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Lymph Node Metastasis from Hilar Cholangiocarcinoma: Audit of 110 Patients Who Underwent Regional and Paraaortic Node Dissection

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Objective
To assess the status of the regional and paraaortic lymph nodes in hilar cholangiocarcinoma and to clarify the efficacy of systematic extended lymphadenectomy.

Summary Background Data
There have been no studies in which regional and paraaortic lymphadenectomies for hilar cholangiocarcinoma have been routinely performed. Therefore, the metastasis rates to the regional and paraaortic nodes, the mode of lymphatic spread, and the effect of extended lymph node dissection on survival remain unknown.

Methods
This study involved 110 patients who underwent surgical resection for hilar cholangiocarcinoma with lymph node dissection including both the regional and paraaortic nodes. A total of 2,652 nodes retrieved from the surgical specimens were examined microscopically.

Results
Of the 110 patients, 52 (47.3%) had no involved nodes, 39 (35.5%) had regional lymph node metastases, and 19 (17.3%) had regional and paraaortic node metastases. The incidence of positive nodes was significantly higher in the patients with pT3 disease than in those with pT2 disease. The pericholedochal nodes were most commonly involved (42.7%), followed by the periportal nodes (30.9%), the common hepatic nodes (27.3%), and the posterior pancreaticoduodenal nodes (14.5%). The celiac and superior mesenteric nodes were rarely involved. The 3-year and 5-year survival rates were 55.4% and 30.5% for the 52 patients without involved nodes, 31.8% and 14.7% for the 39 patients with regional node metastases, and 12.3% and 12.3% for the 19 patients with paraaortic node metastases, respectively. Of the 19 patients with positive paraaortic nodes, 7 had no macroscopic evidence of paraaortic disease on intraoperative inspection. The survival in this group was significantly better than in the remaining 12 patients.

Conclusion
The paraaortic nodes and the regional nodes are frequently involved in advanced hilar cholangiocarcinoma. Whether extended lymph node dissection provides a survival benefit requires further study. However, the fact that long-term survival is possible despite pN2 or pM1 disease encourages the authors to perform an aggressive surgical procedure with extended lymph node dissection in selected patients with hilar cholangiocarcinoma.

Hilar cholangiocarcinoma represents about half of all malignant bile duct tumors and is the most difficult to treat.[1–3] Because surgical resection is the best therapeutic strategy, the goal has been complete removal of all cancer tissue, despite the difficulties associated with resection. Recently, hepatectomy with en bloc resection of the extrahepatic bile duct has been found to offer a better chance of long-term survival.[4–16] Nodal status is an important predictor of survival after resection.[8,11,13–17] Some authors have reported a benefit from hepatectomy with lymph node dis-

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Table 1. SURGICAL PROCEDURES PERFORMED IN 110 PATIENTS

Procedure	Total	With PD	With PV
Right trisegmentectomy with S_1	13	0	8
Right lobectomy with S_1	32	6	13
Left trisegmentectomy with S_1	9	1	4
Left lobectomy with S_1	38	0	9
Central bisegmentectomy with S_1	5	0	1
Other segmentectomies	7	1	1
Bile duct resection only	6	2	0

S_1, combined resection of the caudate lobe; PD, pancreatoduodenectomy; PV, portal vein resection and reconstruction.

Table 2. DEFINITION OF REGIONAL LYMPH NODE GROUPS

TNM classification	This Study
N1	N1
Hilar	Pericholedochal (No. 12h, 12c, 12b)
Cystic duct	
Pericholedochal	
N2	N2
Periportal	Periportal (No. 12 p, 12a)
Periduodenal	Common hepatic (No. 8a, 8p)
Peripancreatic	Posterior pancreaticoduodenal (No. 13a)
Celiac	Celiac (No. 9)
Superior mesenteric	Superior mesenteric (No. 14)

Numbers in parentheses indicate lymph node group according to the classification by the Japanese Society of Biliary Surgery.

section.[4–7,13–17] However, the incidence of paraaortic lymph node metastasis, the mode of lymphatic spread, and the effect of dissection of the regional and paraaortic lymph nodes on survival are unknown because regional and paraaortic lymphadenectomies have not been routinely performed in any study.

The purposes of this study were to elucidate the nodal status, including the regional and paraaortic lymph nodes, in patients with hilar cholangiocarcinoma and to clarify the prognostic significance of involved nodes and the efficacy of systematic extended lymphadenectomy.

METHODS

Patients and Procedure

Between 1983 and 1998, 202 patients with hilar cholangiocarcinoma were treated at the First Department of Surgery, Nagoya University Hospital. In 43 (21.3%), laparotomy and/or percutaneous transhepatic biliary drainage alone was performed because of advanced disease or poor general condition. The remaining 159 (78.7%) underwent resection of tumor with (n = 120) or without (n = 39) systematic extended lymphadenectomy, including both the regional and paraaortic nodes. Of the 120 patients who underwent resection with extended lymphadenectomy, 10 were excluded because they had invasive cancer extending from the hepatic hilum down to the distal bile duct. Thus, 110 patients were enrolled in this study. There were 80 men and 30 women, with a mean age of 60.1 ± 10.1 years (range 24–78).

Hepatectomy was performed in 104 (94.5%) of the 110 patients. Extrahepatic bile duct resection was performed in the remaining six patients. Combined portal vein resection with reconstruction (n = 36, 32.7%) and pancreatoduodenectomy (n = 10, 9.1%) were also performed in selected patients (Table 1). Extended lymph node clearance was carried out as follows. After en bloc resection of the primary tumor and nodes of the hepatoduodenal ligament and the head of the pancreas, with skeletonization of the portal vein and hepatic artery, the paraaortic connective tissue containing the lymph nodes was dissected between the levels of the celiac and inferior mesenteric arteries. The left renal vein and the right renal artery were skeletonized between the aorta and the inferior vena cava.

A total of 2,652 nodes (24.1 nodes/patient), including 1,524 regional, 984 paraaortic, and 144 paragastric or paracolic nodes, were retrieved from the 110 fresh surgical specimens. A single representative section per node was microscopically examined with hematoxylin and eosin staining.

Definition of Lymph Node Group

Nodal status and primary tumor extension were evaluated using the TNM classification of the International Union Against Cancer (UICC).[18] The regional lymph nodes were defined as the cystic duct, pericholedochal, hilar, periportal, periduodenal, peripancreatic, celiac, and superior mesenteric nodes. Because the definitions of the regional nodes are obscure, the Japanese Society of Biliary Surgery's rules[19] were used to define the topographic relations of the lymph nodes to surrounding structures. In this study, the hilar, cystic duct, and pericholedochal nodes in the TNM system were lumped together as the pericholedochal nodes. The periportal and proper hepatic nodes in the hepatoduodenal ligament were considered together. Nodes on the posterior surface of the pancreatic head were defined as the posterior pancreaticoduodenal nodes. The common hepatic nodes were located around the common hepatic artery (Table 2). The pericholedochal, periportal, common hepatic, celiac, and paraaortic nodes were dissected in all patients. The superior mesenteric, paragastric, and paracolic nodes were resected in selected patients.

Statistical Analysis

Results were expressed as means ± standard deviation. Statistical analysis was performed using the Fisher exact

Table 3. RELATION BETWEEN NODAL STATUS AND PRIMARY TUMOR EXTENSION

pT	Group 1 pN0 (n = 52)	Group 2		Group 3 pM1 (n = 19)
		pN1 (n = 13)	pN2 (n = 26)	
pT2 (n = 42)	28	7	4	3
pT3 (n = 68)	24	6	22	16

pN status in group 3 is classified as pM1 because of positive paraaortic nodes. Group 1, no nodal metastases; Group 2, regional lymph node metastases; Group 3, paraaortic node metastases.

probability test and the Mann-Whitney test, where appropriate. Postoperative survival was calculated using the Kaplan-Meier method. Differences in survival curves were compared using the log-rank test. $P < .05$ was considered statistically significant.

RESULTS

Regional and Paraaortic Nodal Status

The 110 patients were classified into three groups according to nodal status. Group 1 consisted of 52 (47.3%) patients without involved nodes. Group 2 consisted of 39 (35.5%) patients with regional lymph node metastases only. The remaining 19 (17.3%) patients had paraaortic lymph node metastases (group 3). Group 2 included 13 patients with pN1 disease and 26 patients with pN2 disease (Table 3). The extent of lymph node involvement was correlated with the primary tumor extension. There were no patients with pT1 disease in this series. The incidence of positive nodes was significantly greater in the patients with pT3 disease than in those with pT2 disease (64.7% vs. 33.3%, $P < .005$). The incidence of positive paraaortic nodes was significantly higher in the patients with pT3 disease than in those with pT2 disease (23.5% vs. 7.1%, $P < .05$).

The most common site of metastasis was the pericholedochal nodes (Table 4). The incidence of metastasis in this node group (42.7% overall, 79.5% in group 2, and 84.2% in group 3) was significantly ($P < .05$) greater than the incidence in the periportal (30.9%) and common hepatic nodes (27.3%). The incidence of metastasis to the paraaortic nodes (17.3%) was greater than that to the posterior pancreaticoduodenal nodes (14.5%). Although the celiac nodes were defined as regional nodes, the incidence of metastasis was low (6.4%). All eight patients with positive superior mesenteric, paragastric, or paracolic nodes had positive paraaortic nodes.

Of the 2,652 lymph nodes surgically resected, 382 (14.4%) contained metastases (Table 5). The actual involvement rate, defined as the number of involved nodes divided by the number of dissected nodes, was 20.1% in the pericholedochal nodes, 15.4% in the periportal nodes, 15.0% in the common hepatic nodes, and 12.5% in the posterior pancreaticoduodenal nodes. The actual involvement rate in the paraaortic nodes was 14.0%, which was not significantly different from the rates in the periportal, common hepatic, or posterior pancreaticoduodenal nodes. The actual involvement rates of all the regional nodes were significantly greater in group 3 than in group 2.

Table 4. INCIDENCE OF NODAL INVOLVEMENT

Lymph Node Group	Overall (n = 110)	Group 2 (n = 39)	Group 3 (n = 19)
N1			
Pericholedochal	47/110 (42.7)	31/39 (79.5)	16/19 (84.2)
N2			
Periportal	34/110 (30.9)	18/39 (46.2)	16/19 (84.2)*
Common hepatic	30/110 (27.3)	18/39 (46.2)	12/19 (63.2)
Posterior pancreaticoduodenal	16/110 (14.5)	8/39 (20.5)	8/19 (42.1)
Celiac	7/110 (6.4)	1/39 (2.6)	6/19 (31.6)*
Superior mesenteric	4/23	0/8	4/7
M1			
Paraaortic	19/110 (17.3)	0/39 (0.0)	19/19 (100)*
Paragastric or paracolic	6/44	0/16	6/10

Data are given as patients with positive nodes/patients who underwent node dissection (%).
* $P < .01$ vs. group 2 patients.
Group 2, regional lymph node metastases; Group 3, paraaortic node metastases.

Table 5. ACTUAL NUMBER OF INVOLVED NODES AND DISSECTED NODES

Lymph Node Group	Overall (n = 110)	Group 2 (n = 39)	Group 3 (n = 19)
N1			
Pericholedochal	67/334 (20.1)	41/138 (29.7)	26/45 (57.8)*
N2			
Periportal	62/402 (15.4)	30/147 (20.4)	32/84 (38.1)*
Common hepatic	56/374 (15.0)	28/159 (17.6)	28/51 (54.9)†
Posterior pancreaticoduodenal	24/192 (12.5)	9/74 (12.2)	15/40 (37.5)*
Celiac	15/196 (7.7)	1/82 (1.2)	14/37 (37.8)†
Superior mesenteric	5/26	0/10	5/6
M1			
Paraaortic	138/984 (14.0)	0/329 (0.0)	138/290 (47.6)†
Paragastric or paracolic	15/144	0/35	15/66
Total	382/2652 (14.4)	109/974 (11.2)	273/619 (44.1)†

Data are given as involved nodes/dissected nodes (%).
* $P < .005$ and † $P < .0001$ vs. group 2.
Group 2, regional lymph node metastases; Group 3, paraaortic node metastases.

Paraaortic Node Metastases

The pericholedochal or periportal nodes were involved in all patients in group 3 (Table 6). The common hepatic or posterior pancreaticoduodenal nodes were involved in 15 (78.9%) patients. These nodes were not involved in the remaining four (21.1%) patients.

The actual number of involved paraaortic nodes was 1 to 36: 3 or fewer in 10 patients, 4 to 10 in 4 patients, and more than 10 in 5 patients. Macroscopic inspection during surgery found that 7 (36.8%) patients had negative paraaortic nodes and 12 had positive nodes. There was a significant difference in the number of involved paraaortic nodes between the former and the latter patients (1.9 ± 0.9 vs. 10.4 ± 10.2, $P < .01$).

Complications and Death

Several kinds of postoperative complications occurred. Pleural effusion was the most common, followed by wound sepsis and then liver failure.[20,21] Although the complication rate for all 110 patients was as high as 63%, no postoperative complications were related directly to the extended lymphadenectomy. Because we did not dissect the neural plexus around the superior mesenteric artery, no diarrhea requiring treatment developed after surgery.

Five patients died of multiple organ failure within 30 days after surgery, and another six patients died of liver failure or multiple organ failure in the second to fifth postoperative month. The remaining 99 patients were discharged from the hospital in good condition. Thus, the 30-day death rate was 4.5% (5/110), and the overall hospital death rate was 10.0% (11/110). All 11 patients who died in the hospital had undergone major hepatectomy after percutaneous transhepatic biliary drainage.

Survival

Survival was closely associated with the extent of nodal involvement. The 3-year and 5-year survival rates (includ-

Table 6. PATTERN OF LYMPH NODE METASTASES IN 19 PATIENTS WITH POSITIVE PARAAORTIC NODES

Pericholedochal	Periportal	Common Hepatic	Posterior Pancreaticoduodenal	Paraaortic	No. of Patients
+	+	+	+	+	4
+		+	+	+	1
+	+	+		+	6
+		+		+	1
+	+		+	+	2
	+		+	+	1
+	+			+	1
+				+	1
	+			+	2

+, presence of involved node.

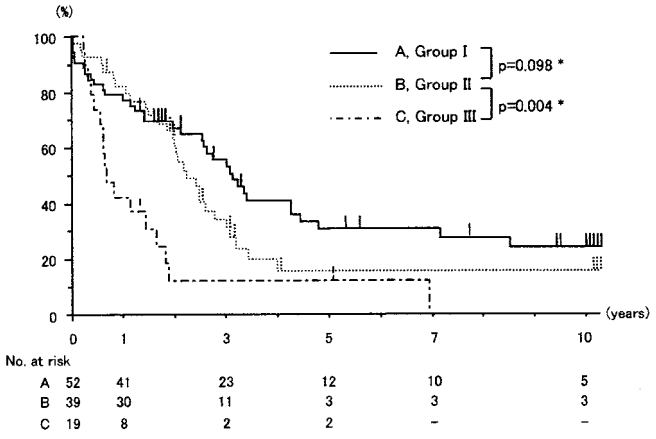

Figure 1. Survival according to nodal status in 110 patients with hilar cholangiocarcinoma who underwent resection with regional and paraaortic lymphadenectomy (all deaths included). Group 1, patients without lymph node metastasis; group 2, patients with regional lymph node metastasis; group 3, patients with paraaortic node metastasis. *, by log-rank test.

ing all deaths) were 55.4% and 30.5% in group 1, 31.8% and 14.7% in group 2, and 12.3% and 12.3% in group 3, respectively (Fig. 1). The actual number of patients surviving more than 5 years was 12 in group 1, 3 in group 2, and 2 in group 3. The difference in the survival rate between groups 1 and 2 was marginal ($P = .098$), but it was highly significant ($P = .004$) between groups 2 and 3. Among group 2 patients, no significant difference in survival existed between patients with pN1 and pN2 disease (3-year survival, 23.1% vs. 37.1%; 5-year survival, 23.1% vs. 13.9%; median survival, 29.2 vs. 25.0 months).

The outcome in group 3 was analyzed according to the macroscopic appearance of the paraaortic nodes (Fig. 2). The survival rates for the 7 patients in whom the paraaortic nodes were macroscopically negative on intraoperative inspection were significantly better than those for the 12 patients in whom the paraaortic nodes were macroscopically positive (5-year survival, 28.6% vs. 0%; median survival, 22.1 months vs.7.6 months; $P < .001$). The survival rates for the seven patients with macroscopically negative nodes were almost equal to those for the patients in group 2. In contrast, the outcome of the 12 patients with macroscopically positive nodes was not significantly different from that of the 43 patients with unresectable tumor.

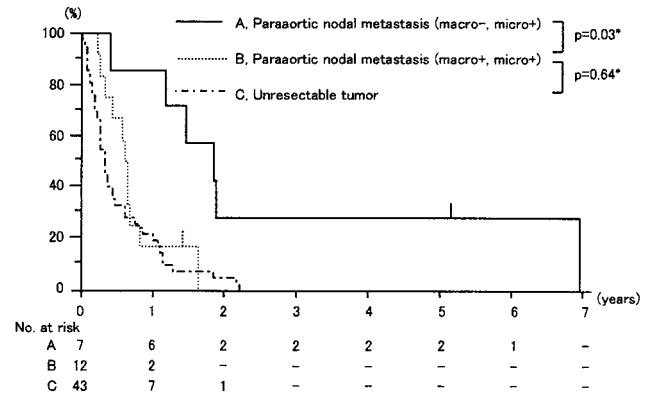

Figure 2. Survival in patients with paraaortic nodal metastases or unresectable tumor (all deaths included). Paraaortic nodal metastasis (macro-, micro+), patients in whom the paraaortic nodes were macroscopically negative on intraoperative inspection; paraaortic nodal metastasis (macro+, micro+), patients in whom the paraaortic nodes were macroscopically positive. *, by log-rank test.

Of the five patients with lymph node metastasis who survived more than 5 years, one had pN1 disease, two had pN2 disease, and the remaining two had paraaortic node metastasis (Table 7). All these patients underwent major hepatectomy with negative resection margins. Two of these patients died (at 83 and 126 months after surgery). The remaining three patients were alive as of this writing with no signs of recurrence.

DISCUSSION

Hilar cholangiocarcinoma is characterized by tumor extension with lymph node metastasis and neural invasion.[4–17] Therefore, an understanding of the pattern of lymph node spread is critical to determine the extent of lymph node dissection. The incidence of nodal involvement in resected specimens has been reported to range from 30% to more than 50%.[3,6,10,11,13,15] The metastasis rate of 52.7% in our series was consistent with these results. The incidence of lymph node metastasis in cholangiocarcinoma increases with increasing depth of carcinoma invasion in the primary tumor.[8,11,22–24] We also showed a correlation between primary tumor extension and nodal involvement. The node-positive rate in our patients with pT3 disease exceeded 60%.

In this study, the pericholedochal nodes in the hepatoduodenal ligament were the most common sites of metastasis. These nodes appear to be key stations for lymphatic spread toward the peripancreatic and more distant lymph nodes. The periportal, common hepatic, and posterior pancreaticoduodenal nodes also exhibited a high incidence of metastatic involvement. This implies that these three groups are important regional nodes. The lymphatic pathways in the hepatoduodenal ligament and around the head of the pancreas are anatomically complicated, with a network connecting each lymph node.[25,26] In a dye staining study, lymph from the pericholedochal nodes was shown to flow to the posterior pancreaticoduodenal, retroportal, posterior common hepatic, and paraaortic nodes.[27] Kayahara et al,[22] in a clinicopathologic study of middle bile duct cancer, defined two lymphatic pathways: one from the hepatoduodenal ligament to the superior border of the pancreas or retropancreatic area, and the other to the celiac trunk by means of the common hepatic artery. Such pathways have also been demonstrated in studies of gallbladder cancer.[28,29] Taking these observations into consideration, lymphatic metastases from hilar cholangiocarcinoma appear to spread first to the pericholedochal nodes in the hepatoduodenal

Table 7. DATA OF 5-YEAR SURVIVORS WITH LYMPH NODE METASTASIS

Patient	Age/Sex	Surgery (segments resected)	Histology	Nodal Status*							Follow-Up (months)
				PC	PPo	CH	PPa	C	SM	PA	
1	62/M	S1, 5, 6, 7, 8	Well	1/9	0/6	0/7	0/2	0/5	0/2	0/7	121, alive
2	55/M	S1, 4, 5, 7, 8	Mod	1/5	0/2	1/3	0/2	0/3	ND	0/7	162, alive
3	48/M	S1, 2, 3, 4	Well	1/3	1/4	1/8	0/4	0/2	ND	0/5	126, dead
4	65/M	S1, 2, 3, 4	Mod	2/2	2/3	2/3	0/1	0/1	ND	2/11	83, dead
5	62/M	S1, 4, 5, 8	Mod	0/3	1/12	0/1	0/3	0/0	ND	1/16	61, alive

Well, well-differentiated adenocarcinoma; Mod, moderately differentiated adenocarcinoma; PC, pericholedocal node; PPo, periportal node; CH, common hepatic node; PPa, posterior pancreaticoduodenal node; C, celiac node; SM, superior mesenteric node; PA, paraaortic node; ND, not dissected.
* Number of involved nodes/number of dissected nodes.

ligament, then to spread widely toward the posterosuperior area around the pancreatic head, portal vein, and common hepatic artery.

Involvement of the celiac nodes was found in only seven (6.4%) patients, six of whom had positive paraaortic nodes. Although the incidence of metastasis to the superior mesenteric nodes was 17.4% (4/23), this does not reflect the complete picture, because these nodes were dissected only in selected patients. No involvement of the superior mesenteric nodes was found in patients without positive paraaortic nodes. This implies that the true metastasis rate to the superior mesenteric nodes is low, probably similar to that of the celiac nodes. The celiac and superior mesenteric nodes are classified as regional nodes in extrahepatic bile duct cancer according to the TNM system. This might be true in distal bile duct cancer,[22,23] but it is not the case in proximal bile duct cancer. In hilar cholangiocarcinoma, the celiac and superior mesenteric nodes should be classified as distant nodes.

Another important finding in our study was the unexpectedly high incidence of metastasis to the paraaortic lymph nodes (17.3%). This incidence was slightly greater than that to the posterior pancreaticoduodenal nodes, a regional nodal basin. In the patients with pT3 disease, the metastasis rate to the paraaortic nodes was 23.5%. The actual involvement rate of the paraaortic nodes was 14.0%, similar to the rates for the regional nodes. We have previously reported that the metastasis rate to the paraaortic nodes was 38.3% in patients with pT2 or more advanced gallbladder cancer.[30] Compared with this extremely high incidence in advanced gallbladder cancer, the metastasis rate in hilar cholangiocarcinoma is low. Regardless, it is important to be aware that the paraaortic nodes are often involved, especially in advanced hilar cholangiocarcinoma.

The unexpectedly high incidence of paraaortic nodal involvement does not indicate the presence of skip metastasis, because all these patients also had positive regional nodes. The paraaortic nodes are regarded as the final nodes in the abdominal lymphatic system from the bile duct. The common hepatic and retropancreatic pathways are the main routes to the paraaortic nodes.[22,28,29] Our results support the existence of such pathways. In some patients, however, the paraaortic nodes were involved despite a lack of involvement of the common hepatic and posterior pancreaticoduo-

Table 8. 5-YEAR SURVIVORS WITH LYMPH NODE METASTASIS IN PREVIOUS REPORTS

Author	Period	Resection	Node-Positive	5-Year Survivors with Positive Node
Sugiura[6]*	1973–1991	83	42	3
Klempnauer[33]	1971–1995	151	44	2
Nakeeb[3]	1973–1995	109	NA	0
Ogura[11]	1976–1995	66	34	0
Iwatsuki[10]	1981–1996	72†	25	0
Kosuge[14]	1980–1997	65	30	4
Miyazaki[13]	1981–1998	93	48	1¶
Neuhaus[15]	1988–1998	95†	51	3¶
Todoroki[16]	1976–1998	98	50	3¶
Present series	1983–1998	110	58	5

* Multicenter study.
† Including liver transplantation.
¶ By personal communication because the number of 5-year survivors was not documented in the report.

denal nodes. This suggests the existence of a pathway from the nodes in the hepatoduodenal ligament directly to the paraaortic nodes.

The overall complication rate of 63% in this series was slightly greater than that found in most recent published reports, in which it was 37% to 65%.[3,9,13,15,31,32] However, the common complications in this study were pleural effusion and minor wound infection. These minor complications may have been excluded from the list of complications in previous studies. The point is that no postoperative complications were related directly to the extended lymphadenectomy. In addition, our death rate was acceptable, equal to or better than that in published reports,[3,5–16] although we performed a more extended hepatectomy and lymphadenectomy. These observations negate the concern that extended lymphadenectomy including paraaortic node dissection may increase the postoperative rates of death and complications.

Our results confirm that the prognosis in patients with hilar cholangiocarcinoma is strongly affected by the lymph node status.[4,6,10,11,14–17,33] A range of 5-year survival rates from 0%[10,11] to more than 30%[14] has been reported for patients with lymph node metastasis. This variability is probably due to the limited number of patients assessed and the short study periods. We therefore reviewed previous studies that included at least 50 patients undergoing resection (Table 8). A limited number of 5-year survivors with involved nodes were reported by six authors; the remaining three authors reported no 5-year survivors. None of the patients with paraaortic node metastasis were alive at 5 years. In our series, five patients with involved nodes (one with pN1 disease, two with pN2 disease, two with involved paraaortic nodes) survived more than 5 years after hepatobiliary resection. This may have been the result of the extended lymphadenectomy or accurate pathologic examination.

There is controversy about the indications for dissection of the paraaortic nodes. This dissection is not technically difficult and can yield precise staging information. Of the seven patients in whom the paraaortic nodes were macroscopically negative on intraoperative inspection, two survived more than 5 years after hepatobiliary resection. In contrast, the prognosis of the 12 patients with macroscopically positive nodes was dismal. Therefore, in patients with widespread nodal involvement on intraoperative inspection, aggressive paraaortic node dissection is not indicated. However, regional node metastasis does not make a tumor unresectable, as was previously reported.[34]

In conclusion, an understanding of the pattern of lymph node spread is essential to determine the extent of lymph node dissection in patients with hilar cholangiocarcinoma. The pericholedochal nodes are the key stations for lymphatic spread. The nodes at the posterosuperior area of the pancreatic head are important regional nodes. The paraaortic nodes are often involved in advanced disease. Whether extended lymph node dissection provides a survival benefit requires further study. However, the fact that long-term survival is possible despite pN2 or pM1 disease encourages us to perform an aggressive hepatobiliary resection with extended lymph node dissection in selected patients with hilar cholangiocarcinoma.

References

1. Tompkins RK, Saunders K, Roslyn JJ, et al. Changing patterns in diagnosis and management of bile duct cancer. Ann Surg 1990; 211: 614–621.
2. Schoenthaler R, Phillips TL, Castro J, et al. Carcinoma of the extrahepatic bile ducts: the University of California at San Francisco experience. Ann Surg 1994; 219:267–274.
3. Nakeeb A, Pitt HA, Sohn T, et al. Cholangiocarcinoma: a spectrum of intrahepatic, perihilar, and distal tumors. Ann Surg 1996; 224:463–475.
4. Nimura Y, Hayakawa N, Kamiya J, et al. Hepatic segmentectomy with caudate lobe resection for bile duct carcinoma of the hepatic hilus. World J Surg 1990; 14: 535–544.
5. Tashiro S, Tsuji T, Kanemitsu K, et al. Prolongation of survival for carcinoma at the hepatic duct confluence. Surgery 1993; 113:270–278.
6. Sugiura Y, Nakamura S, Iida S, et al. Extensive resection of the bile ducts combined with liver resection for cancer of the main hepatic duct junction: a cooperative study of the Keio Bile Duct Cancer Study Group. Surgery 1994; 115:445–451.
7. Miyagawa S, Makuuchi M, Kawasaki S. Outcome of extended right hepatectomy after biliary drainage in hilar bile duct cancer. Arch Surg 1995; 130:759–763.
8. Pichlmayr R, Weimann A, Klempnauer J, et al. Surgical treatment in proximal bile duct cancer: a single-center experience. Ann Surg 1996; 224:628–638.
9. Su CH, Tsay SH, Wu CC, et al. Factors influencing postoperative morbidity, mortality, and survival after resection for hilar cholangiocarcinoma. Ann Surg 1996; 223:384–394.
10. Iwatsuki S, Todo S, Marsh JW, et al. Treatment of hilar cholangiocarcinoma (Klatskin tumors) with hepatic resection or transplantation. J Am Coll Surg 1998; 187:358–364.
11. Ogura Y, Kawarada Y. Surgical strategies for carcinoma of the hepatic duct confluence. Br J Surg 1998; 85:20–24.
12. Ishiyama S, Fuse A, Kuzu H, et al. Results of surgical treatment and prognostic factors for hepatic hilar bile duct cancer. J Hepatobiliary Pancreat Surg 1998; 5:429–436.
13. Miyazaki M, Ito H, Nakagawa K, et al. Parenchyma-preserving hepatectomy in the surgical treatment of hilar cholangiocarcinoma. J Am Coll Surg 1999; 189:575–583.
14. Kosuge T, Yamamoto J, Shimada K, et al. Improved surgical results for hilar cholangiocarcinoma with procedures including major hepatic resection. Ann Surg 1999; 230:663–671.
15. Neuhaus P, Jonas S, Bechstein WO, et al. Extended resections for hilar cholangiocarcinoma. Ann Surg 1999; 230:808–819.
16. Todoroki T, Kawamoto T, Koike N, et al. Radical resection of hilar bile duct carcinoma and predictors of survival. Br J Surg 2000; 87:306–313.
17. Bhuiya MMR, Nimura Y, Kamiya J, et al. Clinicopathologic factors influencing survival of patients with bile duct carcinoma: multivariate statistical analysis. World J Surg 1993; 17:653–657.
18. International Union Against Cancer (UICC). TNM classification of malignant tumors. 5th ed. New York: Wiley-Liss; 1997.
19. Japanese Society of Biliary Surgery. General rules for surgical and pathological studies on cancer of biliary tract. 4th ed. Tokyo: Kanehara; 1997.
20. Nagino M, Kamiya J, Uesaka K, et al. Complications of hepatectomy for hilar cholangiocarcinoma. World J Surg (in press).
21. Nimura Y, Kamiya J, Kondo S, et al. Aggressive preoperative management and extended surgery for hilar cholangiocarcinoma: Nagoya experience. J Hepatobiliary Pancrat Surg 2000; 7:155–162.

22. Kayahara M, Nagakawa T, Ohta T, et al. Role of nodal involvement and the periductal soft tissue margin in middle and distal bile duct cancer. Ann Surg 1999; 229:76–83.
23. Kurosaki I, Tsukada K, Hatakeyama K, et al. The mode of lymphatic spread in carcinoma of the bile duct. Am J Surg 1996; 172:239–243.
24. Tio TL, Cheng J, Wijers OB, et al. Endoscopic TNM staging of extrahepatic bile duct cancer: comparison with pathological staging. Gastroenterology 1991; 100:1351–1361.
25. Deki H, Sato T. An anatomic study of the peripancreatic lymphatics. Surg Radiol Anat 1988; 10:121–135.
26. Ito M, Mishima Y, Sato T. An anatomical study of the lymphatic drainage of the gallbladder. Surg Radiol Anat 1991; 13:89–104.
27. Shirai Y, Yoshida K, Tsukada K, et al. Identification of the regional lymphatic system of the gallbladder by vital staining. Br J Surg 1992; 79:659–662.
28. Fahim RB, McDonald JR, Richards JC, et al. Carcinoma of the gallbladder: a study of its modes of spread. Ann Surg 1962; 156:114–124.
29. Tsukada K, Kurosaki I, Uchida K, et al. Lymph node spread from carcinoma of the gallbladder. Cancer 1997; 80:661–667.
30. Kondo S, Nimura Y, Hayakawa N, et al. Regional and paraaortic lymphadenectomy in radical surgery for advanced gallbladder carcinoma. Br J Surg 2000; 87:418–422.
31. Tsao J, Nimura Y, Kamiya J, et al. Management of hilar cholangiocarcinoma: comparison of an American and a Japanese experience. Ann Surg 2000; 232:166–174.
32. Gerhards MF, Gulik TM, Wit L, et al. Evaluation of morbidity and mortality after resection for hilar cholangiocarcinoma: a single-center experience. Surgery 2000; 127:395–404.
33. Klempnauer J, Ridder GJ, Werner M, et al. What constituted long-term survival after surgery for hilar cholangiocarcinoma? Cancer 1997; 79:26–34.
34. Burke EC, Jarnagin WR, Hochwald SN, et al. Hilar cholangiocarcinoma: Patterns of spread, the importance of hepatic resection for curative operation, and a presurgical clinical staging system. Ann Surg 1998; 228:385–394.