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Hepatocellular carcinoma: Prognostication beyond size and number

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Hepatocellular Carcinoma (HCC) is one of the man causes of death in cirrhosis. Apart from chronic hepatitis B, hepatitis C and alcoholic cirrhosis, metabolic syndrome associated NASH is emerging as an important risk factor for HCC. Robust radiological diagnostic criteria for HCC have been defined thus obviating the need for liver biopsy in more than 90 percent of cases. While early HCC (small <3 cm) in a patient with child A cirrhosis can be effectively treated by resection or ablation, most patients presenting with advanced HCC have limited treatment options. Prognostication of HCC is extremely important while selecting patients for transplantation so that post-transplant recurrence can be minimized. The Milan criteria and the University College of San Francisco (UCSF) criteria are based on the principle of size and number of tumors, which are regarded as an indirect marker of tumor aggressiveness and biology. Vascular invasion is an important predictor of recurrence and while major vascular invasion is a contraindication to transplant, there is no direct measure of micro-vascular invasion. Although high levels of Alpha-Fetoprotein (AFP) and Des-Gamma-Carboxy-Prothrombin (DCP) have been shown to adversely affect prognosis, the search for a perfect marker that would determine tumor biology remains elusive. Ongoing research is now focusing on tumor biology to select treatment options including candidates for transplant. Tumor biology can be assessed by serum biomarkers, tissue biomarkers, molecular (gene) markers, histological markers and specialized radiological features. Gene expression profiling has allowed stratifying HCCs into several clinically relevant subgroups that were previously unrecognized by conventional methods. Specific gene signatures of aggressiveness, micro-vascular invasion, recurrence and risk of metastases have been developed. HCC-associated micro RNAs have also been assessed as diagnostic and prognostic biomarkers. 18FDG PET/CT has been shown to provide excellent prognostic information. Tumors that are PET avid show poor differentiation, micro-vascular invasion, are associated with higher AFP levels and have a higher risk of recurrence after transplant or resection. ^{18}FDG PET/CT may have a role in identifying patients within Milan or UCSF criteria who may have higher recurrence risk post-transplant and therefore may not be offered transplant as well as identifying patients outside standard criteria who may have a low recurrence risk and therefore may be offered transplant. To conclude, evidence suggests that intrinsic biologic characteristics of the tumor in terms of proliferation and invasiveness lead to very different clinical outcomes. Numerous biomarkers, and imaging with ^{18}FDG PET/CT have been studied that provide additional information for HCC biologic behavior, metastasis and recurrence compared to traditional radiological and histo-pathological features.

Biography

Kaiser Raja is a Senior Consultant Physician in Liver Diseases and Liver Transplantation. He is the Chief Hepatologist for the Integrated Liver Care Team at Aster DM Healthcare Group in India running multi-organ transplant centers at Aster CMI Hospital, Bangalore and at Aster Medcity in Kochi, India. He has completed his post-graduate medical training in Internal Medicine and Gastroenterology from the renowned Postgraduate Institute of Medical Education and Research, Chandigarh India. Following that he has done an Advanced Liver Diseases and Transplant Hepatology Fellowship from the Mount Sinai Medical Center, New York. He has several publications to his credit. His areas of interest are chronic viral hepatitis, autoimmune liver disease, liver cancer and post transplantation care.

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