Symposium III

Factors Affecting Survival after HCC Recurrence in Liver Transplantation

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The early results of liver transplantation (LT) in patients with advanced HCC were poor because of frequent tumor recurrence. Since the introduction of the Milan criteria by Mazzaferro and colleagues in 1996 (1), the survival outcome has improved. Now, LT is regarded as the best treatment modality for patients with early HCC. However, about 10-20% of patients still experience recurrence, even though they meet the favorable selection criteria (2,3). The patients who experience recurrence after LT show rapid progression of recurrent disease and have a very poor prognosis because the rate of progression of recurrent HCC is more rapid after transplantation than after hepatic resection (4). However, some patients have a good prognosis if they are appropriately treated after the recurrence (5). Therefore, it is important to predict not only who can experience recurrence but also who can survive longer after recurrence.

A few studies investigated prognostic factors affecting survival after recurrence in patients who underwent LT for HCC, but uniformly demonstrated better outcomes in patients with surgically treated post-transplant HCC recurrence (Table 1) (5-10). The majority of patients with post-transplant recurrence of HCC present with multifocal disease that is not amenable to local therapy. In that minority of cases where localized recurrence is detected, however, direct treatment by surgery or ablation warrants consideration (2). While it is clear that patients selected for surgical treatment are a subgroup with the best pre-operative variables, and the numbers of patients in these studies is too small to allow firm conclusions, it appears reasonable to consider surgical/ablative treatment of recurrent HCC when the tumor is confined to a single anatomic site that is readily amenable to treatment with low expected morbidity or to multiple sites that is controllable to local therapy for all.

In terms of the site of recurrence, liver and lung (2,5,7) is better than bone, brain, lymph node, and peritoneum. Although selection bias confounds comparisons of the outcomes according to the site of recurrence, early detection and aggressive local therapy for liver and lung lesions leads to long-term survival. A long-term survival in 3 patients who even underwent retransplantation for the graft with recurred HCC has been reported (5,6).

On the other hand, tumor biology of primary HCC was associated with the survival after recurrence

Table 1. Radical treatments of recurrent HCC after transplant

Study (Reference No.), year, type of LT	Treated radically	Liver resection (LT)	Lung resection	Others	Patient survival (%)
Regalia (10), 1998, DDLT	7 (33%)	2	2	3	57 (4 yr)
Schlitt (6), 1999, DDLT	15 (38%)	3 (2)	8	4	47 (5 yr)
Roayaie (9), 2004, DDLT	18 (32%)	5	7	6	47 (5 yr)
Kornberg (8) , 2009, DDLT	7 (44%)	2	2	2	(65 months)*
Shin (5), 2010, LDLT	4 (14%)	1 (1)	1	2	75 (3 yr)
Taketomi (7), 2010, LDLT	9 (53%)	Not accessible	3	6	88 (3 yr)

*overall survival.

(2,5,8,9). The patients whose tumor had major vascular invasion and/or poorly differentiated tumor had poor prognosis after recurrence. Malignant phenotype of the recurrent HCC may be quite different and more aggressive than that of the primary HCC. However, the biology of the primary tumor seems to be associated with early recurrence on multiple sites that is one of the poor prognosis factors after recurrence and that is unacceptable reason to curative surgical treatment.

In summary, tumor recurrence after transplantation generally carries a poor prognosis; however, that subset of patients with recurrence that is amenable to curative treatment has a materially better outlook. Clearly, selection bias confounds comparison between surgically and non-surgically treated patients. Nevertheless, complete elimination of single-site recurrences by surgical/ablative treatment, when feasible, seems reasonable. Apart from surgery, there is no evidence to support any currently available treatment for recurrent HCC, t best my knowledge to date. Therefore, early detection according to the well designed protocol and aggressive treatment according to the risk-benefit analysis may only give a chance of curative treatment for recurred HCC.

References

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