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(1) TITLE:

Outcome of surgical treatment of hilar cholangiocarcinoma: a special reference to postoperative morbidity and mortality

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Abstract

Background/Purpose

Radical resection for hilar cholangiocarcinoma is still associated with significant morbidity and mortality. The aim of this study was to analyze short-term surgical outcomes and to validate our strategies, including preoperative management and selection of operative procedure.

Methods

We surgically treated 146 consecutive patients with hilar cholangiocarcinoma with a management strategy consisting of preoperative biliary drainage, portal vein embolization, and selection of operative procedure based on tumor extension and hepatic reserve. Major hepatectomy was conducted in 126 patients, and caudate lobectomy or hilar bile duct resection in 20 patients.

Results

The overall 5-year survival rate was 35.5%, with overall in-hospital mortality and morbidity rates of 3.4% and 44%, respectively. Hyperbilirubinemia (total bilirubin >5 mg/dL, persisted for>7 postoperative days) and liver abscess were the most frequent complications. Five among 9 patients with liver failure (total bilirubin >10 mg/dL) encountered in-hospital mortality. Four out of 5 mortality patients had suffered circulatory impairment of the remnant liver due to other complications. Multivariate analysis revealed that operative time is a single independent significant predictive factor (odds ratio, 1.005; 95% confidence interval, 1.000–1.010, P=0.04) for postoperative complications.

Conclusions

Aggressive resection for hilar cholangiocarcinoma, performed in accordance with strict management strategy, achieved acceptable low mortality. Prolonged operative time was a risk for morbidity following hepatobiliary resection.

Introduction

Surgical treatment of hilar cholangiocarcinoma still remains a challenge for the surgeon, because it usually requires several modalities to obtain detailed information about cancer spread as well as a complicated operative procedure. During the last decade, the resection rate of hilar cholangiocarcinoma has been increasing, due to the use of major hepatectomy [1]. Recently, low postoperative mortality (< 5%) following hepatobiliary resection has been reported from high-volume centers [2-8]. However, morbidity rates have been still remained in a high range (> 40%) even in reports from the institutes where many procedures are performed [2-8].

Most previous studies on the prognosis of hilar cholangiocarcinoma have analyzed various clinicopathologic variables, focusing on their influence on long-term survival. Factors affecting the morbidity or mortality associated with surgical treatment of hilar cholangiocarcinoma, especially in hepatobiliary resection, still remain unclear. Although only curative resection could offer long-term survival in cases of hilar cholangiocarcinoma, the surgical procedures should be safe and reliable. Therefore, it is necessary to perform detailed evaluations of postoperative short-term results, as well as to analyze long-term survival of patients with hilar cholangiocarcinoma.

We evaluated the surgical outcome of our consecutive surgically treated hilar cholangiocarcinoma patients, with special attention to complications following hepatobiliary resection, in order to validate our strategies for preoperative management and selection of operative procedures.

Patients and Methods

146 patients with hilar cholangiocarcinoma, including 16 patients (11%) of intrahepatic cholangiocarcinoma (ICC) involving the hepatic hilus, who underwent surgery with curative intent between January 2001 and December 2008, were included in this study. There were 31 women and 115 men, with a median age of 68.5 years (range, 40-82 years). The patients were treated in accordance with our departmental guidelines, which were established in 1999 for patients with hilar cholangiocarcinoma [2].

The lesions were classified according to the Bismuth classification [9] as follows: type I, no obstruction of the confluence of the right and left hepatic ducts, in 21 patients (14%); type II, limited obstruction to the confluence, in 35 patients (24%); type IIIa or IIIb, extended obstruction to the right or left ductal ramifications, in 26 (18%) and 34 patients (23%), respectively; and type IV, extended bilateral obstruction, in 30 patients (21%).

Pathologic staging of the diseases was conducted in accordance with the criteria established in the 6th edition of the International Union Against Cancer.

Preoperative management of the patients and selection of operative procedure

Preoperative biliary decompression was performed to reduce serum bilirubin concentration below 2 mg/dL for all patients with jaundice and to control segmental cholangitis. Previously, single or multiple percutaneous transhepatic biliary drainage (PTBD) was used for drainage. Since 2005, single or double endoscopic naso-biliary drainage (ENBD) of future remnant liver was adopted as an initial drainage. Second ENBD catheters were placed to drain biliary trees in the future remnant liver that were not decompressed by the first catheter, or to control of cholangitis. Alternatively, PTBD was employed when drainage by ENBD was not effective or a third catheter was required. To evaluate longitudinal cancer spread, precise cholangiography was performed via the indwelled catheter. When the lesion was diagnosed as a papillary or nodular tumor, intraductal ultrasonography (IDUS), cholangioscopy, and biopsy were performed through the route of PTBD or papilla of Vater, using endoscopy to diagnose extensive intraepithelial spread of the tumor [10]. 118 patients with obstructive jaundice (median serum total bilirubin concentration of 7.9 mg/dL; range, 2.1–29.3 mg/dL) underwent preoperative biliary drainage. Eleven patients without jaundice also received biliary drainage of the future remnant liver, for the purpose of preventing jaundice and recovering portal flow. Two other patients without jaundice underwent PDBD to perform percutaneous cholangioscopy (PTCS). In the remaining 15 patients, no biliary drainage was placed before the operation.

Helical computed tomography (CT), replaced in recent years by multidetector-row CT, and if possible IDUS were performed to diagnose extraductal

spread of the tumor, especially to detect vascular invasion.

Preoperative portal embolization (PE) of the liver to be resected was performed when right trisegmentectomy, right hepatectomy or left trisegmentectomy were planned. When right hepatectomy or left trisegmentectomy was intended, limited PE was performed for the patients whose indocyanine green retention rate at 15 minutes (ICG R15) after relief of jaundice was no more than 15%. At 2 weeks after PE, the patients with ICG R15 ≤ 20% were judged as candidates for right hepatectomy or left trisegmentectomy. Similarly, when patients were slated for performing right trisegmentectomy, PE was performed for only the patients with ICG R15 ≤10%, and surgery was conducted for the patients with ICG R15 ≤ 15% at 2 weeks after PE. Patients with lesions that mainly invaded the left hepatic duct, and did not infiltrate beyond the anterior and posterior bifurcation of the right hepatic duct, underwent left hepatectomy at ICG R15 ≤ ~20%. In patients for whom future remnant hepatic reserves were not sufficient for major hepatectomy, caudate lobectomy or hilar resection including the hilar and cystic plate [11] was planned only when the lesion could be completely resected by the procedure. Overall, right-side hepatectomy, left-side hepatectomy, caudate lobectomy, and hilar bile duct resection were conducted in 78, 48, 2, and 18 patients, respectively (Table 1).

Surgical technique

Systematic lymphadenectomy of the hepatoduodenal ligament, including the nodes around the head of the pancreas, was routinely performed. This procedure is accomplished by skeletonizing the portal vein and hepatic artery. The portal vein resection and reconstruction with macroscopic infiltration by the tumor were completed before hepatic parenchymal dissection and hepatic ductal division [12, 13]. Since 2005, if the preoperative image diagnosis showed a tumor neighboring the portal bifurcation, the bifurcation was preemptively resected using a “no-touch” technique [14]. Hepatic arteries that were determined to have cancer invasion were resected *en bloc* with the bile duct and reconstructed by direct suture or *in situ* grafting of the right epigastric artery, using a microscopic technique. When infiltration of tumor proceeded too peripherally to allow reconstruction, arterio-portal shunting was performed [15].

The concomitant resection of the portal vein and hepatic artery were performed in 65 (45%) and 20 (14%) patients, respectively.

Liver transection was performed using the forceps clamp crushing method, during both hepatic artery and portal vein clamping, for 15 minutes with 5 minutes intervals. In every patient who underwent hemihepatectomy or more extensive resection, *en bloc* resection of the caudate lobe and extrahepatic bile duct was conducted. Intraoperative frozen section diagnosis of the stump of the hepatic duct was not performed because the ducts were always divided at the separating limit from the vasculature [16]. Biliary tract reconstruction was made by bilio-enterostomy using a Roux-en-Y jejunal limb, and external biliary stents were placed throughout every anastomosis.

Pancreatoduodenectomy was performed for the patients with evidence of an invasive lesion in the intrapancreatic bile duct, diagnosed by preoperative examinations or intraoperative frozen section. Reconstruction during pancreatoduodenectomy was conducted by end-to-side pancreaticojejunostomy using a modified Child's method. When the *in situ* lesion in the stump of the intrapancreatic duct was proven by intraoperative frozen section, the remnant entire intrapancreatic bile duct was resected with preservation of the pancreatic parenchyma. Pancreatoduodenectomy concomitant with major hepatectomy (hepatopancreatoduodenectomy) was performed in 20 patients. The combination of vascular resection and pancreatoduodenectomy with each type of hepatectomy were listed on Table 1.

Definition of Morbidity and Mortality

Operative mortality included all in-hospital deaths. Regarding operative morbidity, all postoperative complications that lengthened the hospital stay were considered. Postoperative hepatic insufficiency was defined by a rise in serum total bilirubin concentration as follows: total bilirubin level more than 10.0 mg/dL during the postoperative period was defined as liver failure; levels above 5 mg/dL that persisted beyond 7 postoperative days were defined as hyperbilirubinemia. Postoperative incidents that resulted in organ failure or required another surgery or interventional radiology were treated as complication. Conversely, minor

complications such as pleural effusion (even if thoracic drainage was necessitated), wound infection, clinically silent pancreatic fistula, and bile leakage from the transection surface of the liver healing spontaneously without radiological intervention and never prolonged the hospital stay were not counted as morbidity.

Statistics

Results are expressed as median values, with the respective ranges indicated within parentheses. The relationship between the postoperative morbidity and the dichotomous variables was evaluated by Chi-square test, or Fisher's exact test. Statistical significance of continuous variables was determined by the Mann-Whitney *U* test. A multivariate logistic regression analysis was performed to identify factors associated with postoperative complications. The survival curve was generated by the Kaplan-Meier method. Results were considered significant when the *P* values were less than 0.05. The statistical analyses were performed using statistical analysis software StatView^{TM}.

Results

The patient characteristics and perioperative variables stratified into 2 groups of with or without major hepatectomy; these are summarized in Table 2. Most of the patients without major hepatectomy were classified as stage I and II and were significantly different from those with major hepatectomy. ICG R15 and incidence of preoperative cholangitis were higher in patients without major hepatic resection. The operative time of the patients in the major hepatectomy group was shorter than for those without major hepatectomy, despite the high frequency of combined portal reconstruction. The R0 resection rate for patients without major hepatectomy (90%) was similar to the rate for patients with major hepatectomy (87%). The overall median length of a postoperative hospital stay was 38 days (range: 16–226 days) in all: 38 days (range: 16–159 days) in patients who underwent major hepatectomy, and 35 days (range, 17–226 days) in those who underwent caudate lobectomy or hilar bile duct resection (Table 2),

Overall morbidity rate was 44.5%: 41.3% for patients with major hepatectomy and 45% for those without major hepatectomy. In-hospital mortality was encountered in 5 of 146 patients (3.4%). All patients with mortality had undergone major hepatectomy; thus, the mortality rate in major hepatectomy group was 3.9% (Table 3). Twenty patients (15.9%) suffered hepatic insufficiency: 11 (8.7%) of these had hyperbilirubinemia and 9 (7.2%) had liver failure. Although hyperbilirubinemia was one of the most frequent complications, the patients did not encounter any lethal events, and were discharged after a median of 43 (33-103) days of hospitalization. In contrast, among 9 liver failure patients, 5 died in the hospital. In 4 of these 5 cases, liver failure was induced by hepatic circulatory impairment: 2 patients underwent transarterial embolization of the hepatic artery for hemorrhage from pseudoaneurysm associated with pancreatic juice leakage; one patient suffered postoperative flow disturbance of reconstructed right portal vein due to distortion; and one patient suffered liver abscess followed by severe DIC that caused massive gastrointestinal hemorrhage and shock. Only one patient who underwent right trisegmentectomy with portal reconstruction encountered liver failure without any causative events and died during the hospitalization. The remaining 4 patients with liver failure recovered and could return directly to their homes after a median hospitalization of 111 (34-149) days. All patients who suffered liver or intra-abdominal abscess, except the patient with DIC, were treated with radiological interventions and recovered without any surgery. Relaparotomies in postoperative acute periods were required in 3 patients: 2 patients with intra-abdominal bleeding, and the aforementioned patient with insufficient flow in the reconstructed portal vein. In one patient who underwent hepatopancreatoduodenectomy, a relaparotomy was performed 4 months after the initial surgery because the spontaneous pancreaticocutaneous fistula had been persistent and required fistulo-jejunostomy.

To evaluate the factors influencing the postoperative complications following hepatobiliary resection, we performed univariate analysis on the characteristics and perioperative variables from patients who underwent major hepatectomy (Table 4). Operative time of the patients with complication was significantly longer (P=0.006) than that of the patients without. As postoperative variables, maximum total bilirubin level during the postoperative period was

significantly elevated in patients with complications. We also performed a multivariate analysis, selecting 3 each of preoperative and operative variables for which *P*-value were less than 0.2 in univariate analysis, and using a logistic regression model. This analysis could identify prolonged operative time as the only independent predictive factor for postoperative complications (odds ratio, 1.005; 95% confidence interval, 1.000–1.010, P =0.04).

The overall 1-, 3-, and 5-year survival rates were 81.4%, 52.9%, and 35.5%, respectively, with a median survival time of 39 months (Fig. 1). Forty-one patients died of tumor recurrence, 7 patients of other disease, and the remaining 93 patients are now alive either with recurrence (n =8) or without any sign of recurrence (n= 85).

Discussion

In the treatment of hilar cholangiocarcinoma, several studies have been advocating *en bloc* major hepatectomy to purchase the negative histologic margins and to improve the survival [2, 3, 6, 17-19]. However, extended liver resection for hilar cholangiocarcinoma still remains a challenge for the surgeon, because the liver has been injured by long-term jaundice. Major hepatic resection in this setting is associated with significant risk for postoperative hepatic insufficiency and other complications. Recent retrospective reports concerning large series of surgically treated hilar cholangiocarcinoma reveal mortality rates between 0 and 7.5% [2-8]. The remarkable improvement in mortality can probably be attributed to advanced surgical techniques and decreases in postoperative hepatic failure, the most frequent cause of in-hospital death following major hepatectomy. These decreases can in turn be attributed to perioperative cautious management, e.g. reduction of jaundice for recovering of damaged liver function [20], early treatment of segmental cholangitis [21], and use of preoperative portal embolization [22].

Similarly, in our institute, a management strategy for hilar cholangiocarcinoma including preoperative biliary drainage and portal embolization had been employed for prospective cohort study [2]. We also determined the indication of portal embolization based on the value of ICG R15 after reducing jaundice. Moreover, the indication of right-sided hepatectomy or left trisegmentectomy was strictly defined by the value of ICG R15, 2 or more weeks after PE. The resulting

mortality — 3.4 % in all patients and 3.9% in major hepatectomy patients — means our strategy was successful in managing the patients and selecting appropriate operative procedures.

Contrary to the remarkable improvement of mortality, morbidity rates of 14-62.3% still remains in a high range [2-8]. Major hepatectomy with vascular resection and/or pancreatic resection is still considered to be high-risk surgery. Indeed, in this study, all liver failure induced disturbed circulation of the remnant liver, such as embolization of the hepatic artery for hemorrhage from pseudoaneurysm, led the patients to in-hospital death. Thus, even though the remnant hepatic reserve is enough for the patient to survive, co-existence of complications could pose a risk of liver failure. Therefore, more meticulous intraoperative technique and postoperative care is essential in order to avoid postoperative mortality leading to impairment of hepatic circulation. Especially for postoperative infectious complications, more precise assessment for precautions against biliary infection might be effective [23]. Although hyperbilirubinemia (defined by the maximum level of serum total bilirubin concentration beyond the 7th day after the operation) was not proved as a lethal situation in this study, the condition is still important because liver failure could be easily induced by other complications.

By analyzing the factors influencing the occurrence of postoperative complications, prolonged operative time was revealed as the only independent factor in this study. While the odds ratio of the factor is low, the median operative time of the patients who suffered complications was significantly longer than that of patients who did not (607 vs. 667 ml; P=0.006). Other reports have demonstrated that a high morbidity rate is significantly related to the opportunities for perioperative homologous transfusion [5], and occurrence of preoperative cholangitis or cholecystitis [3] following hepatobiliary resection. However, these trends were not evident in the present study. Prolonged surgical time was also associated with high morbidity rate in a report that analyzed data from patients who underwent hepatectomy primarily for hepatocellular carcinoma, rather than cholangiocarcinoma as in this study [24]. Although the warm ischemic time during dissection of the hepatic parenchyma or reconstruction of the hepatic vessels could not be collected in this study, we speculate that the prolonged surgical time might be associated with the ischemic time of the

remnant liver, and contribute to the postoperative morbidity. Consequently, surgeons should take all measures to shorten the total ischemic time during hepatobiliary resection.

The role of preoperative biliary drainage is still under debate [25]. We believe that preoperative biliary decompression as well as portal embolization for patients who underwent major hepatectomy play important roles in the prevention of postoperative mortality [2, 3]. Previously, PTBD with multiple drainage catheters was employed for biliary drainage. In recent years, the introduction of preoperative portal vein embolization followed by extended liver resection and advancement of endoscopic technique and equipment have changed preoperative drainage strategies [26, 27]. In our institute, endoscopic naso-biliary drainage has been performed since 2005 as a first choice for biliary decompression for future remnant hepatic lobes. In comparison between the patients with and without postoperative hepatic insufficiency, endoscopic drainage including diagnostic usage without drainage was revealed to be more advantageous than PTBD (data was not shown). The endoscopic transduodenal approach might be less invasive and contribute to postoperative fair hepatic function. However, in this study, as the strategy for biliary drainage had changed historically, the real effect of the endoscopic approach should be re-evaluated in larger patient's series.

Although positive ductal margin is one of the negative prognostic factors of postoperative survival [28], the histological curability rate reported in recent papers with low mortality ranged from 61 to 80% [3, 4, 6-8]. Concerning the curability rate, 90% of patients in this study without major hepatectomy (18 out of 20 patients) are comparable with those with major hepatectomy. Hilar bile duct resection or caudate lobectomy with extrahepatic bile duct resection could be an important option for patients with poor hepatic reserve.

Conclusions

Despite the relatively high morbidity, aggressive resection for hilar cholangiocarcinoma, when performed in accordance with strict management strategy, achieved acceptable low mortality. To attain even better short-term outcomes, it will be necessary to perform further refinements of intraoperative and postoperative

management, such as decreasing operative time and reducing complications related to operative procedures.

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Figure legends

Figure1: The survival curve for the 146 study patients.

The overall 1-, 3-, and 5-year survival rates were 81.4%, 52.9%, and 35.5%, respectively.

Table 1. Surgical procedures performed

	with PVR (n=65)	with AR (n=20)	with PD (n=24)
Right hepatectomy (n=69)	40	3	16
Right trisegmentectomy (n=9)	4	1	1
Left hepatectomy (n=43)	18	10	3
Left trisegmentectomy (n=5)	2	1	0
Caudate lobectomy (n=2)	0	0	1
Hilar bile duct resection (n=18)	1	5	3

PVR: Combined resection of the portal vein, AR: Combined resection of the hepatic artery,

PD: pancreatoduodenectomy

Table 2. Comparison of characteristics and perioperative variables of the patients according to types of operation

Characteristics and variables	Total (n=146)	With major hepatectomy (n=126)	Without major hepatectomy (n=20)	*p*
Age (range) (yr)	68.5 (40-82)	67.5 (40-79)	71.5 (57-82)	0.03
Gender (male/ female)	115 / 31	97 /29	18 / 2	0.08
Disease (HC/ ICC)	130 / 16	110 / 16	20 / 0	0.13
Bismuth's classification (I/ II/ IIIa/ IIIb/ IV)	21 / 35 / 26 / 34 / 30	12/26/24/34/30	9/9/2/0/0	<0.0001*
Preoperative jaundice present	118	100	18	0.37
Preoperative maximum serum T.Bil (range) (mg/dL)	5.8 (0.2-29.3)	7.6 (0.2-29.3)	5.5 (1.7-25.0)	0.38
Preoperative biliary drainage present	131	112	19	0.69
Preoperative cholangitis present	27	20	7	0.04
Biliary access (PTBD/ Endoscopy)	60 / 86	52 / 74	8 / 12	0.91
Portal vein embolization performed	66	66	-	-
ICG R15 (range) (%)	11.4 (3.4-25.8)	10.7 (3.4-20.4)	16.6 (10.0-25.8)	0.001
Operative time (range)(min)	633 (385-1010)	629 (385-979)	731 (387-1010)	0.02
Blood loss (range)(mL)	1500 (270-5840)	1550 (270-5840)	1260 (540-3170)	0.02
Combined arterial resection performed	20	15	5	0.11
Combined portal vein resection performed	65	64	1	0.0001
RBC transfusion performed	27	26	1	0.12
Achieved negative surgical margins	127	109	18	0.66
Stage (UICC) (I/ II/ III/IV)	53 / 67 / 20 / 6	40 / 61 / 20 / 5	13 / 6/ 0 / 1	0.04**
Postoperative hospital stay (range) (days)	38 (16-226)	38 (16-159)	35 (17-226)	0.3

HC: Hilar cholangiocarcinoma, ICC: Intrahepatic cholangiocarcinoma, PTBD: Percutaneous transhepatic biliary drainage, ICG R15:indocyanine green retention rate at 15 minutes, *: Bismuth's type I&II versus III & IV, **: Stage I&II versus III & IV

Table 3. Comparison of postoprative complications according to types of operation

	Total	With major hepatectomy n=126	Without major hepatectomy * n=20
No. of patients with morbidity	65 (44.5%)	56 (41.3%)	9 (45.0%)
Frequency of events			
Hyperbilirubinemia	11	11	0
Liver abscess	11	10	1
Liver failure	9	9	0
Bile leakage	8	7	1
Intra-abdominal abscess	8	6	2
Pancreatic fisutula	8	6	2
Pancreatojejunostomy insufficiency	8	6	2
Intra-abdominal bleeding	7	5	2
Resiratory distress	5	3	2
Sepsis	5	3	2
Hepaticojejunostomy insufficiency	3	3	0
Ileus	3	3	0
Gstrointestinal bleeding	3	2	1
Cholangitis	2	2	0
Portal hypertension	2	2	0
Occlusion of reconstructed portal vein	1	1	0
Outflow disturbance of hepatic vein	1	1	0
Abdominal wall dehiscence	1	1	0
Relaparotomy performed	4	4	0
No. of patients with mortality	5 (3.4%)	5 (3.9%)	0

*: Patients who underwent Caudate lobectomy or hilar bile duct resection

Table 4. Comparison of characteristics and perioperative variables in patients with major hepatectomies based on occurrence of postoperative complications

Characteristics and variables	Without complication n=70	With complication n=56	*P*
Age (range) (yr)	67.0 (40-79)	69.0 (48-76)	0.62
Gender (male/ female)	51 / 19	46 / 10	0.22
Disease (HC/ ICC)	59 / 11	51 / 5	0.26
Bismuth's classification (I, II / III, IV)	53 / 17	35 / 21	0.11
Preoperative jaundice present	53	47	0.26
Preoperative maximum serum T.Bil (range) (mg/dL)	5.9 (0.2-29.3)	4.9 (0.5-25.7)	0.92
Preoperative biliary drainage present	59	53	0.09
Preoperative cholangitis present	13	7	0.35
Biliary access (PTBD/ Endoscopy)	43 / 27	31 / 25	0.49
Portal vein embolization performed	33	33	0.19
ICG R15 (range) (%)	10.5 (3.5-20.4)	10.9 (3.4-20.0)	0.80
Hepatic resection (Rx or R3 / Lx or L3)	43 / 27	35 / 21	0.90
Rx or R3 or L3 resection performed	47	36	0.74
HPD performed	9	11	0.30
Combined portal vein resection performed	37	27	0.60
Combined arterial resection performed	6	9	0.20
Operative time (range)(min)	607 (385-979)	667 (450-902)	0.01
Blood loss (range)(mL)	1490 (270-4815)	1650 (650-5840)	0.20
RBC transfusion performed	20	6	0.26
AST on postoperative day 1 (range) (IU/L)	340 (81-3680)	456.5 (90-4545)	0.12
ALT on postoperative day 1 (range) (IU/L)	288 (54-3080)	404 (53-3400)	0.08
Postooperative maximum serum T.Bil (range) (mg/dL)	2.9 (1.0-6.3)	5.05 (1.3-53.3)	<0.0001
Postoperative hospital stay (range) (days)	32.5 (16-86)	54.0 (19-159)	<0.0001

HC: Hilar cholangiocarcinoma, ICC: Intrahepatic cholangiocarcinoma, PTBD: Percutaneous transhepatic biliary drainage, ICG R15:indocyanine green retention rate at 15 minutes, Rx: Right hemihepatectomy, R3: Right trisegmentectomy, Lx: Left hemihepatectomy, L3: Left trisegmentectomy, AST: Aspartate aminotransferase, ALT: alanine aminotransferase

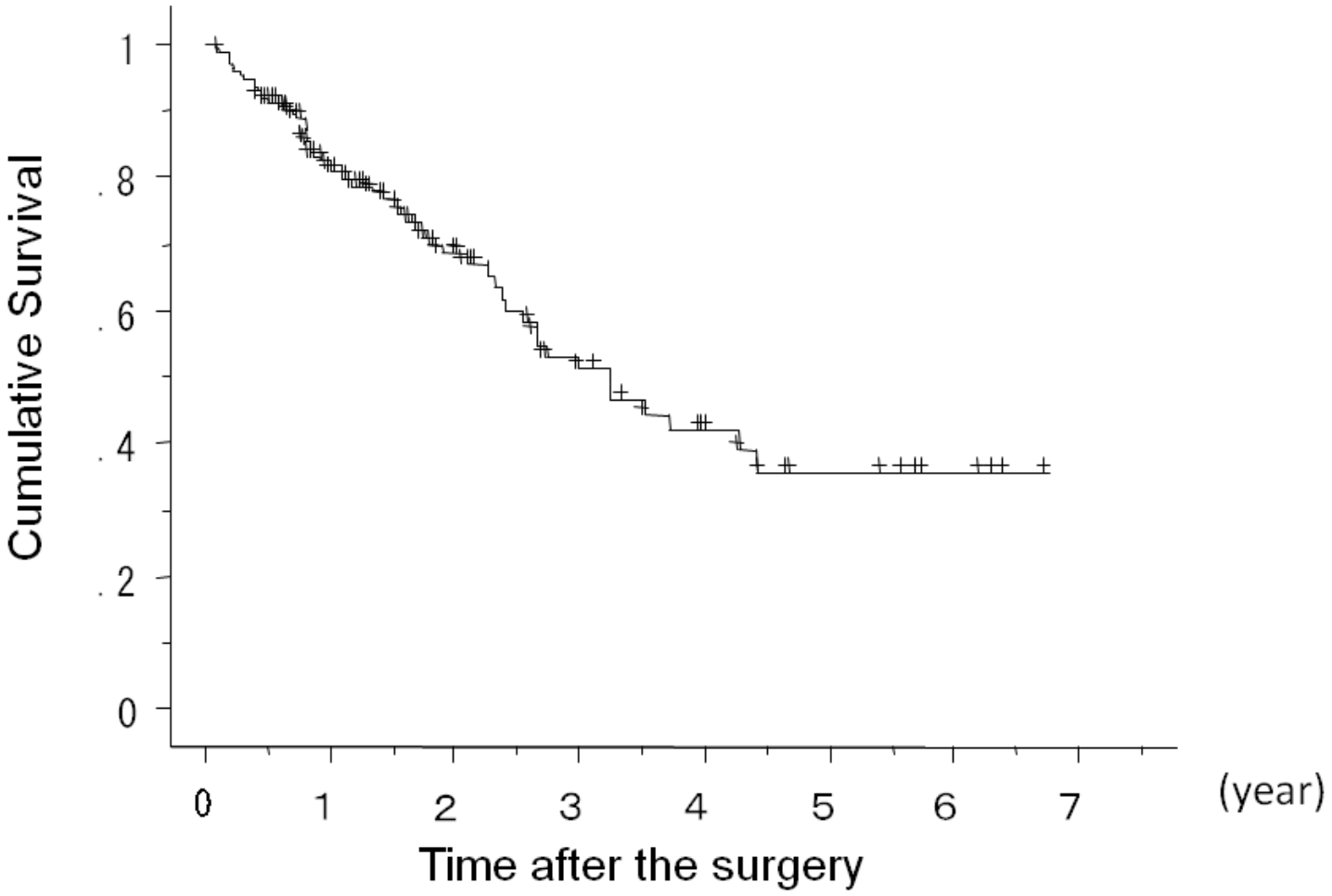

Cumulative Survival
1
.8
.6
.4
.2
0
0
1
2
3
4
5
6
7
(year)
Time after the surgery
No. at risk 146 93 27 8

Figure 1