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Recurrence of B Viral Hepatitis Despite Hepatitis B Immunoglobulin Prophylaxis after Liver Transplantation

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Background: Although favorable outcome following liver transplantation for hepatitis B virus (HBV)-related liver disease was made possible with long-term, high-dose, passive immunoprophylaxis using hepatitis B immune globulin (HBIG), overall recurrence rates with its monotherapy were reported from 15% to 35%. Combination of lamivudine and HBIG showed recurrence rates between 0% and 18% in a few studies. In patients receiving HBIG, HBV reinfection may be the consequence of HBV overproduction coming from extrahepatic sites, an insufficient protective titer of HBIG or the emergence of escape mutants. We undertook this retrospective study to assess recurrence rate and its mechanism after HBIG monotherapy or HBIG+entecavir combined therapy in our clinic.

Methods: The study comprised 157 patients undergoing liver transplantation for hepatitis B-related liver disease during January 2005 through June 2010. One hundred twenty patients was treated with high-dose HBIG monotherapy (Monotherapy group), and 37 patients with combination entecavir and HBIG (Combination group) after liver trasplantation. We adopted indefinite immunoprophylaxis: patients received 10,000 U of HBIG during anhepatic phase, 10,000 U daily during the 6 postoperative days, 10,000 U weekly for 1 month, and 10,000 U monthly for 1 year. After that, 10,000 U was administered in the interval of 4-8 weeks to maintain the anti-HBs level of more than 250 IU/L. Blood samples of 3 patients with HBV recurrence were analyzed for sequencing the "a" determinant of surface antigen gene (S gene), showing the mechanism of HBIG resistance. S gene sequence of HBV genotype adr was used for control.

Results: Overall recurrence rate of HBV was 10.1% (17/157), and recurrence rates of monotherapy group and combination group were 14.2% (17/120) and 0% (0/37), respectively. S gene sequencing of 3 patients showed multiple mutations in all cases. G145R mutation was commonly found, and other mutations were the followings: I126T and P142T in case 1, I126T and F134I/V in case 2 and D144E in case 3. All of recurrent patients were controlled with entecavir therapy (0.5 mg, daily).

Conclusions: As HBV recurrence rate despite high-dose HBIG monotherapy after liver transplantation was 14.2%, we think that the entecavir+HBIG combination protocol could be considered as alternative prophylaxis against HBV recurrence after liver transplantation for HBV-related liver disease.

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Liver Transplantation, Liver Resection and Transarterial Chemoembolization for Multiple Hepatocellular Carcinoma Within Milan Criteria: What is the Best Option?

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Background: Recently, it was reported that surgical resection showed better overall survival than transarterial chemoembolization (TACE) for patients with multiple hepatocellular carcinomas (HCCs) although liver resection is not currently recommended for multiple HCCs. We performed this study to clarify the role of liver resection for multiple HCCs.

Patients and Methods: Among HCC patients who were managed in Yonsei University Health System from January 2003 to December 2008, 160 Child-Pugh A patients who had two or three nodules without vascular invasion and tumor diameter ≤5 cm per radiologic study were enrolled in this study, retrospectively. Long-term outcomes were compared among three treatment modalities such as surgical resection or combined radiofrequency ablation (n=36), TACE (n=107) and Liver transplantation (LT) (n=17).

Results: Disease-control rates of surgical resection and TACE were 19.4% and 10.3%, respectively (p=0.158). The 5-year disease-free survival rates after surgical resection and LT were 11.2% and 87.5%, respectively (p<0.001). The 5-year overall survival rates

after TACE, surgical resection and LT were 28.9%, 48.1% and 80.2%, respectively (p=0.447 at resection vs. LT, p=0.005 at resection vs. TACE). In patients with surgical resection, twelve patients who did not have cirrhosis showed higher 5-year disease-free and overall survival rates than those of patients who had cirrhosis (22.2% vs. 6.2%, p=0.048; 80.8% vs. 25.5%, p=0.006). Surgical resection of 24 patients who had cirrhosis did not show any survival benefit compared to that of TACE (p=0.736).

Conclusion: In multiple HCCs with radiologic two or three nodules, no radiologic vascular invasion and tumor diameter ≤5 cm, surgical resection can be justified only in patients without cirrhosis. LT showed the best oncologic outcomes in these patients.

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Outcome of Direct Local Heparinization of Liver just after Graft Procurement without Systemic Heparinization of Donor in Adult to Adult Living Donor Liver Transplantation

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Research Purpose: Despite excellent outcome of living donor liver transplantation, there are still considerable debates concerning donor safety including morbidity and mortality. We usually use the protocol of systemic heparinization of donor before ligation of vessels. However, we saw the elevation of bleeding tendency and increase of abdominal fluid collection after systemic heparinization. Therefore we introduced direct local heparinization (infusion of perfusate mixed with heparin) just after graft procurement instead of systemic heparinization.

Materials and Methods: Between February 2010 and January 2011, 97 consecutive donors underwent liver resection for living donor liver transplantation. Among them, 47 donors (systemic heparinization group: SHEP group) were performed systemic heparinization and 50 donors (local heparinization group: LHEP group) were direct local heparinization just after graft procurement at bench. We classified patients into two groups as SHEP group and LHEP group by the protocol of heparinization. We retrospectively collected the data such as amount of Jackson-Pratt (JP) drainage, level of JP bilirubin, amount of wound hematoma, amount of abdominal fluid collection, hospital stay of donor and vascular patency of recipient including hepatic artery and portal vein by postoperative doppler ultrasound and CT scan.

Results: The donors included 66 (68%) male and 31 (32%) female with a median age of 29 years (range: 17-59). The median score of Body Mass Index (BMI) was 22.4 (range: 16.6-29.8), the median time of operation was 270 min (range: 180-420) and the median estimated blood loss (EBL) was 300 ml (median, range: 50-700). There was no significant difference in gender, age, BMI, hospital stay, operative time, estimated blood loss (EBL) except abdominal fluid amount, pulmonary effusion amount, left remnant volume(%) of donor and level of total bilirubin in JP at postoperative 5th day between SHEP group and LHEP group. There was no thrombosis or obstruction in the hepatic artery and portal vein after anastomosis in the recipient operation, although there are some cases with stenosis at anastomotic site. One donor of SHEP group was readmitted for management for pneumonia and another donor of the same group underwent reoperation for bleeding control just after the end of hepatectomy and wound closure.

Conclusions: The protocol of systemic heparinization just before vascular ligation is used usually in liver transplantation nowadays. However, systemic heparinization can increase the incidence of minor bile leakage, abdominal fluid collection and pleural fluid more than the method of the direct infusion of perfusate mixed with heparin in this study. And postoperative bleeding and infection can be occurred due to elevation of bleeding tendency, abdominal fluid and pleural fluid. Direct local heparinization of donor graft at bench is as feasible as systemic heparinization.