Imaging in Patients with Cirrhosis: Current Evidence

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KEYWORDS

• Cross-sectional imaging • Cirrhosis • Hepatocellular carcinoma • Evidence

KEY POINTS

- There have been major changes in the management and reporting of hepatocellular carcinoma (HCC) in the last decade.
- Cross-sectional imaging is now pivotal in the management of cirrhotic patients, in particular in the diagnosis and staging of HCC.
- Although diagnostic systems have become relatively well developed, approximately one-third of HCC nodules may have an atypical appearance, necessitating ancillary testing, close follow-up, or biopsy.
- The introduction of standardized diagnostic and reporting systems has improved communication between radiologists and clinicians, but there remains substantial disagreement between radiologists in feature assignment and nodule characterization.
- As our understanding of this disease evolves and imaging techniques improve, standardized diagnostic criteria must continue to evolve in order to provide more accurate, early diagnosis.

Cirrhosis is an increasingly common disease. Its sequelae, including portal venous hypertension and hepatocellular carcinoma (HCC), are major causes of morbidity and mortality, with more than half a million new cases of HCC diagnosed every year worldwide.[1] Cross-sectional imaging plays a central role in the care of cirrhotic patients and is used primarily for the detection and treatment planning of HCC. Unlike other types of malignancy, all major guidelines for the management of HCC accept the imaging diagnosis of HCC without requiring tissue confirmation.[2–6] Thus high-quality imaging, interpretation, and communication of findings are central to the care of cirrhotic patients.

SURVEILLANCE

The target population and method for HCC surveillance vary among liver societies.[7] The American Association for the Study of Liver Disease (AASLD) recommends that patients with cirrhosis, regardless of cause, undergo liver ultrasound every 6 months for surveillance.[2] In addition, noncirrhotic hepatitis B virus carriers should undergo ultrasound surveillance if they are of Asian ethnicity (men >40 years old and women >50 years old), black, or have a strong family history of HCC.[2] The European Society for the Study of the Liver (EASL) recommends surveillance ultrasound of all patients with Child-Pugh stage A and B cirrhosis or Child-Pugh stage C cirrhosis awaiting liver transplantation, noncirrhotic hepatitis B carriers with active hepatitis or a family history of HCC, and noncirrhotic patients with chronic hepatitis C infection and stage F3 liver fibrosis.[3] The Japanese Society of Hepatology (JSH) defines 2 at-risk groups: a high-risk group comprising noncirrhotic patients with chronic hepatitis B or C infection and patients with cirrhosis of other causes and a super–high-risk group comprising patients with

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hepatitis B– or hepatitis C–related cirrhosis.[4] The JSH includes liver ultrasound, alpha-fetoprotein, and other serum markers in its surveillance algorithm for both groups and dynamic contrast-enhanced computed tomography (CT) or MR imaging for the super–high-risk group.[4]

One of the important issues in imaging surveillance for HCC is the use of ultrasonography. Although all major liver societies agree that ultrasound is the imaging modality of choice for HCC surveillance mainly because of the availability, affordability, simplicity, and reasonable overall sensitivity, it is widely acknowledged that ultrasound has a relatively low sensitivity for detecting early stage HCC (within Milan criteria) (63% in a 2009 meta-analysis); detection of early stage disease is important to the success of any surveillance system.[8] In addition, ultrasonography is highly operator dependent; its performance may be even lower at centers without dedicated liver surveillance programs.[8] However, because the performance of CT and MR imaging have mainly been evaluated in the diagnostic setting rather than that of surveillance, there are currently no data that support their use in routine surveillance.[8] Concerns regarding cost, complexity, false positives, and radiation dose in CT have reduced enthusiasm for their use in general surveillance.

There is, however, good agreement among liver societies regarding diagnostic imaging features for HCC. All major systems allow the definitive diagnosis to be made when classic imaging features are present on multiphasic contrast-enhanced CT or MR imaging; in the JSH guidelines, contrast-enhanced ultrasound features can also be used for the diagnosis of HCC.[4]

COMPUTED TOMOGRAPHY AND MR IMAGING TECHNIQUE

Preferential arterial blood supply is one of the hallmarks of HCC. HCC is typically a highly vascular lesion arising in a highly vascular organ, and visualizing the characteristic features of arterial phase hyperenhancement (APHE) and venous phase hypointensity washout feature requires a high-quality multiphasic contrast-enhanced examination with an accurately timed hepatic arterial phase. All published diagnostic criteria emphasize the importance of multiphase contrast-enhanced imaging.

The US Organ Procurement and Transplant Network's (OPTN) policy on the allocation of livers includes specific technical requirements for both contrast-enhanced CT and MR imaging.[5,9] These requirements include minimum contrast media injection rates (3 mL/s for CT and 2 mL/s for most MR imaging agents), high spatial resolution (5-mm slice thickness or less for dynamic series), and multiple dynamic phases (at least 3 phases for CT and 4 phases for MR imaging). Precontrast imaging is optional for CT because of its relatively low yield and added radiation dose. However, for MR imaging, precontrast T_1-weighted imaging is mandatory because it is needed to assess for APHE in intrinsically hyperintense nodules. Both a portal venous and delayed (>120 seconds after contrast media injection) phase are mandated to optimize sensitivity for the detection of the nodule washout feature.

The ideal hepatic arterial phase is transient, and its timing is variable from patient to patient. Visually, lesional enhancement is typically best seen in the late arterial phase when there is robust enhancement of the hepatic arteries, early enhancement of the portal veins, minimal enhancement of the hepatic parenchyma, and no enhancement of the hepatic veins. Several techniques for attaining a well-timed hepatic arterial phase are currently available, including test bolus technique, automated bolus detection, real-time bolus tracking, and single-breath-hold multi-arterial phase methods.[10–15]

DIAGNOSTIC FEATURES OF HEPATOCELLULAR CARCINOMA

Established Imaging Characteristics

Arterial phase hyperenhancement

Arterial phase hyperenhancement is the single most important imaging feature of HCC. It usually appears diffuse or heterogeneous in tumors with necrosis or varying degrees of cellular dedifferentiation (**Fig. 1**) and sometimes rimlike (**Fig. 2**). This feature alone is highly sensitive for HCC (82%–93%) but not as specific.[16–20] For example, cholangiocarcinoma (CC) often demonstrates rimlike hyperenhancement, and high-grade dysplastic nodules may have homogeneous APHE; thus, APHE alone is not sufficient to make the diagnosis of HCC.

Washout feature

The washout feature has a 2-fold definition under the Liver Imaging-Reporting and Data System (LI-RADS); a nodule must be less enhanced than the surrounding liver parenchyma in a venous phase and less enhanced than it was on a previous dynamic phase (see **Fig. 1**). The washout feature has largely been attributed to the diminished portal venous supply of HCC compared with the surrounding liver, such that although an HCC nodule may appear hyperenhancing in an arterial-dominant phase, the liver appears hyperenhancing (and the nodule hypoenhancing) in a