의학석사 학위논문

Analysis of Microscopic Tumor Spread Pattern According to Gross Morphology in Bile Duct Cancer

담관암의 육안적 분류에 따른 종양진행의 특성을 이용한 적절한 절제범위 결정에 관한 연구

2013년 2월

서울대학교 대학원

의학과 외과학 전공

장 예 림

A Thesis of the Master's degree

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February 2013

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지도교수 장 진 영

이 논문을 의학석사 학위논문으로 제출함

2012 년 10 월

서울대학교 대학원

의학과 외과학 전공

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장예림의 의학석사 학위논문을 인준함

2013년 1월

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Analysis of Microscopic Tumor Spread Pattern According to Gross Morphology in Bile Duct Cancer

by

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A Thesis Submitted to the Department of Surgery in Partial Fulfilment of the Requirement for the Degree of Master of Philosophy in Medicine (Surgery) at Seoul National University College of Medicine

January 2013

Approved by thesis committee

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Abstract

Introduction: Surgical resection is the only curative therapy in the extrahepatic bile duct (EHBD) cancer but guideline on optimal resection margin is not established. Therefore, the purpose of this study is to analyze the pattern of microscopic tumor spread and its length according to gross morphology and to suggest optimal resection margin in EHBD cancer.

Methods: From 2007 to 2010, 79 patients with EHBD cancer who underwent curative resection at Seoul National University Hospital were reviewed and analyzed. Pathologic findings including spread pattern of the tumor and its length were reviewed by one specialized pathologist.

Results: Mucosal and mural/perimural spread was seen in 59 (37.3%) and 99 (62.3%) cases, respectively. Gross morphology were classified as papillary (n=13), nodular/nodular infiltrative (n=43), and sclerosing

type (n=23) and spread pattern correlated with gross morphology (p < 0.001). In papillary type, 80.8% showed mucosal spread while sclerosing type had 16.9%. Mean length of tumor spread of each gross type were 4.5 ± 6.3mm, 1.8 ± 6.4mm, and 6.4 ± 6.7mm (p = 0.004), and 90 percentile of the length of tumor spread were 15.6mm, 10.0mm, 15.6mm, respectively.

Conclusions: The pattern of tumor spread correlated with gross morphology and sclerosing type showed the longest tumor spread. Optimal resection margin in EHBD cancer should be 15mm in papillary/sclerosing type and 10mm in nodular/nodular infiltrative type.

Keywords: Bile duct cancer, Surgical resection, Margin, Spread pattern

Student number: 2011-21857

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Introduction

Surgical resection is the only curative therapy in extrahepatic bile duct (EHBD) cancer. Many previous clinicopathologic studies have been shown that negative surgical margin as one of the most important prognostic factor.[1-5] Recent advances in imaging modalities, preoperative biliary drainage, portal vein embolization and surgical strategies made improvement in resectability and the outcome of the surgical treatment for EHBD cancer. Five-year survival rates of 20% up to 45% have been reported after resection of EHBD cancer in recent years.[3,6,7]

However, although preoperative diagnosis for the evaluation of the extent of EHBD cancer has improved in recent years, it is difficult to decide the surgical resection margin preoperatively.[8] EHBD cancer is rarely confined to the short segment since it tends to spread along the bile duct wall longitudinally.[3,9] Still there are no guidelines established regarding the optimal resection margin of EHBD cancer.

Based on the pattern of tumor infiltration in EHBD cancer,

optimal surgical margin were proposed by some groups.[10-14] Since these previous reports focus on the results based on the microscopic findings, application of these data in the operative field seems to have some limitations. Due to the discrepancy between marcoscopic and microscopic finding, practical guidelines are still needed. Therefore, the purpose of this study is to analyze the pattern of tumor spread according to the gross morphology and to suggest the optimal resection margin in EHBD cancer.

Material and Methods

From October 2007 to November 2010, prospectively collected data from 79 patients with EHBD cancer who underwent curative resection at Seoul National University Hospital were analyzed. Preoperatively, the longitudinal extent and depth of the tumor along the biliary tract were evaluated using imaging studies including CT, MRI and percutaneous transhepatic cholangiography (PTC). Bismuth-Corlette classification, pattern of bile duct branching, vascular variation, gross morphologic subtypes, lymph node metastasis, major vessel invasion, liver and pancreas parenchymal invasion were checked for the preoperative surgical planning.

Operation

The surgical procedure was decided by each attending surgeon after considering the balance between the tumor extent and the safety of each surgical procedure. Distant metastasis, extensive lymph node metastasis, bilateral extensive intrahepatic duct

infiltration, involvement of major vessels except focal portal vein invasion, and other systemic poor operative risk factors were contraindications of curative resection. The type of resection was determined by the location and extent of the tumor. In patients with localized bile duct cancer in the hepatoduodenal ligament, EHBD resection was adopted, especially in patients with a poor general condition or high-risk factors. When the tumor was predominantly located in the perihilar bile duct or tumor involvement in the liver parenchyma, unilateral hepatic artery, or portal vein was observed on the preoperative images, an extended hemihepatectomy including caudate lobectomy combined with bile duct resection (BDR) was performed. When the tumor was predominantly located in the distal bile duct, pancreatoduodenectomy (PD) or pylorus-preserving pancreatoduodenectomy (PPPD) were usually performed.[9]

Pathology

All specimens were opened longitudinally along the bile duct, and macroscopic tumor findings were recorded (Fig 1). Gross morphology of the tumor were classified and recorded as papillary,

nodular/nodular infiltrative, and sclerosing. The length of whole bile duct, main lesion, proximal and distal gross margin were also measured and recorded. Specimens were then sent to department of pathology, serially sectioned at 3-to-5 mm slice, fixed in formalin for several days, embedded in paraffin, and stained with hematoxylin-eosin (Fig 2). Shrinkage rate were calculated and recorded based on the whole bile duct length before and after embedding for adjustment of bile duct length. One specialized pathologist thoroughly reviewed the slides of the resected specimen with no knowledge of the imaging findings.

Definition of spread pattern and spread length

The pattern of tumor spread was classified as mucosal spread and mural/perimural spread pattern (Fig 3). Mucosal spread was defined when lateral border of the tumor infiltrated along the mucosal layer, and mural/perimural spread was defined when tumor infiltrated along mural or perimural layer. Each proximal and distal end was examined. Some cases showed different proximal and distal pattern (Fig 4) and length was measured including high grade dysplasia.

Spread length is defined as the longitudinal length of tumor extension from the edge of the tumor to the microscopic margin of the tumor spread. In papillary type, mucosal spread portion in some case was visible although they only extend along mucosal layer. Since measuring visible tumor length does not provide useful information on the decision of resection margin but makes confounding data, we did not include all mucosal spread portions but tumor with height less than 1mm which was not detectable with naked eye. Therefore, we classified papillary type into visible and non-visible type and measured microscopic length of the tumors (Fig5).

In the sclerosing type, many cases does not exhibit protruded lesion. In such cases, the edge of the tumor was defined as the point when mucosal elevation, nodularity, mucosal discoloration, or wall thickening (2 times more than normal bile duct wall) was discontinued.

Measurement of spread length

After evaluation of tumor spread patterns, the length and thickness of the main tumor as well as the microscopic margin

was measured. Using the shrinkage rate, adjusted proximal and distal margin was calculated and it was subtracted from gross margin. The difference is measured as the length of tumor spread. Figure 6 is shows this process.

Other evaluated parameters included thickness of the tumor, perineural invasion and its length and thickness, histologic differentiation. Histologic grade was classified into papillary, well-, moderate-, and poorly differentiated adenocarcinoma. Staging were described in accordance with the 7th edition TNM staging of the American Joint Committee on Cancer (AJCC).[15] Combined dysplasia, skipped spread of tumor, margin status, and its length were also checked.

Statistical analysis

The data was analyzed using SPSS ver. 19.0 (SPSS Inc., Chicago, IL). To determine the differences according to the pattern of tumor spread and gross morphologic subtype, the Student t test, χ^2 test, and one-way ANOVA were used. *P*-values less than 0.05 were considered statistically significant. This study was approved by the Institutional Review Board of Seoul

National University Hospital (H-1007-030-322).

Results

Thirty-seven hilar cholangiocarcinoma and 42 middle-to-distal bile duct cancer were analyzed in this study. Mean age of the total subjects was 66.8 ± 7.2 years and male to female ratio was 56:23. Seventy patients (88.6%) needed preoperative biliary drainage such as percutaneous transhepatic biliary drainage, endoscopic retrograde biliary drainage and endoscopic nasobiliary drainage. Four patients had portal vein embolization before operation (Table 1).

Among 6 (7.6%) with suspected lymph node metastasis in the preoperative imaging with CT and MR, actual lymph node metastasis in the pathologic review was observed in 23 (29.1%) cases. Invasion of hepatic artery and portal vein was suspected in 14 (17.6%) cases whereas microscopic invasion of major vessel was detected in 5 (6.3%) cases (Table 2 and 3).

The operations performed included 37 PD or PPPD, 21 liver resections, and 13 BDR alone. In 6 cases, PPPD with BDR was performed due to the tumor location. There was 1

hepatopancreaticoduodenectomy for the case with synchronous gallbladder cancer and bile duct cancer (Table 2). Caudate lobectomy was performed in all cases with liver resection.

In pathologic reviews, 79 cases were defined as papillary (n=13), nodular/nodular infiltrative (n=43), and sclerosing type (n=23) by the gross morphology. Among papillary gross type, visible papillary and non-visible papillary type was observed in 9 and 4 cases, respectively. Papillomatosis was present in 6 cases, and microscopic skipped lesion was observed in 1 case. Mean length of the tumor was 29.5 ± 11.7 mm, and thickness was 8.8 ± 5.5 mm. Perineural invasion was present in 54 (68.4%) cases. Skipped lesion in the microscopic review was observed in 9 (13.4%) cases. For spread pattern of the tumor, mucosal and mural/perimural spread was seen in 59 (37.3%) and 99 (62.3%) cases, respectively when proximal and distal part was counted separately (Table 3).

Gross type and histologic grade, the length and thickness of the tumor, T stage, and perineural invasion correlated with proximal spread pattern. Papillary (n=10, 32.3%) and nodular/nodular infiltrative gross type (n=16, 51.6%) were

common in mucosal spread cases whereas nodular/nodular infiltrative (n=27, 56.3%) and sclerosing type (n=18, 37.5%) were common in mural/perimural spread type (p = 0.005). Well-differenciation (n=7, 22.6%) and T1 stage (n=12, 38.7%) were more commonly observed in mucosal spread cases (p =0.058, <0.001, respectively). Tumor tended to be thicker (5.9 ± 2.8mm vs. 10.4 ± 6.0mm) and perineural invasion was more common in mural/perimural spread pattern (p <0.001, 0.003, respectively). There no difference in lymph node metastasis or skipped lesion (Table 4). The results were similar with the distal spread pattern (Table 5).

The length of spread was counted proximal and distal spread separately. Mean length of tumor spread of each gross type were 4.5 ± 6.3mm, 1.8 ± 6.4mm, and 6.4 ± 6.7mm (p = 0.004). In papillary type, 80.8% showed mucosal spread while sclerosing type had 16.9% (p < 0.001) When papillary type showed mural/perimural spread, mean length of spread was shorter than that of mucosal spread (1.3 ±1.5mm vs. 5.4 ± 7.8mm). The range of the length of spread in nodular/nodular infiltrative type was -10.3mm to 23.6mm. The minus value of length of spread was

observed in cases with overestimated gross edge mainly due to inflammation by the preoperative endoscopic biliary drainage. Sclerosing type showed the longest length of spread (Table 6).

To figure out the optimal resection margin, histograms and percentiles of length of spread according to the gross type were calculated. In papillary type, majority of the cases were distributed in the 0 ~ 5.0mm range and 50 percentile was 1.8mm. Nodular/nodular infiltrative type showed the widest range with many cases with minus value. Sclerosing type had relatively even distribution through the range of the length and 50 percentile was 5.0mm which was the longest among 3 gross types. Ninety percentile of the length of tumor spread were 15.6mm, 10.0mm, 15.6mm, respectively (Table 6 and figure 7).

Discussion

Characteristics of the growth pattern of hilar cholangiocarcinoma include (1) transmural invasion of bile ducts and radial extension into periductal tissue and adjacent structures and (2) longitudinal extension along the bile ducts.[12] The papillary phenotype has a predominantly intraluminal growth pattern with late transmural extension; this subtype is associated with a more favorable prognosis.[16] In contrast, longitudinal spread along the duct wall with microscopic intramural extension is characteristic of mass-forming and periductal-infiltrating subtypes. [14,17,18] It is this biologic feature that often confounds the ability to obtain histologically negative margins.[3]

Considering surgery is the treatment of choice as it is the only potentially curative therapy for patients suffering from EHBD cancer, obtaining negative resection margin is crucial. However, appropriate surgical margin is not established, and only a few groups have been proposed regarding spread pattern of the bile duct tumor and adequate margin.[10-14]

The longitudinal length of proximal intramural extension was less than 10 mm in most of the previous studies. But this result is in disagreement with studies by Shimada et al.[18] and Hayashi et al.[12] These authors reported that the mean length of submucosal extension is 16.8 and 12.8 mm, respectively.

Nagoya group also reported several studies regarding the pattern of infiltration of hilar bile duct carcinoma. The pattern of infiltration was shown to be closely related to the gross tumor type and the length of ‘submucosal’ extension is usually less than 10 mm and tumor-free proximal resection margin of 5 mm was proposed. Superficial spread of cancer which was defined as mucosal extension of more than 20 mm and it was seen more than 10% of cases.[14] In the study with superficial extension defined as non-invasive carcinoma spread beyond the mass, 20 mm margin was recommended to remove any non-invasive component.[13]

Since these previous reports focus on the results based on the microscopic findings, application of these data in the operative field seems to have some limitations since discrepancy exists between macroscopic and microscopic finding. After embedding, gross specimen shrinks by some degree, and appearance may

become different before and after embedding. For example, visible lateral mucosal spread in gross specimen of papillary type may become equivocal or invisible due to the shrinkage. In such case tumor edge can be different between macroscopic and microscopic view. Considering surgical decision is made on the operative field not by microscopic overview but naked eye supported by results of frozen biopsies, it is reasonable to define the tumor edge by gross edge before embedding.

Spread length in present study was defined as the longitudinal length of tumor extension from the edge of the tumor to the microscopic margin of the tumor spread. However, there were many cases with ambiguous tumor edge. In papillary type, mucosal spread portion with height over 1mm was visible although they only extend along mucosal layer. We classified papillary tumor into visible and non-visible type, and did not include all mucosal spread portions but just tumor with height less than 1mm. In the sclerosing type, many cases did not exhibit protruded lesion. In such cases, the edge of the tumor was defined as the point when mucosal elevation, nodularity, mucosal discoloration, or wall thickening (2 times more than normal bile

duct wall) was discontinued.

The pattern of spread significantly diff among gross morphology, therefore, we analyzed the pattern of tumor spread and its microscopic length of spread. The mean length of tumor spread in papillary type was 4.5 ± 6.3mm, shorter than that of mucosal spread pattern in previous studies. The difference of definition of length of tumor spread may have resulted in this result.

Sclerosing type presented the longest mean length of tumor spread (6.4 ±6.7mm). Sclerosing type had the largest proportion of mural/perimural spread (83.1%) and microscopic margin may differ from gross margin especially in tumor with mural/perimural spread since mural/perimural spread may not accompany mucosal change and be hard to detect in gross specimen. Considering its frequent perineural invasion and discrepancy between gross and microscopic margin, sufficient surgical margin is required in sclerosing type.

In cases with preoperative biliary drainage, tumor extent was overestimated mainly due to inflammation of the bile duct, and the minus value of length of spread was observed. Minus values

were most common in nodular/nodular infiltrative type, therefore, the length of the tumor spread was 1.8 ± 6.4mm.

For the suggestion of optimal resection margin, practical definition of the length of tumor spread and analysis according to gross type was performed in the present study. Ninety percentile of mean length of spread was chosen for the length of optimal margin. Further studies regarding validation and influence on the survival is needed in future.

In conclusion, the pattern of tumor spread correlated with gross morphology and sclerosing type showed the longest tumor spread. Optimal resection margin in EHBD cancer should be 15mm in papillary/sclerosing type and 10mm in nodular/nodular infiltrative type.

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Table 1. Patient characteristics

Parameters		Total (n=79)
Age (years)		66.8 ± 7.2
Sex (M:F)		56:23
Tumor location	Hilar cholangiocarcinoma	37 (46.8%)
	- Bismuth I/II	- 5/13 (13.5%/35.1%)
	- Bismuth IIIa/IIIb	- 14/4 (37.8%/10.8%)
	- Bismuth IV	- 1 (2.7%)
	Mid-distal bile duct cancer	42 (53.1%)
Preoperative biliary drainage		70 (88.6%)
Length of biliary drainage (days)		22.3 ± 12.0
Preoperative portal vein embolization		4 (5.1%)
Length of hospital stay (days)		26.1 ± 12.0

Table 2. Imaging findings and operative methods

Parameters		Total (n=79)
Gross morphology by imaging	Papillary	18 (22.5%)
	Nodular/ N. infiltrative	7 (8.8%)
	Sclerosing	44 (55.0%)
Other imaging findings	Lymph node metastasis	6 (7.6%)
	HA/PV invasion*	9/5 (17.6%)
Operative methods	PD/PPPD	37 (46.8%)
	Bile duct resection alone	13 (16.5%)
	Rt./Ext. Rt. hemihepatectomy +S1[+]	12 (15.2%)
	Lt./Ext. Lt. hemihepatectomy +S1	7 (8.9%)
	PD/PPPD + bile duct resection	6 (5.9%)
	Rt. trisectionectomy +S1	2 (2.5%)
	Hepatopancreatoduodenectomy	1 (2.4%)

[*] Hepatic artery, portal vein

[+] S1, caudate lobectomy

Table 3. Pathologic findings

Parameters			Total (n=79)
Gross morphology		Papillary	13 (16.5%)
		Nodular/ N. infiltrative	43 (54.4%)
		Sclerosing	23 (29.1%)
Histologic differenciation		Well	9 (11.4%)
		Moderate	55 (69.6%)
		Poorly	9 (11.4%)
		Others*	6 (7.6%)
Tumor size		Length (mm)	29.5 ± 11.7
		Thickness (mm)	8.8 ± 5.5
Hilar cholangiocarcinoma (n=37)		Tis/T1	6 (13.2%)
		T2a/T2b	29 (78.4%)
		T3	2 (5.4%)
Mid-distal bile duct cancer (n=42)		T1	6 (14.3%)
		T2	9 (21.4%)
		T3	27 (64.3%)
Lymph node metastasis			23 (29.1%)
Perineural invasion			54 (68.4%)
HA/PV invasion			2/3 (6.3%)
Skipped lesion			9 (13.4%)
Pattern of spread	Proximal side	Mucosal spread	31 (39.2%)
		Mural/perimural spread	48 (60.8%)
	Distal	Mucosal spread	28 (35.4%)

	side	Mural/perimural spread	51 (64.6%)
	Total	Mucosal spread	59 (37.3%)
		Mural/perimural spread	99 (62.7%)

*Papillary (n=3), spindle cell type (n=1), mixed endocrine/exocrine carcinoma (n=2)

+ Hepatic artery, portal vein

Table 4. Differences according to proximal spread pattern

Parameters		Mucosal spread (n=31)	Mural/perimural spread (n=48)	*P*-value
Gross type	Papillary	10 (32.3%)	3 (6.3%)	0.005
	Nodular/ Nodular infiltrative	16 (51.6%)	27 (56.3%)	
	Sclerosing	5 (16.4%)	18 (37.5%)	
Histologic differenciation	Well	7 (22.6%)	2 (4.2%)	0.058
	Moderate	19 (16.3%)	36 (75.0%)	
	Poorly	2 (6.5%)	7 (14.6%)	
	Others*	3 (9.7%)	3 (6.3%)	
Tumor length (mm)		33.1 ± 13.5	27.2 ± 9.9	0.030
Tumor thickness (mm)		6.5 ± 3.8	10.4 ± 5.9	0.002
T stage	Tis/T1	12 (38.7%)	0 (0%)	<0.001
	T2	10 (32.3%)	28 (28.5%)	
	T3	9(29.0%)	20 (41.7%)	
Lymph node metastasis		8 (26.7%)	15 (13.1%)	0.800
Perineural invasion		14 (45.2%)	40 (83.3%)	<0.001
Skipped lesion		5 (20.8%)	4 (9.3%)	0.264

* Papillary (n=3), spindle cell type (n=1), mixed endocrine/exocrine carcinoma (n=2)

Table 5. Differences according to distal spread pattern

Parameters		Mucosal spread (n=28)	Mural/perimural spread (n=51)	*P*-value
Gross type	Papillary	11 (39.3%)	2 (3.9%)	<0.001
	Nodular/ Nodular infiltrative	12 (42.8%)	31 (60.8%)	
	Sclerosing	5 (17.9%)	18 (35.3%)	
Histologic differenciation	Well	7 (25.0%)	2 (3.9%)	0.026
	Moderate	16 (57.1%)	39 (76.5%)	
	Poorly	2 (7.1%)	7 (13.7%)	
	Others*	3 (10.7%)	3 (5.9%)	
Tumor length (mm)		32.7 ± 13.0	27.8 ± 10.7	0.070
Tumor thickness (mm)		5.9 ± 2.8	10.4 ± 6.0	<0.001
T stage	Tis/T1	12 (42.9%)	0 (0%)	<0.001
	T2	12 (42.9%)	26 (51.0%)	
	T3	4 (14.3%)	25 (49.0%)	
Lymph node metastasis		6 (22.2%)	17 (33.3%)	0.435
Perineural invasion		13 (46.4%)	41 (80.4%)	0.003
Skipped lesion		2 (9.5%)	7 (15.2%)	0.709

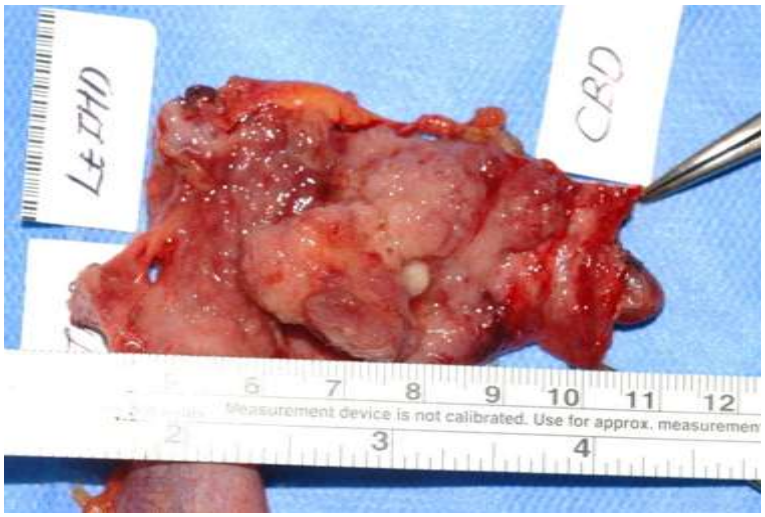
* Papillary (n=3), spindle cell type (n=1), mixed endocrine/exocrine carcinoma (n=2)

Table 6. The length of tumor spread according to gross morphology

	Papillary (n=26)	N/Nodular infiltrative (n=86)	Sclerosing (n=46)	*P*-value
Mucosal spread	21 (80.8%)	28 (32.6%)	10 (16.9%)	<0.001
Mean length of spread (mm, range)	5.4 ± 7.8 (0 ~ 22.5)	2.9 ± 7.0 (-10.3 ~ 23.6)	9.6 ± 7.5 (-4.4 ~ 18.5)	0.058
Mural/perimural spread	5 (19.2%)	58 (67.4%)	36 (83.1%)	<0.001
Mean length of spread (mm, range)	1.3 ± 1.5 (0 ~ 3.6)	1.3 ± 6.1 (-9.2 ~ 23.0)	5.3 ± 6.1 (-4.1 ~ 19.7)	<0.001
Total mean length of spread (mm, range)	4.5 ± 6.3 (0 ~ 22.5)	1.8 ± 6.4 (-10.3 ~ 23.6)	6.4 ±6.7 (-4.1 ~ 19.7)	0.026
50 percentile	1.8mm	0mm	5.0mm	
75 percentile	8.2mm	4.4mm	12.0mm	
90 percentile	15.6mm	10.0mm	15.6mm	

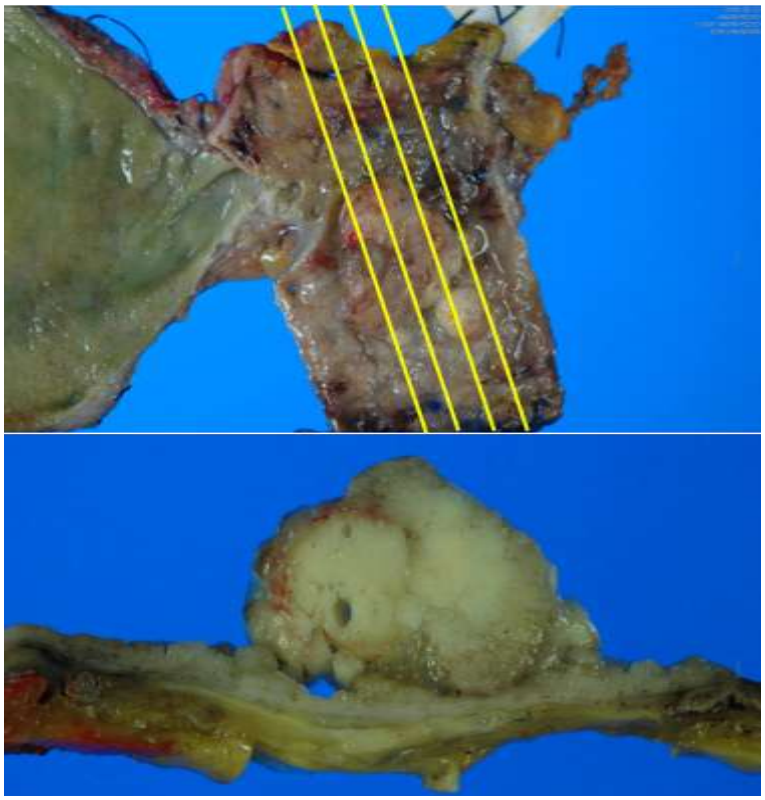
Figures

Figure 1. Picture of gross specimen



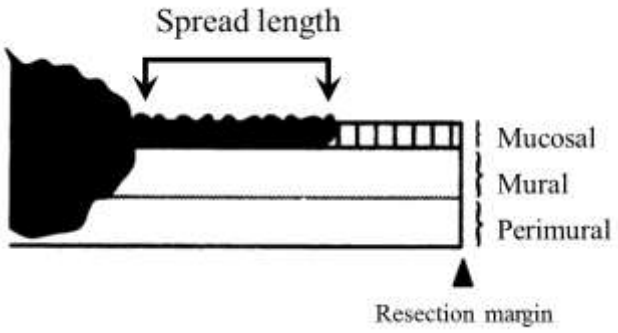
After specimen removal, gross morphologic type, the length of total bile duct, main lesion, proximal and distal margin was measured and recorded. In this case, main lesion was 43mm in longitudinal diameter with 8mm proximal, and 10mm distal margin.

Figure 2. Embedding and serial section of specimen



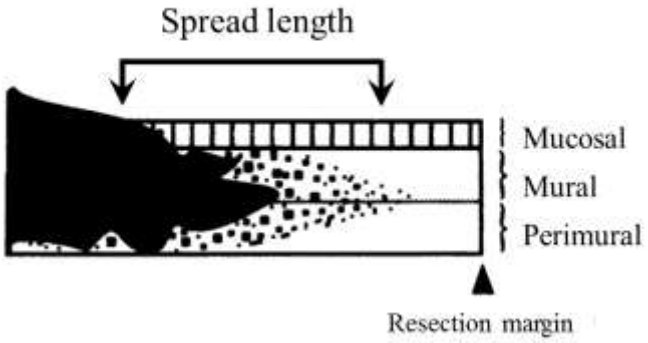
Specimen was embedded and serially sectioned in the department of pathology. Shrinkage rate was recorded for adjustment. Before embedding, the length of whole bile duct was 61mm which was shortened to 51.1mm, therefore, shrinkage rate is 83.8% in this case

Figure 3. Definition of spread pattern



A. Mucosal spread pattern

Lateral tumor infiltration along the mucosal layer

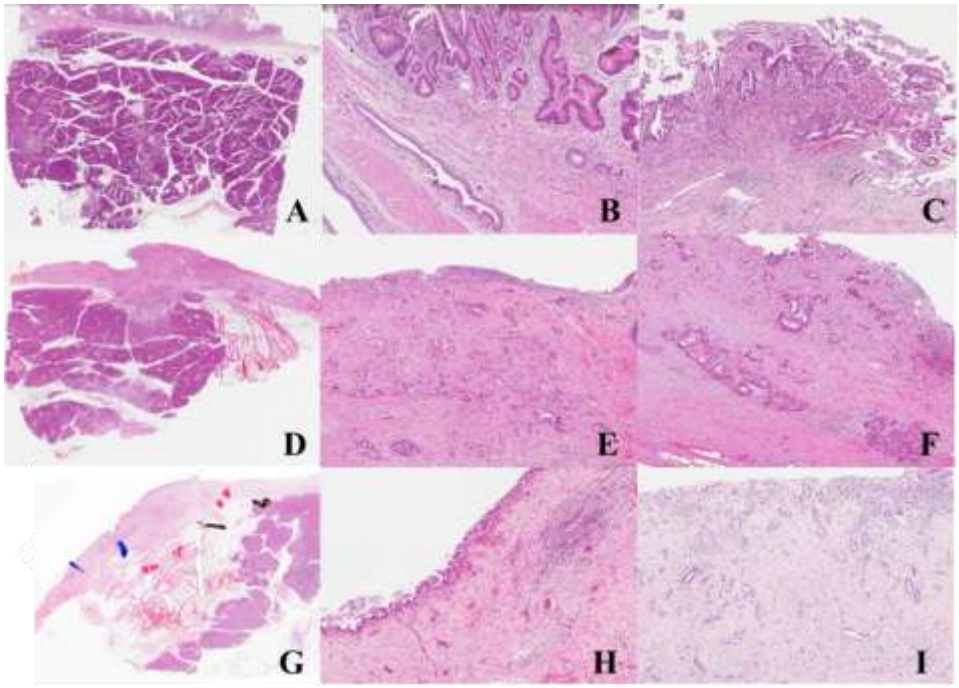


B. Mural/perimural spread pattern

Lateral tumor infiltration along the mural or perimural layer

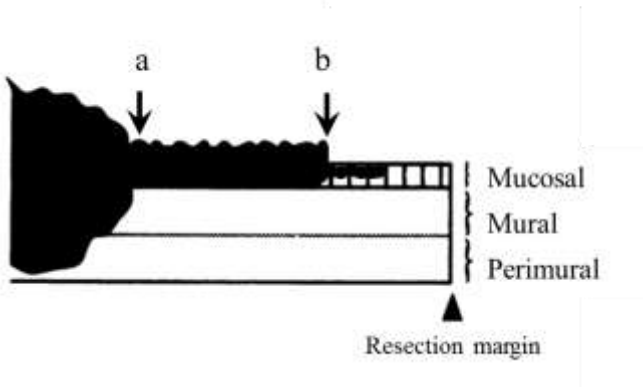
(Figure originally from Sakamoto et al.)

Figure 4. Classification of spread pattern



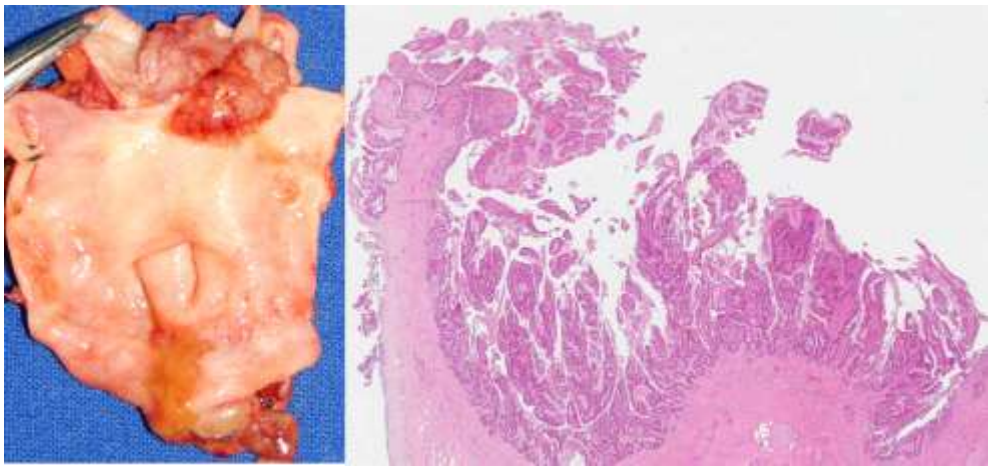
A-C. Mucosal spread pattern; A. Overview of papillary carcinoma; B. Proximal spread (x 50); C. Distal spread (x 50); D-F. Mural/perimural spread pattern; D. overview of nodular type adenocarcinoma; E. Proximal spread (x 40); F. Distal spread (x 40); G-I. Different proximal and distal spread pattern; G.Overview of nodular infiltrative gross type tumor; H. Proximal mucosal spread (x 40), I. Distal mural/perimural spread (x 40)

Figure 5. Visible papillary and non-visible papillary types



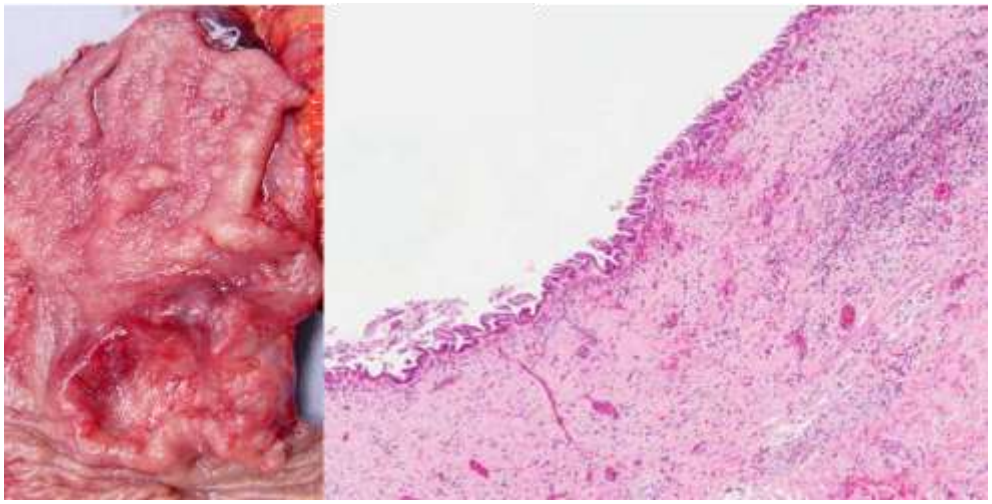
A. Definition of visible and non-visible papillary type

Papillary type tumor is may be visible although they only extends along mucosal layer. Tumor is usually visible when tumor height was over 1mm. In such case, edge of the gross tumor becomes (b). When height was less than 1mm, it is usually non-visible but only seen in microscopic view. The edge of gross tumor becomes (a) in non-visible papillary type.



B. Example of visible papillary type

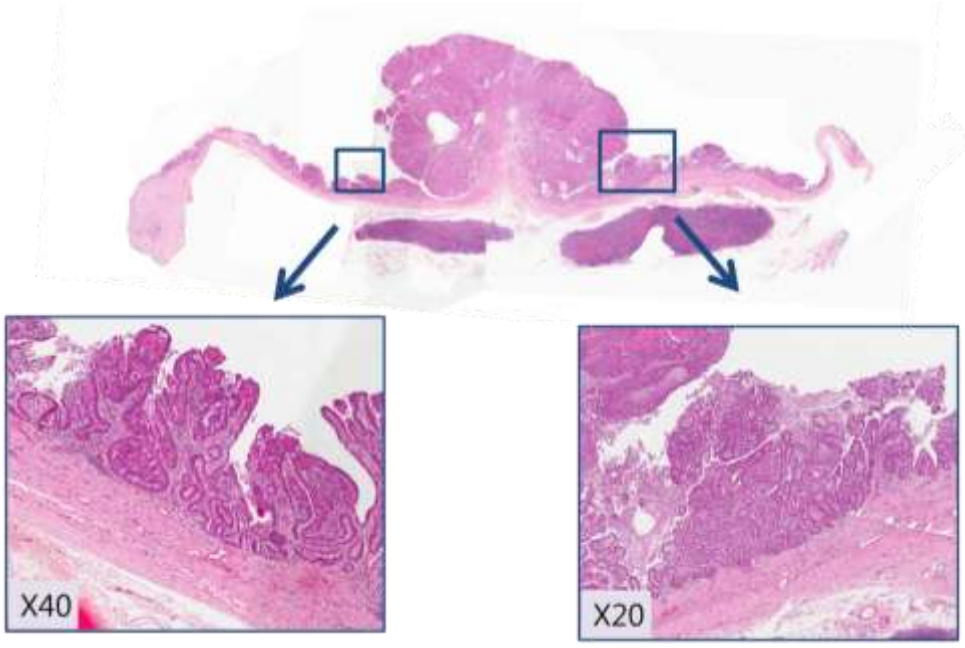
Papillary tumor is seen in the proximal part of the gross specimen. This type of tumor was defined as visible papillary type tumor.



C. Example of non-visible papillary type

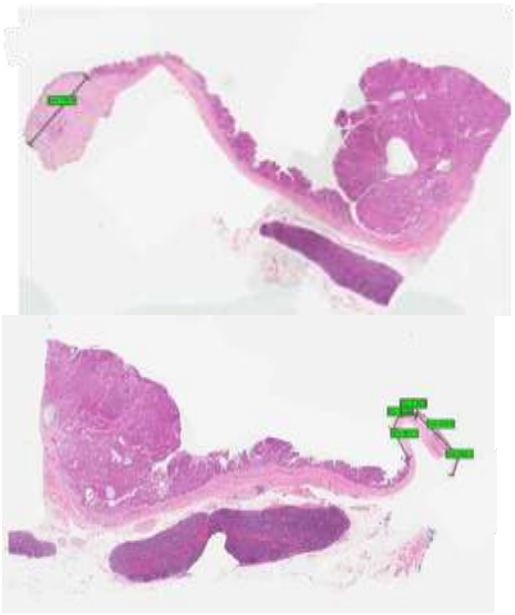
This example is case of tubulopapillary tumor. Mucosal spread was seen in the microscope on proximal side (x50) but no visible tumor is observed beyond gross edge.

Figure 6. Measurement of the length of tumor spread



A. Review of tumor spread pattern

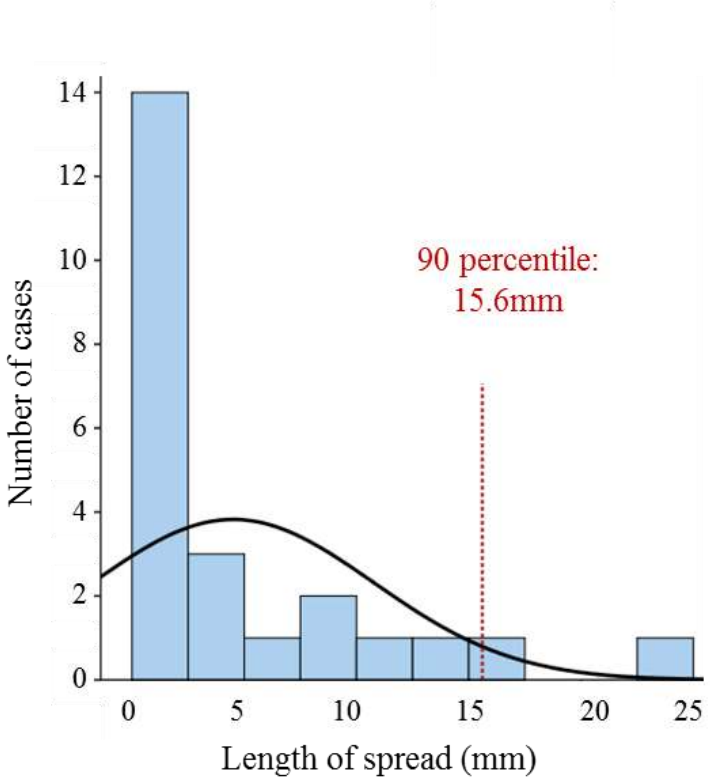
In this case, proximal and distal part was all defined as mucosal spread type.



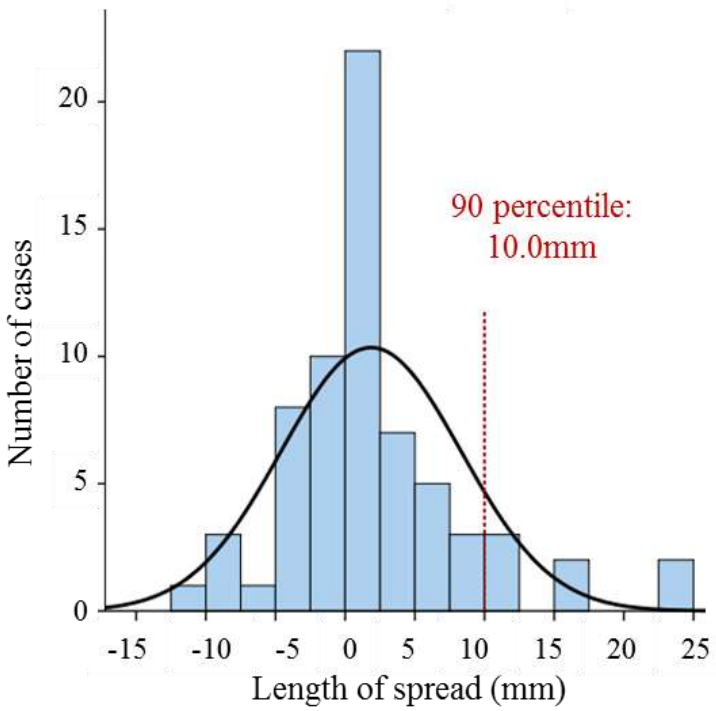
B. Calculation of the length of microscopic tumor spread

Then microscopic margin was measured. In this case, proximal margin was 4.65mm, and distal margin was 7.76mm. When adjusting shrinkage rate, adjusted proximal and distal margin is 5.55mm, and 9.26mm, respectively. Therefore, microscopic length of tumor spread is 2.45mm (8mm-5.55mm) in proximal side, and 0.74mm (10mm-9.26mm) in distal side.

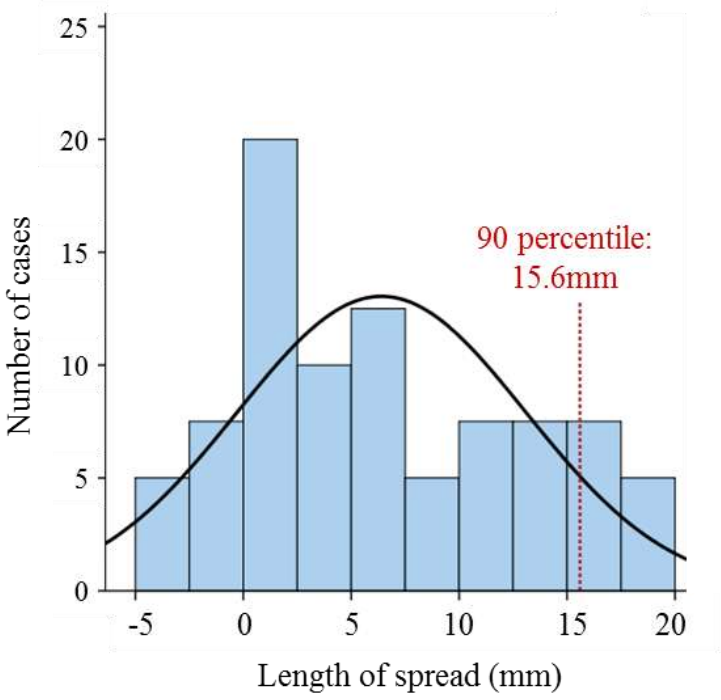
Figure 7. Histogram of length of spread according to gross morphology



A. papillary type



B. Nodular/nodular infiltrative type



C. Sclerosing type

초 록

서론: 담도암에서 수술적 절제는 완치를 기대해볼 수 있는 유일한 치료방법이며, 따라서 종양의 침습 특성과 범위를 정확하게 파악하고 그에 따른 근치적 절제를 하는 것이 중요하다고 할 수 있다. 그러나 담도암의 침습형태에 대한 연구는 미비한 실정이며 그에 따른 근치적 절제를 위한 안전한 절제연의 기준은 아직 확립되어 있지 않은 실정이다. 따라서 이 연구에서는 담도암의 육안적 형태에 따른 침습형태의 차이와 침습 길이를 측정하여 적절한 절제범위를 제시하고자 하고자 한다.

방법: 2007년부터 2010년까지 서울대병원에서 근치적 절제가 가능하였던 79명의 간문부, 중하부 담도암 환자에 대하여 분석을 시행하였다. AJCC 7판을 기준으로 T1, 2, 3이면서 원격전이가 없는 환자를 대상으로 수술시 육안 소견과 수술 후 병리소견을 이용하여 침습형태를 분류하고 그 현미경적 침습길이를 분석하였다.

결과: 점막침습형과 근층침습형은 각각 59 (37.3%)례, 99 (62.3%)례에서 관찰되었다. 종양의 형태에 대한 육안적 분류는 유두형 (papillary type, n=13), 결절형/결절침윤형 (nodular/nodular infiltrative type, n=43), 경화형 (sclerosing type, n=23)으로 나누었는데 유두형에서는 80.8%가 점막침습형태를 보였던 반면, 경화형에서는 16.9%만이 점막침습형태를 보여 육안적 유형이 침습형태와 유의한 연관성을 보였다 ($p < 0.001$). 각 육안적 유형의 현미경적 침습길이

는 4.5 ± 6.3mm, 1.8 ± 6.4mm, and 6.4 ± 6.7mm (p = 0.004)였으며, 90 퍼센타일은 15.6mm, 10.0mm, 15.6mm로 측정되었다.

결론: 담관암의 육안적 유형은 침습형태와 유의한 연관성을 보였고, 그 길이는 경화형이 가장 길었다. 담관암의 적절한 절제연으로서 유두형과 경화형에서는 15mm, 결절형/결절침윤형에서는 10mm가 필요하다.

주요어: 담관암, 수술적 절제, 절제연, 침습양상
학 번: 2011-21857