

Surgical Outcomes and Predicting Factors of Curative Resection in Patients with Hilar Cholangiocarcinoma: 10-Year Single-Institution Experience

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Abstract

Background The surgical resection of hilar cholangiocarcinoma is extremely challenging because the tumor is closely related with the complicated hilar structures. We investigated to identify the outcomes for patients who underwent surgical resection and to identify the parameters that influenced radical resection.

Methods From January 2000 to December 2009, 105 patients underwent surgical resection for hilar cholangiocarcinoma. The clinicopathological parameters and surgical outcomes were retrospectively analyzed.

Results There were 15 operative mortalities (14.3%). Seventy-four patients underwent curative resection (70.5%). The median overall survival time for R0, R1, and R2 were 58, 28, and 19 months, respectively. Caudate lobectomy ($p=0.044$; odds ratio [OR], 4.386) and perineural invasion ($p=0.01$; OR, 0.062) were correlated with curative resection. Total bilirubin levels of more than 3 g/dl just before the operation ($p=0.042$; hazard ratio [HR], 2.109) and extent of resection (R1 and 2 vs R0; $p=0.05$; HR, 2.309) were selected as significantly negative factors affecting overall survival on the multivariate analysis. **Conclusions** Caudate lobectomy and neurectomy may be thought of as adjustable territories by the surgeon's efforts to achieve curative resection. R0 resection achieved through those efforts and liver optimization using preoperative biliary drainage may offer the patients a chance of cure.

Keywords Hilar cholangiocarcinoma · Curative resection · Liver optimization

Introduction

Hilar cholangiocarcinoma (CC) is a malignant cancer arising from the biliary confluence. It is the most common of

malignant tumors arising within the biliary tree. Since hilar CC was first described as a sclerosing carcinoma of the major intrahepatic bile ducts in 1957 by Altemerier W. A. et al.¹ and 13 cases were systemically reviewed in 1965 by Klatskin², its incidence has been increasing worldwide.^{3,4}

Among the treatment modality of hilar, CC surgical resection has been known as an only curative modality. Previous studies reported that local excision should be limited to non-invasive papillary cancer (Tis or T1).⁵ Partial hepatectomy with caudate lobectomy is accepted as a standard treatment by many surgeons. As surgical techniques, equipments, and peri-operative management have been developed, aggressively surgical approaches including portal vein and hepatic artery resection^{6,7} offer possible chance of cure within acceptable morbidity and mortality rates. However, the rates of overall resection and resection with curative intent from previous reports vary widely, ranging from 28% to 95% and from 14% to 95%, respectively.⁸ To optimize liver status, preoperative biliary drainage has been performed in many centers, but the benefits of preoperative biliary drainage and the methods of biliary drainage are still debatable.⁹ Five-year

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survival is poor, ranging from 25% to 40% despite those developments.⁸

This study was primarily designed to evaluate the outcomes of patients with hilar CC who underwent surgical resection and secondarily to identify factors influencing curative resection in a single institution.

Patients and Methods

Patients

From January 2000 to December 2009, 105 patients with hilar CC underwent surgical resection with curative intent at Severance Hospital, Yonsei University Health System, Seoul, Korea. We retrospectively reviewed the medical records of these 105 patients. All patients were followed up at 1 month after operation and then every 2–3 months after that. The median follow-up time was 25 months.

Preoperative Evaluations

All patients underwent computer tomography to evaluate the extent of the tumor, the metastasis of lymph nodes, and the presence of distant metastasis and peritoneal seedings. Biliary drainage was performed in patients with hyperbilirubinemia (total bilirubin, >2 mg/dL) or cholangitis symptoms by impending obstructive jaundice (i.e., fever, leukocytosis, and abdominal pain).¹⁰ Biliary drainage was performed in planned remnant liver. Biliary drainage was removed during operation in many cases, except remnant right side liver because of disturbance of liver mobilization and rotation. To evaluate the involvement and anatomy of the bile duct, cholangiography or magnetic resonance cholangiopancreatography were performed. Preoperative cholangitis was defined as leukocytosis and fever, and treated with antibiotics. The unresectability of the disease was defined as definitive imaging findings of distant metastasis or contralobar vascular invasion of liver undergoing resection. Preoperative portal vein embolization (PVE) was performed to prevent liver failure due to small remnant liver volume (<25% of the total volume of the liver) after liver resection.¹¹

Classification of Disease Status

The diseases were classified by the Bismuth–Corlette classification and Memorial Sloan-Kettering Cancer Center (MSKCC) clinical T-stage criteria for hilar CC.

The Extent of Surgical Resection

The surgical resection was performed by four surgeons. The segmental resection without caudate lobectomy was

firstly tried in all patients with Bismuth type I and II cancers, and all surgeons except one performed caudate lobectomy in patients with Bismuth type III and IV cancers.

Pathological Investigations

Macroscopically, the number, tumor diameter, gross type, and distance of the surgical margins of tumors were evaluated. The gross type about the cut surface of the tumor was categorized into the following: mass forming, periductal infiltration (PI), and intraductal growth type, according to the Liver Cancer Study Group of Japan.¹²

The evaluated microscopic characteristics were histologic type, differentiation, presence of vascular invasion and perineural invasion, margin status, and presence of lymph node metastasis. In the seventh edition of pathological tumor node metastasis (pTNM) classification proposed by the American Joint Committee on Cancer (AJCC), the extrahepatic bile duct tumors have been separated into perihilar (proximal) and distal groups and separate staging classifications defined for each. Finally, tumor stage was defined according to the seventh pTNM classification proposed by the AJCC.

Statistical Analysis

Continuous variables were expressed as median (range). Categorical variables were expressed as number (percentage). Survival curves were obtained by the Kaplan–Meier test. Univariate and multivariate analysis of prognostic factors for survival were performed using Cox's proportional hazard model. Factors having a *p* value of less than 0.05 upon univariate analysis were analyzed in multivariate analysis. Factors influencing the radicality were analyzed using logistic regression. Statistical analysis was performed with SPSS v 15.0 software (SPSS Inc., Chicago, IL, USA). Statistical significance was defined as a *p* value of <0.05.

Results

Baseline Characteristics

The baseline characteristics of 105 patients are presented in Table 1. The median age was 63 years (range, 30–82 years), and male gender predominated (*n*=67, 63.8%). The median preoperative total bilirubin levels at diagnosis and just before operation were 5.9 mg/dl (range, 0.5–34.6) and 1.6 mg/dl (range, 0.3–21.8). After liver optimization using biliary drainage, 72 patients (68.6%) achieved less than 3 mg/dl bilirubin level before operation.

Table 1 Baseline characteristics and preoperative management

Variable	<i>n</i> (%) or median (range)
Sex	
Male	67 (63.8)
Female	38 (36.2)
Age, years	63 (30–82)
Maximal total bilirubin, mg/dl	5.9 (1–35)
Preoperative total bilirubin	1.6 (0.3–21.8)
<3	72 (68.6)
≥3	33 (31.4)
CEA, ng/ml	2.29 (0.01–50.92)
CA 19-9, U/ml	149 (0–20000)
≤37	25 (25.8)
>37	72 (74.2)
Bismuth type	
I	12 (11.4)
II	8 (7.6)
IIIA	39 (37.1)
IIIB	18 (17.1)
IV	28 (26.8)
MSKCC T stage	
T1	64 (61)
T2	15 (14.3)
T3	26 (24.7)
Preoperative biliary drainage	
No	21 (20)
Yes	84 (80)
Portal vein embolization	
No	86 (81.9)
Yes	19 (18.1)
Preoperative cholangitis	
No	66 (62.9)
Yes	39 (37.1)
Neoadjuvant treatment	
No	97 (92.4)
Yes	8 (7.6)

CEA carcinoembryonic antigen, CA 19-9 carbohydrate antigen 19-9, MSKCC Memorial Sloan-Kettering Cancer Center

The most common types of Bismuth–Corelette classification and MSKCC clinical T stage were type IIIA ($n=39$, 37.1%) and T1 ($n=64$, 61%), respectively.

Preoperative Management

Eighty-four patients (80%) underwent preoperative biliary drainage. Percutaneous transhepatic biliary drainage was the most common procedure ($n=52$, 61.9%). Thirty-nine patients (37.1%) were treated for cholangitis. Preoperative PVE was performed in 19 patients with less than 25% future remnant liver volume (18.1%) (Table 1).

Operative Procedure

Table 2 shows the operative procedure according to Bismuth–Corelette classification. Three patients were found to be unresectable cases at the time of laparotomy. For a potentially curative resection, portal vein resection was performed in eight patients. The extent of lymph node dissection was decided by the surgeon. Lymph node (LN) dissection was not performed in six patients. Fourteen patients (13.3%) had hepatoduodenal LN dissection (D1). Seventeen patients (16.2%) had D1+ α dissection (D1+ α included D1 LN and LN around Rt. gastric artery, common hepatic artery, and Lt. gastric artery). Sixty-eight (64.8%) patients had para-aortic LN dissection (D2; D1+ α plus dissection of lymphatic chain above and below the left renal vein).

Table 2 Type of operative procedure according to Bismuth classification

Bismuth	Type of operative procedure (no. of caudate lobectomy)	No. of patients
I	Segmental resection of bile duct	10
	Rt. hemihepatectomy (1) ^a	2
II	Segmental resection of bile duct	6
	Rt. hemihepatectomy (0) ^b	1
	Bypass surgery	1
IIIA	Segmental resection of bile duct ^c	4
	Rt. hemihepatectomy (8)	13
	Extended Rt. hemihepatectomy (5)	6
	Rt. trisegmentectomy (12)	13
	Central bisectionectomy (0)	1
	Palliative external drainage	1
IIIB	Diagnostic laparotomy	1
	Rt. trisegmentectomy (1)	1
	Lt. hemihepatectomy (8)	11
IV	Extended Lt. hemihepatectomy (5)	6
	Segmental resection of bile duct ^d	3
	Rt. hemihepatectomy (1)	1
	Extended Rt. hemihepatectomy (4)	5
	Rt. trisegmentectomy (7)	7
	Lt. hemihepatectomy (2)	3
	Extended Lt. hemihepatectomy (8)	8
Lt. trisegmentectomy (1)	1	

Portal vein resection was undergone in eight cases; five cases in IIIA, three cases in IV

^a Rt. hemihepatectomy was performed because of hepatic artery and perineural invasion

^b Rt. hemihepatectomy was performed because of hematoma developed by percutaneous biliary drainage

^c Segmental resection was performed because of small residual volume and co-morbidity in three cases and posterior branch drained into the common bile duct in one case

^d Segmental resection was performed because of extensive bile duct involvement or distant metastasis

Pathologic Findings

Table 3 shows pathologic findings. The PI type was most common gross type ($n=75$, 71.4%). Microvascular invasion and perineural invasion were found in 41 (40.2%) and 70 patients (68.6%), respectively. The depth of tumor invasion was confined to the liver parenchyma in most patients ($n=82$, 78.1%). However, four patients were diagnosed with

invasion into the ipsilateral portal vein, and five patients were diagnosed with T4 lesions because of invasion of the bilateral second-branch bile duct.

Five patients had LN metastasis in the D1 group ($n=14$). The median number of retrieved LNs was 5 (1–15). In the D1+ α group ($n=17$), the median number of retrieved LNs was 13 (2–29), and the median number of metastatic LNs was 4 (1–9). In the D2 group ($n=68$), the median number of retrieved LNs was 22 (4–60), and the median number of metastatic LNs was 2 (1–16). The common sites of metastasis were the hepatoduodenal ligament and LNs along the common hepatic artery. The LN metastasis rate was 43.8% including para-aortic LN metastasis ($n=8$, 7.6%).

Table 3 Pathologic characteristics

Variables		N=105
Gross type		
	Intraductal growth	9 (8.6)
	Mass forming	12 (11.4)
	Periductal infiltration	75 (71.4)
	Mixed type	6 (5.7)
	Not available	3 (2.9)
Tumor differentiation		
	Well differentiation	18 (18.2)
	Moderate differentiation	66 (66.7)
	Poor differentiation	15 (15.1)
Microvessel invasion		
	No	61 (59.8)
	Yes	41 (40.2)
Perineural invasion		
	No	32 (31.4)
	Yes	43 (42.1)
	Frequent	27 (26.5)
Lymph node metastasis ^a		
	Dx	6
	D1	No 9 (64.3) Yes 5 (35.7)
	D1+ α	No 11 (64.7) Yes 6 (35.3)
	D2	No 33 (48.5) Yes 35 (51.5)
7th AJCC TNM stage		
	I	14 (13.3)
	II	35 (33.3)
	IIIA	8 (7.6)
	IIIB	30 (28.6)
	IVA	7 (6.7)
	IVB	11 (10.5)

IG intraductal growth, PI periductal infiltration, MF mass forming, AJCC T American Joint Committee on Cancer Tumor

^a Dx indicated no dissection of lymph node; D1 is only dissection of hepatoduodenal lymph nodes; D1+ α is D1 plus dissection around Rt. gastric artery, common hepatic artery, and Lt. gastric artery; D2 is D1+ α plus para-aortic lymphadenectomy

Curability

Seventy-four (70.5%) patients underwent potentially curative resection. Nine (8.6%) patients underwent palliative surgery with grossly residual cancer (R2). Among nine patients who underwent palliative surgery, three patients had unresectable disease because of peritoneal seeding and distant metastasis. Six patients underwent R2 resection because further resection was impossible due to small remnant liver volume and family refused extensive resection due to old age and co-morbidities. Twenty-two (21%) patients underwent R1 resection showing positive margin on pathologic report. Table 4 shows the results of univariate and multivariate analyses of factors affecting curative resection. In univariate analysis, bile duct resection with liver resection, caudate lobectomy, and perineural invasion were significantly correlated with curative resection. However, multivariate analysis demonstrated that caudate lobectomy ($p=0.044$, odds ratio [OR]=4.386, 95% confidence interval [CI]=1.041–18.476) was positively correlated and perineural invasion ($p=0.01$, OR=0.062, 95% CI=0.008–0.511) was negatively correlated with curative resection.

Survival Analysis

Operative mortality developed in 15 cases (14.3%). The overall 1-, 3-, and 5-year survival rates were 88.2%, 49.1%, and 34.1%, respectively. The median survival time was 36 months (Fig. 1a).

Overall Survival (OS) According to the Radicality

Comparison of OS according to the radicality is shown in Fig. 1b. The median survival time of R0 resection was 58 months, which was higher than those of R1 (28 months, $P=0.062$) and R2 resections (19 months, $P=0.001$). However, survival of R0 and R1 resection did not show significant difference.

Table 4 Univariate and multivariate analysis of factors associated with curative resection

Variables	Univariate analysis					Multivariate analysis		
	R0	R1	P value	OR	95% CI	P value	OR	95% CI
PVE								
No	58 (75.3%)	19 (24.7%)	0.414	1.747	0.459–6.656			
Yes	16 (84.2%)	3 (15.8%)						
Operation type								
Without liver resection	12 (60%)	8 (40%)	0.047	2.952	1.017–8.574	0.914	1.091	0.224–5.315
With liver resection	62 (81.6%)	14 (18.4%)						
Caudate lobectomy								
No	21 (60.0%)	13 (40.0%)	0.01	3.646	1.356–9.799	0.044	4.386	1.041–18.476
Yes	53 (81.6%)	9 (18.4%)						
Portal vein resection								
No	69 (78.4%)	19 (21.6%)	0.315	0.459	0.1–2.096			
Yes	5 (62.5%)	3 (37.5%)						
Perineural invasion								
No	28 (96.6%)	1 (3.4%)	0.015	0.078	0.01–0.614	0.01	0.062	0.008–0.511
Yes	46 (68.7%)	21 (31.3%)						
Biliary drainage								
No	16 (88.9%)	2 (11.1%)	0.201	0.363	0.077–1.717			
Yes	58 (74.4%)	20 (25.6%)						
Neoadjuvant treatment^a								
No	62 (75%)	22 (25%)	0.999					
Yes	8 (100%)	0 (0%)						

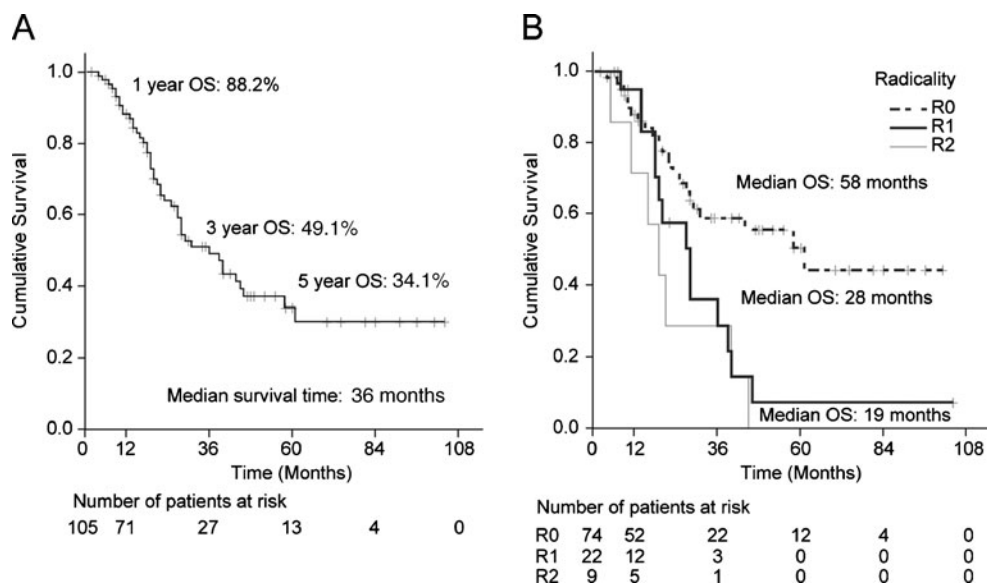
^a Odds ratio can't calculated because neoadjuvant treatment group shows all R0 resection
OR, odds ratio; CI, confidence interval; PVE, portal vein embolization

Factors Affecting the Operative Mortality

PVE ($p=0.024$, OR=3.949, 95% CI=1.203–12.96), operative time ($p=0.01$, OR=1.004, 95% CI=1.001–1.007), liver resection more than hemihepatectomy ($p=0.007$, OR=

6.286, 95% CI=1.655–23.868), and estimated blood loss more than 2,000 ml ($p=0.002$, OR=7.333, 95% CI=2.219–25.26) were negatively correlated with operative mortality in univariate analysis. However, multivariate analysis could not reveal an independent prognostic factor. In

Fig. 1 The overall survival in patients with hilar cholangiocarcinoma. **a** The overall 1-, 3-, and 5-year survival rates were 88.2%, 49.1%, and 34.1%, respectively. The median survival time was 36 months. **b** The overall survival according to the radicality. The median survival time of R0 resection was 58 months and higher than that of R1 ($p=0.062$) and R2 resection ($p=0.001$)



non-PVE group ($n=86$), presence of preoperative cholangitis ($p=0.032$, $OR=6.732$, $95\% CI=1.18-38.405$) was found as a negatively independent prognostic factor for operative mortality in univariate and multivariate analyses. In PVE group ($n=19$), independent prognostic factor was not found because of the small number of patients.

However, the estimated blood loss ($p<0.001$), operation time ($p<0.001$), and the number of patients underwent liver resection more than hemihepatectomy ($p=0.005$) were all significantly higher in PVE group than those in non-PVE group.

Univariate and Multivariate Analysis for OS

Preoperative higher total bilirubin levels, no liver resection, no caudate lobectomy, R1 and 2 resections, and AJCC TNM stage IVB were negatively correlated with OS upon univariate analysis. Multivariate analysis revealed that preoperative total

bilirubin level (higher than 3 g/dl) and radicality (R1 and 2 vs R0) were found to be independent factors negatively affecting OS (Table 5).

Discussion

Surgical resection of the hilar CC offers the only chance of a potential cure. However, this tumor was frequently considered to be an unresectable disease because of its locally advanced status such as opposite vascular invasion of the tumor involved lobe. The overall survival is very low in patients who undergo only palliative treatment.

Because other treatment modalities have showed low efficacy and feasibility, surgical resection has been adopted as an only curable treatment modality by most surgeons. As surgical equipment, techniques, and perioperative management have developed, the extent and indications for

Table 5 Univariate And multivariate analysis for overall survival

Variables		Univariate analysis			Multivariate analysis		
		P	HR	95% CI	P	HR	95% CI
CA-19-9, U/ml	>37 vs ≤37	0.551	1.235	0.617–2.471			
Preop. total bilirubin	≥3 vs <3	0.012	2.416	1.216–4.803	0.042	2.109	1.026–4.335
Preop. biliary drainage	Yes vs No	0.316	1.454	0.699–3.026			
PVE	Yes vs No	0.982	0.99	0.419–2.341			
MSKCC clinical T stage	T2 vs T1	0.065	2.094	0.955–4.593			
	T3 vs T1	0.372	0.651	0.253–1.671			
Liver resection	No vs Yes	0.031	1.948	1.063–3.571	0.907	0.946	0.375–2.391
Caudate lobectomy	No vs Yes	0.006	2.306	1.277–4.163	0.318	1.669	0.611–4.556
Portal vein resection	No vs Yes	0.986	1.011	0.312–3.275			
LN dissection ^a	Dx vs D2	0.618	1.237	0.536–2.854			
	D1 vs D2	0.586	1.247	0.564–2.758			
	D1 + α vs D2	0.206	1.977	0.688–5.68			
Radicality	R1 & 2 vs R0	<0.001	2.994	1.642–5.46	0.05	2.09	1.002–4.361
Tumor differentiation	MD vs WD	0.958	0.98	0.47–2.043			
	PD vs WD	0.306	1.699	0.615–4.695			
MVI	Yes vs No	0.784	1.097	0.567–2.124			
PNI	Yes vs No	0.129	1.673	0.86–3.253			
LN metastasis	Yes vs No	0.368	1.328	0.716–2.462			
Seventh AJCC TNM stage	II vs I	0.47	1.424	0.546–3.715	0.492	1.445	0.506–4.128
	IIIA vs I	0.365	2.119	0.418–10.743	0.316	2.345	0.444–12.396
	IIIB vs I	0.468	1.44	0.537–3.86	0.526	1.419	0.481–4.191
	IVA vs I	0.248	2.283	0.562–9.272	0.55	1.583	0.351–7.143
	IVB vs I	0.042	3.021	1.04–8.776	0.28	1.869	0.601–5.814

HR hazard ratio, CI confidence interval, CA 19-9 carbohydrate antigen, preop. preoperative, PVE portal vein embolization, LN lymph node, WD well differentiation, MD moderate differentiation, PD poor differentiation, MVI microvascular invasion, PNI perineural invasion, MSKCC Memorial Sloan-Kettering Cancer Center AJCC TNM American Joint Committee on Cancer Tumor–Node–Metastasis

^a Dx indicated no dissection of lymph node; D1 is only dissection of hepatoduodenal lymph node; D1+α is D1 plus dissection around Rt. gastric artery, common hepatic artery, and Lt. gastric artery; D2 is N1+α plus para-aortic lymphadenectomy

resection have been expanded. Only bile duct excision did not obtain a negative resection margin in most cases and did not achieve good surgical outcomes.¹³ Nowadays, most centers perform liver resection in addition to bile duct resection, and this combined procedure has yielded improved R0 resection and survival rates.^{14,15} Additionally, combined vascular resection is performed in some centers.^{6,7,16} These studies reported that portal vein resection was a poor prognostic factor, but the portal vein resection group had better long-term survival than did the non-resection group. In our study, portal vein resection did not show statistical significance. However, the significance of portal vein involvement was shown in the MSKCC clinical T stage and seventh AJCC stage. Stages including portal vein invasion showed poor prognosis as prognosis in stage IV disease. Portal vein resection was performed in only eight patients. To identify the role of portal vein resection, many more cases will be needed to be accumulated and studied.

R0 resection is very significant factor for prolonging survival. Because of the contiguity between the caudate lobe and the hilar bile duct, caudate lobectomy has been emphasized and has shown a decrease in recurrence and an improvement in survival.^{17,18} Our data showed that caudate lobectomy was an independent prognostic factor for radicality. Perineural invasion and LN metastasis were frequently reported to be independent prognostic factors, and perineural invasion was an independent prognostic factor in our data,¹⁹ but the extent of LN dissection and the role of neurectomy were debatable. The extent of LN dissection and location of LN metastasis did not show a significant correlation with survival in our data. Our hospital policy was D2 dissection including neurectomy. However, in order to prove the role of this concept, it would be necessary to approve pathological neurectomy and conduct a prospective large-scale study. Our results showed a similar result to previous reports. Nagoya group emphasized the liver resection in types I and II cholangiocarcinoma.²⁰ However, our data showed high frequency of segmental resection in types I and II cholangiocarcinoma. This may be a reason that our study did not show improved results. Aggressive liver resection in types I and II cholangiocarcinoma may improve the results.

The role of preoperative biliary drainage to decompress biliary obstruction is controversial,^{9,21} but a Japanese study group recommended preoperative biliary drainage in patients with cholangitis or who were scheduled to undergo extended hepatectomy because hyperbilirubinemia was associated with dysfunction of the liver, kidneys, and immune system, and an increase in gut mucosa permeability.²² Some recent studies have reported that low serum bilirubin levels after biliary drainage were significantly correlated with lower mortality.^{23,24} In our study, high preoperative bilirubin level was a significant independent factor of survival.

Preoperative biliary drainage was performed in 84 patients (80%), but hyperbilirubinemia was found in 33 patients (31.4%), and 39 patients (37.1%) experienced cholangitis before the operation. This was thought to be a reason for the high operative mortality in our data.

To overcome liver failure caused by small remnant liver volume after extended liver resection, many centers perform PVE.^{25,26} After PVE ranging from 54% to 100%, mortality rate ranging from 0% to 1.7% was reported.^{27,28} However, Hidalgo et al.²⁹ reported a comparable mortality rate in the absence of PVE. In our study, PVE was found as a risk factor of operative mortality in univariate analysis. However, multivariate analysis showed no independent factor. The estimated blood loss and liver resection more than hemihepatectomy showed a marginal significance and were higher in PVE group than those in non-PVE group. To reduce operative mortality, the efforts to perform tailored liver resection saving liver volume and minimize the blood loss should be needed in PVE group. Moreover, some studies reported that colorectal liver metastases progressed after PVE. Therefore, it might be thought that careful attention was necessary when performing PVE.^{30,31}

Conclusion

Although the mortality rate of this study was as high as 14.7%, caudate lobectomy offers a chance of potentially curative resection and improvement of the survival rate. To decompress biliary obstructions, efforts to minimize blood loss and careful selection of patients who could most benefit from an aggressive surgery such as vascular resection may be performed to allow for aggressive resection and reduce operative mortality.

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