Oral Presentation 2

- Presentation Date: Friday, April 24, 2015
- TIME: 14:50-15:50
- Chaired by: Sang Mok lee, Hee Chul Yu

OP-2-1

Proposal of Prediction Model for Early Recurrence after Resection of Huge Hepatocellular Carcinoma ≥10 cm

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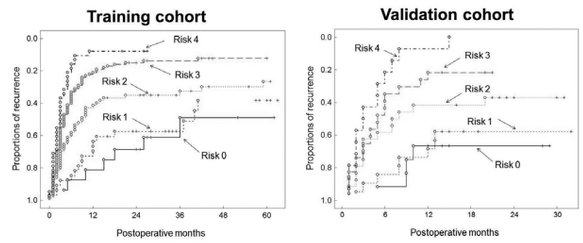
Background: Tumor recurrence is very common after resection of huge hepatocellular carcinoma (HCC). This study intended to evaluate early recurrence and long-term outcomes in patients with huge HCC ≥10 cm after primary resection and treatment of recurrence.
Methods: Recurrence and survival outcomes were retrospectively evaluated in 471 patients with huge HCCs who underwent resection between January 2000 and April 2012.
Results: Mean tumor diameter was 13.6±3.1 cm, with 93% of patients having single tumors. Anatomic and R0 resection rates were 91.1% and 89.4%, respectively. Perioperative mortality rate was 1.7%. Tumor recurrence and patient survival rates were 62.2% and 69.2% at 1 year and 76.0% and 35.5% at 5 years, respectively. Of patients with recurrence, 92.5% received specific treatment. Median patient survival period after initial intrahepatic recurrence was 16 months. Tumor volume did not affect recurrence or survival outcomes. Independent risk factors for tumor recurrence and patient survival were serum alpha-fetoprotein ≥100 ng/mL, hypermetabolic uptake on positron emission tomography, satellite nodules and microvascular invasion. These 4 factors were used to develop a risk prediction model, in which 1-year HCC recurrence rates in patients with 0, 1, 2, 3, and 4 risk factors were 18.7%, 30.3%, 58.7%, 79.0%, and 92.1%, respectively, and their 1-year patient survival rates were 100%, 97.0%, 75.5%, 63.9%, and 42.1%, respectively. Validation study with new 92 patients proved high predictability of our risk prediction model (Fig. 1).
Conclusions: In patients with huge HCCs, hepatic resection with active recurrence treatment resulted in improved long-term survival. Our 4-factor risk prediction model appears to contribute to quantitative postoperative risk estimation for early HCC recurrence and patient survival in patients with HCC ≥10 cm.



Keywords: Hepatocellular carcinoma; Resection; Recurrence; Microvascular invasion

OP-2-2

Does Liver Regeneration Increase the Postoperative HCC Recurrence after Curative Resection?

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This study is to investigate the correlation between the ratio of liver regeneration and HCC recurrence after curative liver resection due to hepatocellular carcinoma (HCC).
We studied total of 420 patients with curative resection for HCC, from Jan 1st of 2006 to Dec 31st of 2009, at a single institution. Among them, we included 54 patients in our study because the patients had 1) anatomical liver resection over sectionectomy, 2) under three tumors, 3) under 5cm in tumor size, 4) no-cirrhotic liver. And we measured liver volumes using VoxelPlus® 2 program of Mevisys company with AP-CT of preoperation and postoperative 7th and 90th day (POD); studied liver regeneration ratio by dividing postoperative residual liver volume with postoperative regenerated liver volume on the 7th and 90th day respectively; and divided the 54 patients into two groups(Group 1 under 1.5 vs Group 2 over 1.5) according to the median ratio(1.5) of liver regeneration on POD 90th day; and compared clinicopathologic characteristics and perioperative outcomes between the groups.
As a result, male were 49 patients (90.7%), median age was 52(29-77), and median follow-up period was 71.0 months (4-101). All patients had hepatitis B viral infection. The median ratio of liver regeneration was 1.305(1.02-2.44)

and 1.52(1.03-4.40) on POD 7th and 90th, respectively. Among the total of 54 patients, 26 was Group 1 and 28 Group 2. There were no statistically significant differences of clinicopathologic characteristics between the groups. But, the median DFS in Group 1 was 68.5 months (12-96), which was better than those(56.0 months (1-98)) in group 2(P=0.019).

In conclusion, among the HBV infected HCC patients with curative resection, postoperative recurrences occurred more as there were more liver regeneration. We think this is probably because tumor recurrence will be activated more by a serial signaling pathway as there was more liver regeneration. And there needs further studies on this issue.

Keywords: Liver regeneration, HCC recurrence, Curative resection

OP-2-3

Prognosis of the Patients with Hepatocellular Carcionoma with Bile Duct Invasion

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Background: Hepatocellular carcinoma(HCC) with bile duct invasion is much rarer than vascular invasion, and therefore, is not well characterized and studied until these days. There is no globally standardized staging system for HCC, but it is known that bile duct invasion on pathologic finding itself is not the independent factor for estimating prognosis of HCC after operation. The purpose of this study is to present the characteristics of HCC with bile duct invasion and to compare the prognosis of that with other prognostic factors.

Methods: Between January 2009 and December 2011, 365 patients underwent hepatic resection at Seoul National University Hospital (SNUH) for HCC. We reviewed all patients' preoperative clinical information such as age and sex, epidemiologic data (underlying liver disease), biochemical data (AFP, PIVKA-II), radiologic data to determine the presence of bile duct invasion, radiologic tumor size and numbers, preoperative treatments (TACE, RFA), operative findings (operation technique, including bile duct resection), pathologic datas such as tumor grade (TNM staging by AJCC), bile duct and vascular invasion, size and Edmondson grade were collected to compare the implications of factors for prognosis. We compared overall survival and recurrence free survival to evaluate the prognosis of bile duct invasion.

Results: Among 365 patients, 13 patients were improved to have bile duct invasion on pathologic and radiologic findings. 286 patients were recurred after operation on 3-5 year follow up, and 70 patients were expired. By comparing the characteristics of the groups with and without bile duct invasion The median age, preoperative tumor size and T-stage had no significant differences. The group with bile duct invasion showed more vascular invasion (11 in 13 (84.6%), than without bile duct invasion group (40.2%). For prognosis, the patients with bile duct invasion showed poor prognosis than without invasion . In multivariant comparison with other prognostic factors, bile duct invasion improved not to have affect for the prognosis of HCC independently, but by subgrouping T-stage, the bile duct invasion was proved to be the independent factor for the prognosis of HCC in early stage (T1 and 2).

Conclusions: Bile duct invasion accompanies vascular invasion in most cases. Bile duct invasion itself is not the independent prognosis factor for HCC. But in early HCC (T1 and T2) with bile duct invasion has poor prognosis.

Keywords: Hepatocellular carcinoma (HCC), Bile duct invasion, Icteric HCC

OP-2-4

Prediction of Post-hepatectomy Liver Insufficiency Using Liver Stiffness Measurement for the Patient with Hepatocellular Carcinoma

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Background: Evaluation of preoperative functional liver reserve is fundamental step to determine the extent of liver resection and predict the postoperative surgical outcomes. Thus, we studied preoperative liver stiffness measurement as well as indocyanine green retention rate at 15 minutes (ICG R15) for prediction of post-hepatectomy liver insufficiency (PHLI).

Materials and Methods: From January, 2012, to December, 2013, curative liver resection was performed for 236 patients with hepatocellular carcinoma at Severance Hospital, Yonsei University College of Medicine, Seoul, Korea. Among them, 160 patients who worked-up preoperatively by Fibroscan as well as ICG R15 were retrospectively analyzed. PHLI was defined as occurrence of ascites causing a delay for removal of surgical drain more than 7 dats after operation or hyperbilirubinemia more than3 mg/dL within 5 days from operation or prolonged PT

INR more than 1.5 more than 5 days after operation.
Results: 35 patients out of 160 patients were compatible to our definition of PHLI. Lower platelet count, higher partial thromboplastin time, higher liver stiffness value, major liver resection and longer operation time were significant factor for the patient with PHLI according to univariate analysis. Liver stiffness score and operation time was significant factor for PHLI on multivariate analysis. AUROC for prediction of PHLI was higher in liver stiffness measurement (cut-off value of 14.0kPa) comparing ICG R 15 (0.765 Vs 0.576).
Conclusions: Liver stiffness measurement showed good ability for predicting postoperative hepatic insufficiency compared to ICG R15. Thus, liver stiffness measurement might be an important non-invasive tool which enables more efficient and tailored management strategies for patients with liver resection.
Keywords: Liver stiffness measurement, Hepatic insufficiency; Hepatocellular carcinoma

OP-2-5

Surgical Outcomes of Laparoscopic Right Hepatectomy Using the Combined Approach Compared with the Conventional Approach

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Background: During laparoscopic right hepatectomy, the conventional approach may limit access to the superior-posterior surface of the right lobe of liver. Also the conventional approach may lead excessive bleeding from right adrenal gland, hepatic vein and caval branches, prolonged ischemia of the remnant liver because of rotation of the hepatoduodenal ligament. Thus we adopted the combined approach to patients who undergoing laparoscopic right hepatectomy to reduce the risks of the conventional approach.
Methods: The combined approach involves initial mobilization of the right lobe of liver within the limits of the possible using the conventional approach, complete dissection of superior-posterior surface of the liver after hilar control of the inflow blood vessel, parenchymal transection and outflow control of right hepatic vein.
Results: We reviewed a clinicopathologic data of 42 patients who underwent laparoscopic right hepatectomy between June 2008 and October 2014 at Asan Medical Center. 13 patients who underwent laparoscopic right hepatectomy using the conventional approach were compared to 29 patients who underwent laparoscopic right hepatectomy using the combined approach. There were no differences between two groups in patient`s characteristics. Patients who underwent laparoscopic right hepatectomy using the combined approach showed significant reduction in mean estimated blood loss (440±268ml vs 263±215ml, p value=0.045) and mean operation time (364±112min vs 288±68min, p value=0.032).
Conclusion: The combined approach results in better operative outcomes compared with the conventional approach in laparoscopic right hepatectomy. The combined approach can be reasonable technique for laparoscopic right hepatectomy.
Keywords: Laparoscopy, Right hepatectomy, Conventional approach

OP-2-6

Outcome of Simultaneous Major Liver Resection with Colorectal Surgery for Patients with Colorectal Cancer Liver Metastases

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Introduction: The optimal surgical strategy in colorectal cancer liver metastases(CRLM) remains still controversial. Several centers are recommend staged operation because high rate of complications, longer operation time and delayed hospitalization in simultaeneous major liver resection(MLR) group. The aim of this study was to compare of outcomes between simultaneous and staged MLR to CRLM.
Method: From June 2003 to September 2012, 80 patients underwent MLR for CRLM. 44 patients underwent simultaeneous MLR and colorectal surgery, and 36 patients underwent metachronous MLR only. Clinicopathologic, operative, and perioperative data and complications were evaluated.
Result: All patient and tumor characteristics are similar in both group. The simultaneous group had a longer rate of operation time(437+-136min vs. 336+-111min, p=0.001). However, estimated blood loss(836.3+-836.5ml vs 739.4+-520.7ml, p=0.547), transfusion rate(34% vs 27%, p=0.631) and hospitalization(15.7+-10.2 day vs 13.9+-5.7 day, p=0.692) were not significant difference in both group. There was no mortality in both group and morbidity(30% vs

25%, p=0.802), and colonic movement normalization rates were similar in the two groups. Considering both surgical procedures(colorectal , p=0.529 + liver resection, p=0.626), there was no significant difference between two group.

Conclusion: MLR can be feasibly and safely performed in selected patients at CRLM with similar perioperative outcomes and morbidities.

Keywords: Colorectal cancer liver metastases, Simultaneous major liver resection

Oral Presentation 3

- Presentation Date: Saturday, April 25, 2015
- TIME: 15:30-16:30
- Chaired by: Kuk Hwan Kwon, Young Hoon Kim

OP-3-1

Influence of Preoperative Transcatheter Arterial Chemoembolization on Gene Expression in the HIF-1α Pathway in Patients with Hepatocellular Carcinoma

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Introduction: Hepatocellular carcinoma (HCC) is a major malignancy of the liver with high-incidence and mortality rates worldwide (Llovet et al., 2003). Due to the complexity and heterogeneity of hepatocarcinogenesis accompanying chronic liver disease, prognosis of HCC remains poor. More than 80 % of HCC patients are diagnosed at an inoperable stage (Okuda et al., 1985), and available treatment options are limited.

Transcatheter arterial chemoembolization (TACE) is a non-curative and the most common treatment modality for HCC. TACE has been shown to improve survival and effectively suppress tumor progression (Zhang et al., 2000). In contrast, other studies have reported that TACE increases the recurrence rate and aggravates prognosis in HCC patients (Harada et al., 1996; Lee et al., 2009). The principle of TACE is to block blood vessels branching to the liver from arteries with lipiodol and/or chemo agents such as adriamycin, leading to hypoxic tumor necrosis with the aim of maximizing anti-tumor effects. Due to the limitation of TACE to stimulate angiogenesis by inducing hypoxia (Li et al., 2004; Wang et al., 2008), combining TACE with anti-angiogenic therapeutics such as sorafenib has been considered a promising strategy to improve clinical outcomes of HCC and several clinical trials including the SPACE study have been conducted (Abou-Alfa, 2011). Thus, the precise effects of TACE on tumor biology of HCC and its prognostic relevance need to be clarified.

Hypoxia is an inevitable feature of solid tumors during tumor progression. Tumor cells experience hypoxia during natural growth (Semenza, 2003), or artificial manipulation to block blood vessels, such as TACE (Bismuth et al., 1992). Although deprivation of oxygen and nutrients could kill tumor cells, the surviving tumor cells or surrounding pre-neoplastic lesions under hypoxia gain an increased capability to survive and metastasize to other organs (Maxwell et al., 1997). HIF-1α plays critical roles in cells upon oxygen deprivation. In hypoxic conditions, HIF-1α is activated to regulate the transcription of downstream effectors driving tumor angiogenesis and epithelial–mesenchymal transition (EMT) integrating cell growth, invasion, motility, and loss of cell adhesion during metastatic cancer progression (Maxwell et al., 1997; Semenza, 2012; Yang et al., 2008). As a prerequisite step for successful dissemination of tumors from primary organs and subsequent colonization in distant organs (Bastid, 2012), EMT has been closely associated with poor prognosis of HCC. HIF-1α is responsible for hypoxia-induced EMT, which contributes to poor clinical outcomes of HCC (Kim et al., 2010; Mima et al., 2013; Ogunwobi and Liu, 2012). Additionally, elevated VEGF levels concomitant with increased angiogenesis in HCC patients undergoing TACE are attributable to activation of HIF-1α signaling (Huang et al., 2005; Wang et al., 2008). However, there is a lack of studies on relationship of expression of HIF-1α and its associated EMT molecules to prognosis of HCC patients subjected to TACE treatment.

In the current study, we investigated for the first time influence of TACE on expression of HIF-1α and its target genes involved in EMT and their prognostic relevance in HCC patients. Our findings provide molecular insights that should aid in improving treatment and prognosis of HCC.

Materials: A total of 50 patients were randomized 1:1 to preoperative TACE or not before curative resection for primary HCC in Ajou Medical Centers in South Korea. Among initial 25 HCC patients undergoing preoperative TACE, we analyzed 10 patients who met inclusion criteria of both the duration from TACE to resection within 50 days and one time of TACE. The interval between TACE and surgery was an average of 26.4 ± 14.5 days ranging from 6 to 49 days. TACE tissues were taken from the viable portion of necrotic HCC tissues. All tissues were obtained with informed consent from the patients, and the study protocol