Screening and Detection of Hepatocellular Carcinoma

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KEYWORDS

• Hepatocellular carcinoma • Tumors • Screening • Treatment

KEY POINTS

- The increasing incidence of hepatocellular carcinoma (HCC) has led to the need to identify patients at risk for HCC so that a program of screening can be undertaken.
- Screening for HCC has led to earlier diagnosis of tumors and thus has aided in initiating optimal medical treatment earlier in the disease course.
- Advances in radiological techniques and the identification of more accurate serum tests to diagnose HCC continue to be important areas of study and exploration.
- As advances in the diagnosis and treatment of HCC continue to be achieved, it is hoped that morbidity and mortality related to HCC can be decreased.

ROLE OF SCREENING FOR HEPATOCELLULAR CARCINOMA

The incidence of hepatocellular carcinoma (HCC) continues to increase worldwide, and especially in westernized countries due to a rising incidence of nonalcoholic fatty liver disease (NAFLD) and a peak in the number of patients with hepatitis C-induced cirrhosis. In contrast to other malignancies, the prevalence of HCC is predicted to continue to escalate over the next 20 to 30 years. The increasing burden of HCC has led to the need to develop a screening system that will help identify tumors when they are small, and thus more likely to be amenable to treatment and optimally to cure. The role of screening for any malignancy is to reduce mortality related to the disease. In order to be successful in this goal, there must be proper identification of the at-risk population, and the most sensitive and specific tests should be applied to this population at the appropriate time intervals (surveillance intervals). There must also be a validated system in place to determine appropriate follow-up of abnormal findings that maximizes the likelihood of detecting false-positive results and minimizes the number of tests needed to confirm the diagnosis of HCC.

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DEFINITION OF THE AT-RISK POPULATION

The population of patients who are at the highest risk of developing HCC are those who benefit most from being entered into a screening program. This population includes those people that have the highest incidence of HCC. It is well known that advanced fibrosis and in particular, cirrhosis of the liver, predisposes to the development of primary liver cancer. The primary question is what is the level of incidence at which screening becomes effective? An intervention is considered effective if it increases life in the population by at least 3 months.[1] Interventions that can be achieved at a cost of less than $50,000/year of life gained are considered cost-effective.[2] There have been several cost-effective analyses for HCC surveillance that have been published.[3–12] These models have varied in regards to the population being studied, the intervention that has been applied for screening, and differences among the sensitivity and specificity of the surveillance tests. The conclusion among these studies has found that surveillance for HCC is cost-effective using ultrasonography[5] among those who have the highest risk of HCC. The at-risk population identified to have the highest risk of development of HCC includes those patients who have cirrhosis of any etiology, as these patients have a 1.5% to 2% incidence per year of developing HCC. Therefore, among patients with cirrhosis of various etiologies, surveillance should be undertaken when the risk of developing HCC is 1.5% per year or greater (**Table 1**).

Patients who have chronic hepatitis B represent a unique population that remains at higher risk of developing HCC without cirrhosis compared with other populations with chronic liver disease. A prospective controlled study by Beasley and colleagues[13,14] showed that the annual incidence of hepatocellular cancer in hepatitis B carriers was 0.5%. The annual incidence increases with age greater than 70 years, with the chance of developing HCC rising to 1%. The incidence of HCC development among hepatitis B carriers with known cirrhosis increased to 2.5%/year. Uncontrolled prospective cohort studies in North America have suggested that the incidence of HCC in chronic hepatitis B carriers varies significantly.[15–17] Non-Asian chronic carriers with long-term inactive disease (anti-HBe positive with low viral loads) who are not cirrhotic appear to have a very low risk of developing HCC.[18–21] Thus, this population may not be worthy of screening for HCC. However, results of many studies have shown that Asian carriers of chronic hepatitis B without cirrhosis remain at increased risk for HCC regardless of their replication status.[18,22–24] Risk of HCC appears to persist also in Asian HBV carriers who lose surface antigen positivity (HBsAg), and thus this population should continue to be screened for HCC.[25] Overall, the annual incidence of HCC in male hepatitis B carriers from South East Asia starts to exceed 0.2% around age 40,[14] and this is unrelated to whether cirrhosis is present or disease activity is high. This is in contrast to Caucasians with chronic hepatitis B, in whom the risk of development of HCC appears to be increased with presence of cirrhosis and greater inflammatory activity. Unlike Asians who lose surface antigen and are at risk of developing HCC, Caucasian HBV carriers who lose surface antigen appear to have a decline in their risk of HCC development.[26,27] In general, recommendations are for Asian men with HBV to begin receiving screening at age 40, and Asian women with HBV to initiate screening at age 50. All hepatitis B carriers with cirrhosis should be screened for HCC regardless of age.

SURVEILLANCE TESTS

There are 2 types of screening tests used to detect HCC: radiological and serologic. Radiological tests include ultrasonography, dynamic contrast computed tomography (CT), and dynamic contrast magnetic resonance imaging (MRI). The most widely used

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