Commentary

Commentary on the article entitled "hepatocellular carcinoma with macrovascular invasion treated with yttrium-90 radioembolization prior to transplantation"

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Provenance: This is an invited Commentary commissioned by Editor-in-Chief Yilei Mao (Department of Liver Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China).

Comment on: Levi Sandri GB, Ettorre GM, Colasanti M, *et al.* Hepatocellular carcinoma with macrovascular invasion treated with yttrium-90 radioembolization prior to transplantation. HepatoBiliary Surg Nutr 2017;6:44-8

Submitted Oct 31, 2016. Accepted for publication Nov 22, 2016.
doi: 10.21037/hbsn.2017.01.09
View this article at: http://dx.doi.org/10.21037/hbsn.2017.01.09

Between 50% to 70% of patients with hepatocellular carcinoma (HCC) are diagnosed at a stage when radical treatment (percutaneous ablation, partial hepatectomy, liver transplantation) are no longer an option (1). Limitations due to size, number and location of tumours, as well as quantity and quality of liver remnant, prohibit partial hepatectomy. Percutaneous radiofrequency ablation can produce good long-term survival in patients with a solitary or a few small HCC nodules (2). Liver transplantation removes not only the tumour, but replaces the underlying cirrhotic liver with a normal liver. It is not surprising that liver transplantation offers the best overall and tumour-free survival in selected patients (1,2).

The Milan criteria [one HCC nodule ≤5 cm, or ≤3 nodules ≤3 cm, and with no macrovascular invasion (MVI)] remain the benchmark for selection of HCC patients for liver transplantation, despite a number of proposed extensions to the Milan criteria to capture patients with an increase number or size of HCC nodules who may achieve similar post-transplant survival outcomes (3). A recent meta-analysis showed that patients with chronic hepatitis and cirrhosis and HCC within the Milan criteria achieved post-transplant survival rates similar to those with non-HCC indications (4).

Improvements in locoregional and systemic treatments have been reported to downstage an advanced staged HCC into an earlier stage, thus making an unresectable HCC to become resectable, and an untransplantable HCC beyond the Milan criteria to become transplantable (within the Milan criteria). The main reasons why after downstaging HCC patients become resectable or transplantable are: shrinkage of tumours, disappearance of secondary tumours, disappearance of tumour venous thrombi and/or hypertrophy of non-tumorous liver. It is important to differentiate between tumour downstaging and neoadjuvant therapy. For tumour downstaging, the tumour is unresectable or untransplantable to start off with, and the downstaging treatment makes the tumour resectable and transplantable. For neoadjuvant therapy, the HCC is resectable or transplantable and the therapy aims to improve long-term survival outcomes after surgical treatment. Similarly, it is important to differentiate between tumour downstaging to liver transplantation and bridging therapy in liver transplantation. Bridging therapy in liver transplantation aims to control progression of the tumour while the patient is put on a waiting list for liver transplantation so that the waiting time for liver transplantation can be prolonged while the long-term

survival of liver transplantation will not be affected.

Yttrium-90 microspheres were first reported by Lau *et al.* to be able to downstage unresectable HCC to become resectable in the year 2004 (5). Subsequently a lot of reports came out, not only supporting that yttrium-90 microspheres can downstage unresectable HCC to become resectable, but also untransplantable HCC to become transplantable (1,2,4,6,7). In actual fact, when HCC is downstaged, the chance of salvage liver transplantation is higher than salvage liver resection as liver transplantation does not depend on the preoperative liver functional status of the patient and the position of the tumour to determine operability. Even when the liver function is decompensating, as long as the HCC has been downstaged to be within the Milan criteria, liver transplantation can still be carried out. The long term survival of these patients after HCC downstaging to be within the Milan criteria has been reported to be similar to those who had initial tumours within the Milan criteria who underwent liver transplantation (1-4,6,7).

Patients with HCC with portal vein tumour thrombosis (PVTT) are in BCLC-stage C. The BCLC recommendation is sorafenib and the median survival of these patients is 11 months (2,6,7). Yttrium-90 microspheres have been recommended in guidelines and in expert consensus statements to be used in HCC with PVTT as numerous reports have shown their effectiveness in these patients (2,7,8). The article written by Levi Sandri *et al.* entitled "*hepatocellular carcinoma with macrovascular invasion treated with yttrium-90 radioembolization prior to transplantation*" which is published in this issue of the Journal (9) is interesting. The authors treated four patients with HCC with PVTT with Yttrium-90 microspheres. In 3 patients, the PVTT staging was V_p1 (third order branch of main portal vein) and in 1 patient it was V_p3 (first order branch of main portal vein). The PVTT staging which they used was based on the staging system of the Liver Cancer Study Group of Japan (10). After treatment with yttrium-90 microspheres, complete thrombus regression was observed in these four patients, enough for these patients to be included in the waiting list for liver transplantation as they were all within the Milan criteria. After liver transplantation a disease-free survival of 39.1 months (range, 1–76 months) was obtained. This article is interesting because although occasional patients with HCC with PVTT had been reported to be downstaged with yttrium-90 microspheres from untransplantable to become transplantable, this report is on a series of four patients who were so treated with good results in long-term overall and disease-free survival.

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Cite this article as: Lau WY. Commentary on the article entitled "hepatocellular carcinoma with macrovascular invasion treated with yttrium-90 radioembolization prior to transplantation". HepatoBiliary Surg Nutr 2017;6(1):49-51. doi: 10.21037/hbsn.2017.01.09

