Hepatocellular carcinoma resection post-selective internal radiation therapy

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1. Introduction

Cure is only possible in hepatocellular carcinoma (HCC) when all cancer cells have been ablated using a single or multi-modality treatment. Unresectable HCC is by definition advanced and the chance of cure is remote. At this stage, local ablative therapy or liver transplantation is no longer an option. The aim of treatment is palliative, mainly to minimise symptoms and to prolong life.

Improvements in locoregional and systemic treatment can convert advanced to earlier-stage HCC and from non-curable to potentially curable disease. This downstaging of tumours differs fundamentally from neoadjuvant therapy which is used to treat patients with curable disease in order to improve the duration of survival after resection. After tumour downstaging in advanced HCC, salvage surgery (either in the form of partial hepatectomy or liver transplantation) is required as complete histological tumour necrosis occurs in only a minority of patients. Studies on tumour downstaging show that neither normalisation of serum alpha fetoprotein nor complete radiological tumour response correlates with the absence of viable tumour cells detected in specimens obtained after salvage liver resection.1

The reasons why HCC becomes resectable or transplantable after tumour downstaging are: the disappearance of either intrahepatic or extrahepatic tumours, shrinkage of tumours, disappearance of portal venous tumour thrombi, and/or hypertrophy of non-tumourous part of the liver.

The pre-requisites for a successful downstaging programme are: the availability of an effective treatment for downstaging, close monitoring of the results of downstaging, an experienced liver surgeon who repeatedly re-evaluates tumour resectability/transplantability and an aggressive surgical approach adopted in treatment of these patients.

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2. Selective internal radiation therapy

Tumour downstaging using yttrium-90 ($^{90}$Y) microspheres has been reported in 0.7–5.6% of patients with unresectable HCC which becomes resectable, and in 11–23% of patients with unresectable HCC which becomes transplantable. The higher liver transplantation rates are a consequence of the improved liver function after surgery while the reverse is true for liver resection. Selective internal radiation therapy (SIRT) with $^{90}$Y-microspheres can also be combined with systemic chemotherapy in order to downstage unresectable to resectable HCC. Salvage liver resection following downstaging with $^{90}$Y-microspheres resulted in a 1-year survival of 84% and a 3-year survival of 27% with better results were reported by other authors.2

The interval between SIRT and salvage liver resection should be at least 8 months in order to ensure adequate tumour shrinkage and hypertrophy of the non-tumorous liver and to allow sufficient time for the non-tumorous liver to recover from the effects of SIRT.

The situation for liver transplantation is more complex and involves consideration of the best use of donor organs and resources. If the HCC has been downstaged to within the Milan criteria and with a serum alpha fetoprotein <400 ng/mL, the outcomes are broadly equivalent to patients who were first selected for liver transplantation based on the same criteria. Most surgeons agree that a minimum interval of 6 months between downstaging and transplantation is essential to identify and exclude patients with rapid tumour regrowth, metastases or portal venous invasion with thrombi. Good results with liver transplantation after downstaging with $^{90}$Y-microspheres have been reported and even for HCC involving the caudate lobe. In a non-randomised study, $^{90}$Y-microspheres were more effective than transarterial chemoembolisation (TACE) in shrinking T3 HCC to transplantable T2 HCC. Overall, SIRT using $^{90}$Y-microspheres appears to be well tolerated with no reported harmful effects on arterial or vascular anastomosis in liver transplantation.

The safety profile of $^{90}$Y microspheres also means that SIRT can be used as bridging therapy to extend the time to patients waiting for a liver donor without affecting post-transplant survival. Riaz et al. (2009) recently suggested that radiation lobectomy/segmentectomy may improve the safety of SIRT, although more data are needed to determine whether these techniques will increase the numbers of patients with unresectable HCC who are downstaged to resectable or transplantable HCC.

3. Conclusion

Downstaging HCC from unresectable to resectable and non-transplantable to transplantable using $^{90}$Y-microspheres is possible with prospective of cure for some patients who previously were considered as non-curable.

Conflict of interest statement

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References