



Liver Cancer: INCREASING INCIDENCE, BUT GREATER THERAPEUTIC OPTIONS

By Christopher Siegel, MD, PhD, FACS

ALTHOUGH HEPATOCELLULAR CARCINOMA (HCC) does not garner the type of publicity breast cancer and colon cancer receive, it clearly remains a major cause of cancer mortality. In the United States, the incidence of liver cancer remains the fifth and ninth leading cause of cancer deaths in men and women with an estimated 13,260 male and 6,330 female deaths in 2011. In contrast to the incidences of colon, lung and breast cancer, which are decreasing, the incidence of liver cancer is increasing.¹

Studies (Davila et al, *Gastroenterology*, 2004) indicate this is in part due to the large number of people infected with viral hepatitis. Because of the latency between viral infection, cirrhosis, and the development of cancer, it has been projected that the number of hepatitis C related liver cancer cases will continue to rise and potentially double over the next 10-20 years (reviewed by El-Serag, *Hepatology* 2002).

The American Association for the Advancement of Liver Disease (AASLD) has developed recommendations for screening populations at risk. For chronic hepatitis B carriers, the guidelines recommend screening Asian males 40 years of age or older, Asian females 50 years of age or older, all hepatitis B carriers with cirrhosis, all hepatitis B carriers with a family history of HCC and African hepatitis B carriers older than 20. Screening should also be offered to patients with cirrhosis related to hepatitis C, alcohol, hemochromatosis, and primary biliary cirrhosis.

Because patients who develop hepatocellular cancer often have cirrhosis as well, treatment algorithms and tumor staging systems have been developed to try to incorporate the degree of hepatic dysfunction in the recommendations for treatment.

For example, the treatment recommendation for a patient with a small tumor but with advanced cirrhosis may be different than a patient with the same size tumor but much better liver function and reserve. Multiple staging systems have been described to try to determine the best way to segregate patients to the appropriate treatment algorithm. One current commonly used algorithm is the Barcelona Clinic Liver Cancer (BCLC) staging classification. This staging system takes into account underlying liver function as represented by the patient's Child-Pugh-Turcotte score, as well as, tumor size, vascular involvement, the presence of extrahepatic disease and the patient's performance status.

Multiple tools have been added to the armamentarium for the treatment of hepatocellular cancers. These can be separated into three categories: surgical, medical and radiological. Surgical options include resection, ablation and transplantation.

In a patient with HCC and no underlying cirrhosis, the goal should be resection if possible. In a study by Llovet et

al. (*Hepatology* 1999), excellent five year survival rates were reported (74%) for patients with a normal bilirubin and no portal hypertension who were treated with resection. Aarii et al. (*Hepatology* 2000) reported similar survival rates for 1,318 patients who underwent resection for the treatment of small (< 2 cm) hepatocellular cancers.

Most patients with hepatocellular cancers and early stage tumors are not candidates for resection based on poor underlying liver function and inadequate liver reserve. Based on a publication by Mazzaferro et al. (*NEJM* 1996) the United Network for Organ Sharing (UNOS) currently gives special consideration to patients who have a liver cancer that is less than 5 cm in size or have three or fewer tumors, no individual tumor larger than 3 cm. These criteria have become known as the Milan criteria. Patients that satisfy these requirements can be placed on the transplant list and are awarded enough points that they can often be transplanted relatively quickly. In Ohio they often can be transplanted within 3-6 months. Transplant recipients who met Milan criteria were found to have a 75% four-year survival.

Ablation may be a possible treatment for patients with small tumors, < 3 cm, with hepatic dysfunction severe enough to preclude them from resection. This treatment modality employs either cold (cryoablation) or heat (radiofrequency/microwave) to destroy tumors. Interventional radiologists and radiation oncologist also have effective treatments which can be offered to appropriate candidates.

Within the last several years, sorafenib, a multiple kinase inhibitor, was FDA approved for the treatment of unresectable hepatocellular carcinoma. In a randomized control trial, sorafenib was shown to increase survival over best supportive care.

With so many options now available for the treatment of hepatocellular carcinoma, trials are now underway to evaluate the effect of combining various treatments to obtain better long term survival. In addition, efforts are underway to educate the general population on the importance of screening high risk groups at regular intervals. By finding cancers earlier and having multiple tools to treat patients, new found hope has been given to curing this disease.

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Reference

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