

Surgical Outcome of Hilar Plate Resection: Extended Hilar Bile Duct Resection Without Hepatectomy

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Abstract

Background We have done curative or palliative extended extrahepatic bile duct resection at the level of the hilar plate for selected patients with cholangiocarcinoma with hilar spreading, calling this procedure “hilar plate resection” (HPR), but the results of evaluating the clinical benefits of HPR for cholangiocarcinoma with hilar spreading have not been reported.

Patients and Methods Fifty-two patients with cholangiocarcinoma underwent HPR: the curative procedure was performed in 28 patients (cHPR group) and the palliative in 24 patients (pHPR group). In the same period, 128 patients with cholangiocarcinoma underwent major hepatectomy with intrahepatic cholangiojejunostomy (Hx group). These groups were compared in terms of post-operative complications and survival.

Results There were no significant differences in the rate of patients with post-operative complications and in post-operative hospital stay. The overall cumulative 5-year survival rates for each procedure (Hx group, cHPR group and pHPR group) were 40, 38 and 11 %, respectively. There was no significant difference between the Hx and cHPR groups in survival rates ($p=0.87$).

Conclusion In conclusion, HPR appears to be safe and feasible for selected patients with cholangiocarcinoma. However, the indications for HPR should be restricted.

Keywords Hilar bile duct resection · Hepatectomy ·
Cholangiocarcinoma · Palliative surgery

Introduction

Hilar cholangiocarcinoma or distal cholangiocarcinoma with hilar spreading continues to be among the most difficult cancers to manage in terms of staging and performing curative resection. In the treatment of hilar cholangiocarcinoma, several studies have advocated en bloc major hepatectomy to achieve negative histologic margins and improved survival.^{1–6}

Since these extended surgical procedures have serious problems, including high morbidity, especially with post-operative liver failure, various parenchyma-preserving hepatectomy procedures with potential curability have been

proposed, such as caudate lobectomy alone, caudate lobectomy combined with medial segmentectomy, anterior segmentectomy and central bisegmentectomy.^{2,4,5,7–11} However, these procedures were often dubbed “noble” operations, because their curability and low surgical risk were associated with heavy demands on the surgeon.

We know that there are some patients with distal cholangiocarcinoma with longitudinal spread remaining in the hilar portion (extrahepatic portion), without infiltration beyond the bile duct wall (distal cholangiocarcinoma with hilar spreading). These lesions should be treated thoroughly so as not to leave cancer at the proximal side of the bile duct. We also know that there are a few patients with Bismuth type I hilar cholangiocarcinoma without infiltration beyond the bile duct wall. These tumours are likely to have superficial spreading, which would be difficult to accurately diagnose preoperatively.¹² It remains unknown whether, for patients with such a non-invasive tumour, extended hepatectomy would be appropriate. Some patients having hilar cholangiocarcinoma with non-invasive and limited spreading lesions could be treated with bile duct resection without hepatectomy.

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Conventional hilar bile duct resection (CHBDR) at the level just above the bile duct confluence would likely result in cancer-positive margins due to superficial tumour in hilar malignancies.^{12,13} Therefore, we have done extended extrahepatic bile duct resection at the level of the hilar plate for selected patients, calling this procedure hilar plate resection (HPR).

The results of a retrospective study evaluating the clinical benefits in patients who underwent HPR for cholangiocarcinoma are reported.

Patients and Methods

Surgical Indications

As shown in our previous report, from 2000 to 2004, we choose various operative procedures according to evaluation of intraductal longitudinal spread by precise cholangiography. Preoperative diagnosis and operative strategy for hilar cholangiocarcinoma in this period were shown in previous our report in 2004.¹

Since 2004, HPR has mainly been used for the following types of patients: (1) patients with distal cholangiocarcinoma with hilar spreading and (2) selected patients with hilar cholangiocarcinoma without infiltration beyond the bile duct, with longitudinal spread remaining in the area of resection of HPR and with the no obvious suspicions of spreading to caudate branch. These diagnoses were mainly made by precious cholangiography.¹ Most patients with invasive tumour in the perihilar portion were diagnosed to be candidates for major hepatectomy.

We have also used this operation as a palliative procedure for patients with insufficient future remnant hepatic reserve for major hepatectomy, with severe systemic comorbidities (e.g. cerebral infarctions, moderate to severe ischemic heart

disease) or with decreased performance status. It was determined that these patients could undergo no residual tumour or microscopic residual tumour resection by HPR, even if the procedure was done with palliative intention. If the patient was found to have a macroscopic residual tumour resection with HPR, non-operative treatment was selected.

Operative indications for major hepatectomies or vascular combined resection were described in our previous report.²

Patients

From August 2000 to October 2010, 52 patients with cholangiocarcinoma (32 patients with hilar and 20 patients with distal cholangiocarcinoma with hilar spreading) underwent HPR at the Department of Surgery II, Hokkaido University Hospital.

In the same period, 128 patients underwent major hepatectomy with intrahepatic cholangiojejunostomy for cholangiocarcinoma (124 patients with hilar cholangiocarcinoma and 4 patients with distal cholangiocarcinoma with hilar spreading). A total of 180 patients were evaluated in this study (Table 1). Patients' performance status (PS) was evaluated by the Eastern Cooperative Oncology Group score.¹⁴

Surgical Procedure of HPR

Nodal clearance around the pancreatic head and skeletonization of the portal vein and the hepatic artery were performed first. The portal vein and the hepatic artery were then separated from the surrounding tissue upward to the hilar plate, where the duct cannot be further separated from the vasculature. This was considered "the limit of ductal transection without hepatectomy", which is at the right edge of the posterior portion of the right portal vein and the right edge of the umbilical portion of the left portal vein.^{15,16} Then, the gallbladder with the "cystic plate" was

Table 1 Characteristics of patients in this study

Characteristics	Hilar plate resection (<i>N</i> =52)	Major hepatectomy (<i>N</i> =128)	<i>p</i> value
Age (years)	72 (52–83) ^a	69 (44–81) ^a	0.03
Gender (male/female)	45/7	95/33	
Preoperative diagnosis			
Hilar cholangiocarcinoma	32	124	<0.01
Distal cholangiocarcinoma with hilar spreading	20	4	
Preoperative complications			
Cardiac disease	8	9	0.10
Cerebral disease	1	2	1
Respiratory disease	4	0	<0.01
Lower performance status	5	0	<0.01
Diabetes mellitus	11	22	0.67
Body mass index	21.3 (16.1–29.7) ^a	21.8 (16.5–31.5) ^a	0.51
Preoperative albumin	3.9 (2.6–4.8) ^a	3.7 (2.5–4.6) ^a	0.37

^a Numbers show median number, and numbers in parentheses show range of each parameter

resected toward the hepatic hilum. Finally, the extrahepatic duct at the hilar plate was resected. The portions resected in HPR are shown in Fig. 1. The difference between HPR and CHBDR, which used to be performed by many surgeons, is the level of ductal resection. In a patient with HPR, the bile ducts at the level of the hilar plate were resected. On the other hand, in a patient with CHBDR, the hilar bile ducts were usually resected around the level of the confluence of bilateral hepatic ducts. The bile duct portions resected in CHBDR and HPR are shown in Fig. 1.

Depending on the anatomical characteristics, there were three to five or more divided duct stumps to be anastomosed. A Roux-en-Y cholangiojejunostomy was then performed. In this procedure, two orifices in the jejunum were created due to the distance between the ducts.¹⁷ Our surgical procedure for pancreaticoduodenectomy and hepatectomies for cholangiocarcinoma has been described previously.^{2,3,15,18}

Pathological Diagnosis and Analysis

In this report, the clinical features and histological findings were described using the seventh edition of the American Joint Committee Cancer Classification.¹⁹ Tumour type in the present study was classified according to the fifth edition of the Japanese General Rules for Classification of Biliary Tract Carcinoma currently used in Japan.²⁰

The pathological diagnosis protocol was based on prior studies.¹² The bile duct of the specimen was opened

longitudinally, pinned to a board and immediately fixed in 10 % formalin. The surgical margin was diagnosed by experienced pathologists. Descriptions of margin status in this report follow the second edition of the Japanese Classification of Biliary Tract Carcinoma: hepatic margin status (HM), distal (duodenal) cut-end margin (DM) and dissected periductal structure margin (EM).²⁰ Patients with a cancer-free margin 5 mm or less in any direction were considered cancer-positive. Cases with a cancer-free margin of more than 5 mm in any direction from the biliary stump including the periductal margin were considered surgical margin-negative. Superior margin status was calculated by the macroscopic distance from the middle point of the confluence of the right and left hepatic bile ducts, as reported by Shimada et al.⁸ When there were multiple bile ducts on the right and left sides, the mean of the bile duct of each side was used.

Statistical Analysis

Statistical calculations were performed using Stat Flex (Artech Co., Ltd., Osaka, Japan) and “Exact Test” produced by Prof. S. Aoki (<http://aoki2.si.gunma-u.ac.jp/exact/exact.html>). Chi-squared, Fisher’s exact and Mann-Whitney’s *U* tests were used as appropriate. Cumulative survival after surgery was calculated using the Kaplan-Meier method. The log-rank test was used to compare cumulative survival. A Cox proportional regression hazards model was used for multivariate analysis. Values of $p < 0.05$ were considered significant.

Results

Clinical Characteristics

Table 1 shows the patients’ characteristics. There were a few differences in clinical characteristics between patients who underwent HPR (HPR group) and those who underwent major hepatectomy (Hx group) (Table 1). The patients were older in the HPR group than in the Hx group ($p < 0.01$), there were more patients with hilar cholangiocarcinoma in the Hx group and there were more patients with lower performance status and respiratory complications in the HPR group.

HPR was performed with curative intention in 28 patients (cHPR group) and with palliative intention in 24 patients (pHPR group). In the cHPR group, there were 11 cases of hilar cholangiocarcinoma and 17 of distal cholangiocarcinoma with hilar spreading. In the pHPR group, there were 21 cases of hilar cholangiocarcinoma and 3 of distal cholangiocarcinoma with hilar spreading.

The reasons for performing pHPR were insufficient future remnant hepatic reserve for major hepatectomy ($n = 17$), low PS ($n = 5$) and bilateral superficial tumour spreading beyond the resection limit ($n = 2$).

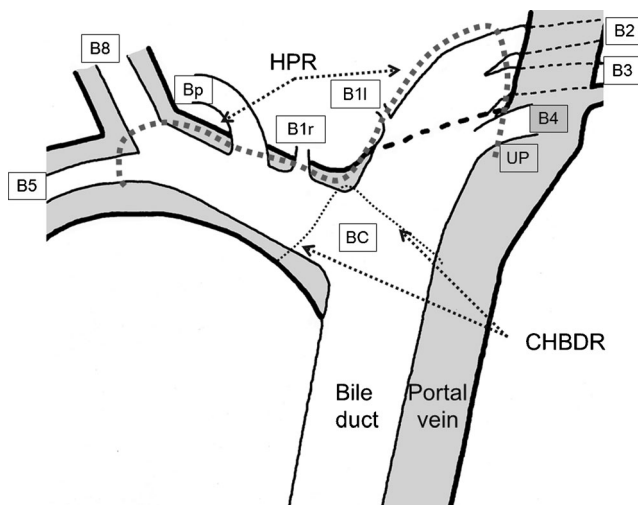


Fig. 1 Schematic of hilar plate resection (HPR) and conventional hilar bile duct resection (CHBDR). In HPR, the extrahepatic ducts are resected to the limit of ductal transection without hepatectomy, which is at the right edge of the posterior portion of the right portal vein and the right edge of the umbilical portion of the left portal vein. In CHBDR, the extrahepatic bile ducts are resected at the level just above the bile duct confluence (BC). Thick lines indicate the level of the hilar bile ducts resected with HPR and CHBDR. UP umbilical portion, Bp bile duct of the posterior segment, B1r bile duct of right caudate lobe, B1l bile duct of left caudate lobe, B2 bile duct of segment 2, B3 bile duct of segment 3, B4 bile duct of segment 4, B5 bile duct of segment 5, B8 bile duct of segment 8

Table 2 Operative results in this study

Clinical factor	Hilar plate resection (N=52)	Hepatectomy (N=128)	p value
Operative procedure			
Right hepatectomy	–	71	–
Left hepatectomy	–	43	–
Trisegmentectomy	–	13	–
Other hepatectomy	–	1	–
With PD	23	23	<0.01
Operation time (min)	625 (417–1,010) ^a	634 (426–1,023) ^a	0.66
Operative Bleeding (mL)	1,310 (485–3,670) ^a	1,690 (510–8,590) ^a	<0.01
Blood transfusion (cases)	6	38	0.01
Number of bile ducts reconstructed	5 (3–8)	3 (1–5)	<0.01
Post-operative complications (cases)			0.46 ^b
Clavien-Dind IIIa	17	44	
Clavien-Dind IIIb	0	1	
Clavien-Dind IVa	4	4	
Clavien-Dind IVb	0	0	
Clavien-Dind V	1	6	0.67
Pancreatic fistula ^a	16	26	0.17
Anastomotic insufficiency of CJ	4	5	0.28
Organ/space surgical site infections	4	19	0.23
Post-operative hospital stay (median)	38 (17–340) ^a	38 (16–172) ^a	0.90

PD pancreaticoduodenectomy,
CJ intrahepatic
cholangiojejunostomy

^a Numbers show medians, and numbers in parentheses show the range of each parameter

^b Frequency of post-operative complications (Clavien-Dind IIIa to IVb)

Operative Results

Operative results of the HPR group and Hx group in the same period are shown in Table 2. There were no differences in length of operation time, morbidity and post-operative hospital stay. However, there were significant differences in operative blood loss (number of patients requiring blood transfusion) and number of bile ducts reconstructed (Table 2).

Pathological Results with HPR

The pathological results of the HPR group are shown in Table 3. The median length of the bile duct from the bile duct confluence was 17 (5–41) mm on the right side and 16 (10–41) mm on the left side. There were no significant differences between the cHPR group and the pHPR group in the lengths of the bile ducts in the hilar lesions.

Table 3 Pathological results of hilar plate resection

	cHPR, N=28	pHPR, N=24	p value	
Length of bile duct (median length)				
Right side	17 (5–41) ^a mm	17 (10–41) ^a mm	17 (5–35) ^a mm	0.15
Left side	16 (10–41) ^a mm	16 (11–41) ^a mm	16 (10–35) ^a mm	0.48
Tumour type				
Papillary	16	10	6	
Nodular	29	16	13	
Flat	7	2	5	
Margin				
Negative	19	15	4	<0.01
Positive	33	13	20	
HM-positive	25	9	16	0.03
In situ	11	4	7	
Invasive	14	5	9	
DM-positive	10	2	8	0.03
In situ	7	1	6	
Invasive	3	1	2	
EM-positive	15	5	10	0.02

HM proximal (hepatic) cut-end margin (patients with a cancer-free margin 5 mm or less in width were considered cancer-positive), DM distal (duodenal) cut-end margin (patients with a cancer-free margin 5 mm or less in width were considered cancer-positive), EM dissected periductal structure margin (patients with a cancer-free margin 5 mm or less in width were considered cancer-positive)

^a Numbers show medians, and numbers in parentheses show the range

The histological margins were positive in 33 patients. The pHPR group had more patients with a positive histological margin than the cHPR group ($p < 0.01$).

Survival

The overall cumulative survival rates of the hilar and distal cholangiocarcinoma patients (128 patients in the Hx group, 28 patients in the cHPR group and 24 patients in the pHPR group) were 58, 54 and 37 % at 3 years and 40, 38 and 11 at 5 years, respectively (Fig. 2). There was no significant difference between the Hx group and the cHPR group in survival rates ($p = 0.87$). The survival rate of the pHPR group was significantly lower than that of the Hx group ($p = 0.03$). The survival rate of the pHPR group was lower, but not significantly, than that of the cHPR group ($p = 0.08$).

Next, to clarify the effect on survival of the surgical margin, the survival of the cHPR group was evaluated. The overall cumulative survival rates of patients who were surgical margin-free and patients with a surgical margin of less than 5 mm were 72 and 33 % at 3 years and 63 and 11 % at 5 years, respectively. There were significant differences between the two groups ($p = 0.02$).

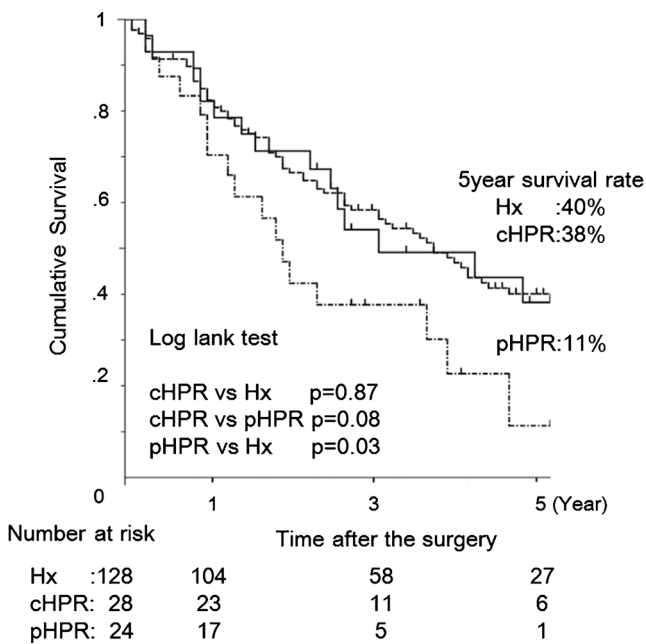


Fig. 2 Post-operative survival in resected patients with hilar and distal cholangiocarcinoma according to surgical procedure. There was no significant difference between the Hx and the cHPR in survival rates ($p = 0.87$). The survival rate of the pHPR group was significantly lower than that of the Hx group ($p = 0.03$). The survival rate of the pHPR group was lower, but not significantly, than that of the cHPR group ($p = 0.08$). Hx hepatectomy, cHPR group patients who underwent hilar plate resection with curative intention, pHPR group patients who underwent hilar plate resection with palliative intention

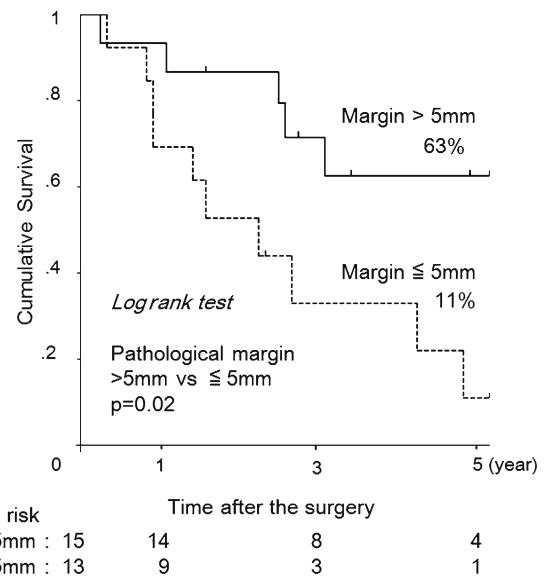


Fig. 3 Post-operative survival in 28 patients of the hilar plate resection with curative intention. Patients with a surgical margin less than 5 mm have significantly worse survival than other patients ($p = 0.02$)

Discussion

With recent improvements in diagnostic and preoperative management, many surgeons have adopted an aggressive approach to hilar malignancies with satisfactory results.²¹⁻²⁵ Our previous report showed that the survival of patients treated with right hepatectomy was significantly higher.¹ This was most likely due to the fact that right hepatectomy enables en bloc resection of the hepatic ductal confluence and its surrounding structures, because the confluence lies on the right side of the hepatic hilum. Ikeyama et al. also showed that, even with a Bismuth type I or II tumour, hilar cholangiocarcinoma of the nodular and infiltrating types should be treated by right hepatectomy.¹³ These reports determined the operative strategy for hilar cholangiocarcinoma. Today, there is no doubt that major hepatectomy is the first-choice treatment for hilar cholangiocarcinoma.

However, several questions remained unsolved. One question was whether these extended procedures would be appropriate for patients with hilar or distal cholangiocarcinoma with hilar spreading. The second question was how to treat hilar cholangiocarcinoma patients with insufficient liver function or with lack of future remnant liver reserve for hepatectomy, as well as those with severe systemic complications. The present results are the key to resolving these questions.

HPR is a unique technique for complete extrahepatic bile duct resection. In this procedure, the extrahepatic bile ducts were resected at the level of the hilar plate. Therefore, we believe that HPR differs from hepatic parenchyma-preserving resections and CHBDR.

Shimada et al. were the first to report a similar procedure in 2002.⁸ They discussed five patients with

hilar cholangiocarcinoma who underwent extended bile duct resection, and they concluded that their procedure was indicated for hilar cholangiocarcinoma in selected cases with a papillary or nodular appearance.

Aydin et al. also reported a similar procedure.²⁶ They discussed 10 cases with hilar cholangiocarcinoma who underwent “high hilar resection”. There were several differences between Aydin’s procedure and our HPR. Their operation required parenchymal resection, including about 1–1.5 cm of the hilar part of segments 5 and 4b; they also partially resected segment 1. HPR was a complete hepatic parenchyma-preserving operation.

These previous studies had only small numbers of patients; therefore, the results of the present 52 cases of HPR for cholangiocarcinoma are the first to show the procedure’s safety. The present data show that there were no significant differences in morbidity and mortality compared with major hepatectomies, even though the present cases of HPR included more patients with severe systemic comorbidities or lower performance status. These results show that HPR for selected patients with extrahepatic cholangiocarcinoma appears to be an appropriate operation given its safety and survival.

The present data showed that the median bile duct lengths from bile duct confluence to hepatic stump resected in this procedure were 17 (5–41) mm on the right side and 16 (10–41) mm on the left side (Table 3). We believe that identification of both the limit of ductal resection and the length of the bile duct resected is extremely important for biliary surgery.¹⁵ Shimada et al. previously reported similar results.⁸ Masunari et al. analysed the length from the confluence of the hepatic duct to the “limit of the bile duct transected with hepatectomy”.¹⁶ They showed that the length from the confluence of the hepatic duct measured about 25 and 30 mm on the right and left sides, respectively. These results showed that the length of the resected hepatic duct that the surgeon could resect without hepatectomy was less than 20 mm.

The present data showed that selected patients in the cHPR group in whom a cancer-free margin of more than 5 mm in any direction (cancer-free) was obtained would have a satisfactory survival result (Fig. 3). This may explain the low survival rate in the pHPR group. The number of cancer-free patients was significantly higher in the pHPR group than in the cHPR group (Table 3).

Even though there were several clinical benefits of HPR, it is our view that the indications for HPR should be restricted. There were several problems with this procedure: anatomical difficulties requiring specialized technique and lengthy operation time; a relatively high cancer-positive rate even in the cHPR group, despite the fact that HPR was done for selected patients as described before; and a survival rate significantly worse in patients with a surgical margin of less than 5 mm than in surgical

margin-free patients. Therefore, further investigations would be needed to determine suitable candidate for performing cHPR.

It is still unknown whether this palliative procedure is indicated in hilar malignancies. The 5-year survival rate was significantly worse in the pHPR group than in the Hx group. Furthermore, this procedure had a relatively high morbidity as a palliative procedure. Nevertheless, some patients would derive clinical benefit such as a stent-free life, and a few patients showed long-term survival. A randomized trial would be almost impossible because of the very limited number of patients who present with this disease.

In conclusion, HPR appears to be safe and feasible for selected patients with cholangiocarcinoma. However, the indications for HPR should be restricted. Considering the clinical benefit and the associated problems, HPR appears to be indicated for tumours with or without superficial cancer spread limited to less than 10 mm above the bile duct confluence.

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