative HCC, Satellite Nodule, and Multifocal HCC with Literature review

19. In lesions more than 1 cm, the combination of AP hyperenhancement and portal venous and/or delayed phase washout appearance is highly specific for HCC in patients with cirrhosis or other risk factors for HCC. A1
20. In lesions more than 1 cm, the combination of AP hyperenhancement and threshold growth is highly specific for HCC in patients with cirrhosis or other risk factors for HCC. A1
21. In lesions more than 2 cm, the combination of AP hyperenhancement and capsule appearance is highly specific for HCC in patients with cirrhosis or other risk factors for HCC. A1
22. In lesions more than 20 mm without AP hyperenhacement but with one or more of the following washout, capsule enhancement or threshold growth—there is high probability of HCC. Likewise observations 10–20 mm but with two or more of the above features—there is high probability of HCC. B1
23. AFP alone may be nonspecific as a screening modality. But in the presence of other imaging characteristics increases the degree of confidence and can play a role in decision making. B1

INDETERMINATE NODULE—WHAT CONSTITUTES INDETERMINATE NODULES, BIOPSY *VS* ALTERNATE MODALITY *VS* FOLLOW-UP LR3

Indeterminate nodules are commonly seen in cirrhotic patients and pose a diagnostic dilemma for clinicians. Challenges to biopsy include the high frequency of benign nodules in the cirrhotic liver, cost, false negative rates, and the increased complications associated with thrombocytopenia or coagulopathy, both common in patients with cirrhosis.[1–9,77] In most studies, incidence of nodule progression to HCC is 14–23%[77,78]

The incidence of HCC development and which indeterminate lesions are most likely to progress to HCC is not

yet established. Previous studies cite factors such as age, chronic viral hepatitis, low platelet count, alcohol and hepatitis C, male gender, and hepatitis C as risks for the development of HCC, although these factors have not been specifically identified as risk factors for progression of an indeterminate nodule[79]

Such patients are best reviewed by multidisciplinary Liver Tumor Board. For most indeterminate nodules discovered on surveillance imaging, follow-up imaging in 3 months is recommended based on the approximately 3-month median interval to "progression" of indeterminate nodules to HCC.[80]

Up to 21% incidence of HCC in the cirrhotic population with indeterminate nodules suggests early intervention is appropriate for some at higher risk. A randomized trial by Zhang *et al.* found a 37% reduction in HCC mortality with routine 6-month surveillance exams, which allows for earlier intervention.[81] In the least, early follow-up imaging, biopsy, or empiric treatment should be considered for those at highest risk, such as indeterminate nodules in men with hepatitis C.

According to the KLCSG-NCC Korea practice guidelines, either biopsy or follow-up could be used for nodules without the typical enhancement pattern of HCCs, i.e., arterial-phase enhancement and "washout" on contrast-enhanced CT or MRI. This is quite different from the AASLD or EASL-EORTC guidelines, as biopsy is advocated for all indeterminate nodules on imaging work-up by contrast enhanced scans. First, neither the AASLD diagnostic algorithm nor the EASL-EORTC diagnostic algorithm would be appropriate to diagnose early HCCs, which frequently show atypical enhancement patterns. Second, biopsy of small (<2 cm) nodules may not be technically possible in some patients and may possess a risk of sampling bias or a serious diagnostic difficulty, as well as a potential risk of tract seeding. Third, the low prevalence of malignancies among the 1–2 cm indeterminate nodules (14–23%) also justifies follow-up strategy (reference). Fourth, no outcome study has shown that survival is prolonged by performing a biopsy for indeterminate nodules >10 mm rather than following them closely for growth. Thus, this option of follow-up strategy is clinically feasible.[82]

Key Statements: Indeterminate nodule

24. All arterially enhancing lesions which show no corresponding feature of washout, threshold growth or capsular enhancement or lesions more than 20 mm without any of the above features. Alternatively, lesions less than 20 mm which show only one of the above features are considered indeterminate. A1
25. Any other nodule, which the radiologist can neither assign as benign, HCC or alternate malignancy is considered indeterminate. A1
26. In cirrhotic patients with an indeterminate mass, there are insufficient data comparing biopsy to repeat imaging. A1. USG visibility, serial change in AFP, and recent history of treatment for HCC may help in decision making. B2

HYPOVASCULAR HYPOINTENSE NODULES

It was reported that a substantial proportion of nonhypervascular hypointense nodules (≥1 cm) or isovascular hypointense nodules (>1 cm) are pathologically diagnosed as HCCs or high-grade dysplastic nodules (HGDNs).[83–86] Moreover, approximately 10–30% of these nodules show arterial-phase hypervascularization on follow-up. The clinical impact of these nodules on patients' outcome is gaining attention. Patients with nonhypervascular hypointense nodules show shorter recurrence-free survival after radiofrequency ablation and lower overall survival (OS) rate after liver resection. Despite their clinical significance, currently LI-RADS is the only criteria that stratifies risk of nonhypervascular hypointense nodules by scoring LR-3 or LR-4, depending on ancillary findings.[8] One of the reasons why these nodules are not stated in other guidelines might be the challenge to differentiate HCCs from HGDNs noninvasively. Although there have been attempts to differentiate HCCs from HGDNs in these nodules using ancillary findings such as mild to modest T2 hyperintensity and diffusion restriction or initial nodule size (>1–1.5 cm in diameter), the results are controversial to date.[87] Nonetheless, these nonhypervascular hypointense nodules should be addressed as potentially malignant with intense close interval follow-up, because a substantial number of the nodules are pathologically early HCCs, and they potentially progress to classic HCCs.

Key Statements: Indeterminate nodule

27. At present available evidence or expert opinion does not agree on any single recommendation or key statement.

ANCILLARY FINDINGS (TABLE 6)

Mild or moderate T2 hyperintensity comparing to the liver is highly suggestive of malignancy. Cirrhotic and dysplastic nodules are characteristically isointense or hypointense on T2WI, and only very rarely appear mild/moderately hyperintense. This feature can be useful for the differentiation between a dysplastic nodule and a small HCC, especially when the latter presents as a hypervascular nodule without washout.[88–91] HCCs tend to show minimal to mildly increased signal intensity on T2-WI, with specificity and a positive predictive value ranging between 73%-100% and 72%–100%, respectively. The addition of T2-WI hyperintensity to the AASLD criteria improved the detection rate of HCC, especially in nodules <20 mm, by increasing sensitivity from 67.6% to 79%.[88–91] Sofue *et al.* evaluated the imaging features in MRI associated with the upgrade to a LI-RADS 5 category and verified that the risk factors in the 56 LR-4 observations, which were upgraded to LR-5, included mild to moderate T2 hyperintensity ($P < 0.001$) and growth ($P < 0.001$)[92]. Hyperintensity on T2-WI and DWI could also be useful in differentiating hypovascular HCCs from dysplastic nodules, which are perceived as hypointense nodules in the HPB phase. However, many well-differentiated HCCs and some small, moderately differentiated HCCs can be isointense or hypointense in T2-WI, and both metastasis and ICCs can show mild T2 hyperintensity.[92] DWI measures the random motion of water molecules inside a voxel of tissue. DWI hyperintensity (relative to liver parenchyma) is expected within an HCC because of its highly cellular tissue. In contrast, benign nodules usually present a similar microstructure to their surrounding tissues, and therefore, free water movement is preserved. As such, DWI may be useful in detecting HCC among benign nodules and arterially enhancing pseudo-lesions, assessing response to treatment, because treatment-induced necrotic and inflammatory tissue result in a loss of cellular density and an increase in membrane permeability with subsequent diminished restriction of diffusion.[89–91]

All reports seemed to agree that DWI, as a diagnostic criterion for HCC, improved the sensitivity of conventional MRI, and the greatest benefit lied in the combined use of both (pooled sensitivity and specificity: 93% and 84% combined, respectively). However, cirrhotic parenchyma may itself show restricted diffusion, presumably owing to the abundance of fibrotic tissue, which results in reduced HCC conspicuity in DWI.[93,94] In patients at risk of HCC with fatty liver infiltration, if a suspicious lesion has a lower fractional fat content than that of the background liver, then it is an ancillary feature favoring HCC. However, this only applies in the presence of fatty liver infiltration and must be differentiated from hepatic fat sparing areas by way of confirmation of the different enhancement pattern from that of background liver, which is better performed using subtraction technique. Absence of iron deposition in a suspicious lesion within an iron-overloaded liver parenchyma is highly suggestive of premalignancy or malignancy, because high-grade dysplastic nodules and HCC cells lose the ability to concentrate iron.[8] Applies to solid masses that unequivocally have a lower fractional iron content than background liver. Liver iron deposition can be shown as signal loss on the second echo of a dual-echo sequence or as abnormal hypointensity on T2 or T2*-weighted images, however not specific to HCC, as it may also be observed in other malignancies, such as ICC, and nonmalignant processes such as confluent fibrosis. Intralesional fat than background liver tissue[88–91] reflects fatty metaplasia frequently histologically observed in early HCCs—sensitivity, specificity ranging from 12% to 37%/68%–91%, respectively. High-grade and occasionally low-grade dysplastic nodules may also show intralesional fat.

An increase in diameter less than the threshold growth is an ancillary feature that favors HCC; however, there is no stipulated minimum increase in diameter for its use as an ancillary feature.[8]

Corona enhancement defined as a zone (or rim) of perilesional enhancing parenchyma seen in hypervascular and progressed HCC in the late arterial or early portal venous phase, which fades to isoenhancement in the subsequent phases. It represents the rapid drainage of contrast material from the arterially hyperenhancing lesion to the peritumoral parenchyma, carried by the tumor draining vessels, just a few seconds after the tumor itself begins to enhance.

The presence of intralesional or perilesional hemorrhage in the absence of previous biopsy, intervention, or trauma is also an ancillary feature favoring HCC, as it is associated with HCC expansion. In MRI, blood products usually manifest as areas with predominantly high signal intensity on T1-WI and heterogeneous and predominantly low-signal intensity on T2-WI. Owing to T2* shortening, there may be signal loss on the second echo of a dual-echo gradient-echo sequence.

LI-RADS may provide a good example on how to deal with the aforementioned ancillary findings in the noninvasive diagnosis of HCCs. For the diagnosis of "probably HCC (LR-4)", morphologic findings such as fatty metamorphosis and nodule in nodule architecture as well as the findings on T2-weighted imaging, DWI, and HPB phase imaging are considered as favoring malignancy. Hypointensity on the HPB phase is also considered as an ancillary finding for malignancy. In a recent prospective cohort study, which considered the diagnoses of "LR-5" and "LR-4" as definitive for HCC, sensitivity increased from 42.3% to 65.4%, without decreasing specificity (96.4%) in US detected small nodules (≤2 cm).[95] In a study by Tang *et al.*, the use of ancillary features in combination with major features increases the sensitivity while preserving a high specificity for

the diagnosis of HCC.[70] Min *et al*., in their study adding at least two ancillary features improved accuracy (88.1%, $P < 0.0001$) and sensitivity (88.1%, $P < 0.0001$) without changing specificity (87.8%, $P = 1.0$)[94]. However, up-scoring and down-scoring using ancillary findings are one of the main causes of increased interobserver variability in LI-RADS.[96]

Nodule-in-nodule architecture refers to the presence of a nodule within a larger nodule or mass—corresponds to the nodule-in-nodule growth pattern observed at histologic evaluation suggesting progressed HCC within a dysplastic nodule or early HCC.[97] The subnodule, corresponding to the progressed HCC, typically shows AP hyperenhancement as well as hyperintensity on T2-weighted images, and if a HPB agent is given, hypointensity is in the HPB phase.[98] The surrounding parent nodule, corresponding to more well-differentiated tissue, typically is T1 hyperintense, T2 hypointense, and AP hypoenhancing or isoenhancing. The parent nodule may be fatty or iron rich (siderotic); the inner nodule usually contains less fat and reflecting the iron "resistance" of neoplastic hepatocytes, less iron, the sensitivity, and specificity of this feature for the diagnosis of HCC has not been established.[98]

Mosaic architecture within a mass represents randomly distributed internal nodules or compartments differing in enhancement (in the dynamic vascular phases or if a HPB agent is administered, in the HPB phase), attenuation, intensity, shape, and size and often separated by fibrous septations. Frequently observed in large HCCs and reflects the mosaic configuration observed at pathologic examination. This feature helps in the differentiation of HCC from ICC.[99]

Key Statements: Ancillary Findings

28. Adoption of ancillary findings though helpful to increase the confidence of the radiologist in reporting a lesion on case to case basis are at present subjective in nature. The reporting radiologist/institution can decide about their adoption. B2

Key Statements: Subcentimeter

29. Subcentimeter hypervascular lesions showing two or more of the features of washout, rim enhancement, or threshold growth can be considered as suspicious for HCC in the correct clinical setting. Ancillary features of diffusion restriction and hypointensity on the HPB phase may help in further characterization. B2

SUBCENTIMETER HCC

The first emerging question is the characterization of subcentimeter hypervascular nodules that show AP enhancement and "washout", diffusion restriction or hyperintensity on T2-weighted imaging and hypointensity on the HPB phase.[100] In contrast to AASLD and EASL-EORTC guidelines, KLCSG-NCC Korea practice guidelines and LI-RADS include a category for these HCCs (<1 cm). KLCSG-NCC Korea practice guidelines indicate that HCCs can be diagnosed by a combination of the typical hallmark features of HCCs in ≥2 imaging modalities and increased serum alpha-fetoprotein levels with a rising trend over time for liver nodules <1 cm in patients with suppressed hepatitis activity.[5] LI-RADS suggests that arterial-phase enhancing nodules (<1 cm) showing two finding among "washout", "capsule", or "threshold growth" can be scored as LR-4, indicating "probably HCC".[5,8] Recent studies report that in subcentimeter (<1 cm) hypervascular nodules showing typical imaging findings of HCC on gadoxetic acid–enhanced MRI and DWI, 89.9–100% of the nodules progress to overt HCCs (≥1 cm) within 12 months, and all nodules (100%) > 5.5 mm turn to overt HCC within a year in patients with history of HCC, including a case of portal vein invasion.[100] To date, there are no studies regarding clinical outcome of subcentimeter HCCs between immediate treatment and imaging follow-up strategy after detection. However, given the high progression rate to typical HCCs (89.9–100%)[101,102] and better prognosis of very early stage HCC than early stage HCC, diagnosis of subcentimeter HCC would be clinically beneficial by providing two different options including immediate treatment and intense follow-up.

TREATMENT OPTIONS BASED ON IMAGING

Literature Review

Using BCLC system, patients classified as having early-stage HCC, are suitable for treatment with potentially

curative therapies (resection, transplantation, or ablation). Patients with intermediate-stage HCC are asymptomatic (performance status (PS) score, 0) with multinodular tumors but without vascular invasion or extrahepatic spread are eligible for locoregional therapy (TACE). Those with advanced-stage HCC are either symptomatic (PS score, 1–2) or have evidence of vascular invasion or extrahepatic spread; these patients are eligible for chemotherapy using sorafenib. Finally, patients with terminal-stage HCC have either severe cancer symptoms (PS score, 3–4) or severely decompensated cirrhosis (Child-Pugh class C) and should receive symptomatic treatment only. The BCLC system has been externally validated and is endorsed AASLD and EASL.[103]

Preferred first-line treatment for (HCC) remains liver transplantation when proper indications are met. Unfortunately, the number of patients awaiting transplant far outstrips the number of available organs. Resection also offers acceptable long-term survival in suitable patients, with low-volume tumor burden, well-preserved liver function, and no significant portal hypertension.[103–105]

Ablative therapies are typically most effective at treating small HCCs (≤3 cm in diameter). As tumor diameter increases above 3 cm, treatment results improve when ablation is combined with chemoembolization rather than being used as a stand-alone treatment. LRT is not purely palliative, in selected clinical settings ablative treatments offer equivalent opportunities for OS relative to surgical resection[105–110] They are also used as a neoadjuvant therapy intended to "downstage" or bridge patients to transplant or resection. Recently, stereotactic body radiation therapy has emerged as a potential alternative to percutaneous ablative techniques for all of the above indications.[111,112] A large number of studies have confirmed the efficacy of radiofrequency ablation (RFA) in early RFA provided 5-year survival rates of 40–90%.[105–110] *Irreversible electroporation (IRE) is indicated in patient with peribiliary and centrally located tumors as IRE is a nonthermal technique and causes damage to the collagenous structures. It uses ultra-short pulses of very high voltage at direct electric current.[113]

Endovascular techniques include transarterial embolization (TAE) with embolic particles alone, TACE, and selective internal radiation therapy (SIRT). Exclusion criteria for these techniques often focus on the extent of underlying liver disease and tumor burden. Surprisingly, given the theoretical risk of rendering the liver globally ischemic, hepatic arterial embolization techniques tend to be well tolerated even in the setting of portal vein thrombosis. HCC may parasitize blood flow from extrahepatic collateral arteries, and failure to recognize a vessel feeding the tumor may lead to incomplete treatment. TACE is the most widely used locoregional therapy for patients with intermediate HCC. Treatment is associated with partial responses in 15%–65% of patients, and OS benefits were reported in a meta-analysis of RCTs[114–16] TACE has also been studied as a neoadjuvant therapy to transplantation or resection. However, the survival benefit of this technique is still debated despite present data suggesting a positive impact of bridging treatments on both tumor recurrence and patient/graft survival following transplantation.[117–119] Recently, TACE with drug-eluting beads has been found to be more efficacious with less systemic toxicity than the established conventional TACE technique of direct infusion of chemotherapeutic agents emulsified in ethiodized oil, followed by bland embolization.[117–120]

SIRT (also called transarterial radioembolization [TARE]) with beta-emitting Y90 beads has also shown the ability to effectively downstage patients for potential transplant or resection. Potential disadvantages to SIRT compared with TACE and TAE include the need for more extensive arteriography for treatment planning as well as additional logistical hurdles and cost involving radiotherapeutic dose planning.[120] Many published articles

Key Statements: Treatment Options Based On Imaging

30. There is a concurrently published guideline by INASL on which treatment modality to be used in which clinical setting the following are nonoverlapping guidelines suggesting impact of imaging on choice of treatment modality.
31. Along with stage of the disease/performance status of the patient, location on imaging (subcapsular, peribiliary, and perivascular) can help decide the mode of therapy. B1
32. RFA is recommended in early stage HCC. A1
33. Microwave ablation (MWA) is an alternative option for lesions close to vascular structures as it has less heat sink effect and reduces treatment time. B1
34. Irreversible electroporation is recommended for peribiliary and centrally located tumors. B2
35. cTACE is recommended in intermediate stage HCC. A1 Imaging should include information about the presence or absence of extrahepatic blood supply to the lesion as this determines the success of the treatment. B1
36. Drug-eluting beads (DEB) has a better safety profile than conventional TACE with no survival advantage. A1. DEB-TACE is recommended in the treatment of HCCs larger than 6 cm. B2
37. Radioembolization (TARE) is an alternative to TACE in intermediate stage HCC because of its safety profile. B1
38. TARE is recommended with main portal vein thrombus (PVT) and for large unresectable tumors. A1

regarding TARE in HCC has shown consistent outcomes in OS, ranging from 15.4 months to 17.2 months in BCLC B stage. Although many studies have not shown differences in OS, several studies have demonstrated that TARE had a longer time to progression than TACE, thus TARE may have better role in a bridge to transplantation at centers with a long wait time. In addition, TARE was more effective in downstaging patients from United Network for Organ Sharing T3 to T2 than TACE. TARE with or without external beam radiotherapy is frequently being used in patients with portal vein thrombosis (tumoral or bland).[120–123]

Therapeutic regimens using different combinations of ablative techniques, transarterial techniques, systemic therapy, and surgical treatments are also commonly utilized, given the theoretical benefits of a multifaceted treatment regimen compared with monotherapy.[114–122]

TREATMENT RESPONSE EVALUATION

RECIST criteria following loco-regional treatment are misleading post therapy changes in tissue viability often do not result in corresponding changes in lesion size. Modified RECIST (mRECIST), Choi and EASL-ESORTC criteria has been developed; only well-delineated arterially enhancing lesions can be selected as target lesions for mRECIST evaluation[124–126]

Tumor ablation results in an area of necrosis, which appears as an area of hypodensity that may exhibit a thin, uniform peripheral rim of contrast enhancement in the arterial and/or portal venous phases, which may represent reactive hyperemia or granulation tissue. At MRI, necrosis after tumor ablation demonstrates low and high signal intensity on T2-weighted and T1-weighted imaging, respectively, because of coagulation necrosis. Hyperintensity on T1-weighted images may be due to hemorrhage or proteinaceous material within the ablated area (because of T1 hyperintensity of the tumor on the T1-weighted images, subtraction imaging is recommended on the contrast enhanced images). Cystic necrosis of tumor may also demonstrate hyperintensity on T2-weighted imaging. On DCE CT/MR, areas of nodular or crescentic enhancing tissue in close proximity to the ablated lesion is suspicious of residual or recurrent HCC[124–127] Also, peripheral enhancement that becomes hypodense in the equilibrium/delayed phase is more suspicious of residual or recurrent tumor.[127–129] Evaluation of the pretreatment scan could help to distinguish viable tumor as a side-by-side comparison could demonstrate whether the area of necrosis completely covers the tumor seen on pretreatment imaging. Nontumorous wedge-like enhancement often at the periphery of an ablated lesion secondary to iatrogenic arteriovenous shunting.

TACE usually results in liquefaction necrosis and the tumor when adequately embolized shows no enhancement in follow-up imaging. When lipiodol is used in conjunction with TACE, follow-up imaging with MRI may be the preferred modality as the extremely radiodense lipiodol may interfere with CT evaluation of marginal enhancement in residual or recurrent tumor.[130] Focal washout of lipiodol during follow-up suggests the presence of viable tumor.[129,130] For the best possible comparison of images, serial posttreatment follow-up is ideally performed with the same modality used to assess the presence of the tumor before and after LRT. The assessment of response will depend on the intent of treatment, namely whether or not treatment is with curative or with palliative intent. For curative treatments such as resection, transplantation, or locally ablative treatments of small solitary lesions without residual tumor, the goals are to detect tumor recurrence or new tumor formation. A suggested surveillance program would include both imaging and tumor marker assessments at 3 month intervals for the first year, 6-month intervals for the second year, and annually thereafter. For treatments with palliative intent or control of tumor growth, such as with regional or systemic therapies, the goal of response assessments is to determine disease progression and symptom control, if present. Following chemoembolization, an evaluation of therapeutic response should be performed 1–6 months following the intervention, with a determination of impact on both lesions that were therapeutically targeted and any others that may not have been therapeutically targeted. Following ablation, imaging at 3 months may provide baseline information on response once the inflammatory changes and hemorrhage related to the procedure have resolved. Subsequent imaging and tumor marker assessments every 3 months for the first 2 years will allow documentation of stability or disease progression and guide further interventions if disease progression is noted. If there is no disease progression for 2 years, these evaluations could be done annually.[125–129]

Kamel *et al.* found that DWI can quantify tumor necrosis after chemoembolization to a greater degree than gadolinium-enhanced MRI. Early after treatment with Y, tumors demonstrate a decrease in enhancement and an increase in ADC, without a statistically significant change in tumor size.[130]

FDG-PET has also been shown to be of value in the detection of tumor recurrence after LRT. Potential drawbacks that may be encountered when using FDG-PET are false-negative results because of a partial volume effect when dealing with small lesions (<1 cm) or because of diabetes/immune-compromised/infection and false-positive results because of abscess formation.[131]

Liu *et al.* reported 100% specificity and 36% sensitivity of CT for the depiction of residual or recurrent tumor seen as enhancing soft tissue and not necessarily arterially enhancing.[94] Dromain *et al.* found that MRI is known to be superior to CT for the evaluation of HCC after performing lipoidol TACE.[132] Treated HCC sometimes shows a thin

and peripheral pseudocapsule that enhances on hepatic arterial and delayed phases.[133–36] Further following TARE, there is reduction in hypervascularity initially with complete necrosis developing up to 6 weeks after treatment. DWI tumor response assessed at 1 month preceded anatomic size change at 3 months.[133–36] Some patients following TACE and TARE may show perfusion-related change in the treated lobe or segment without any mass effect often appearing as hypodense on portal venous phase. There is no correlation to loss of hepatic function following TARE; however, following TACE, this may represent transient perfusion-related ischemic response.[133–36]

Key Statements: Treatment Response Evaluation

39. Transient hyperemia manifested by thin, uniform enhancement of the treated zone is an expected finding after RFA, TACE, or transarterial radioembolization and represents a transient physiologic response to thermal injury and embolization to the hepatic parenchyma. This should decrease over time (3–12 months). A1
40. Foci of persistent nodular arterial enhancement with washout or persistent enhancing tissue at short-term follow-up suggests malignancy and should be evaluated further for need of additional directed therapy. A1
41. Subtraction images can be a helpful adjunct for differentiating hemorrhage from enhancing tumor on MRI. A1

NON-HCC MALIGNANCY (LR-M)

A mass with features suggestive of malignancy (diffusion restriction, growth, signal intensity different than background liver T2 hyperintensity, iron, or fat sparing) but lacking specific features of HCC (classic APHE and washout/capsule appearance, intralesional fat, or blood products) may be appropriately classified as LR-M.[8] This is important to differentiate for maintaining high specificity for imaging diagnosis of HCC. LR-M observations may still be HCC, or other malignancies, such as ICC, hepatocholangio carcinomas, or metastases. ICCs tend to be more cellular and vascular at their periphery while having a more fibrotic and watery stroma centrally. This concentric histologic structure accounts for the characteristic "targetoid" enhancement pattern of these lesions.[137–39] As mentioned above, rim-like APHE suggests malignancy other than HCC, whereas APHE not limited to a rim favors HCC.[8,9] At portal venous and delayed phase imaging with extracellular agents, a pattern of delayed or progressive central enhancement emerges was reported in 42%–96% of lesions.[137–39] Other ancillary features associated with ICC include hepatic capsular retraction, peripheral biliary duct dilation, central T2 hypointensity, and target appearance on diffusion-weighted images. While there is ample evidence supporting the classic imaging features of ICC, few studies test the ability of these features to help differentiate ICC from HCC, and fewer studies focus on these lesions in patients with defined risk factors or cirrhosis (i.e. the LI-RADS population). The studies that have attempted to determine the discriminatory power of diagnostic imaging for differentiating HCC from ICC have focused on atypical HCC in the comparison group. Despite these limitations, target appearance on HPB phase images and presence of rim-like APHE and peripheral "washout" may help differentiate ICC from HCC.[137–139] To date, only a few publications have described the imaging appearance of hepatocholangio carcinomas-biphenotypic tumors. A majority of cases report rim APHE with washout appearance in the periphery along with delayed central enhancement. Rarely, these tumors may display features of HCC or have both HCC and ICC features. Most of the data are however retrospective, no prospective data are available to better quantify the diagnostic accuracy of the above described imaging features.[139]

Key Statements: Non-HCC Malignancy

42. Any lesion with rim hypervascularity, rim washout, targetoid appearance, and delayed central enhancement is suspicious for non-HCC malignancy. A1
43. Imaging features are not sufficiently specific to make noninvasive diagnosis of non-HCC malignancy. Biopsy is required when specific diagnosis is likely to alter management decisions. B1

PORTAL VEIN TUMOR THROMBUS

Macrovascular tumor thrombus precludes surgical treatment options such as resection or liver transplantation, while bland thrombus may alter the surgical approach.

Specific imaging features of macrovascular invasion include direct extension of a parenchymal tumor mass into an adjacent vessel and the presence within an occluded vein of arterial enhancing neovessels seen as thin tubular hyperenhancing "threads and streaks" within a portal venous or hepatic venous thrombus.[140–44] Thrombosed main portal vein ≥23 mm suggests intraluminal tumor, reported sensitivity and specificity of 63% and 100%; however, acute bland thrombosis also may result in luminal expansion.[140–44] Sorrentino found a sensitivity of 87% using AP hyperenhancement as a diagnostic feature.[144] DW imaging enables discrimination between bland and neoplastic portal vein thrombi.[140–144] In a statement by Chinese expert consensus, the imaging features of PVTT include solid lesions within the portal vein in all the phases of intravenous-enhanced three-phase CT, especially with enhancement of contrast in the AP and washout in the portal venous phase of the procedure.[140]

Key Statements: Portal Vein Tumor Thrombus

44. PVTT should be suspected with tissue showing early arterial enhancement and wash out of the thrombus within expanded PV on dynamic CT/MR of liver and/or unequivocal enhancing soft tissue in vein, regardless of visualization of parenchymal mass. A1

CONTRAST ENHANCED ULTRASOUND

Literature Review

CEUS can accurately differentiate between benign and malignant focal liver lesions with a sensitivity of 93% and a specificity of 90% (hyper/isoenhancing on PV phase, hypoenhancing on the PV, and delayed phase). CEUS can be used as a second-line diagnostic tool indeterminate focal liver lesions on conventional grayscale USG or contrast-enhanced CT.[145–149]

CEUS can diagnose tumor enhancement with enhancing tumor seen on AP with a sensitivity 88%–100% and specificity of 92.5%, respectively.[145–149] According to a meta-analysis, CEUS can accurately differentiate between benign and malignant focal liver lesions with a sensitivity of 93% and a specificity of 90%, and the diagnostic performance of CEUS is similar to that of contrast enhanced CT (CECT) and contrast enhanced MRI (CEMRI).[150]

For lesions seen on CT/MR but not on USG, CEUS can help in localization for tissue diagnosis, allowing for differentiating the central necrotic portion of the tumor from the viable enhancing tissue aiding in targeting tumor for tissue diagnosis. Furthermore, CEUS could improve the diagnostic accuracy from 42%–44% to 89%–92% for lesions that have been found to be inconclusive on CECT and improve the diagnostic confidence level. Hence, CEUS can be used as a second-line diagnostic tool for the evaluation of incidentally found indeterminate focal liver lesions on conventional grayscale US or contrast-enhanced CT.[150,151]

Small HCCs, those less than 2 cm in size, were accurately diagnosed using CEUS with a sensitivity of 81% and a specificity of 86%.[147–149] HCC usually appears as a hypervascular lesion in the AP and as a hypovascular lesion in the PVP or the delayed phase, depending on differentiation. Enhancement patterns vary depending on the degree of differentiation. Poorly differentiated HCC frequently presents with an atypical enhancement pattern. Hence, careful assessment is needed to evaluate nodular lesions in patients with chronic liver disease.

In the comparison of imaging modalities, HPB-enhanced MRI showed better sensitivity than both contrast-enhanced CT (74%) and CEUS (72%), and when Gd-EOB-DTPA and CEUS were used together in the evaluation, the sensitivity improved up to 90%. In addition, when CEUS and MDCT were used together to assess tumor vascularity, the combination of the evaluation techniques improved the sensitivity for differentiating HCC from benign nodules in patients with liver cirrhosis, by decreasing the false-negative rate.[150,151]

Portal vein thrombosis is frequently observed in patients with liver cirrhosis or HCC. In these patients, differentiation between tumor thrombosis and bland thrombosis is critical to determine treatment plans. Furthermore, even if there is portal vein thrombosis without definite evidence of a mass-forming lesion in the liver on conventional US, a careful further examination is needed to check whether there is an undetected infiltrative HCC. Although Doppler US was used to diagnose tumor thrombosis in previous research, the sensitivity and the diagnostic accuracy were only about 20% and 50%, respectively. On CEUS, tumor thrombosis can be diagnosed, when there is an enhancement in the AP, in which the sensitivity, and the diagnostic accuracy can be improved to 88%–100% and 92.5%, respectively.[142] The diagnostic performance of CEUS was found to be significantly lower in patients with chronic hepatitis than in patients without chronic liver disease. This might be because of technical difficulties such as limited time for the whole liver assessment; limited sonic window because of anatomical changes such as atrophy of the right hepatic lobe; heterogeneous enhancement of the liver parenchyma because of the arterioportal shunt, which is often found in cirrhotic livers;

and the relatively less extensive enhancement of the liver parenchyma as compared with the normal liver.[151]

During the RFA of inconspicuous lesions, fusion imaging with conventional grayscale US and CECT or CEMR can be used for RFA guiding. If the lesion is inconspicuous even with fusion imaging with conventional grayscale US, CEUS can be used additionally. According to a previous study, about 83% of HCC, which were inconspicuous on fusion imaging with conventional grayscale US, were well visualized after CEUS.[152] After RFA of the hepatic tumor, it is essential to evaluate the treatment response. Although CECT has been used for this purpose, there are several limitations, including possible harmful effects of radiation and the iodinated contrast agent and an inaccurate assessment of the ablated margin. Furthermore, even though a residual viable tumor is detected on CECT, it is sometimes difficult to visualize and target the residual viable tumor on conventional grayscale US, particularly immediately after RFA.[153] Because CEUS can overcome these disadvantages, it can be used in the evaluation of the post-RFA response. For hypervascular lesions such as HCC, if the intratumoral vascularity, which was noted before treatment, disappears on postprocedural CECT or CEUS, complete ablation of the tumor can be confirmed. For hypovascular lesions such as metastasis, successful ablation can be confirmed if the ablated zone does not show enhancement on CECT or CEUS, including the target lesion. It is important to secure a sufficient safety margin (>5 mm) to ablate satellite nodules around the main lesion and to prevent marginal recurrence. According to previous studies, the diagnostic accuracy of CEUS (93.8%–100%) for the evaluation of the RFA treatment response with either SonoVue or Sonazoid was comparable with CECT or CEMR.[152,153] The optimal time to assess the treatment response to RFA is 3 h after the procedure because the treated tumor margin is the most clearly perceived at this time. Uniform rim enhancement can be seen up to 30 days after RFA, and this rim enhancement should not be misdiagnosed as marginal tumor recurrence. Efforts have also been made to evaluate the treatment response after TACE with CEUS. Although CEUS could detect residual intratumoral vascularity after TACE in previous studies, it is not feasible to use it as an evaluation tool after TACE because of the difficulty in evaluating multiple lesions, deeply located lesions, and poorly enhancing, or diffusely growing lesions[152–154]

Key Statements: Contrast Enhanced Ultrasound

45. CEUS has adjunct role in characterization of targeted lesion seen on cross-sectional imaging. It can help guide tissue diagnosis. A1
46. CEUS is comparable in performance to both contrast-enhanced CT and MRI in the evaluation of ablation treatment for local recurrence and the assessment of ablation volume viability especially in the immediate postprocedure setting. A1

STRUCTURED REPORTING TEMPLATE AND MINIMUM DATA SET (TABLE 7)

Literature Review

Structured reports provide superior description and evaluation of the clinical question and improve the confidence of referring physicians. Brook *et al.* reported structured reports provided more complete reporting of 12 key features.[154] In a study by Poulos *et al.*, 50–80% surgeon perceived improvement is seen in structured reports l.[155]

Key Statements: Structured Reporting Template and Minimum Data Set

47. Structured template based reporting should be adopted by each institute for better consistency and reproducibility of findings LIRADS Nomenclature is recommended A1.

STAGING OF HCC

Literature Review

Prognosis of HCC patients takes into consideration tumor stage, liver function, physical status, and treatment efficacy. Conventionally, HCC has been classified by the tumor-node-metastasis staging systems-based on data from patients who underwent curative resections, and liver function is not considered.[156] There are several other clinical staging systems taking into account imaging criteria and clinical and liver function parameters.

According to Organ Procurement and Transplantation Network policy, only nodules that satisfy imaging criteria for definite HCC or that are proven by means of biopsy to be HCC should contribute to the

staging.[157] Imaging-detected nodules that are suspicious but not diagnostic for HCC usually are ignored for staging purposes.[158] Detection of microvascular invasion and differentiation of the two causes of multifocality (intrahepatic metastasis or multicentric carcinogenesis) are not part of routine radiologic staging, as imaging methods for these purposes have not yet been validated. With emerging understanding of HCC genomics, there is no doubt that personalized approaches will be introduced in clinical practice based on molecular targeted therapies.

FDG PET-CT shows suboptimal sensitivity was found to be higher in poorly differentiated HCCs. PET-CT positivity was identified as an independent poor prognostic factor for disease-free survival. When actual explant correlation is done −41% of the Milan patients fall outside the criteria. Adding [18F]FDG PETCT to the assessment algorithm of patients planned for liver transplantation, resection, or ablation may identify patients at risk for recurrence after each procedure.[156–158] PET-CT may identify patients who, despite being outside the Milan criteria, have favorable biological tumor characteristics. [18F]FDG PET-CT into the initial workup of HCC patients planning to undergo transplantation often reveal unexpected distant metastases.[158–161] FDG PET has only a limited role in the diagnosis of HCC, and it provides valuable prognostic information for liver surgery, transplantation, and palliative treatment.[157–163]

Key Statements: Staging of HCC

48. PET-CT has potential value in the diagnosis of extrahepatic disease in advanced tumors before offering TARE or considering for liver transplant. A1

Key Statement: Recent Advances

49. At present, none of the recent advances have shown any incremental benefit to be adopted into routine clinical practice. However, they are very promising and could benefit the patient in the large volume tertiary centers on case by case basis. B1

RECENT ADVANCES

Dual-energy CT utilizes the principal of differential attenuation of different tissues with polychromatic X-ray beam (80–140 kvp). Virtual noncontrast and iodine maps can be generated.[164] Given that iodinated contrast material provides greater X-ray attenuation at low-tube voltage settings through an increased photoelectric effect, it is expected that low kVp images of dual-energy data sets will be more sensitive than high-kVp images in detecting hypervascular liver lesions such as HCC, despite the higher noise levels[165]

IVIM-DWI (Intravoxel incoherent motion DWI) is able to differentiate the vascular contribution to overall water molecule movement using sufficient b-values, and it additionally calculates three perfusion parameters: true molecular diffusion, (which is pure molecular diffusion), pseudodiffusion, and the perfusion fraction. Several studies reported the usefulness of IVIMDWI parameters in the detection and characterization of liver lesions and the monitoring of treatment response after chemotherapy.[165]

The fundamental principle of perfusion CT/MR or DCE-MRI is based on the temporal changes in tissue enhancement after intravenous administration of contrast media. Perfusion imaging techniques such as perfusion CT and DCE-MRI provide qualitative and quantitative data on the regional and global changes in blood flow of HCCs and background liver parenchyma. Clinical applications include (1) lesion characterization and detection (2) prognostic information based on tumor vascularity; and (3) monitoring response to treatment.[164–170]

CONFLICTS OF INTEREST

The authors have none to declare.

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