ANNALS OF SURGERY
Vol. 229, No. 1, 76–83

Role of Nodal Involvement and the Periductal Soft-Tissue Margin in Middle and Distal Bile Duct Cancer

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Objective
To determine the pattern of middle (Bm) and distal (Bi) bile duct cancers in an attempt to optimize surgical treatment.

Summary Background Data
Lymph node involvement and neural plexus invasion are the prognostic factors most amenable to surgery in Bm and Bi disease. However, a detailed analysis of these factors has not been conducted.

Methods
Fifty patients with Bm and Bi disease (Bm 14 patients, Bi 36 patients) were examined histopathologically. A precise determination was made of lymph node involvement and neural plexus invasion. Important prognostic factors were examined by clinicopathologic study to apply these findings to surgical management.

Results
Frequencies of nodal involvement for Bm and Bi disease were 57% and 71%, respectively. The inferior periductal and superior pancreaticoduodenal lymph nodes were most commonly involved. Neural plexus invasion occurred in 20% of patients, particularly involving the plexus in the hepatoduodenal ligament and pancreatic head. Tumor was present at the surgical margin in 50% and 14% of patients with Bm and Bi disease, respectively. Five-year survival rates were 65% in the absence of nodal metastasis and 21% with nodal metastasis. A significant correlation existed between absence of tumor at the surgical margin and survival. A Cox proportional hazard model projected absence of tumor at the surgical margin, followed by nodal involvement, as the strongest prognostic variables.

Conclusions
Absence of tumor at the surgical margin and nodal involvement are important independent prognostic factors in Bm and Bi disease. Skeletonization of the hepatoduodenal ligament, including portal vein resection, is necessary for patients with Bm disease, and a wide nodal dissection is essential in all patients.

The survival rate for periampullary carcinoma is low among the malignant gastrointestinal diseases. The prognosis of bile duct cancer is better than that of carcinoma of the head of the pancreas.[1] Pancreatobiliary carcinoma is characterized by tumor spread by neural invasion and lymph node metastasis.[2–4] Nodal involvement and nerve plexus invasion are important prognostic factors that may be surgically resectable. We already have reported that a radical resection is necessary for pancreatobiliary cancer.[2–6] However, even after curative surgery, some patients still have recurrence.

The goal of the current study was to determine the pattern of tumor spread, including nodal involvement and nerve plexus invasion, and other factors that may affect long-term survival. We also discuss the implications for the surgical treatment of carcinoma of the middle or distal bile duct.

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Accepted for publication August 3, 1998.

PATIENTS AND METHODS

Fifty patients with carcinoma of the middle (Bm) and distal (Bi) bile duct who underwent resection at Kanazawa

University Hospital from 1973 to 1997 were examined histopathologically. These 50 patients comprised 14 patients with Bm and 36 with Bi. There were 37 men and 13 women, with an average age of 65 years (range 34 to 84 years). Seven of the 14 patients with Bm were treated by pancreaticoduodenectomy (PD), and the other 7 patients underwent extrahepatic bile duct resection. All of the patients with Bi underwent PD. Seven patients with PD underwent concomitant portal vein resection. A radical lymphadenectomy, including the paraaortic lymph nodes, was performed in 28 patients.

After careful gross descriptions of the primary tumors were made, the resected specimens with attached peripancreatic lymph nodes were immediately fixed in 10% buffered formaldehyde solution. After serial 5-mm-thick sections were made, these tissues were embedded in paraffin and stained with hematoxylin and eosin. The site of tumor origin usually was determined at the time of both gross and histopathologic examinations.

Pathologic diagnoses were determined in accordance with *General Rules for Surgical and Pathological Studies on Cancer of Biliary Tract.*[7] On the basis of these guidelines, a numeric classification of the major lymph nodes was defined as follows:

- Number 8, nodes along the common hepatic artery
- Number 9, nodes around the celiac artery
- Number 10, nodes at the splenic hilum
- Number 11, nodes along the splenic artery
- Number 12, nodes in the hepatoduodenal ligament
- Number 13, posterior pancreaticoduodenal nodes
- Number 14, nodes around the superior mesenteric artery
- Number 15, nodes along the middle colic artery
- Number 16, paraaortic nodes
- Number 17, anterior pancreaticoduodenal nodes.

For number 12 lymph nodes, several subgroups were defined:

- 12a, nodes along the hepatic artery
- 12b, nodes along the bile duct
- 12c, nodes around the cystic duct
- 12p, nodes posterior to the portal vein
- 12abp$_1$, nodes along the superior hepatoduodenal ligament
- 12abp$_2$, nodes along the inferior hepatoduodenal ligament.

For number 13 and 17 lymph nodes, two subgroups were defined: a, those above the papilla of Vater, and b, those below the papilla.

For number 14 lymph nodes, four subgroups were defined:

- 14a, nodes at the origin of the superior mesenteric artery

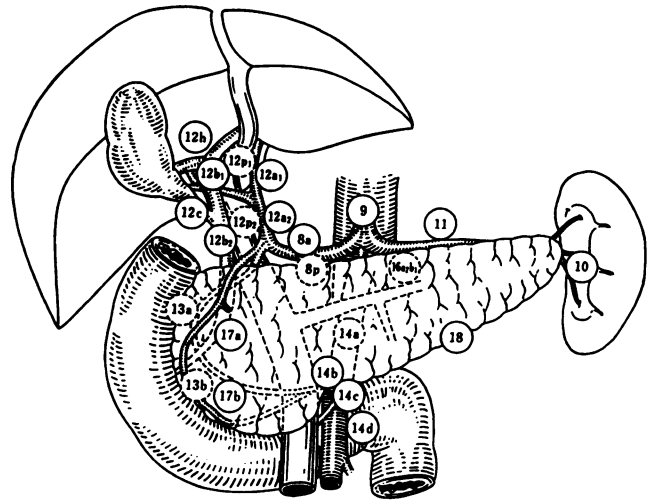

Figure 1. The major lymph nodes involved with bile duct cancer.

- 14b, nodes at the origin of the inferior pancreaticoduodenal artery
- 14c, nodes at the origin of the middle colic artery
- 14d, nodes at the origin of the jejunal arteries.

For paraaortic lymph node, four subgroups were defined:

- 16a$_1$, nodes around the aortic hiatus of the diaphragm
- 16a$_2$, nodes from the superior margin of the celiac trunk to the inferior margin of the left renal artery
- 16b$_1$, nodes from the inferior margin of the left renal artery to the superior margin of the inferior mesenteric artery
- 16b$_2$, nodes from the superior margin of the inferior mesenteric artery to the aortic bifurcation.

Between numbers 1 and 7 lymph nodes were perigastric lymph nodes (Fig. 1).[2,7]

Nodal involvement for Bi was classified into five groups as proposed by the Japanese Society of Biliary Surgery[7]:

- n$_0$, no evidence of regional lymph node involvement
- n$_1$, nodal involvement in a primary lymph node group close to the tumor (numbers 12b$_2$ and 13a)
- n$_2$, lymph node metastasis in the secondary lymph node group (numbers 8, 12 except 12b$_2$, and 13b)
- n$_3$, lymph node metastasis in the third group (numbers 9, 13b, 14, 16a$_2$, 16b$_1$, and 17)
- n$_4$, lymph node metastasis in the fourth group (beyond the third group).[2,4]

Nodal involvement for Bm also was classified into five groups:

- n$_0$, no evidence of regional lymph node involvement
- n$_1$, nodal involvement in the primary lymph node group close to the tumor (numbers 12b$_1$, 12b$_2$, and 12c)
- n$_2$, lymph node metastasis in the secondary lymph node group (numbers 8, 12a$_1$, 12a$_2$, 12p$_1$, 12p$_2$, and 13a)

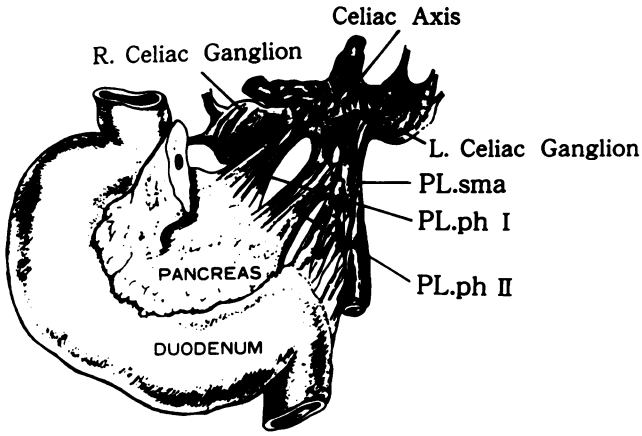

Figure 2. Anatomic location of plexus pancreaticus capitalis.

- n_3, lymph node metastasis in the third group (numbers 9, 13b, 14, $16a_2$, $16b_1$, and 17)
- n_4, lymph node metastasis in the fourth group.[4]

Extrapancreatic neural plexuses are defined by the Japan Pancreas Society's *Classification of Pancreatic Carcinoma*[8] as follows:

- Celiac plexus (PL ce)
- Superior mesenteric arterial plexus (PL sma)
- Common hepatic arterial plexus (PL ch)
- Plexus within the hepatoduodenal ligament (PL hdl)
- Pancreatic head plexus I (PL ph I), which extends from the right celiac ganglion to the upper medial margin of the pancreas
- Pancreatic head plexus II (PL ph II), which extends from the superior mesenteric artery to the medial margin of the uncinate process (Fig. 2).[9,10]

Curative resection was defined by absence of tumor at the surgical margin (proximal hepatic transection line, distal bile duct transection line, and dissected periductal soft tissue) and the complete removal of all lymph node metastases ($n \leq D$ where n refers to the most distant group of lymph node involvement and D refers to the most distant group included in the lymph node dissection).

Statistical analyses included the chi square test with Fisher's exact test when appropriate. Patient survival was calculated by the Kaplan–Meier method,[11] and the significance of differences between survival rates was determined by using the generalized Wilcoxon method. $P < 0.05$ was considered statistically significant. Multivariate analysis was performed using the Cox proportional hazard model.[12] Statistical calculations were performed using the SPSS (SPSS, Japan, 6.1) advanced statistics module.

RESULTS

Relation Between Depth of Tumor Invasion and Nodal Involvement

Table 1 shows the relation between the degree of the tumor invasion and nodal involvement. The single patient with mucosal cancer had no nodal involvement. Half of the patients with fibromuscular layer invasion or subserosal invasion had nodal involvement. Only one patient with fibromuscular layer disease had secondary nodal involvement. However, 28 (76%) of the 37 patients with serosal exposure, pancreatic invasion, or both, had nodal involvement. Half of these 28 patients had involvement of the third group of lymph nodes. Four of these 28 patients had paraaortic node involvement.

Frequency and Distribution of Lymph Node Involvement

The frequency of nodal involvement for patients with Bm was 57% (8/14). The frequency of involvement of nodes 8, 12, 13a, and 13b was 7%, 50%, 7%, and 7%, respectively. The $12abp_2$ node was involved frequently. There were no patients with number 14 node involvement. Figure 3 demonstrates the relation between nodes 8, 9, $12abp_1$, $12abp_2$, 13a, 13b, and 16. All except two patients had $12abp_2$ involvement. One patient had $12abp_1$ involvement, and the other had node 8 involvement.

The frequency of nodal involvement for patients with Bi was 71% (25/36). Node 8 was involved in 1 of the 36 patients (3%). No involvement of node 9 was present. The frequency of involvement of 12, 13a, 13b, 17a, and 17b nodes was 22%, 50%, 11%, 3%, and 0%, respectively. One or more number 14 nodes were involved with cancer in 10 of 36 patients (28%), whereas the frequency of involvement of subgroups 14a, 14b, 14c, and 14d was 14%, 17%, 0%, and 6%, respectively. Of all the number 14 nodes, 14b was the most frequent site of involvement. Paraaortic nodes (number 16) were involved with tumor in 3 patients (8%). One of the three patients with paraaortic node involvement had no involvement of other lymph node groups. Figure 4 demonstrates the relation among nodes $12abp_1$, $12abp_2$, 13a, 13b, 14a, 14b, and 14d. Only 1 patient without evidence of 13a involvement had 13b involvement. In addition, 1 patient without evidence of 13a metastasis had ≥1 number 14a

Table 1. RELATION BETWEEN DEPTH OF TUMOR INVASION AND LYMPH NODE INVOLVEMENT

Depth of Tumor	n_0	n_1	n_2	n_3
M (n = 1)	1	0	0	0
FM (n = 6)	3	2	1	0
SS (n = 6)	3	3	0	0
SE, SI (n = 37)	9	12	2	14

Four patients with SE, SI disease had paraaortic lymph node metastasis.
M = mucosa; FM = fibromuscular layer; SS = subserosal; SE, SI = serosal exposure and/or pancreas invasion; n_0 = no evidence of regional lymph node involvement; n_1 = nodal involvement in primary group; n_2 = nodal involvement in secondary group; n_3 = lymph node metastasis in the third group.

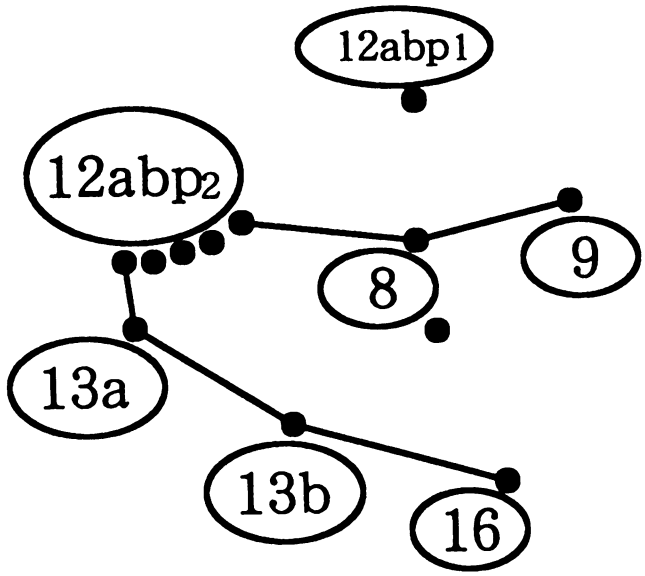

Figure 3. Correlation of lymph nodes (in particular, 12, 13a, 13b, 14a, 14b, and 14d) in patients with positive lymph node involvement in middle bile duct disease. Each solid circle indicates each patient with lymph node involvement. Solid circles of the same patient were linked by line.

nodes involved. All patients with 14b node involvement had 13a or $12abp_2$ node involvement. Involvement of 14a and 14b nodes was closely related to involvement of 13a and $12abp_2$ nodes. Thirty-three of 34 patients with nodal involvement had involvement of $12abp_2$ or 13a nodes; the one exception had involvement of 13b, 14d, and 14a nodes.

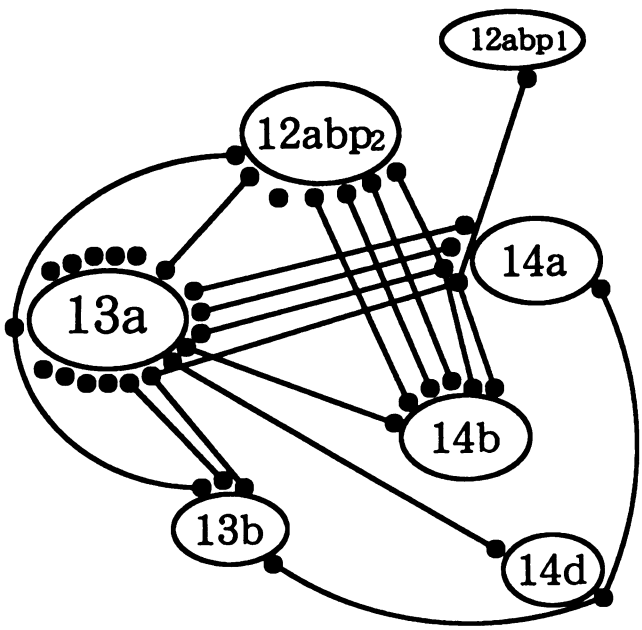

Figure 4. Correlation of lymph nodes (in particular, 12, 13a, 13b, 14a, 14b, and 14d) in patients with positive lymph node involvement in distal bile duct disease. Each solid circle indicates each patient with lymph node involvement. Solid circles of the same patient were linked by line.

Table 2. RELATION BETWEEN DEPTH OF TUMOR INVASION AND NEURAL INVASION

Depth of Tumor	pn_0	pn α	pn β
M (n = 1)	1	0	0
FM (n = 6)	4	2	0
SS (n = 6)	1	2	3
SE, SI (n = 37)	2	2	33

M = mucosa; FM = fibromuscular layer; SS = subserosal; SE, SI = serosal exposure and/or pancreas invasion; pn_0 = no neural invasion; pn α = neural invasion in the bile duct wall; pn β = extrabiliary neural invasion.

Relation Between Depth of Tumor Invasion and Neural Invasion

The relation between the depth of tumor invasion and neural invasion is summarized in Table 2. The one patient with mucosal disease had no neural invasion. Two of the 6 patients (33%) with fibromuscular layer disease had neural invasion. All except one patient with subserosal disease had neural invasion. Three patients with subserosal disease had extrabiliary neural invasion (pn β). Plexus invasion was observed in 10 patients (28%).

Distribution of Nerve Plexus Invasion

The distribution of extrapancreatic neural plexus invasion in patients with Bi and Bm is summarized in Table 3. Of the patients with Bm, two had PL hdl invasion. However, among the patients with Bi, seven of eight patients with plexus invasion had tumor in PL ph I. Five of these seven patients had PL hdl invasion. One patient had only PL hdl invasion. Another patient had advanced plexus invasion that consisted of PL hdl, PL ph I, PL ph II, and PL sma. Plexus invasion around the superior mesenteric artery was obvious at surgery.

Table 3. DISTRIBUTION OF PLEXUS INVASION

Localization	Bm	Bi
PL hd1	1	1
PL hd1, ch	1	
PL hd1, ph I		5
PL ph I		1
PL hd1, ph I, ph II, sma		1

PL hd1 = plexus within hepatoduodenal ligament; PL ch = common hepatic arterial plexus; PL ph I = pancreatic head plexus I; PL ph II = pancreatic head plexus II; PL sma = superior mesenteric plexus; Bm = middle bile duct cancer; Bi = distal bile duct cancer.

Table 4. FACTORS ASSOCIATED WITH NONCURATIVE RESECTIONS

Factor	Bm	Bi
EM	7	4
DM	2	0
HM	4	0
n > R	2	4

HM = proximal hepatic transection line; DM = distal bile duct transection line; EM = dissected periductal soft tissue; n > R = group of lymph node involvement > group of lymph node dissection; Bm = middle bile duct cancer; Bi = distal bile duct cancer.

Factors Associated With Noncurative Resections

Fourteen patients had noncurative resections: 7 (50%) of the 14 patients with Bm and 7 (14%) of the 36 patients with Bi. The factor most frequently associated with recurrence was a positive dissected periductal soft-tissue margin (all patients with Bm and four of seven with Bi). A positive proximal hepatic transection line margin was observed in four of seven patients with Bm. Two patients with Bm and 4 patients with Bi had resections that were noncurative because of n > D (Table 4). All patients with Bm with a positive dissected periductal soft-tissue margin had involvement near the portal vein. Of the four patients with Bi with a positive dissected periductal soft-tissue margin, two had involvement of the extrapancreatic nerve plexus (PL ph I) at the cut surface, two had involvement in the retropancreatic area near the common bile duct, and one had portal vein involvement.

Survival

Death occurred within 30 days of surgery in one patient who underwent radical pancreaticoduodenectomy with combined resection of the portal vain in 1982. A complication developed in 30% of patients, usually pancreatic fistula (13 patients, 26%). Intraabdominal bleeding and abscess were seen in three patients. The overall 3- and 5-year survival rates, including death during surgery, for our patients were 47% and 35%, respectively. The survival time after resection showed a significant correlation with nodal involvement ($p < 0.01$) (Fig. 5). The 3- and 5-year survival rates for 16 patients without nodal involvement were 86% and 65%, respectively. The 3- and 5-year survival rates for 34 patients with nodal involvement were 30% and 21%, respectively. However, 5 patients with nodal involvement lived >5 years. One of the 4 patients with paraaortic node involvement is alive 27 months after resection without evidence of recurrence.

The 3- and 5-year survival rates for 8 patients without neural invasion were 63% each. The 3- and 5-year survival rates for 42 patients with neural invasion were 45% and 29%, respectively. No significant difference existed between the two groups (Fig. 6). Also, no significant difference with regard to the presence or absence of plexus invasion was observed.

The overall survival time after resection showed a significant correlation with the absence of tumor at the surgical margin ($p < 0.001$) (Fig. 7). The 3- and 5-year survival rates for 36 patients with absence of tumor at the resection margins were 64% and 48%, respectively. Thirteen (36%) of these 36 patients were alive at 5 years. However, of 14 patients with tumor present at a resection margin, there were no survivors beyond 43 months.

Univariate and Multivariate Analyses

Age, neural invasion, tumor location, and gender were not associated with survival. However, depth of tumor, lymph node involvement, and involvement of the surgical margin were significant prognostic factors. Lymph node

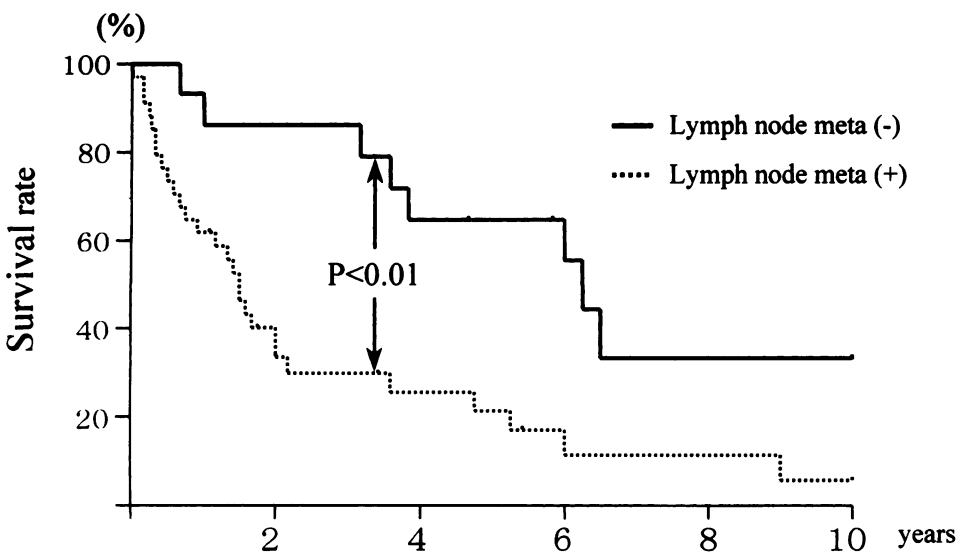

Figure 5. Survival of patients with or without lymph node involvement after resection for middle and distal bile duct cancer.

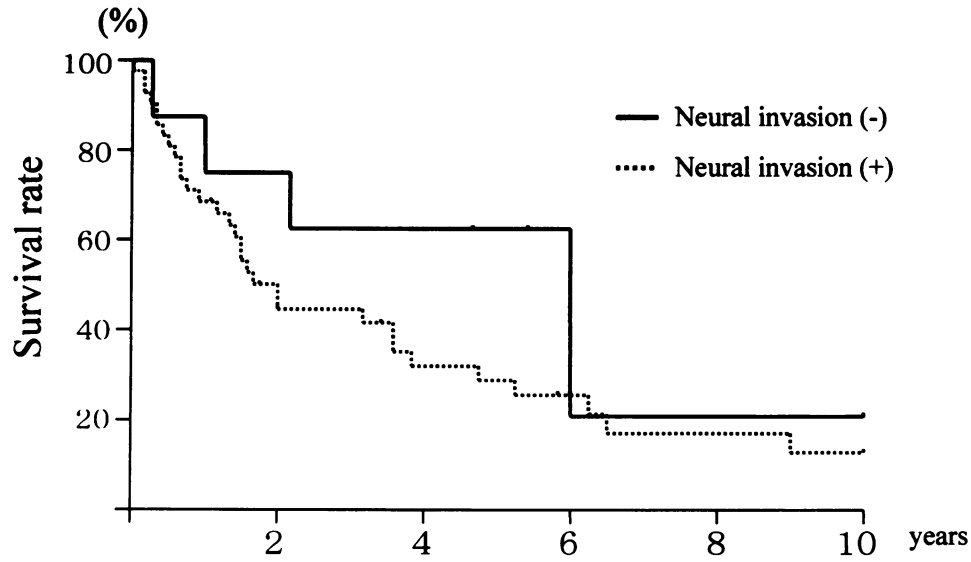

Figure 6. Survival of patients with without neural invasion after resection for middle and distal bile duct cancer.

involvement and a positive surgical margin were significant independent predictors of poor prognosis (Table 5).

DISCUSSION

Pancreatobiliary carcinomas are characterized by tumor spread by neural invasion and lymph node metastasis.[2–4,9,13,14] Detailed knowledge of the pattern of lymph node involvement and neural plexus invasion would help guide the surgeon in determining the optimal extent of lymph node and nerve plexus dissection for Bm and Bi. Tio et al[15] have reported that the incidence of lymph node metastasis in common bile duct cancer increased with increasing depth of tumor infiltration. In our previous study of Bi,[2] the degree of nodal involvement increased with increasing tumor infiltration into the pancreas. Our present study also demonstrated that there was a correlation between depth of tumor invasion and nodal involvement.

Few reports concerning the frequency of nodal involvement in Bm have been published. In the present study, the frequency of nodal involvement in Bm was 57%, and no significant difference was found between the tumor location and nodal involvement when compared with Bi (71%). Lymphatic flow is an important concept in determining the surgical approach.[2,9] However, the lymphatic pathway in Bm is diffuse and complicated. Because the number of patients with Bm is small, it is difficult to draw conclusions regarding the precise lymphatic pathway in this disease. However, two lymphatic routes are suggested by our clinicopathologic study: a lymphatic pathway from the hepatoduodenal ligament to the superior border of the pancreas or retropancreatic area, and a pathway to the celiac trunk by the common hepatic artery. Kurosaki et al[14] have reported that metastatic lymph nodes in Bm were widely distributed, involving nodes around the superior mesenteric artery or in the paraaortic area.

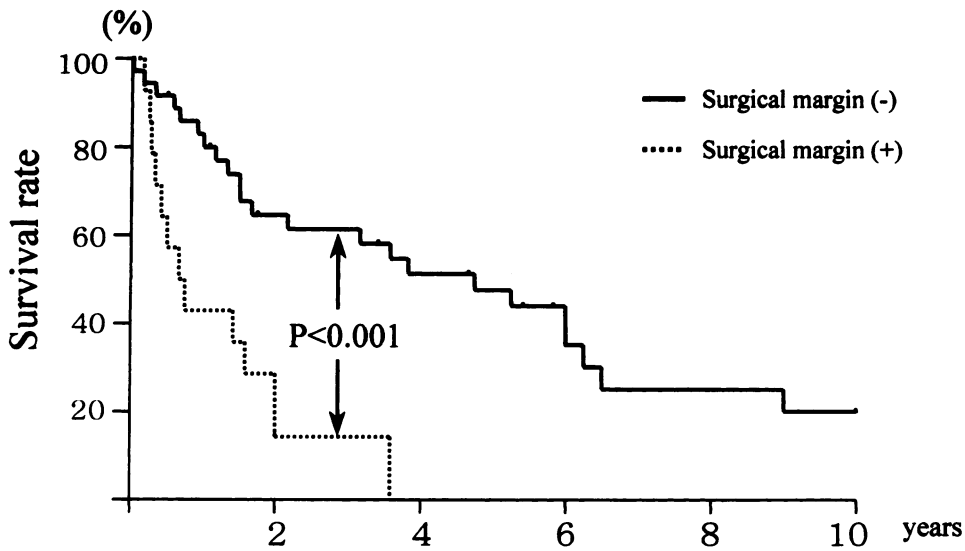

Figure 7. Survival of patients with absence or presence of tumor at the resection margins for middle and distal bile duct cancer.

Table 5. RESULTS OF UNIVARIATE AND MULTIVARIATE ANALYSES

Risk Factor	Number of Patients	Survival (%)			p value	
		1-year	3-year	5-year	Univariate Analysis	Multivariate Analysis
Age						
≦65 yr	22	82	45	39	0.52	—
>65 yr	28	60	49	32		
Depth of tumor						
≦SS	13	76	76	76	0.03	0.105
>SS	37	67	37	20		
Lymph node metastasis						
Absent	16	86	86	65	0.002	0.017
Present	34	62	30	21		
Neural invasion						
Absent	8	75	63	63	0.27	—
Present	42	69	45	29		
Histologic margin						
Negative	36	80	61	48	0.0005	0.015
Positive	14	43	14	0		
Tumor location						
Bm	14	63	31	31	0.50	—
Bi	36	72	57	38		

SS = subserosa; Bm = middle bile duct cancer; Bi = distal bile duct cancer.

The frequency of nodal involvement in Bi has been reported to range from 23% to 81%.[2,7,15,16] Tio et al[15] have reported that 20 of 33 patients (61%) with common bile duct cancer had lymph node involvement. Lygidakis et al[16] have reported a frequency of nodal involvement of 30% (6 of 20 patients, all with only local nodal involvement). In our study, the rate of lymph node involvement was 69%. Lymphatic pathways in Bi have been reported to be nearly the same as those in carcinoma of the head of the pancreas.[2] Specifically, in that study, there was a correlation between involvement of the pericholedochal lymph nodes (12abp2 and 13a) and involvement of the lymph nodes around the superior mesenteric artery (number 14, particularly 14a and 14b). Nodal status was an important prognostic factor. However, in our series, 5 patients with nodal involvement lived >5 years. In addition, 1 patient with paraaortic lymph node involvement is alive 27 months after resection without evidence of recurrence. We suspect that the performance of extended lymphadenectomy[5] contributed to these favorable outcomes.

Another important pattern for the spread of bile duct cancer is neural plexus invasion, as with pancreatic cancer.[3,4,9,13] Neural invasion was encountered more frequently when the tumors invaded the subserosa. Bhuiya et al[13] have reported that perineural invasion was an important prognostic factor, and the overall incidence of perineural invasion was 81% for biliary tract cancer. In the present study, the incidence of neural invasion for Bi and Bm was 86%. However, few precise studies on the location of nerve plexus invasion in bile duct cancer have been published.[4] Our study shows that the PL hdl (plexus within the hepatoduodenal ligament) and PL ph I (pancreatic head plexus I) were the most important sites of plexus invasion for Bm and Bi, respectively. Neural invasion was one of the most important factors contributing to a positive dissected periductal soft-tissue margin. These results suggest that plexus dissection in the hepatoduodenal ligament, around the hepatic artery, and of the pancreatic head plexus I is necessary in the treatment of Bm and Bi. Neural invasion, especially extrapancreatic nerve plexus invasion, was an important prognostic factor for pancreatobiliary tract cancer.[13,17] In particular, nerve plexus invasion was an important factor for a poor prognosis. However, in our series, neural invasion was not an important factor for a poor prognosis because of the small number of patients with nerve plexus invasion and radical surgical approach.

Tompkins et al[18] have reported that the Whipple procedure for middle- or lower-third lesions had a 50% survival rate at 19.5 months and a 27% 5-year survival rate. The French Surgical Association Survey has reported similar results.[19] In our series, the overall 5-year survival rate was 35%. Thirteen patients in our series have lived >5 years after resection. However, it is difficult to perform a curative resection in patients with advanced bile duct cancer because of local invasion of the hepatic artery, portal vein, or both, as well as distant metastasis. The location of the primary lesion has been reported to be the most important prognostic consideration.[14,18] In general, Bm has been reported to have a poorer prognosis than Bi.[18] In our study, however, no significant difference in survival between patients with Bm and Bi was found.

Tumor involvement of the surgical margin has been reported to be an important prognostic factor in patients with gastrointestinal tract cancer.[20–22] Adam et al[20] have re-

ported the clinical importance of tumor involvement of the circumferential margin for local recurrence and prognosis of rectal cancer. Wilett et al[21] also have reported that the peripancreatic surgical margin was an important prognostic factor for pancreatic cancer. Langer et al[22] have shown that the mean survival time was more than twice as long in patients with tumor-free surgical margins than in those having margins with tumor (42 *vs.* 18 months). Our data also show that the survival rate for patients with negative surgical margins is significantly longer than for those with positive surgical margins. Our multivariate analysis also shows that absence of tumor at the surgical margin is the most important independent prognostic factor.

The patterns of nodal involvement and tumor extension (especially neural invasion), as well as the results of our multivariate analysis, indicate that pancreaticoduodenectomy combined with skeletonization of the hepatoduodenal ligament is an adequate surgical choice. The hepatic artery, portal vein, lymphatic vessels, and nerve branches are located in the hepatoduodenal ligament. The main site of surgical margin involvement in Bm was the periductal soft tissue adjacent to the portal vein. Our finding that the periductal soft-tissue margin was involved by tumor in 50% of resections for Bm is important in determining surgical strategy. It is necessary to resect the portal vein in patients with serosal invasion to maintain enough distance between the main tumor and the surgical margin. It is relatively easy to obtain an adequate surgical proximal hepatic transection and distal bile duct transection lines in addition to resecting the portal vein. However, obtaining negative surgical margins in the periductal soft tissue adjacent to the proper hepatic artery is difficult. Some Japanese surgeons have attempted a complete ligamentectomy to obtain a clear surgical margin.[23] Lygidakis et al[16] also have reported an aggressive surgical procedure with combined resection of the portal vein and hepatic artery for advanced carcinoma. However, complete ligamentectomy has been reported to be accompanied by high morbidity and mortality rates[23] and should be undertaken only after careful consideration.

In conclusion, our results indicate that absence of tumor at the surgical margin, especially dissected periductal soft tissue, and absence of nodal involvement are important prognostic factors in bile duct cancer. Skeletonization of the hepatoduodenal ligament, including portal vein resection, is necessary for patients with Bm, and wide nodal dissection is essential in all patients.

References

1. Michelassi F, Erroi F, Dawson PJ, et al. Experience with 647 consecutive tumors of the duodenum, ampulla, head of the pancreas, and distal common bile duct. Ann Surg 1989; 210:544–556.
2. Kayahara M, Nagakawa T, Ueno K, et al. Lymphatic flow in carcinoma of distal bile duct based on a clinicopathologic study. Cancer 1993; 72:2112–2117.
3. Kayahara M, Nagakawa T, Konishi I, et al. Clinicopathological study of pancreatic carcinoma with particular reference to the invasion of the extrapancreatic neural plexus. Int J Pancreatol 1991; 10:105–111.
4. Kayahara M, Nagakawa T, Tsukioka, Y, et al. Neural invasion and nodal involvement in distal bile duct cancer. Hepato-Gastroenterology 1994; 41:190–194.
5. Nagakawa T, Kurachi M, Konishi K, Miyazaki I. Translateral retroperitoneal approach in radical surgery for pancreatic carcinoma. Jpn J Surg 1982; 12:229–233.
6. Nagakawa T, Nagamori M, Futagami F, et al. Results of extensive surgery for pancreatic cancer. Cancer 1996; 77:640–645.
7. Japanese Society of Biliary Surgery. General Rules for Surgical and Pathological Studies on Cancer of Biliary Tract, 4th ed. Tokyo: Kanehara, 1997.
8. Japan Pancreas Society. Classification of pancreatic carcinoma, 1st ed. Tokyo: Kanehara, 1996.
9. Kayahara M, Nagakawa T, Futagami F, et al. Lymphatic flow and neural plexus invasion associated with carcinoma of the body and tail of the pancreas. Cancer 1996; 78:2485–2491.
10. Yoshioka H, Wakabayashi T. Therapeutic neurotomy on head of pancreas for relief of pain due to chronic pancreatitis. Arch Surg 1958; 76:546–554.
11. Kaplan E, Meier P. Nonparametric estimation from incomplete observation. J Am Stat Assoc 1958; 53:457–462.
12. Cox DR. Regression models and life tables. J R Stat Soc 1972; 34:187–220.
13. Bhuiya MMR, Nimura Y, Kamiya J, et al. Clinicopathologic studies on perineural invasion of bile duct carcinoma. Ann Surg 1992; 215:344–349.
14. Kurosaki I, Tsukada K, Hatakeyama K, Muto T. The mode of lymphatic spread in carcinoma of the bile duct. Am J Surg 1996; 172: 239–243.
15. Tio TL, Cheng J, Wijers OB, et al. Endosonographic TNM staging of extrahepatic bile duct cancer: comparison with pathological staging. Gastroenterology 1991; 100:1351–1361.
16. Lygidakis NJ, van der Heyde MN, van Dongen RJAM, et al. Surgical approaches for unresectable primary carcinoma of the hepatic hilus. Surg Gynecol Obstet 1988; 66:107–114.
17. Nakao A, Harada A, Nonami T, et al. Clinical significance of carcinoma invasion of the extrapancreatic nerve plexus in pancreatic cancer. Pancreas 1996; 2:357–361.
18. Tompkins RK, Thomas D, Wile A, Longmire WP. Prognostic factors in bile duct carcinoma: analysis of 96 cases. Ann Surg 1991; 194:447–457.
19. Reding R, Buard JL, Leveau G, Launois B. Surgical management of 552 carcinomas of the extrahepatic bile ducts (gallbladder and periampullary tumor excluded): results of the French Surgical Association Survey. Ann Surg 1991; 213:236–241.
20. Adam IJ, Mohamdee MO, Martin IG, et al. Role of circumferential margin involvement in the local recurrence of rectal cancer. Lancet 1994; 44:707–711.
21. Wilett CG, Lewarndrowski K, Warshaw AL, et al. Resection margins in carcinoma of the head of the pancreas. Ann Surg 1993; 217:144–148.
22. Langer JC, Langer B, Taylor BR, et al. Carcinoma of the extrahepatic bile ducts: results of an aggressive surgical approach. Surgery 1985; 98:752–759.
23. Mimura H, Kim H, Takakura N, et al. Radical bloc resection of hepatoduodenal ligament for carcinoma of the bile duct with double catheter bypass for portal circulation. Surg Gynecol Obstet 1988; 167:527–529.