Oral Presentation VIII

VIII-1

Prognostic Factors for Gallbladder Cancer in the Laparoscopy Era: Iatrogenic Bile Spillage Worsens the Prognosis

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Purpose: Hepatobiliary surgery has changed dramatically in the recent decades with the advent of laparoscopic techniques. The aim of this retrospective study was to compare survival rates according to stages, adjusting for important prognostic factors.

Methods: A retrospective study of a 17-year period from January 1994 to April 2011 was carried out. The cases studied were divided into 2 time period cohorts, those treated in the first 9 years (N=109) and those treated in the last 7 years (N=109).

Results: An operation with curative intent was performed on 218 patients. The 5-year survival rates according to the depth of invasion were as follows: 86% with T1, 56% with T2, 45% with T3, 5% with T4. The overall median survival improved in the last 7 years. The number of cases of incidental gallbladder cancer (GBC) found during 3919 laparoscopic cholecystectomies (LC) was 96 (2.4%). A total of 112 cases were discovered incidentally by the pathologist. Incidental GBC revealed a better survival rate (p=0.003). Iatrogenic bile spillage was found in 20 perforations of the gallbladder during LC, 16 preoperative percutaneous transhepatic gallbladder drainages (PTGBD) and 16 percutaneous transhepatic biliary drainages (PTBD). These patients showed a significantly lower survival rate than patients without iatrogenic bile spillage ($p < 0.01$). It was found that chemoradiation may improve overall survival ($p < 0.001$). Univariate analysis revealed that the following factors significantly influenced survival: T-stage, time period, type of surgery, incidentality, differentiation, iatrogenic bile spillage, surgical margin, peineual, lymphatic and venous invasion, lymph node involvement and chemoradiation therapy. Multivariate analysis also revealed that time period, type of surgery, iatrogenic bile leakage, surgical margin, lymphovascular invasion, lymph node involvement, and chemoradiation therapy had significant effects.

Conclusions: This study found that the prognosis of GBC is still determined by the stage at presentation due to the aggressive biology of this tumor. Iatrogenic bile spillage and tumor violation is a risk factor that influences the prognosis of GBC. Early diagnosis, radical resection and appropriate adjuvant therapy can increase overall survival.

VIII-2

Can Common Bile Duct Resection Increase the Survival in Advanced Gallbladder Cancer?

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Introduction: In advanced gallbladder cancer, the surgical resection is the only treatment for cure. However, there is no consensus for common bile duct resection during radical surgery. The aims of this study were to identify predictors of survival and assess the necessity of common bile duct (CBD) resection in advanced gallbladder cancer.

Methods: We reviewed the medical records of 64 patients with advanced gallbladder cancer who underwent cholecystectomy except R2 resection and D0 lymph node dissection from March 2000 through June 2011 at Severance hospital, Yonsei University College of Medicine, Seoul, Korea. The survival outcomes and clinicopathological characteristics were reviewed between the CBD resection group and the non-CBD resection group.

Results: Of the 64 patients, 34 patients (53.1%) underwent common bile duct resection. Overall survival rates did not differ significantly between the CBD and non-CBD resection groups (at 1 year: 79% vs 88%, at 3 years: 53% vs 68% and at 5 years: 53% vs 58% re-

spectively; P=0.461). However, the CBD resection group had a shorter recurrence-free survival (at 1 year: 60% vs 82%, at 3 years: 58% vs 79% and at 5 years: 49% vs 76%: P=0.057). The numbers of acquired lymph nodes, tumor invaded lymph nodes and Lymph nodes around hepatoduodenal ligament were more in CBD resection group. Because the pathological staging was higher (P=0.02), the survival was poorer in CBD resection group.

Conclusions: Although CBD resection didn't increase the survival, CBD resection may be needed for more accurate nodal status evaluation.

VIII-3

Is T Stage the Only Significant Factor to Determine the Extent of Surgery for T2 Gallbladder Cancer?

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Purpose: The T stage is only factor to determine surgical extension of gallbladder cancer. We hypothesized that perineural invasion can be another predictive factor to determine surgical extension because it is very powerful prognostic factor of gallbladder cancer.

Materials and Methods: 89 patients with gallbladder carcinomas underwent operation at our surgical department over a period of 20 years from 1991 to 2011. The survival rate of these data were retrospectively analyzed and reviewed. Especially, microscopic findings were reconfirmed by one pathologist.

Results: Of 89 patients studies(5.6% Tis , 12.3% T1, 31.4% T2, 37.0% T3, 11.2% T4), overall 3yr and 5yrs survival rate were 52.4%, 46.4%, and 28 patients who were T2 stage was 75%, 58.3%. 9 case of T2 and other 19 patient underwent simple cholecystectomy and extended cholecystectomy, each other and there 5yrs survival rate were 66.6%, 46.6%. In univariate analysis, perineural invasion as well as the LN metastasis, lymphatic invasion, vessel invasion and distant metastasis were associated with survival. ($P<0.05$) In the multivariate analysis, only perineural invasion had an impact on survival rate ($P<0.05$).

Conclusions: Perineural invasion is significant prognostic factor for T2 gallbladder cancer. T stage and perineural invasion, independently, can be a criteria to predict survival as well as determining factor of extended cholecystectomy on patients who diagnosed T2 gallbladder cancer by phathology.

VIII-4

Changing Trend of Biliary Microbiology and Antibiotics Susceptibilities

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Background: Traditionally, Escherichia and Klebsiella are known to be the most common genus cultivated from bile in biliary obtruction. However, rapidly changing medical environment may have changed the microbiology of infected bile. The aim is to identify changing trends of microorganisms, and to examine the susceptibilities of the organisms against currently recommended antibiotics in biliary infection.

Methods: All bile cultures done between 1998 and 2010 at Seoul National University Hospital, a tertiary center, were reviewed. 3,425 organisms were isolated from 2,217 cultures carried out in 1,403 patients. The results of cultures were reviewed for types of organism and antibiotics susceptibilities. To test the adequacy of antibiotics, a unique efficacy grading system that reflects susceptibility and trend was devised. The efficacy of antibiotics were graded A, B, or C according to the proportion of the sensitive strains. The +, 0, - following the grade indicated increasing, stationary, and decreasing trend, respectively.

Results: The 5 most frequently isolated organisms were Enterococcus (22.7%) followed by Escherichia, Pseudomonas, Klebsiella, Enterobacter in decreasing order (13.2%, 10.9%, 10.3%, 7.2%, respectively). The trend of annual incidence showed growing emergence of Enterococcus ($P<.001$). Among Enterococcus, proportion of E. faecium has become dominant (50.6%) with yet growing tendency (P=.026). Also incidence of vancomycin-resistant Enterococcus (VRE) showed increasing trend ($P<.001$). Among many clinical factors,

benign causes of obstruction and non-operative treatment were found to harbor more risk for enterococcal growth by multiple regression analysis (P=.001 and P=.027, respectively). Many commonly used antibiotics were inadequate for coverage of frequently encountered organisms. Enterococcus in particular showed poor susceptibility against all of the tested antibiotics. Streptomycin showed excellent efficacy against various species of Enterococcus. Amikacin, imipenem, meropenem, and piperacillin-tazobactam were the antibiotics that showed excellent efficacy against the remaining 4 frequent organisms. However, the susceptibility of Pseudomonas to imipenem and meropenem showed significantly decreasing trend (P<.001 and P=.015, respectively), which implies their questionable effectiveness currently and in the near future.

Conclusions: Unlike previous reports, Enterococcus has emerged as the most frequently isolated organism from bile. Importance of enterococcal infection should be recognized. Furthermore, reevaluation of currently recommended antibiotics is needed as most of them showed inadequate coverage of the frequently encountered organisms in bile. The changes and trend of microbiology in bile demonstrated by the current study should be taken into consideration when confronting biliary obstruction in clinical practice.

VIII-5

Clinical and Histologic Characteristics of Intraductal Papillary Neoplasms of the Bile Ducts: Comparison with Pancreatic Intraductal Papillary Mucinous Neoplasms

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Purpose: Current version of WHO classification completely integrated the term 'biliary papilloma(tosis)' and papillary bile duct tumors into 'intraductal papillary neoplasms of the bile ducts (IPNB)', which is now drawing great interest because of its similarities between intraductal papillary mucinous neoplasm of the pancreas (IPMN-P). The authors investigated the clinicopathologic characteristics and survival outcome of IPNB and compared it with IPMN-P.

Methods: Data were collected from 51 patients who underwent surgery at Seoul National University Hospital from 2000 to 2009, whose pathologic diagnosis corresponded to IPNB. Pathological slides were thoroughly reviewed by a specialized pathologist. Clinicopathologic characteristics were compared with our previously reported data of 213 IPMN-P.

Results: IPNB patients were at mean age of 62.8 years, and male to female ratio was 2.2 to 1 with median follow up of 43.5 months. Eighteen patients (35.3%) had mucin secretion. Forty-four patients (86.3%) underwent curative resection which included 23 hepatobiliary resection (52.3%), 6 bile duct resection (13.6%), and 15 pancreatoduodenectomy (34.1%). Histologic subtypes were defined as 3 gastric (5.9%), 36 intestinal (70.6%), 11 pancreatobiliary (21.6%), and 1 oncocytic (2.0%) type. There was no difference in curative resection rate, lymph node metastasis or mucin secretion between 4 histologic subtypes. Proportions of invasive cancer were 100%, 8.3%, and 18.2% of gastric, intestinal, and pancreatobiliary type IPNB (p=.081). Invasive cancer was identified in 43 cases (84.3%). Tumors were confined to bile duct in 37 cases (72.5%) and 3 (5.9%) had lymph node metastasis. Among 43 invasive cancers, tumor morphology was identified as papillary (n=16, 37.2%), tubular (n=23, 53.5%), and mucinous (n=2, 4.7%) carcinoma. When compared with 213 IPMN-P, IPNB had lower rate of curative resection (86.3%[IPNB] vs. 97.7%[IPMN-P], p=.002), higher proportion of invasive cancer (84.3% vs. 27.7%, p<.001), higher rate of positive resection margin (23.5% vs. 2.3%, p<.001), more frequent intestinal type epithelium (70.6% vs. 17.8%, p<.001) and lower incidence of mucinous carcinoma (4.7% vs. 27.1%, p=.003). Overall 5-year survival rate of IPNB was 62.3% and curative intended resection had survival benefit with marginal significance (p=.051). After curative intended resection, invasive papillary cancers had most favorable survival outcome followed by tubular and mucinous carcinoma (p=.002). Histologic subtypes or mucin secretion were not significant prognostic factors of IPNB, as were in IPMN-P.

Conclusions: IPNBs have favorable survival outcome with 5-year survival rate of 62.3%. In comparison with IPMN-P, IPNBs have higher incidence of invasive cancer with positive resection margin, and intestinal type epithelium were more frequently observed.