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Original Article

High hilar resection and portojejunal anastomosis: a novel surgical option for Bismuth-Corlette type IIIb hilar cholangiocarcinoma

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Abstract: Objective: To explore the feasibility of applying high hilar resection and portojejunal anastomosis for Bismuth-Corlette type III b hilar cholangiocarcinoma treatment. Methods: From 2004 to 2009, 25 cases of Bismuth-Corlette type III b hilar cholangiocarcinoma underwent surgical treatment in Shandong University Qilu Hospital. They were divided into 2 groups according to the different operation method received, i.e., high hilar resection and portojejunal anastomosis (PJA) and bile duct plasty and cholangiojejunal anastomosis (CJA). Clinical and follow-up parameters were analyzed retrospectively. Results: Two groups of patients had comparable parameters including age, gender and preoperative assessments. High hilar resection and portojejunal anastomosis (PJA) were performed in 13 patients and bile duct plasty and cholangiojejunal anastomosis (CJA) were conducted in 12 patients. R0 resection rate was similar between the two groups (92.3% vs. 83.3%, P>0.05). However, left hemihepatectomy rate was significantly lower in the PJA group compared to the CJA group (7.7% vs. 83.3%, P=0.001). Operation time and intra-operative blood loss volume were also significantly reduced in the PJA group. Postoperative complications rate and survival rate were comparable between the two groups. Conclusion: High hilar resection and portojejunal anastomosis (PJA) represents onebetter choice for patients with Bismuth-Corlette type III b hilar cholangiocarcinoma, especially for patients with relatively poor health conditions.

Keywords: Hilar cholangiocarcinoma, Bismuth-Corlette type III b, portojejunal anastomosis

Introduction

Hilar cholangiocarcinoma (HC) originates from the hepatic duct epithelium, occurring at multiple sites including the common hepatic duct, the right/left hepatic duct, and at the confluence of the right/left hepatic ducts. About 2% of all malignant cancers are hilar cholangiocarcinoma [1]. The incidence rate of HC is increasing in recent years [2]. HC is a highly invasive tumor located adjacent to hepatic portal while the symptoms of HC are of no specificity and generally appear very late. Thus, about 45% of the patients with HC have neural invasion or lymph node metastasis when they are diagnosed, and death generally occurs within six months post-diagnosis for untreated patients [3]. Surgical resection is currently regarded as the only effective treatment for prolonging the lives of patients [2]. Bismuth-Corlette classification is the most commonly used classification system for HC, which defines that the Bismuth-Corlette type III b HC involves the common hepatic duct and the left hepatic duct [4]. We have used high hilar resection and portojejunal anastomosis (PJA) in treating hilar cholangiocarcinoma since 2004. In the present study, we retrospectively retrieved the data from the patients with Bismuth-Corlette type III b HC treated with high hilar resection and portojejunal anastomosis (PJA) in Shandong University Qilu Hospital, and the essential values of this novel operation procedure were emphasized.

Subjects and methods

Subjects

From February 2004 to February 2009, a total of 25 patients with Bismuth-Corlette type IIIb

Table 1. Characteristics of the included patients

Variables	PJA group (n=13)	CJA group (n=12)	*P*-value
Age (y)	62.1 ± 7.6	59.3 ± 8.3	0.385
Gender (male:female)	8:5	9:3	0.673
TBIL at hospitalization (μmol/L)	244.0 ± 178.3	201.5 ± 139.9	0.516
CEA at hospitalization (ng/mL)	6.4 ± 5.8	6.7 ± 6.3	0.810
Left hemihepatectomy (n)	1	10	0.001
Operation time (h)	4.2 ± 1.3	5.8 ± 1.5	0.011
Intraoperative blood loss (mL)	202.3 ± 138.5	450.0 ± 219.5	0.002
Blood transfusion (n)	1	6	0.030
Length of hospital stay (d)	20.4 ± 3.8	28.8 ± 8.4	0.006

HC underwent operation in Shandong University Qilu Hospital. The diagnosis was confirmed by postoperative pathological examination. Preoperative demographics and clinical information of the patients were retrospectively obtained from the patients' medical records, and follow-up study was conducted. The patients were divided into two groups according to two different surgical procedures (PJA vs CJA) received. High hilar resection and portojejunal anastomosis (PJA) were performed for 13 patients and bile duct plasty and cholangiojejunal anastomosis (CJA) were conducted for 12 patients. Hepatic function and tumor biomarkers (AFP, CA19-9 and CEA) were determined routinely after hospitalization. Preoperative imaging including abdominal ultrasonography, abdominal computed tomography (CT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), and cholangiography through percutaneous transhepatic biliary drainage (PTBD) were performed. Patients with the level of total bilirubin (TBIL) higher than 400 μmol/L or patients with poor medical conditions, PTBD was performed prior to operation.

Frozen section assessment for tumor specimen was performed during the operation to determine the tumor invasion of the surgical margin.

Follow-up study

Follow-up study was performed for all the patients. After the operation, abdominal ultrasonography and serum CA19-9 was determined every 3 months, while a chest X-ray was taken every 6 months for each patient. Other information was interviewed by telephone until the patient passed away, or reached the end of current study observation (December 31, 2012). No loss of follow-up was found.

Statistical analysis

All statistical analysis was performed using SPSS 19.0 software package. Student *t* test and Fisher exact probability test was used for the analysis. Postoperative survival rate of the patients was plotted by Kaplan-Meier curve and compared by log-rank test. $P<0.05$ was considered statistically significant.

Results

Clinical characteristics

Two groups of patients were comparable in terms of age, gender and preoperative assessments (**Table 1**). Common symptoms included jaundice (21/25, 84%), upper abdominal pain (9/25, 36%), itching (8/25, 32%), decreased appetite (5/25, 20%), fever (2/25, 8%) and weight loss (2/25, 8%). Preoperative imaging including abdominal ultrasonography, CT, MRI, MRCP, and cholangiography through PTBD were performed for 25 (100%), 23 (92.0%), 13 (52.0%), 13 (52.0%), and 10 (40.0%) patients, respectively. Preoperative PTBD was performed for 6 and 4 patients in the PJA group and the CJA group, respectively (46.2% vs. 33.3%, $P>0.05$).

Operation process

The main procedures in the high hilar resection and portojejunal anastomosis operation (PJA) were outlined below: (1) hepatoduodenal ligament was divided and skeletonized (**Figure 1A**); (2) gallbladder was divided retrogradely and resected; (3) common hepatic duct, right and left hepatic duct, and portal vessels were divided. With specific emphasis to identify any potential tumor invasion. In general, the hepatic duct was divided retrogradely until 1 cm away from the tumor proximal end, and the tumor was removed along with the liver tissues within 1 cm around the tumor. The left and right branches of the portal vein were divided for at

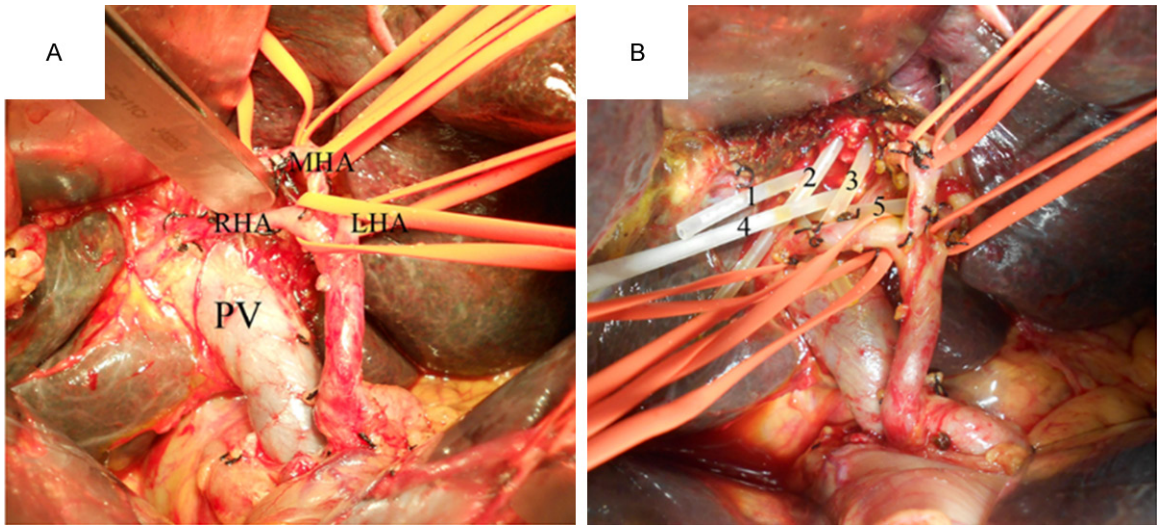

Figure 1. A. Hepatoduodenal ligament was divided and skeletonized; B. All the bile duct radicals must be anastomosed.

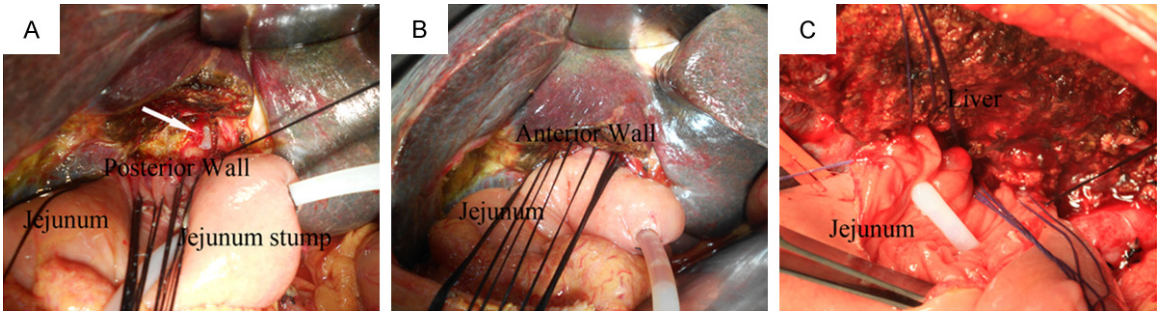

Figure 2. A and B. Exact suture techniques must be performed in anastomosing jejunum with bile duct walls or adjacent liver tissues; C. Left hemihepatectomy and portojejunal anastomosis.

least 2 cm to gain an adequate exposure of caudate lobe. For patients with only left hepatic artery involvement, the left hepatic artery was ligated and resected. For patients with main portal vein involvement, part of the main portal vein wall was resected and followed by repair or end-to-end anastomosis; however, anastomosis of autologous grafts with the main portal vein was conducted in cases of deep operation site or high anastomotic tension. For patients with the involvement of the left branch of the portal vein, the left hemiliver and the ipsilateral caudate lobe were divided and resected; (4) resection of ipsilateral caudate lobe was performed for patients whose left hemiliver was resected. For other patients, part of the caudate lobe was resected; (5) bile duct radicals were carefully inspected, and bile duct stents were used if necessary, then portojejunal anastomosis was performed. During this process, all the bile duct radicals must be anastomosed (**Figure 1B**). Exact suture techniques must be performed in anastomosing jejunum with bile duct walls or adjacent liver tissues (**Figures 2A** and **3B**). Large bile duct should be anastomosed with the adjacent liver tissue to reduce the risk of developing bile duct stenosis after the operation, and bile duct stent should be used if necessary (**Figure 2A**) to avoid the postoperative mechanical compression caused by local recurrence of tumor.

Bile duct plasty and cholangiojejunal anastomosis (CJA) was performed for indicated patients in current study. Left hemihepatectomy was also performed if necessary.

For the patients in the PJA group, left hemihepatectomy and portojejunal anastomosis (**Figure 2C**) were performed for 1 patient with left portal vein involvement, while high hilar

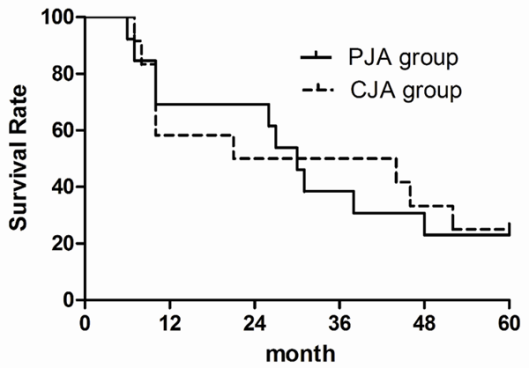

Figure 3. No statistically significant difference was found between the 2 groups.

Table 2. Postoperative complications in PJA and CJA groups

Complication	PJA group (n=13)	CJA group (n=12)	*P*-value
Pleural effusion	3 (23.1%)	5 (50.0%)	0.411
Biliary infection	4 (30.8)	2 (15.4%)	0.645
Bile leakage	0 (0)	1 (8.3%)	0.480
Liver failure	0 (0)	1 (8.3%)	0.480
Infectious diseases	1 (7.8%)	4 (33.3%)	0.160
Lymphorrhea	1 (7.8%)	0 (0)	1.000
Gastroplegia	0 (0)	1 (8.3%)	0.480
Intestinal leakage	1 (7.8%)	0 (0)	1.000
Total	5 (38.5%)	7 (58.3%)	0.434

resection and portojejunal anastomosis were performed for the other 12 patients. Frozen section assessment confirmed that R0 resections were achieved in 12 (92.3%) patients, R1 resection was achieved in 1 patient with large tumor and poor medical conditions that could not tolerate the extended resection. For the 12 patients in the CJA group, R0 resections were achieved in 10 patients (83.3%) that received left hemihepatectomy and caudate lobe resection, while R1 resections were achieved in 3 patients with poor conditions that could not tolerate the extended resection or left hemihepatectomy. Left hemihepatectomy rate was statistically lower in the PJA group compared with the CJA group (7.7% vs. 83.3%, P=0.001). The operation time was 4.2 ± 1.3 h (ranging from 2.5 to 7.2 h) and 5.8 ± 1.5 h (ranging from 3.8 to 8.5 h) in the PJA and CJA groups, respectively. Intraoperative blood loss volume was 202.3 ± 138.5 mL (ranging from 50 to 500 mL) in the PJA group and 450.0 ± 219.5 mL (ranging from 100 to 800 mL) in the CJA group. Blood transfusion was needed for 1 (7.7%) patient in the PJA group and 6 (50.0%) patients in the CJA group. Statistical analysis revealed that significant differences existed in operation time, intraoperative blood loss volume, and rate of blood transfusion (**Table 1**).

Postoperative complications

Mortality and morbidity are defined as death or complications occurring within 30 days of surgery. Liver failure was defined as the level of total bilirubin increased to more than 10 mg/dL (171 μmol/L) after the operation [5, 6]. Infectious complications included wound sepsis, intraabdominal abscess and bacteremia. Postoperative complications were found in 12 (48.0%) patients (**Table 2**) and it tended to be lower in the PJA group compared with the CJA group, although it did not reach statistical significance (38.5% vs. 58.3%, P=0.051) possibly due to the relatively small sample size (n=25) of patients.

The average length of hospital stay was 25.4 ± 6.3 d (ranging from 18 to 48 d) for the 25 patients indicated. Significant difference was found in the length of hospital stay between the PJA group and the CJA group (20.4 ± 3.8 d vs. 28.8 ± 8.4 d, P<0.05). No in-hospital death was found.

Postoperative survival rate

For the 25 patients included, the 1-, 3-, and 5-year postoperative survival rate was 68%, 44%, and 24%, respectively. However, the 1-, 3-, and 5-year postoperative survival rate was 69%, 38%, and 23% for the patients in the PJA group, and 67%, 50%, and 25% for the patients in the CJA group. No statistically significant difference was found between the 2 groups (P>0.05, **Figure 3**).

Discussion

Portojejunal anastomosis

Portojejunal anastomosis (PJA) has been firstly developed by Kasai as an effective treatment for children with congenital biliary atresia in 1974 [7]. However, very few studies have used PJA operation in treating hilar cholangiocarcinoma. High hilar resection and portojejunal

anastomosis has been used as a novel surgical option for treating hilar cholangiocarcinoma in our hospital since 2004.

Some critical procedures exist in this operation. As residual tumor and the involvement of lymph node are two independent prognostic factors [8], lymph nodes around the hepatoduodenal ligament, pancreatic head, and common hepatic artery should be removed, connective tissues around the hepatoduodenal ligament should also be resected [5]. Skamoto E *et al.* [9] reported that the length of submucosal extension was usually less than 10 mm, and a tumor-free proximal resection margin of 5 mm appeared to be adequate in hilar cholangiocarcinoma. And liver tissue 1 cm around the tumor was resected in the present study. The caudate lobe is located posterior to the bile duct bifurcation and portal vein. Many branches of bile ducts in the caudate lobe enter the bile duct bifurcation [8], and one or more branches of short hepatic veins enter the inferior vena cava. Studies had reported that caudate lobe involvement was found in about 40% to 80% of the patients with hilar cholangiocarcinoma, and R0 resection of caudate lobe was critical in treating these patients [10]. Hemi- or part caudate lobe resection was performed for different patients in the operation.

Importantly, we have found many differences between the portojejunal anastomosis that had developed by Kasai and the one we had used in treating hilar cholangiocarcinoma, which includes the complete skeletonization of the hepatoduodenal ligament and the resection of hepatic portal and tissues within 1 cm around the tumor in treating hilar cholangiocarcinoma but not congenital biliary atresia.

Advantages of high hilar resection and portojejunal anastomosis

Treating with high hilar resection and portojejunal anastomosis can significantly reduce the requirement of left hemihepatectomy and accelerate the postoperative restoration of liver function. The extent of liver resection has been demonstrated as an independent factor that affects the postoperative survival [11]. Tomoo Kosuge *et al*. [12] reported that less-extensive procedures are beneficial for patients with less-advanced disease if clear resectional margins are secured. In another study performed by Jane I. Tsao *et al.* [13] that compared the outcomes of 255 patients with hilar cholangiocarcinoma, the postoperative survival period was found associated with clear resectional margins but not extent of liver resection. High hilar resection and portojejunal anastomosis can effectively facilitate the reconstruction and anastomosis of the multiple biliary radicals without ligation of any bile duct, and increase the residual liver volume to improve the prognosis of the patients. Moreover, all bile duct radicals are drained to the jejunum without ligation, cholestatic rate is reduced and the compression of the vessels confined to the Glisson sheath sre also relieved because of the lack of dilated bile ducts, thus, postoperative portal hypertension rate decreases. Postoperative liver function restoration is accelerated accordingly, which is great beneficial to the reduction of postoperative complications, infectious diseases especially, and patients' recovery [14, 15].

Resection margins free of tumor is an independent prognostic factor, and R0 resection can substantially increase the survival rate, which has been confirmed by numerous previous studies [5, 16-18]. However, as a R0 resection requires an extended resection, it is unrealistic for the patients with poor medical conditions that could not tolerate the operation. Fortunately, high hilar resection and portojejunal anastomosis can effectively reduce the liver resection volume which makes it a feasible option for patients with relatively poor conditions to achieve R0 resection.

Treating with high hilar resection and portojejunal anastomosis can decrease the volume of intraoperative blood loss, and shorten the operation time. Numerous studies have demonstrated that the volume of blood transfusion and operation time were two important factors that influenced the long-term survival rate and possibility of developing postoperative complications in patients with hilar cholangiocarcinoma or other malignant tumors [19-22]. In another study performed by Ercolani G *et al.* [18], volume of blood transfusion has been regarded as the most important factor that influences the operative mortality. The findings of the present study demonstrated that high hilar resection and portojejunal anastomosis could effectively simplify the operation process

by reducing the extent of resection and dissection of great vessels. Thus, operation time is shortened, and the volume of blood transfusion is reduced.

Previous study revealed that intraoperative blood transfusion and operative time were the most predictive intraoperative variables associated with length of hospitalization [23]. Statistical analysis of the present study also revealed the patients in the PJA group recovered more quickly and soon discharged.

In summary, high hilar resection and portojejunal anastomosis can significantly decline the requirement of hemihepatectomy, shorten the operation time, reduce the volume of blood loss and shorten the length of hospital stay. Meanwhile, its prognosis was the same with hemihepatectomy operation. High hilar resection and portojejunal anastomosis represents a novel and feasible surgical choice for patients with Bismuth-Corlette type III b hilar cholangiocarcinoma, especially for patients with relatively poor conditions. However, as the sample size of this study is relatively small, further follow-up studies are warranted to validate our findings. Further analysis of its applications on other types of cholangiocarcinoma, type III a and type IV especially, are also undertaken.

Disclosure of conflict of interest

None.

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