**Oral Presentation VII**

**VII-1**

**Outcome of Hepatic Resection for Hepatocellular Carcinoma Followed by Salvage Liver Transplantation**

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**Background:** Liver transplantation (LT) is the best treatment option for hepatocellular carcinoma (HCC) meeting the Milan criteria (MC). However, due to limited organ availability, hepatic resection (HR) followed by salvage LT in case of recurrence or liver cirrhosis progression could be an alternative strategy. This study aimed to evaluate the outcome of such alternative strategy compared with those of primary LT.

**Patients and Methods:** From September 1994 to December 2011, 653 patients underwent HR for HCC. 323 (49.4%) fulfilled the MC on pathologic review and were enrolled. Univariate and multivariate analyses were performed to identify predictive factors of recurrence after HR. Their survival outcomes were compared with those of similar patients who had LT as primary treatment.

**Results:** After a mean follow-up of 57 months, 5-year disease-free, and overall survival rates were 51.5 and 76.2%, respectively. Risk factors for recurrence included microscopic vascular invasion (McVI) (hazard ratio [HR] 2.273 [range, 1.558-3.317]), and liver cirrhosis (HR, 2.829 [range, 1.841-4.348]). Patients with HCC without McVI or underlying cirrhosis showed significant favorable survival outcome compared with others. 22 patients underwent salvage liver transplantation after initial HR. 5-year survival rates of those patients was 85.9% and 77.3% when calculated from the date of initial HR and salvage LT, respectively, comparable to that of 79.1% in 56 patients treated by primary LT (p=0.368, and 0.375, respectively) [figure1].

**Conclusions:** Despite satisfactory survival outcomes, HR for HCC meeting MC should be restricted to patients without liver cirrhosis. Salvage LT for recurred HCC after HR is a valid treatment option for selected patients with favorable outcome.

**VII-2**

**Risk-based Screening Protocol for Hepatocellular Carcinoma Recurrence after Living-Donor Liver Transplantation**

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**Purpose:** This study intends to establish an actual risk-based long-term screening protocol for hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT).

**Materials and Methods:** The study population 334 patients with HCC who underwent primary living-donor LT with follow-up period of ≥5 years. Patient medical records were reviewed retrospectively.

**Results:** Overall 10-year patient survival rate was 67.5%, with 4.8% perioperative mortality. HCC recurred in 68 (21.4%) of 318 surviving patients during a mean follow-up period of 77 months. HCC recurrence rate was 20.7% at 5 years and 22.2% at 10 years. Annual recurrence rate was 11.4%, 6.6%, and 2.0% during the first, second, and third year, respectively. In patients within Milan criteria, annual incidence of HCC recurrence was highest during first 3 years, while thereafter only six cases of sporadic recurrence occurred during next 8 years; in patients beyond Milan criteria, recurrence was very common during first 3 years, but not after 3 years. Increases in alpha-fetoprotein (AFP) were determined to be an initial indication to perform further imaging studies to diagnose recurrence in 43 patients (63.2%), whereas recurrence was detected incidentally on protocol screening imaging in another 25 patients (36.8%) in the absence of AFP rise. There was a close correlation between pretransplant AFP level and AFP rise after HCC recurrence. The 43 patients who showed a progressive rise or high levels of AFP before or at the time of HCC recurrence, the pretransplant AFP levels were >200 ng/mL in 26 (60.5%), 21-200 ng/mL in 9 (20.1%), and ≤20 ng/mL in 8 (18.6%) patients. By
contrast, in the 25 patients who showed no AFP rise at diagnosis of HCC recurrence, the pretransplant AFP levels were >200 ng/mL in three (12%), 21-200 ng/mL in 10 (40%), and ≤20 ng/mL in 12 (48%) patients. Reversely, the sensitivity of AFP rise for HCC recurrence was 89.7% (26 of 29) in patients with pretransplant AFP >200 ng/mL, 47.4% (nine of 19) in patients with pretransplant AFP 21-200 ng/mL, and 40% (eight of 20) in patients with pretransplant AFP ≤20 ng/mL. After tumor progression, this proportion increased to 96.6% (28 of 29 with pretransplant AFP >200 ng/mL), 78.9% (15 of 19 with pretransplant AFP 21-200 ng/mL), and 60% (12 of 20 with pretransplant AFP ≤20 ng/mL).

Conclusions: The annual risk of posttransplant HCC recurrence was significantly different depending on whether or not the patients met the Milan criteria. All patients beyond the Milan criteria are recommended for more frequent follow-up with blood tumor marker tests and imaging studies for the first 3 years. Beyond the third year posttransplantation, all groups should be followed up less frequently as outlined.

Long-term Results for Living Donor Liver Transplant Recipients with Hepatocellular Carcinoma using Intraoperative Blood Salvage with Leukocyte Depletion Filter

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Background: Massive intraoperative bleeding during liver transplantation (LT) often requires large amounts of blood products. Although IBS is a proven method with blood saving effects and reduces complications and cost, the safety of its use has been an issue in HCC patients. Recent studies of LDF reported near complete removal of cancer cells in both experimental and clinical settings. To investigate long-term outcomes of living donor liver transplantation (LDLT) recipients with hepatocellular carcinoma (HCC) who underwent intraoperative use of intraoperative blood salvage (IBS) and leukocyte depletion filter (LDF).

Methods: Two hundred thirty living donor LT recipients with HCC from two transplantation centers, February 2002 to December 2007 were included. Group 1 (n=121) used intraoperative IBS with LDF and group 2 (n=109) did not.

Results: Amount of autotransfused, filtered red blood cells (RBCs) in group 1 was 1,590.2±1,486.8 mL which corresponded to 5.9 units of allogenic leukocyte-depleted RBCs saved. The median follow up times were 53 (range, 8-95) and 33 months (range, 6-95) in groups 1 and 2, respectively. Recurrence free survival rates of 1, 3, and 5-years in group 1 and 2 were 91.3%, 83.3%, 83.3% and 84.6%, 79.0%, 77.4%, respectively. There was no statistically significant difference between two groups (P=0.314).

Conclusions: IBS using LDF substantially decreased the amount of allogenic RBCs transfusion, and more importantly, it did not seem to increase the long-term cancer recurrence rate. Therefore, the use of IBS with LDF appears to be safe for LT recipients with HCC.

Excessive Graft Regeneration Has Detrimental Effects on Small-for-Size Graft in Living Donor Liver Transplantation

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Purpose: The major premise for a successful adult-to-adult living donor liver transplantation (LDLT) is appropriate liver regeneration of the graft. However, liver dysfunction, also called small-for-size syndrome (SFSS), sometimes develops despite a rapid restoration of liver mass. The aim of this study was to evaluate the impact of the graft regeneration rate on the development of SFSS.

Materials and Methods: We retrospectively reviewed 35 adult-to-adult LDLT recipients with a graft-to-recipient weight ratio (GRWR) of <0.8% using 25 right lobe grafts and 10 left lobe grafts. The graft
regeneration rate was expressed with the ratio of graft volumes measured by computed tomography at approximately postoperative day 10 to those measured during the operation. The graft dysfunction score (range, 0-3) was calculated as a sum of the presence of hyperbilirubinemia (1), coagulopathy (1), or asci tes (1) after surgery, and SFSS was defined as having met all of these criteria.

Results: Six recipients developed SFSS. The graft regeneration rate of the SFSS (+) group was higher than the SFSS (-) group (2.12±0.39 vs. 1.70±0.29, P=0.016). Receiver operating characteristic curve analysis indicated the cut-off value of a graft regeneration rate of 1.86 for the graft dysfunction score. The dysfunction score was positively correlated with the graft regeneration rate (P<0.01). In the group with a GRWR of <0.7% (n=13), 4 of 8 recipients with a graft regeneration rate of ≥1.86 developed SFSS, whereas none of the recipients with a graft regeneration rate of ≤1.86 developed SFSS.

Conclusions: In conclusion, excessive graft regeneration has detrimental effects on hepatic function after LDLT.

Antiviral Treatment for Hepatitis B Virus Recurrence Following Liver Transplantation

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Research Purpose: The purpose of this study was to identify factors associated with recurrence of hepatitis B virus (HBV) following liver transplantation (LT) for HBV-related disease and to recognize the outcome of treatment for HBV recurrence.

Material and Methods: 667 liver transplantations were done for HBsAg-positive adult patients in our institute. HBV prophylaxis was done by hepatitis B immunoglobulin (HBIG) monotherapy or HBIG and entecavir combination therapy. Patients received induction therapy with basiliximab and maintenance immunosuppression with a 3 drug regimen of calcineurin inhibitor, mycophenolate and steroids.

Results: 553 LT recipients' medical records were ret-
respectively analyzed. There were 65 cases (11.8%) of HBV recurrences during median follow-up of 51 months. Median time to HBV recurrence was 22 months. Preoperative HBeAg positivity, HBV DNA $10^5$ IU/mL, HBIG monotherapy, acute rejection and hepatocellular carcinoma (HCC) in the explant liver were significant factors for recurrence of HBV in univariate analysis. In multivariate analysis, preoperative HBV DNA load of more than $10^5$ IU/mL, HBIG monotherapy and HCC in the explant liver were independent risk factors for HBV recurrence following LT. Patients with HBV recurrence had significantly reduced survival compared to those who remained HBsAg negative. Patient survival at 10 years was 54.2% for HBV recurrence patients and 95.1% for patients without HBV recurrence. Among patients with HBV recurrence, HBsAg seroclearance was achieved after antiviral therapy in 23 patients (35.4%). Recurrence of HBV led to graft failure in 9 cases. When censored for patient death or other causes of graft failure, graft survival after HBV recurrence was 83.7% at 10 years. 36 patients received lamivudine as 1st line treatment and 16 patients (44.4%) achieved HBsAg seroclearance. 23 patients died, 4 due to HBV-related graft failure. 14 patients received entecavir as 1st line treatment. 5 patients achieved HBsAg seroclearance. There were 4 deaths, including 1 due to HBV-related graft failure. 

Conclusions: In the era of antiviral therapy, recurrence of HBV after LT is not detrimental and patient survival is relatively acceptable.