Resection for Hepatocellular Carcinoma

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Hepatocellular Carcinoma (HCC) continues to present major challenges in management, which is further complicated by the presence of associated chronic liver disease. Key issues in surgical resection of HCC include the site, size, and number of lesions, the severity of the chronic liver disease, and the size of the functional liver remnant. *De novo* HCC in the absence of chronic liver disease can be treated by major liver resection with little risk of postoperative liver failure. Liver resection can also be used a bridge to liver transplantation as it affords the possibility of determining the pathologic grade of the tumortumor and its invasiveness, and thereby the prognosis. This review summarizes the current treatment approaches to surgical resection for HCC. (J Clin Exp Hepatol 2014;4:S90–S96)

Treatment

Recommendations for treatment of HCC should be based on randomized controlled trials or meta analyses, rather than by non randomized clinical trials or observational studies. However, there is a paucity of robust evidence regarding the treatment of HCC. Interventions have not been thoroughly tested against each other. Hence the strength of evidence for most interventions is less than desirable. Therefore treatment decisions must be taken by a multi-disciplinary group which comprises hepatologists, surgeons, radiologists, interventional radiologists, pathologists, nurses, palliative care physicians, patient education specialists, and pharmacists. Treatment decisions must be made in a tumortumor board meeting.

In India, the problem is compounded by the fact that the country is large, and there is considerable variation in the expertise and technology available for the treatment of HCC. It is inconceivable that HCC shall be treated only in a few centers with state-of-the art services. While treatment guidelines must therefore be treated with caution, the right of every patient with HCC to standardized care has placed a huge burden on healthcare systems to deliver for these patients. Although prevention of HBV related cancer is still the priority, yet, treatment of the established HCC is also necessity.

The radical treatment options are:

a) Surgical resection
b) Liver transplantation
c) Local ablative techniques such as
   a. Radiofrequency ablation (RFA)
   b. Percutaneous ethanol injection (PEI)

No randomized data is available at this time comparing these three approaches. Hence existing guidelines are dependent on cure rates with these treatment approaches.

HEPATOCELLULAR CARCINOMA IN THE ABSENCE OF LIVER DISEASE

HCC in background of healthy liver (without cirrhosis or chronic hepatitis) may occur occasionally.[1] There are two types: a) the classical sporadic variety, and b) the fibrolamellar variant. The fibrolamellar variant is characteristic in the female preponderance, absence of AFP elevation, and in the presence of lymph node involvement. These tumors present only as mass lesions and at an advanced stage. Despite this advanced stage at presentation, resection can be done as the healthy liver has a normal ability to regenerate. Survival following resection is over 50% at 5 years.[2]

HEPATOCELLULAR CARCINOMA IN THE PRESENCE OF LIVER DISEASE

Resection for HCC has several advantages: a) it requires no waiting time, b) allows pathologic examination of the tumortumor and therefore prognostication, and c) atleast in theory, does not preclude future liver transplantation. In this role it is used a bridge to transplantation.

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Abbreviations: AFP: alpha-fetoprotein; AFP/TTV: AFP to tumor volume; ASA: American Society of Anesthesiologists; BCLC: barcelona clinic liver cancer; CT: computerized tomography; CTP: child-turcotte-pugh; CUSA: cavitary ultrasound suction aspirator; FDG-PET: fludeoxyglucose positron emission tomography; FLR: functioning liver remnant; HBV: hepatitis B virus; HCC: hepatocellular carcinoma; HPB: hepato-pancreato-biliary; HVPG: hepatic venous pressure gradient; MELD: model for end-stage liver disease; PEI: percutaneous ethanol injection; POLT: primary orthotopic liver transplantation; PVE: portal vein embolization; RFA: radiofrequency ablation; TACE: transarterial chemoembolization; UCSF: University of California, San Francisco
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However, liver resection is clearly inferior to liver transplantation when applicable as a long term treatment modality in HCC *with* liver disease as.

a) There is the potential to miss satellite lesions and non-visible tumor
b) The remaining liver tissue continues to present a risk of developing new HCC;
c) There is a risk of deterioration of liver function either immediately following hepatic resection or later.

It is important to emphasize that liver transplantation is not applicable to all tumors (Milan, UCSF or other criteria), and liver resection is not suitable in patients with decompensated liver function. Further, liver transplantation requires the availability of cadaveric or living donors, and a specialized transplant setup. Liver resection can, on the other hand, be performed in any center where adequate surgical, medical and radiologic facilities are available. Currently there exists in India, larger numbers of successful hepato-pancreato-biliary (HPB centers) as opposed to liver transplant centers although this situation is rapidly changing. Recent meta-analysis has shown comparable survival figures in patients with early HCC treated (intention-to-treat strategy) by resection or transplantation. There is also some data that primary orthotopic liver transplantation (POLT) may be more cost effective than resection with salvage transplantation in HCC in Child A cirrhotics.[3]

RESECTION IN PATIENTS WITH UNDERLYING CHRONIC LIVER DISEASE

Assessment of the Severity of Liver Fibrosis or Cirrhosis

Assessment of the severity of liver fibrosis or cirrhosis is crucial. Clinical pointers are a) Child-Pugh or MELD scores, b) platelet counts, c) splenomegaly and d) esophageal varices.

Large series have reported 10 year recurrence-free survivals of 22% of 22800 patients who have undergone liver resection for HCC. The results are best in patients who have a single tumortumor with a simple nodular appearance where there is no vascular invasion or intrahepatic metastases.[4] Overall, the application of resection and the results following resection are governed by patient, liver and surgeon factors (Figure 1).

Selection of Candidates for Resection

For selection of candidates for resection use following criteria:

a) Rule out extrahepatic metastases. It is desirable to perform a CT of the chest prior to resection or transplantation. This is because HCC does metastasize to the lymph nodes, lungs or bone. A bone scan is not a routine requirement. FDG-PET scans have low sensitivity of 55%; however, with increasing grade or stage, higher yields upto 100% may be available.[5]
b) Assessment of the extent of the hepatic disease: the location, size and number of tumors, their proximity to major vessels, and whether they are peripheral in location or central deep in the liver all influence the resectability. First the residual volume after resection must be calculated based on the imaging. In normal livers, residual volumes of as low as 20% are acceptable in tumor resections, but in patients with fibrosis or cirrhosis, higher residual volumes are necessary. Patients with Child A liver status may withstand major hepatectomies, but Child B category patients may only be subjected safely to minor resections. Tumor size alone may not be a deterrent to safe resections. Reports of over 45% five

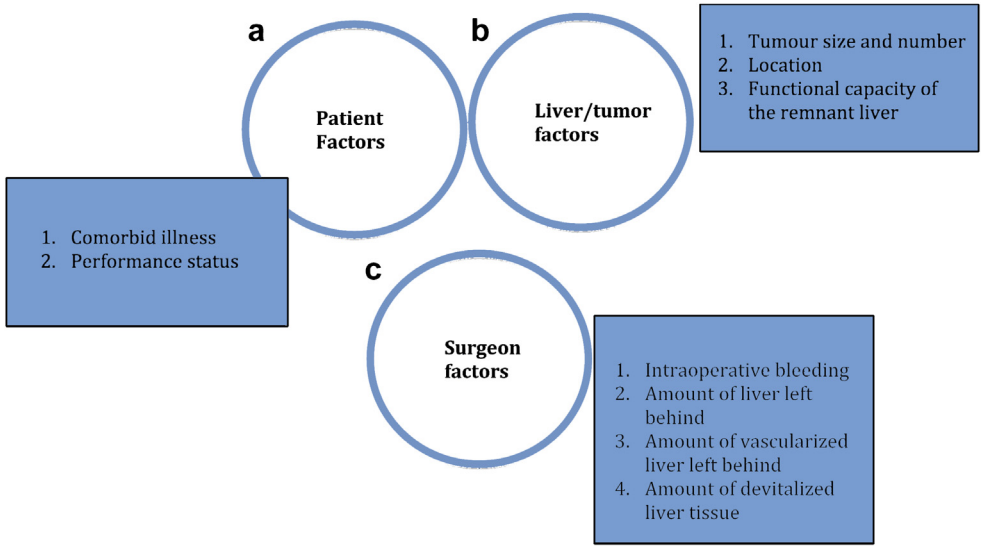

Figure 1 The results of liver resection for HCC depends on three important criteria: a) patient factors, b) liver factors, and c) surgeon factors.