Hepatocellular Carcinoma and Other Liver Lesions

Reena Salgia, MD[a], Amit G. Singal, MD, MS[b,c,*]

KEYWORDS

• Liver cancer • Liver mass • Diagnosis • Treatment

KEY POINTS

- Hepatocellular carcinoma (HCC) is the most common primary liver tumor, with most cases developing in a background of cirrhosis or chronic hepatitis B virus infection.
- Benign liver lesions and other malignancies, such as cholangiocarcinoma, should be considered in the differential diagnosis of a liver mass, particularly in patients without pre-existing chronic liver disease.
- The most common modality for diagnosis of HCC is contrast-enhanced magnetic resonance imaging or 4-phase computed tomography, with characteristic findings of arterial enhancement and delayed phase washout.
- The Barcelona Clinic Liver Cancer staging system is endorsed by the American Association for the Study of Liver Diseases and remains the most commonly used staging system in clinical practice.
- Treatment decisions for HCC should be individualized after accounting for a patient's tumor burden, liver function, and performance status. Given the multitude of potential treatment options, a multidisciplinary approach to care is recommended for optimal communication and treatment delivery.

INTRODUCTION

Hepatocellular carcinoma (HCC) is currently the sixth most prevalent cancer worldwide and the third leading cause of cancer-related death.[1] It is one of the leading causes of morbidity and mortality in patients with cirrhosis. Furthermore, it has a rapidly rising incidence in the United States and Europe, largely driven by the burden of advanced hepatitis C virus (HCV) and nonalcoholic steatohepatitis (NASH) cases.[2,3]

Disclosures: Dr Singal is on the speaker bureau for Bayer/Onyx Pharmaceuticals.
[a] Division of Gastroenterology and Hepatology, Henry Ford Hospital, 2799 West Grand Boulevard, Suite K7, Detroit, MI 48202, USA; [b] Division of Digestive and Liver Diseases, University of Texas Southwestern Medical Center, 5959 Harry Hines Boulevard, POB 1, Suite 420, Dallas, TX, USA; [c] Harold C Simmons Cancer Center, University of Texas Southwestern Medical Center, 2201 Inwood Road, Dallas, TX 75390, USA
* Corresponding author. Division of Digestive and Liver Diseases, University of Texas Southwestern Medical Center, 5959 Harry Hines Boulevard, POB 1, Suite 420, Dallas, TX 75390-8887.
E-mail address: amit.singal@utsouthwestern.edu

Med Clin N Am 98 (2014) 103–118
http://dx.doi.org/10.1016/j.mcna.2013.09.003 **medical.theclinics.com**
0025-7125/14/$ – see front matter

Prognosis for patients with HCC depends on tumor stage at diagnosis, with curative options available only for patients diagnosed at an early stage. Unfortunately, two-thirds of patients with HCC are diagnosed at an advanced stage, when curative options no longer exist and median survival is less than 1 year.[4,5] Despite improvements in therapy, prognosis for patients with HCC remains poor, with 5-year survival rates of only 18%.[4,6] With increasing availability of new treatment options for patients with HCC, treatment decisions have become more complex and challenging.[7] The aim of this review was to provide an up-to-date summary of the diagnosis and management of HCC.

RISK FACTORS

More than 90% of HCC develop in patients with chronic liver disease.[3,8,9] Cirrhosis, the most well-recognized risk factor, is associated with an annual risk of 2% to 7%.[10] HCV-associated cirrhosis is the causative agent largely responsible for the increase in incidence of HCC in the United States and Europe. The incidence of HCC in patients with HCV cirrhosis is up to 2% to 6% per year, although this can be significantly decreased by successful antiviral therapy.[11,12] However, the most frequent risk factor for HCC worldwide is chronic HBV infection, accounting for more than 50% of all cases.[13] Other risk factors include older age, male gender, obesity, diabetes, aflatoxin exposure, and alcohol and tobacco use.[14,15] However, predictive models for HCC based on these known risk factors have been limited by modest accuracy to date, and further refinement is still needed before their routine use in clinical practice.[11,16–18] Inclusion of novel biomarkers or genetic risk factors might improve HCC risk stratification.

SURVEILLANCE

Surveillance for HCC is recommended in high-risk populations, most notably patients with cirrhosis. The goal of surveillance is to detect tumors at an early stage when they are amenable to curative therapy so as to reduce mortality.[8,19] A randomized controlled trial (RCT) from China demonstrated a survival benefit with surveillance using ultrasound and alpha fetoprotein (AFP) in patients with chronic hepatitis B virus infection.[20] Although a similar RCT has not been performed in patients with cirrhosis, several prospective cohort studies, after adjusting for lead-time bias, have demonstrated that cirrhotic patients undergoing surveillance have earlier stages of disease and better survival than patients who had not undergone surveillance.[21–23] However, fewer than 20% of patients with cirrhosis undergo HCC surveillance, contributing to high rates of advanced tumor stage at presentation.[24–26]

The American Association for the Study of Liver Disease (AASLD) endorses HCC surveillance in high-risk patients using ultrasound alone every 6 months.[8] Although ultrasound has a pooled sensitivity of 63% for detecting HCC at an early stage in prospective cohort studies, its sensitivity in clinical practice is substantially lower at 32%.[27–29] AFP appears to be beneficial in clinical practice, increasing sensitivity for early-stage HCC to 63.4%, when used in combination with ultrasound.[28] Although investigators are attempting to identify novel biomarkers, a large multicenter study demonstrated that AFP, at a cutoff of 10.9 ng/mL, is more sensitive for early-stage HCC than other biomarkers, including des-gamma carboxy-prothrombin (DCP) and lens culinaris-agglutinin reactive fraction of AFP (AFP-L3).[30] Further studies are needed to better evaluate the potential role of new biomarkers before their routine use in clinical practice. Until that time, ultrasound and AFP remain the optimal HCC surveillance strategy.