



# Hepatectomy bridges to transplant—the road to cure?

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Liver transplantation and hepatic resection are effective surgical strategies for hepatocellular carcinoma (HCC). In the current issue of *Annals of Surgery*, Professor Pinna and colleagues applied a cure model to compare both treatments (1). Comparison was made in terms of cure rate. Interestingly, curation has never been concisely defined in clinical practise. In the standard survival model, patients are considered disease-free after R0 resection but are always at risk of recurrence. It is arguable, particularly for HCC, whether disease clearance equates curation, as more than half of patients recur in 5 years after radical resection (2). In epidemiology, statistical cure is achieved when the mortality of the patients treated for a specific disease return to that in the general population (3). However, statistical cure is neither practical in clinical sense, as patients surviving with disease are also considered cured.

In professor Pinna's study, a modification of statistical cure was adopted using disease recurrence as the endpoint. The patient is considered cured when his risk of recurrence is equivalent to risk of *de novo* HCC in the general population. A cure fraction provides the probability of returning to the population risk after the specific treatment. This cure model provides further insights into disease status after surgical treatment. A meta-analysis reported 5-year disease-free survivals for HCC as 62.5% after liver transplantation and 35.6% after hepatic resection (4). In the Kaplan Meier survival model, the status of any patients without recurrence is identical, regardless of the treatment received. This may be debatable as patients who underwent resection, albeit tumour free, are constantly at higher risk of recurrence comparing to transplant recipients. The

oncological benefits of transplantation may be considerably higher. In this multicentre retrospective series, the cure fractions after liver transplantation and hepatic resection were 74.1% and 24.1% respectively. Transplant recipients are three times more likely to return to normal risk than patients undergoing liver resection. The proposed cure model effectively quantified the genuine advantage of the more radical treatment. The concept is simple and the figure is easy to comprehend.

However, comparison is only valid when the patient is eligible for both treatments. While sufficient remnant function is paramount for resection, transplantation is applicable to end-stage liver disease, but with strict limitation in tumour burden. Hereby the clinical question is whether to resect or transplant resectable early stage tumours. From the result of the study, the answer is an obvious oncological advantage for liver transplantation. However, access to transplant is limited by organ shortage. Patients with live donor can be offered the option to transplant with the oncological benefits balanced with donor risk. Patients without live donor have a dim chance to acquire a deceased graft with their relatively preserved liver function. Professor Pinna and colleagues suggested that hepatic resection could be performed as neoadjuvant treatment with the prospect of a future transplant. We prefer the term 'bridging' in this context, as resection offers temporary control, instead of enhancement of the transplant's treatment effect. Hepatectomy bridging to liver transplantation provides the highest possible chance of cure to these patients. The excess operative mortality and morbidity, as well as the infective and cardiovascular

complications related to immunosuppression are the price to pay. One might question the necessity of an ultra-major operation in the absence of active disease, but the relative high probability of recurrence and the possibility of it being non-transplantable have to be considered. Supported with data from the cure model, we believe bridging hepatic resection and definitive liver transplantation remains a viable approach in pursuit for curation of HCC.

Several limitations must however be mentioned about this study. The authors did not exclude patients ineligible for either liver transplantation or liver resection. This largely limited the clinical applicability. Only patients eligible for both treatments benefit from a comparison between two options. Moreover, patients in the study receiving liver transplantation and hepatic resection represented heterogeneous populations with different liver function and tumour status. The resection group had larger tumours and lower Model For End-Stage Liver Disease (MELD) score, albeit statistically insignificant. These factors potentially confound cure probability. Nevertheless, the authors must be congratulated for successful application of the cure model to surgical treatments of HCC. Treatment effects were effectively quantified. The study results supported definitive transplantation bridged by hepatic resection to achieve cure for HCC.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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