

Role of Imaging in Surveillance and Diagnosis of Hepatocellular Carcinoma

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KEYWORDS

• Hepatocellular carcinoma • Screening • Liver • MR • Ultrasound • LI-RADS

KEY POINTS

- Prognosis for hepatocellular carcinoma (HCC) is dependent on tumor stage at diagnosis, with small, localized, early-stage tumors more amenable to curative treatment options.
- Screening guidelines have been made by various organizations to improve early detection in at-risk populations.
- Ultrasound is the most commonly used screening tool with increased interest in use of MRI in specific populations.
- Imaging-based diagnosis of HCC has been incorporated into all recent clinical guidelines and is used to determine the extent of tumor burden, guide treatment options, and prioritize patients for organ transplantation.
- The Liver Imaging Reporting and Data System (LI-RADS) was created by the radiology community as a tool for standardized reporting and consistent lexicon; its expanded use necessitates further evaluation and validation of its categories.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the second leading cause of cancer mortality worldwide with more than 700,000 deaths each year.¹ The global distribution closely follows the distribution of hepatitis B (HBV) and hepatitis C (HCV) infections, with the greatest burden in developing countries where these infections are endemic. Interestingly, recent trends have shown a decline in viral hepatitis in East Asian countries, such as China and Korea, owing to the increased vaccination against HBV, whereas rates

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have rapidly increased in developed countries, such as the United States and Japan, where a large aging adult population acquired HCV infection through intravenous drug use and blood transfusions between the 1960s and 1980s. Recent advances in the treatment of HCV may alter this trend; however, antiviral treatment is projected to decrease the number of cases of cirrhosis by only 5%, as most patients are unaware of their infection status and do not receive treatment.² Additionally, the epidemic of metabolic syndrome and subsequent development of nonalcoholic fatty liver disease (NAFLD) increasingly contributes to the rise in HCC in developed countries.^{3–5} Regardless of etiology, underlying liver cirrhosis is the single most important risk factor for development of HCC, identified in approximately 80% to 90% of all cases.⁶

The prognosis for patients with HCC is dependent on tumor stage at diagnosis. Early-detected HCCs are amenable to curative resection and transplantation, with a 5-year survival rate of nearly 70%, compared with a median survival of less than 1 year with advanced HCC.⁷ Early detection, however, can be difficult, as many HCCs remain subclinical until more advanced stages or are only seen incidentally on imaging.^{6,8–15} Thus, it is important to have close active surveillance in high-risk patients to diagnose cirrhosis and HCC when the disease burden is small.

HEPATOCELLULAR CARCINOMA SCREENING AND SURVEILLANCE

The World Health Organization established tenets of cancer screening approximately 50 years ago, emphasizing that the success of a screening program is dependent on identification of a disease that has high associated morbidity and mortality; effective and available treatment; and an acceptable, safe, and relatively inexpensive surveillance tool.¹⁶ Cancer screening and surveillance programs, such as for breast, colon, and prostate cancer, have traditionally focused on a cost-effective method to reduce mortality, and have often been implemented with high degrees of success.¹⁷ However, there are limitations that include poor availability and utilization rate, suboptimal sensitivity of screening tests, and limited access to treatment options. For example, the fecal occult blood test and the prostate-specific antigen, although widely available and relatively inexpensive, have received substantial criticism due to downstream physical, psychological, and financial harm. Further analysis of screening programs has resulted in ongoing revised clinical practice.¹⁸

In contrast to prospective trials that have proven screening efficacy with other malignancies, such as breast cancer, studies evaluating screening for HCC are more limited. One large-scale randomized controlled trial performed in China by Zhang and colleagues¹⁹ demonstrated survival benefit in patients with chronic hepatitis B in a study population of approximately 19,000 patients undergoing screening and surveillance with ultrasound and alpha-fetoprotein (AFP) every 6 months. Despite poor patient compliance, there was a significant 37% reduction in mortality in the screened group. Despite these promising results, this patient population was that of HBV and not cirrhosis. To date, there are no similar large-scale trials evaluating screening in cirrhosis.

Many worldwide professional organizations have produced HCC screening guidelines in at-risk groups in which the incidence of HCC is sufficiently high enough for a surveillance program to be deemed cost-effective.^{20–23} These guidelines provide both an evidence-based and consensus approach to HCC screening, and have been supported by a number of studies that have concluded a survival benefit due to earlier diagnosis.^{19,24–26} Although there is substantial overlap among the different guidelines, variation does exist in HCC surveillance recommendations, specifically the targeted population and means of screening (Table 1). The 2017 guideline update

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