

**KAHBPS-PP-2-1**

**Liver regeneration is remotely controlled by the spleen by way of combination effects of hepatocyte growth factor and transforming growth factor  $\beta$  -1**

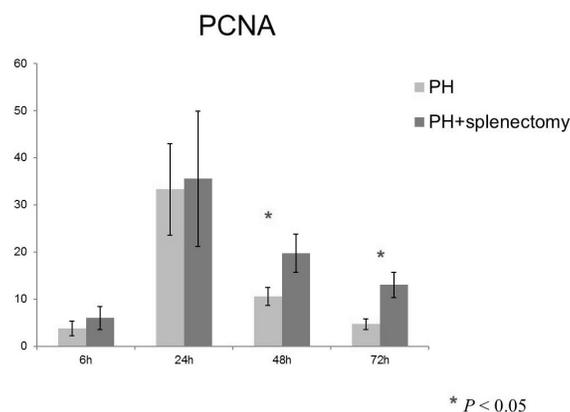
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**(Purpose)** It has been proposed that partial hepatectomy (PH) when combined with splenectomy enhances the regenerative capacity of the liver, most probably due to the removal of Transforming growth factor (TGF)- $\beta$ 1 release from the spleen. The role of spleen, however, should be further clarified considering combination effects of related factors. **(Methods)** Male Sprague-Dawley rats were divided into three groups: control (n=6), 70% PH (PH; n=24), and PH combined with splenectomy (PHS; n=24). The improvements in liver function and liver regenerative capacity (using Ki67 stain and liver weight) were investigated 6 h, 24 h, 48 h, and 72 h after operation in each group. The effect of a splenectomy on the plasma concentrations of HGF and TGF- $\beta$ 1 in the portal vein was investigated by ELISA. The following parameters were also evaluated: liver function tests (ALT and AST), T $\beta$ II Immunohistochemistry and HGF western blot of the liver. **(Results)** Significant increase in Ki67 positive cells and liver regeneration rate (%) were noticed in the PHS group at 48 hours after operation compared with the PH group. The plasma concentration of TGF- $\beta$ 1 and HGF of the portal vein in the PHS rats was significantly lower and higher than in the PH rats for each period, respectively (P<0.05). In addition, compared with the PH

groups, the PHS had better liver functions (P<0.05). Both TGF- $\beta$ 1 protein and mRNA expression level in the spleen were strongest at 48 hours after PH. TGF- $\beta$ 1 type II receptor (T $\beta$ R-II) expression in the liver after PH was assessed immunohistochemically. The expression of T $\beta$ R-II decreased at 12 hours and returned to preoperative level at 24 hours after PH in both groups without significant difference. **(Conclusion)** We found that TGF- $\beta$ 1 was produced and secreted by the spleen during the early phase of liver regeneration and removal of the spleen enhanced proliferation of hepatocytes. In addition, spleen regulated liver regeneration by influencing the concentration of HGF in the portal flow. Taken all into consideration, splenectomy could be carefully considered to the selected patients with jeopardized regenerative capacity of the liver.

**COMPARISON OF LIVER REGNERATION BETWEEN PH GROUP AND PHS GROUP**



**Fig.** Comparison of liver regeneration between PH and PH+splenectomy groups.

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## KAHBPS-PP-2-2

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### Comparative study of pure laparoscopic versus open left hemihepatectomy using multivariate analysis

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**(Purpose)** The objective of this study was to compare the results of pure laparoscopic left hemihepatectomy (LLH) versus open left hemihepatectomy (OLH) in both benign and malignant condition with multivariate analysis. **(Methods)** From October 2007 to December 2013, LLH (n=63) and OLH (n=125) which were performed by a single surgeon were investigated. Patient demographics, preoperative data, clinical perioperative outcomes, and tumor characteristics in patients with malignancy were compared between both groups. Moreover, multivariate analysis of prognostic factors associated with early discharge, complication was executed. **(Results)** The mean operative time was longer in LLH group rather than the OLH group significantly ( $248.89 \pm 53.50$  min vs  $177.23 \pm 68.13$  min,  $p < 0.0001$ ). But, the LLH group had a significantly shorter post operative hospital stay than the OLH group ( $9.53 \pm 3.30$  days vs  $14.68 \pm 11.09$  days,  $p < 0.0001$ ). Multivariate analysis of prognostic factors associated with complication revealed that OLH had nearly 3 times the risk than LLH (odd ratio=2.876, 95% CI 1.093-7.571,  $p=0.0324$ ). **(Conclusion)** LLH, as laparoscopic major hepatectomy, was safe and feasible procedure in selected patients. There was no mortality and no case to be converted open surgery due to major

bleeding. LLH had shorter hospital stay, less operative blood loss. In multivariate analysis, LLH had less risk of complication. The authors suggest prudentially that LLH seems to be a reasonable treatment option in selected patients.

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## KAHBPS-PP-2-3

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### Do young patients with hepatocellular carcinoma after hepatectomy had a poor prognosis?

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**(Purpose)** Young patients with malignancy have more aggressive disease and a poor outcome than old patients with identical disease. However, many studies reported that outcomes in young patients with hepatocellular carcinoma (HCC) are controversial. The aim of present study was to compare the clinicopathological characteristics and outcome between young HCC patients and elderly HCC patients **(Methods)** Between 2006 and 2010, 1,124 HCC patients underwent hepatectomy. The clinicopathological characteristics were retrospectively reviewed. The patients aged  $\leq 40$  years at diagnosis of HCC were defined as young HCC patients. **(Results)** One-hundred three patients (9.2%) were young HCC patients, and 1021 patients were older patients. The incidence of HBV, AFP levels, and ICG-R15 in young patients were higher than that in older patient ( $P < 0.05$ ). The disease-free survival and overall survival in older patients higher than in young patients, but there were no statistically significant differences between the two groups. In young patients, increased platelet counts,

decreased tumor size, microvascular invasion, portal vein invasion, and serosal involvement were closely associated with tumor recurrence after liver resection. **(Conclusion)** There were no statistically significant differences in disease-free survival and overall survival between the two groups, despite AFP levels in young HCC patients were higher than in older patients.

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### KAHBPS-PP-2-4

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#### Laparoscopic left lateral sectionectomy in patients with cirrhosis

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**(Purpose)** Laparoscopic treatment is considered as standard procedure for left lateral sectionectomy (LLS), showing better outcome compared to open LLS. However, safety of laparoscopic LLS in patients with cirrhosis is still unclear. We aim to investigate the safety and reproducibility of laparoscopic LLS even in cirrhotic patients. **(Methods)** We evaluated data of 107 patients who underwent laparoscopic LLS between July 2003 and July 2013. The patients were classified into two groups according to the presence of pathologically proven cirrhosis or not; group A (presence of cirrhosis; n=22) and group B (absence of cirrhosis; n=85). Intraoperative and postoperative functional outcomes were compared between two groups. **(Results)** There were no differences between two groups in terms of median operation time and blood loss (162.5 min vs. 180 min; P=0.960 and 300 mL vs. 200 mL; P=0.144). The rate of transfusion was also similar between two groups (13.6% vs. 7.06%; P=0.387). Conversion to laparotomy occurred

in no patient in group A and one patients in group B (1.18%; P=1.000). Postoperative peak results of total bilirubin was higher in group A than group B (median 1.3 mg/dL vs. 1.10 mg/dL; P=0.023). However, there was no difference in postoperative complication rate (18.18% vs. 22.35%; P=0.778) and hospital stay (7 days vs. 7 days; P=0.719). In patients with hepatocellular carcinoma, no statistically significant difference in disease free survival (P=0.988) and overall survival (P=0.409) between patients with (n=19) or without cirrhosis (n=21). **(Conclusion)** Laparoscopic LLS is safe and reproducible even in patients with cirrhosis.

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### KAHBPS-PP-2-5

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#### Sorafenib inhibits migration and invasion of hepatocellular carcinoma cells through suppressing matrix metalloproteinase expression

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**(Purpose)** Sorafenib increases the survival rate of patients with advanced hepatocellular carcinoma (HCC) by inhibiting Raf kinase and receptor tyrosine kinase activity, but the involvement of sorafenib in fibrosis and the epithelial-mesenchymal transition (EMT) remains unclear. **(Methods)** To elucidate the effects of sorafenib on EMT progression and matrix metalloproteinase (MMP) activity, the levels of E-cadherin, N-cadherin, and MMPs were evaluated in HepG2 human HCC cells induced by hepatocyte growth factor (HGF). A scratching cell migration assay, matrigel cell invasion assay, and immunohistochemistry were per-

formed to examine the effects of sorafenib on tumor metastasis and MMP expression. **(Results)** Sorafenib inhibited HGF-induced EMT and suppressed cell migration and invasion. Treatment with sorafenib significantly reduced the HGF-enhanced expression levels of MMPs, suggesting that the inhibition of MMP activity contributes to suppression of cellular motility and invasiveness in HepG2 cells. Neutralization of MMP activity by MMP-2/9 antibodies, broad-spectrum MMP inhibitor, or selective gelatinase inhibitor resulted in significant suppression of HGF-induced EMT and cell migration/invasion. Western blot analysis showed increased phosphorylation of c-Met and ERK in the HGF treatment group, while sorafenib and anti-MMP-2/9 antibody decreased the levels of phosphorylated c-Met and ERK. Sorafenib treatment and MMP inactivation blocked the HGF-induced c-Met and ERK pathway cascade. These results indicate that inhibition of the MEK/ERK pathway contributes to the beneficial effect of sorafenib on tumor progression and that sorafenib inhibits tumor metastasis by reducing MMP activity via the MEK/ERK pathway. **(Conclusion)** The results of our study demonstrated that sorafenib exerts beneficial anti-tumor effects by preventing MMP activity in an HGF-induced tumorigenic model of HCC. Our data provide in vitro evidence that sorafenib suppresses HGF-induced-EMT and cell migration/invasion by decreasing MMP expression levels. Sorafenib treatment and MMP inactivation suppressed HGF-induced c-Met and MEK/ERK pathways, suggesting that sorafenib inhibits tumor progression through the suppression of MMP activity and the MEK/ERK pathway.

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## KAHBPS-PP-2-6

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### Pure laparoscopic right hemihepatectomy for a patient with HCC following sequential transcatheter arterial chemoembolization and right portal vein embolization (A VIDEO CLIP)

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**(Purpose)** The aim is to confirm pure laparoscopic right hemihepatectomy for a patient with HCC following sequential transcatheter arterial chemoembolization and right portal vein embolization **(Methods)** Preoperative sequential selective transcatheter arterial chemoembolization (TACE) and PVE could increase the rate of hypertrophy, mainly by decreasing the arterial flow in the embolized liver, suppression of arterioportal shunts. The patient underwent sequential TACE 7 wks ago and RPVE 4 wks ago before pure laparoscopic right hemihepatectomy. **(Results)** The remnant left liver volume was increase from 30.8% to 41.2%. The selective isolation technique was used when the hepatoduodenal ligament was dissected. The operative time was 330 mins and estimated blood loss was 350 ml. There was no operative complication. **(Conclusion)** Pure laparoscopic right hemihepatectomy could be equally applied to a patient with HCC following sequential transcatheter arterial chemoembolization and right portal vein embolization.

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**KAHBPS-PP-2-7**

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**Comparison of technical handling and luminal patency between interposed PTFE grafts with interrupted rings versus continuous spiral rings in LDLT using modified right lobe graft**

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**(Purpose)** Due to shortage of vein allograft, synthetic grafts such as polytetrafluoroethylene (PTFE) have been used for reconstruction of the middle hepatic vein (MHV) tributaries of right liver graft during living donor liver transplantation. There are two types of 10 mm-sized ringed PTFE grafts available, in which each has interrupted rings (GORETEX) or continuous spiral rings (IMPRA). With accumulation of surgical experience, we found that unique location of V8 anastomosis close to the graft right hepatic vein (RHV) often led to buckling transformation of PTFE graft and subsequent luminal stenosis and thrombosis. This study primarily intended to compare the technical handling and luminal patency according to different types of outer rings of interposed PTFE grafts. **(Methods)** A prospective case-controlled study was performed with randomized allocation of PTFE grafts with interrupted rings (n=60) or continuous rings (n=30). We have used GORETEX graft for 5 years, thus it be-

came the control group. To avoid buckling transformation of PTFE graft, following modifications were used: when V8 was <1.5 cm apart from graft RHV, we made unification venoplasty of RHV and V8; otherwise, we made V8 composite patch long to provide some redundancy working as a short side branch. **(Results)** Regarding on handling feasibility, GORETEX was superior to IMPRA for bench work because it has a thinner vessel wall and thinner outer rings. In contrast, IMPRA was superior for implantation because its spiral rings permits some flexibility in length adjustment and more resistant to instrumental clamping. The 6-month luminal patency was 68.3% in GORETEX group and 70% in IMPRA group (p=0.97). No noticeable complications including graft infection occurred, but graft migration into the stomach occurred in one case of GORETEX group. Regarding on V8 anastomosis located within 3 cm from graft RHV, 3-month patency rate was equally 96% in two groups. **(Conclusion)** Mid-term luminal patency rates of PTFE grafts were similar regardless of types of outer rings. GORETEX appears to be easier for handling, whereas IMPRA has advantage of longitudinal flexibility. We think that both material are worthy of clinical application for MHV reconstruction of right liver graft during living donor liver transplantation.

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## KAHBPS-PP-2-8

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### Donor safety and recipient liver function following right-lobe liver transplantation from donor with gilbert syndrome

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**(Purpose)** Donor safety is the most important point of living donor liver transplantation (LDLT). Gilbert syndrome is an autosomal recessive condition that is a common cause of non-hemolytic unconjugated hyperbilirubinemia, and its prevalence is not negligibly low in healthy population. Gilbert's syndrome can be classed as a minor inborn error of metabolism. This study intended to assess donor safety and recipient liver function following right-lobe LDLT from donor with Gilbert syndrome. **(Methods)** Among 2140 right-lobe graft donors performed between 2002 and 2011, we identified 12 donors (0.6%) who showed serum total bilirubin level >2 mg/dL. They were clinically diagnosed of Gilbert syndrome, but genetic mutation study was not performed **(Results)** Mean donor age was 24.6 years (range: 18-44) and 11 were male. All met the preoperative evaluation conditions of right liver donation except for unconjugated hyperbilirubinemia. Serum total bilirubin level of donors was 2.3 mg/dL (range: 2.0-2.5) before surgery and 2.2 mg/dL (range: 1.6-4.7) at 1 year after surgery. Preoperative direct bilirubin level was 0.4 mg/dL (range: 0.2-0.7). Preoperative indocyanine

green retention rate at 15 minutes was 8.3% (range: 0.2-15.8). All donors recovered uneventfully following right-lobe graft donation. All recipients recovered uneventfully and are alive to date with serum total bilirubin level of normal limit except one recipient. **(Conclusion)** LDLT with donors of Gilbert syndrome can be safely performed, but special attention should be paid for meticulous preoperative evaluation.

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## KAHBPS-PP-3-1

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### The significance of 2cm size and the value of imaging studies in determining the management of non-functioning pancreatic neuroendocrine tumor

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**(Purpose)** The enhanced accessibility of diagnostic imaging studies have led to an increase in the incidental detection of small non-functioning pancreatic neuroendocrine tumors (NF-pNETs). Currently, 2cm is a widely used reference in determining the need for more aggressive treatment. We aimed to re-analyze the implication of 2cm as reference and the value of imaging studies in determining the management plan of NF-pNET. **(Methods)** 172 consecutive NF-pNET patients who underwent surgery between 1995 and 2014 were identified. Clinical characteristics, imaging study results and outcome of these patients were retrospectively analyzed. **(Results)** Tumors with size  $\geq 2$ cm in preoperative imaging were associated with T3 (HR 9.5 (3.21~28.15),  $p < 0.001$ ), and lymph node metastasis (HR 4.94 (1.63~14.95),  $p = 0.002$ ). The distributions of