



REVIEW ARTICLE

Imagiological Diagnosis of Gastrointestinal Diseases – Diagnostic Criteria of Hepatocellular Carcinoma



Pedro Boal Carvalho^{a,*}, Eduardo Pereira^b

^a Gastroenterology Department, Centro Hospitalar do Alto Ave, Guimarães, Portugal

^b Gastroenterology Department, Hospital Amato Lusitano, Unidade Local de Saúde de Castelo Branco, Castelo Branco, Portugal

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Abstract Hepatocellular carcinoma (HCC) is one of the leading causes of neoplastic morbidity and mortality worldwide, and despite recent treatment advances, the prognosis remains dismal, with a 5-year mortality rate of 85%.

The surveillance and timely diagnosis is therefore of crucial importance in order to improve survival rates and alleviate the health burden imposed by the HCC.

Previously, HCC diagnosis warranted liver biopsy, an invasive process with limited diagnostic accuracy. In the past 15 years, HCC diagnosis based solely on imaging criteria was accepted by all the major national and international guidelines, and is now widely employed across the globe.

Current European guidelines for the HCC diagnosis support the use of both dynamic contrasted computer tomography as well as magnetic resonance imaging for the non-invasive diagnosis of HCC for nodules >1 cm in a cirrhotic liver. The non-invasive diagnosis of HCC depends on radiological hallmarks, such as homogeneous contrast uptake during the arterial phase and wash-out during the venous and late phases, but while such tumoral behaviour is frequent in nodules >2 cm, high-end equipment and superior expertise is often needed for the correct diagnosis of early HCC.

Nevertheless, the accuracy of imaging techniques for the diagnosis of HCC is permanently improving, and supports the progressively reduced need for liver biopsy during liver nodule workout in a cirrhotic liver.

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* Corresponding author.

E-mail address: Pedroboalcarvalho@gmail.com (P. Boal Carvalho).

PALAVRAS CHAVE

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Diagnóstico Imagiológico de Doenças Gastrointestinais – Critérios Diagnósticos do Carcinoma Hepatocelular

Resumo O carcinoma hepatocelular (CHC) é uma das principais causas de morbi-mortalidade a nível mundial, e apesar de avanços no tratamento, o prognóstico é sombrio, com uma mortalidade aos 5 anos de 85%.

Assim, reveste-se de particular importância a vigilância e diagnóstico precoce do CHC, de forma a alterar substancialmente as taxas de sobrevivência desta neoplasia.

Previamente, o diagnóstico do CHC exigia a realização de uma biópsia hepática, uma técnica invasiva com acuidade diagnóstica limitada. Nos últimos 15 anos, o diagnóstico baseado em técnicas de imagem foi sendo progressivamente aceite pelas principais recomendações nacionais e internacionais, e é agora extensamente aplicado em todo o mundo.

As recomendações europeias mais recentes para o diagnóstico do CHC aceitam a utilização de tomografia computadorizada contrastada e ressonância magnética contrastada para o diagnóstico não invasivo de CHC em nódulos >1 cm no fígado cirrótico. Este diagnóstico depende da presença de alterações imagiológicas típicas, como a hiper captação homogénea de contraste na fase arterial e o wash-out nas fases portal e tardia, características frequentes em nódulos >2 cm, mas de difícil identificação em CHC de dimensões reduzidas.

Em conclusão, as técnicas imagiológicas para o diagnóstico do CHC apresentam uma acuidade diagnóstica progressivamente mais elevada, e permitirão reduzir significativamente a necessidade de biópsia hepática durante a abordagem de nódulos hepáticos num fígado cirrótico.

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1. Hepatocellular carcinoma epidemiology

Hepatocellular carcinoma (HCC) is the third most common tumour worldwide and the second leading cause of cancer-related deaths.¹ The overall 5-year survival of patients with HCC is 15%, indicating its generally poor prognosis. However, 40% of patients who are diagnosed with the disease localized to the liver have improved 5-year survival rates of 30%.¹

Cirrhosis is the most important risk factor for HCC. More than 80% of the cases of HCC occur in the setting of cirrhosis, and in these patients, HCC is the leading cause of death.² Importantly, up to 20% of patients with HCC in the setting of HBV infection develop without evidence of cirrhosis. Among patients with cirrhosis, alcohol, tobacco, obesity, diabetes, older age, and male gender are associated with an increase in the risk for the development of HCC.¹

Moreover, the risk of HCC in cirrhotic patients depends on the aetiology of cirrhosis; 2–8% per year in hepatitis C-related liver cirrhosis, 2.5% per year in chronic hepatitis B-related cirrhosis, and <2% in primary biliary and autoimmune cirrhosis.^{3,4}

2. HCC surveillance

National and society guidelines recommend surveillance programmes for HCC^{5–8} on the basis of reduced mortality^{9,10} and cost-effectiveness.¹¹ Current European Association for the Study of the Liver (EASL) guidelines support HCC surveillance in cirrhotic patients Child–Pugh A and B, Child–Pugh C included in transplant lists, non-cirrhotic HBV carriers with active hepatitis or family history of HCC, and

non-cirrhotic patients with chronic hepatitis C and advanced liver fibrosis.⁵

Liver ultrasound (US) is the diagnostic procedure of choice across all major guidelines,¹² with a pooled sensitivity for HCC of almost 95% in a recent meta-analysis.¹³ In experienced hands, US allows for the detection of diminutive nodules (Fig. 1); in a Japanese study, the average size of the detected malignancy was 1.6 ± 0.6 cm, and remarkably, the tumour was larger than 3 cm in only 2% of the patients.¹⁴ Despite being operator-dependent, with difficult identification of a focal malignant nodule in a cirrhotic liver, US is affordable, easily accepted by patients and with no associated risks, allowing for its progressively wider use. Therefore, in patients where surveillance is warranted, liver US should be performed every 6 months.⁵

The use of serological markers, such as alpha-fetoprotein (AFP), des-gamma-carboxy prothrombin (DCP) and glycosylated AFP (AFP-L3), although incorporated in Japanese⁷ and Asian-Pacific,⁸ are not presently supported in the EASL guidelines for HCC surveillance.⁵ AFP in the surveillance setting has been shown to improve HCC detection compared to US alone in just 6–8% of the patients,¹⁵ as only 20% of early-HCC present with elevated AFP serum levels. Additionally, AFP leads as well to an increase in the number of false positives, and consequently, in the cost for HCC diagnosis.^{5,6}

Dimension is of crucial importance in liver nodules, as less than half the nodules <1 cm in a cirrhotic liver correspond to HCC,^{16,17} but more than 90% of nodules >3 cm lead to the diagnosis of HCC.¹⁸ The rate of HCC in nodules between 1 and 2 cm is 66% and almost 80% in nodules 2–3 cm.^{2,19} Therefore, the current challenge in HCC diagnosis is the detection and

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