Comparative Study of Living and Deceased Donor Liver Transplantation as a Treatment for Hepatocellular Carcinoma

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BACKGROUND: Living donor liver transplantation (LDLT) is an important treatment option for unresectable hepatocellular carcinoma (HCC), but whether recurrence and survival in LDLT differ from those in deceased donor liver transplantation (DDLT) remains controversial.

STUDY DESIGN: A retrospective analysis was performed between patients with HCC who underwent LDLT in a Japanese institute (n = 133) and those who underwent DDLT in a United States institute (n = 362).

RESULTS: Although there was a difference in patient background characteristics (eg, body mass index, donor age, Model for End-Stage Liver Disease [MELD] score), tumor aggressiveness represented by Milan criteria and microscopic vascular invasion were comparable between the 2 groups. The cumulative 5-year recurrence rates of the LDLT group and the DDLT group were similar (14.8% vs 19.0%, p = 0.638), but overall survival in the LDLT group was significantly better than that in the DDLT group (84.2% vs 63.5%, p < 0.0001). Separate multivariate analysis identified different preoperative predictive factors for HCC recurrence (salvage transplantation and Des-gamma-carboxy prothrombin >300 in the LDLT group, beyond Milan criteria in the DDLT group). Combined multivariate analysis of the 2 groups identified recipient's body mass image >30 kg/m^2 as an independent risk factor for overall survival; the technique of transplantation (LDLT or DDLT) was not found to be a risk factor.

CONCLUSIONS: When compared between the institutes where LDLT or DDLT were the first treatment choices for unresectable HCC, recurrence rates were comparable. Living donor liver trasplantation is a viable treatment option for unresectable HCC, providing recurrence rates similar to those achieved with DDLT. (J Am Coll Surg 2015;220:297−304. © 2015 by the American College of Surgeons)

The efficacy of liver transplantation (LT) as a treatment option for unresectable hepatocellular caricinoma (HCC) is well established because it removes both the tumor and the cirrhotic liver that is at risk of developing future malignancy.[1] The Milan criteria (1 nodule with a maximal diameter of 5 cm or up to 3 nodules with a maximal diameter of 3 cm) are widely accepted for selection of patients with HCC for LT, and using them helps achieve post-transplant long-term survival comparable to that in patients without HCC.[1]

In the United States, approximately 7,000 new patients with HCC are put on the waiting list for deceased donor liver transplantation (DDLT) each year, and 15% die during the waiting period without receiving an LT due to the relative shortage of deceased donors.[2] Because long waiting time for DDLT increases the risk of tumor progression and drop out from the waiting list, living donor liver transplantation (LDLT) has been proposed as an alternative.[3,4] However, the impact of the source

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Abbreviations and Acronyms

BMI = body mass index
DCP = des-gamma-carboxy prothrombin
DDLT = deceased donor liver transplantation
HCC = hepatocellular carcinoma
LDLT = living donor liver transplantation
LT = liver transplantation
MELD = model for end-stage liver disease
MSMC = Mount Sinai Medical Center

of the graft (ie, DDLT or LDLT) on the treatment outcome remains controversial. Some previous reports have demonstrated worse overall and disease-free survivals for patients treated by LDLT for HCC[5-7]; others have shown similar outcomes between LDLT and DDLT.[8,9] Because most published studies were conducted in Western countries, where the large majority of LT are DDLT, a possible bias for selection of treatment may exist such that patients within Milan criteria are preferentially treated with DDLT and those beyond Milan criteria are relegated to LDLT; this is clearly the case in the United States, where the organ allocation system assigns higher priority to patients with HCC within Milan criteria.[10]

In many Asian countries, especially Japan, the availability of organs from deceased donors is quite limited, so the first treatment option for patients with unresectable HCC is LDLT.[4,11] We aimed to compare the treatment outcomes between LDLT and DDLT in settings when they were the first treatment choice for unresectable HCC. Therefore, we compared LDLT in 133 patients from Kyushu University (Japan) and DDLT in 362 patients from Mount Sinai Medical Center (NY), both major transplant centers in their respective countries. The primary endpoint was recurrence rate after LT, because it is generally the most important factor that determines long-term outcomes after LT.

METHODS

Patients

Between January 2002 and December 2010, 386 patients with a diagnosis of HCC underwent primary DDLT at Mount Sinai Medical Center (New York, NY), and 133 patients underwent primary LDLT at Kyushu University Hospital (Fukuoka, Japan). After approval by the Mount Sinai Medical Center (MSMC) Institutional Review Board and Kyushu University Ethical Committee, data were extracted from database records and from hospital and office charts. Only patients with histologically proven HCC in their explants were included in this study.

At Kyushu University Hospital, the eligibility criteria for LDLT at the beginning of the study period were: no modality except LT available to cure HCC, end-stage liver disease; no extrahepatic metastasis; and no major vascular invasion such as portal vein or hepatic vein. There was no restriction on the tumor size or tumor number. Because initial data demonstrated that patients with both HCC $>$ 5 cm and serum des-gamma-carboxy prothrombin (DCP) levels $>$300 mAU/mL had poor prognosis,[4] the policy changed in 2007 to exclude such patients from transplant candidacy.

At MSMC, the eligibility criteria for DDLT were: unresectable HCC within Milan criteria and tumor beyond these limits that was down-staged by nonsurgical treatment and maintained within Milan criteria for 6 months.

Because the series performed in MSMC included 24 patients (6.3%) with pathologic T4b tumors, but none were included in the Kyushu University Hospital cohort, these 24 patients were excluded from the comparative analysis. Therefore, 362 DDLT patients from MSMC (DDLT group) and 133 LDLT patients from Kyushu University Hospital (LDLT group) were enrolled in this study.

Preoperative assessment for hepatocellular carcinoma

Preoperative diagnosis and staging of HCC was with thoracic and abdominal CT and/or MRI. Routine biopsies were not performed. Tumors were staged according to the American Liver Tumor Study Group modified Tumor-Node-Metastasis (ALTSG-TNM) classification.[12]

Donor evaluation and selection

The selection criteria for partial liver graft from living donor in Kyushu University was based on volumetric analysis, and details are described elsewhere.[13,14] Briefly, the left lobe was initially considered for the graft. The right lobe was chosen if the estimated left lobe with the caudate lobe volume of the donor was less than 35% of the standard liver volume of the recipient. The person was excluded as a donor candidate if the remnant liver volume was less than 35% of the total liver volume. If the CT or ultrasound study showed the possibility of steatosis in the donor liver, short-term intensive treatment for hepatic steatosis was prescribed before surgery.[15]

Postoperative management and follow-up

The transplantation procedures of both institutes have been described previously.[13,16] In both institutes, postoperative immunosuppressive therapy consisted of a triple-drug regimen of cyclosporine or tacrolimus in