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REVIEW / *Abdominal imaging*

Diagnosis of hepatocellular carcinoma: An update on international guidelines

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Abstract Imaging is essential for the successful management of patients with or at risk of developing hepatocellular carcinoma (HCC). If ultrasound remains the key screening modality, computed tomography and magnetic resonance imaging (MRI) can play a major role in the characterization and noninvasive diagnosis of nodules in patients at risk of developing HCC. Each technique has succeeded in adapting to the wide histological spectrum of focal liver lesions. In this review, we discuss recent advancements in imaging techniques and evaluation — notably diffusion-weighted imaging, contrast-enhanced ultrasound, and liver-specific MRI contrast agents — as well as their addition to international guidelines and reporting systems such as the Liver imaging reporting and data system (LI-RADS).

In France, as in many countries worldwide, the incidence of primary liver cancer has significantly increased since the 1980s [1]. In the United States, a study that estimated the incidence of cancer and associated mortality rates in upcoming years reported that primary liver cancer is expected to become the third largest cause of death by cancer by 2030, behind lung and pancreatic cancer but in front of bowel cancer [2]. On one hand, this increase in the incidence of liver cancer may be attributed to an increase in the incidence of chronic liver disease particularly alcohol-related liver disease and liver steatosis in Western countries but, on the other hand, this increase may be due to improvements in

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cirrhosis patient care, which gives hepatocellular carcinoma (HCC) the extra time it needs to appear and develop [3,4]. Particularly in patients with liver steatosis, HCC does not develop after several years of progressive cirrhosis, but rather tends to appear during the preclinical stage, which raises many questions about our current screening strategies [5,6].

Over the last 15 years, imaging has played an ever-growing role in the diagnosis and staging of HCC. Radiologists are involved in many of the key steps of HCC patient management, including assessment of the severity of chronic liver disease using noninvasive techniques [7–9], screening of patients at risk of developing HCC, noninvasive diagnosis of HCC and other nodules that can develop in cirrhotic livers [10], and patient surveillance. Interventional radiology is another important aspect of patient management: radiologists obtain samples for pathological analysis via image-guided liver biopsy and perform both palliative and curative percutaneous and endovascular procedures [11–13].

Knowledge in the field of HCC imaging is growing rapidly and has prompted international medical societies to regularly update their guidelines. In this review, we discuss the main achievements in the field of HCC imaging over recent years, as well as the consequences of imaging advances on different international guidelines and reporting systems.

Hepatocarcinogenesis

HCC is a complex multistage process in which liver cells repeatedly accumulate epigenetic and genetic damage that progressively gives rise to populations of precancerous cells that then undergo malignant transformation [14–20]. This process can either occur gradually over time – starting with the appearance of hyperplasic foci that progress into dysplastic nodules and then early-stage HCC before eventually developing into malignant HCC – or occur as *de novo* HCC. Following the notable initiative of the Japanese pathologist M. Kojiro, the nomenclature related to hepatocarcinogenesis was updated and improved in 2009 [18]. This resulted in harmonized and more specific pathological criteria for defining the different types of precancerous hepatocellular nodules (also known as precursor lesions) and malignant lesions (Fig. 1) [19]:

- cirrhotic nodules (formerly referred to as regenerative nodules): these nodules typically arise in the setting of cirrhosis – usually by the thousands – and appear small, well-defined, and surrounded by an even layer of peripheral fibrous scar tissue. Microscopic dysplastic foci sometimes arise within these cirrhotic nodules and are thought to progressively develop into dysplastic nodules;
- dysplastic nodules: generally with a diameter of 1–1.5 cm, these nodules are classified as low-grade dysplastic nodules (L-DN) or high-grade dysplastic nodules (H-DN) based on the degree of cytologic atypia and architectural changes. Histologically, L-DNs tend to appear different from regenerative nodules, and are therefore considered precancerous lesions with a slightly higher risk of becoming malignant. On the other hand, the histological features of H – DNs are similar to those of well – differentiated HCCs, though they are differentiated based on a lack of stromal invasion. H-DNs and should be considered as advanced HCC precursors with a high risk of malignant transformation;
- early HCC: early HCC tumors are vaguely nodular, generally measure < 2 cm, and are typically differentiated from H-DNs by stromal invasion, which is defined as tumor cell invasion into the portal tracts or fibrous septa. The invasive potential of early HCC lesions is low, and they do not display the typical histological features of tumor aggressiveness such as the presence of a tumor capsule, satellite nodules, or microvascular/macrovascular invasion;

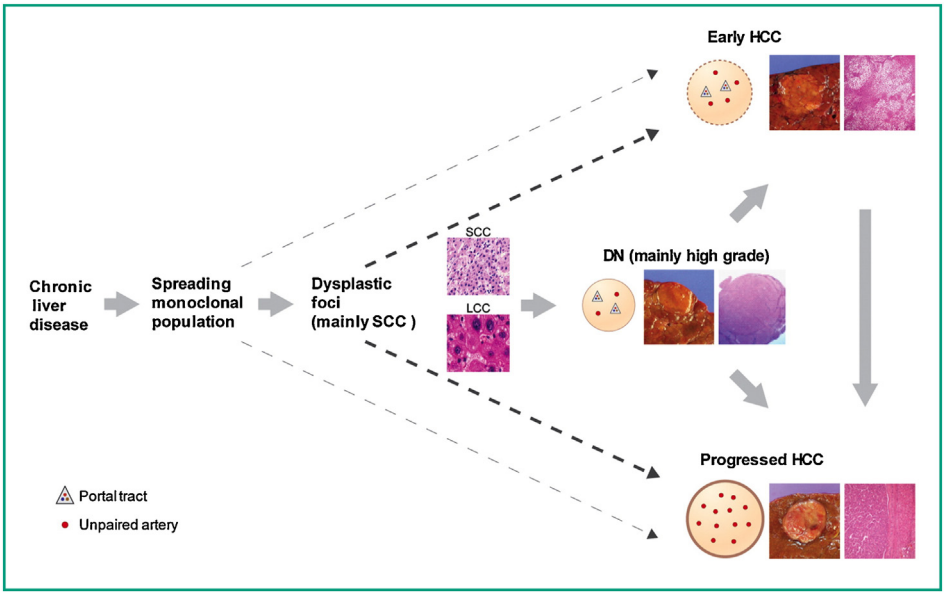

Figure 1. Schema showing the progression of precursor nodules towards malignancy during hepatocarcinogenesis. DN: dysplastic nodule; HCC: hepatocellular carcinoma; LCC: large liver cell change; SCC: small liver cell change.
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