

Liver Transplantation for Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the most common primary hepatic malignancy with an annual incidence of over one million cases worldwide. The single most important risk factor for the development of HCC is cirrhosis; however, the risk of developing HCC varies with the etiology of cirrhosis. Cirrhosis as a result of chronic viral hepatitis, however, accounts for most primary liver cancer worldwide and numerous epidemiological studies have established a clear association between chronic viral infection and development of HCC.

Liver transplantation (LTX) is conceptually an attractive therapy for HCC in a cirrhotic liver because it incorporates the radical resection of a total hepatectomy combined with liver replacement. While initial results were disappointing, better outcomes have been consistently achieved by refining the selection criteria, with a focus on tumor characteristics, including in particular size, number, lobar distribution, and vascular invasion. A landmark study by Mazzaferro et. al. published in 1996 set the stage for the current guidelines and policies, which are currently

in use to allocate hepatic allografts to those patients with HCC, often referred to as the Milan criteria.

Whether the Milan criteria, and the resulting UNOS policies, are too restrictive has been a controversial issue without a clear resolution. Clearly the use of physical characterization of HCC, e.g. size and number, and pathological characteristics, e.g. degree of differentiation and microvascular invasion, are only surrogate markers for biologic behavior. Genetic markers, such as degree of mutational load, may provide more sensitive predictors for recurrence after liver transplantation.

Future developments in the area of liver transplantation for HCC will focus on improved prognostic testing, use of novel antiproliferative agents, novel immunosuppressive protocols and timely application of liver transplantation. The shortage of livers for transplantation is the limiting factor in the application of this life-saving procedure for a previously dismal prognosis. Living donor liver transplantation is one option to the use of conventional brain-dead donors, however other concerning options of donor sources, such as transplant tourism and executed prisoners, jeopardize broader acceptance of liver transplantation for treatment of HCC.