

Oral Presentation X

X-1

A 10-year Experience of Surgical Treatment for Cholangiocarcinoma at Low-volume Hospital

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Research Purpose: Cholangiocarcinoma is a rare malignancy and its prognosis has been kept poor. This study was performed to investigate the clinical characteristics and survival outcome of patients who underwent surgery for cholangiocarcinoma in our hospital.

Materials: Between 2001 and 2010, 73 patients underwent surgical treatment for cholangiocarcinoma in Dankook University Hospital. The patients were divided into three groups according to tumor location, intrahepatic cholangiocarcinoma (IHC), perihilar and distal bile duct cancer (PBDC and DBDC). The clinical manifestation, laboratory findings, surgical treatment and pathological results were compared between groups. Survival outcomes were analyzed according to tumor location, surgical radicality, cell differentiation, period, total bilirubin level including overall and disease free survival duration.

Results: Nineteen (26.0%) patients had IHC, 33 (45.2%) had PBDC, and 21 (28.8%) had DBDC. Male patients were dominant in IHC and DBDC. Incidental detection of tumor was made only in 6 (8.2%) patients but 26 (35.6%) patients were diagnosed in non-jaundiced stage. Of the 26 non-jaundiced patients, 15 were in IHC, 10 were in PBDC and only 1 was in DBDC. About three quarters underwent surgical resection but radical resection was possible in only 33 (45.2%) patients. In DBDC, palliative surgery was performed in only 1 patient. Median follow-up duration was 17.1 months. The overall 3-year and 5-year survival rate of all cholangiocarcinoma patients were 36.1% and 33.5%. Survival rates were significantly related to curative resection ($p < 0.001$), cell differentiation ($p < 0.001$), initial bilirubin level ($p = 0.044$) and period ($p = 0.032$). However, tumor location didn't affect survival duration.

Conclusions: Surgical resection was most frequently performed in DBDC. Curative resection, well-differentiated tumor and early detection in non-jaundiced stage were significantly related to a better prognosis in patients with cholangiocarcinoma. Further study and effort to diagnose early cholangiocarcinoma are warranted.

X-2

Prognostic Factors Following Surgical Resection of Distal Bile Duct Cancer

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Research Purpose: Although various diagnostic tools and surgical standardization for distal bile duct cancer have been developed and survival rate has been improved, prognosis after surgery is not satisfactory. Moreover, although several prognostic factors for distal bile duct cancer have been suggested, there are still many controversies. This study was conducted to analyze the prognostic factors of distal bile duct cancer after surgery and to find factors to enhance survival.

Materials and Methods: 244 patients who underwent pylorus-preserving pancreaticoduodenectomy (PPPD) or Whipple's procedure in Samsung Medical Center from Feb 1995 to Jun 2011 were analyzed retrospectively. 167 patients (68.4%) were male and 77 (31.6%) female patients were enrolled, and their median age was 63 years old (31-88). Median follow-up duration was 19 (2-177) months. 174 patients (71.3%) underwent PPPD and 70 patients (28.7%) underwent classical Whipple's procedure. All the patients were pathologically proved with distal bile duct adenocarcinoma. We investigated the postoperative complications, survival, and prognostic factors after resection of distal bile duct cancer. Chi-square test, Student T test and Kaplan-Meier analysis were used for this study.

Results: The postoperative morbidity and mortality rates were 45.1% and 1.6%, respectively. Five-year survival rate was 47.0% and median survival duration was 62.1 (17.3-104.7) months. Preoperative elevated

CA 19-9 level ($p=0.035$), positive resection margin ($p=0.008$), T stage ($p=0.002$), and lymph node status ($p=0.023$) were significantly independent prognostic indicators by multivariate analysis of resectable distal bile duct cancer.

Conclusions: As expected, surgical resection margin was proved to be a significant worse prognostic factor. Therefore, intraoperative frozen section should be utilized very aggressively to achieve R0 resection. For the distal bile duct cancer with elevated preoperative CA 19-9 level or advanced stage, additional study on postoperative adjuvant treatment may be warranted.

X-3

The Survival Outcome and Prognostic Factors for Extrahepatic Bile Duct Cancer Focused on Worse Behavior of Middle Bile Duct Cancer

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Introduction: The aim of this study was to analyze the survival outcome and the clinicopathological factors that influence survival of extrahepatic bile duct cancer according to the location of the tumor after surgical resection.

Patients and Methods: From January 2001 to November 2011, 86 patients underwent resection for intrahepatic bile duct cancer. In 28 patients of them, tumor was confined at intrahepatic bile duct (DBD group) and in remaining 58 patients, tumor was involved and suprapancreatic portion of bile duct with or without involvement of intrahepatic bile duct (MBD group). We analyzed retrospectively clinicopathological characteristics and survival outcomes in two groups.

Results: In MBD group, rate of R1 resection (27.6% Vs 0%, $P=0.001$) and perineural invasion (82.5% Vs 46.4%, $P=0.001$) were significantly higher than DBD group. However, rate of advanced T stage (T3 and T4) was significantly lower in MBD group than DBD group (43.8% Vs 75.0%). The disease free and overall 3 year survival rates were significantly lower in MBD

group (25.7% Vs 62.5%, $P=0.001$ and 38.7% Vs 68.0%, $P=0.001$). On multivariate analysis, location of tumor (MBD Vs DBD, RR 3.766, 95% CI 1.406-10.086, $P=0.008$) and differentiation of tumor (MD and PD/WD, RR 3.623, 95% CI 1.218-8.608, $P=0.018$) were significant independent prognostic factors.

Conclusions: Extrahepatic bile duct cancer involved middle bile duct showed significantly poor prognosis than cancer confined in the intrapancreatic portion of the bile duct. Type of surgical procedure had not a significant impact on outcome and if R0 resection can be achieved, segmental bile duct resection can be performed with oncologic safety as pancreaticoduodenectomy in patients with middle bile duct cancer.

X-4

Validation of 6th and 7th Edition AJCC Staging of Perihilar Cholangiocarcinoma

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Background: Perihilar cholangiocarcinoma (PHCC) was classified as extrahepatic bile duct tumor together with distal bile duct cancer but it was handled separately for the first time in the 7th AJCC cancer staging. Some major changes include down staging of hepatic parenchymal invasion, simplification of T3 based on unilateral vascular invasion, and defining of stage IVA based on unresectability. The aim was to compare and evaluate the 6th and 7th AJCC cancer staging of PHCC and to validate the 7th edition.

Methods: Pathologic report, radiologic findings, and R status of 318 patients who underwent surgery for PHCC at Seoul National University Hospital from 1990 to 2011 were examined. TNM staging by 6th and 7th edition was done according to the pathologic report and the radiologic findings. Survival analysis was done using life table and Gehan's Wilcoxon method.

Results: In the 6th edition, there were 4 patients (1.1%) of stage 0, 27 (7.1%) of IA, 74 (19.6%) of IB, 69 (18.3%) of IIA, 87 (23.0%) of IIB, 17 (4.5%) of III, and 40 (10.6%) of IV. By the 7th edition, there were 4

(1.1%) of stage 0, 27 (7.1%) of I, 104 (27.5%) of II, 37 (9.8%) of IIIA, 87 (23.0%) of IIIB, 23 (6.1%) of IVA, and 36 (11.3%) of IVB. By the change to the 7th edition, 36 patients (11.3%) mainly in stage IIA (6th ed.) were down-staged, 4 patients (1.1%) up-staged, and the remaining 273 patients (85.8%) remained in the same corresponding stage. The cumulative survivals of PHCC according to the 6th and 7th edition are illustrated in Fig 1 and 2, respectively. According to the 6th edition, the survival curves of stage IIA and IIB failed to show significant difference ($p=0.541$). For the 7th edition, the difference was also insignificant between stage IIIA and IIIB ($p=0.605$). The median survival durations of these stages were even reversed with IIIB showing longer survival (18.2 vs. 20.2 months). Major problem of 7th edition was that Bismuth type 4 is T4 and stage IVA by definition. When stratified accordingly, the survival curve of stage IVA was similar to IIIA ($p=0.908$) and IIIB ($p=0.128$). When Bismuth type was ignored, the survival curves were much better stratified. Thus, the 7th edition was examined without reference to Bismuth type in this study.

Conclusions: There were minor stage shifts, mainly owing to down-staging of hepatic invasion from T3 to T2 in the 7th edition. This change affected the survival stratification only slightly. The problem of poor discrimination of stage IIA and IIB by the 6th edition remains as stage IIIA and IIIB are the corresponding stages by the 7th edition. Bismuth type 4 PHCC does not share common prognosis, because some of these underwent curative resection. Pathologic depth of invasion or vascular invasion is more important rather than Bismuth type itself in determining resectability. Current staging which considers Bismuth type 4 as T4 must be revised. Discrete PHCC staging is certainly necessary, but the current system needs more improvements.

X-5

Role of Resection for Bismuth Type IV Hilar Cholangiocarcinoma and Analysis of Determining Factors for Curative Resection

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Introduction: In the past, Bismuth type IV hilar cholangiocarcinomas (HCCA) had been considered unresectable. However, extended liver resection provides long-term survival in selected patients with Bismuth type IV HCCA. This study was intended to evaluate the role of resection for Bismuth type IV HCCA and to explore the determining factors for curative resection.

Methods: Forty of 159 patients with Bismuth type IV HCCA underwent surgical resection between 2000 and 2010 at Seoul National University Hospital. Among them, 33 patients (82.5%) had curative-intended major hepatic resection (CIR). Clinicopathological features and survival were investigated and disease extent and anatomical variations were analyzed to explore the factors which enable curative resection in Bismuth type IV HCCA.

Results: Mean age of the patients was 60.1 years. The type of operation included right-sided hepatectomy ($n=16$, 48.5%) and left-sided hepatectomy ($n=17$, 51.5%). R0 resection rate was 63.6% (21/33). The rate of CIR with A2 bile duct variation (A2 BDV; hilar trifurcation type) was significant higher than that with other type of BDV ($n=13$, 39.4% vs. $n=18$, 14.4%; $p<0.001$). The length of hilum to left 2nd bile duct confluence and the tumor infiltration over left 2nd bile duct confluence of right-sided CIR was significantly shorter than that of left-sided CIR (10.8 ± 4.9 , 2.7 ± 0.8 vs. 16.5 ± 8.4 , 7.0 ± 5.3 mm, $p=0.029$). Patients undergoing left-sided CIR had higher proportion of tumors invading less than 5mm over the right 2nd confluence than those undergoing right-sided CIR with marginal significance ($n=10$, 76.9% vs. $n=6$, 40%; $p=0.067$). There were no significant differences of other anatomical variation such as hepatic artery, portal

vein, and Ohkubo type of hilar confluence. The survival rates after CIR was significantly higher than those after non-CIR (3YSR 28 vs. 0%, $p=0.006$). Adjuvant radiotherapy (RT) was statistically single significant prognostic factor in patients with Bismuth type IV HCCA (median survival 23 vs. 12 months, $p=0.042$)

Conclusions: A2 BDV, the length of hilum to contralateral 2nd bile duct confluence and the tumor infiltration over 2nd confluence of right-or left- dominant Bismuth type IV HCCA were important for CIR. Carefully selected patients with Bismuth type IV HCCA can be candidate for CIR with expected prolonged survival.