Central Lobectomy

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19.1 Introduction

Hilar cholangiocarcinoma, also known as Klatskin tumor or proximal extrahepatic cholangiocarcinoma, is an uncommon adenocarcinoma which arises from the epithelial cells of the biliary confluence of the right and left hepatic ducts. It accounts for nearly two thirds of cholangiocarcinoma and therefore is the most frequently encountered biliary tumor [1]. The estimated incidence of hilar cholangiocarcinoma is around 1:250,000 population. The cause for hilar cholangiocarcinoma is still unknown, although a variety of chronic inflammatory conditions of the biliary tree, such as sclerosing cholangitis, choledochal cysts, oriental cholangiohepatitis, and biliary parasitic disease, have been reported to increase the risk of bile duct cancers [2].

Unlike intrahepatic or distal cholangiocarcinoma, which can be treated with hepatic resection or pancreaticoduodenectomy, respectively, surgical management of hilar cholangiocarcinoma has evolved since its original description. In earlier decades, surgical management was primarily palliative with generally poor outcomes [3]. Early reports of resection of hilar cholangiocarcinoma typically involved resection of the biliary tree with hepaticojejunostomy [4]. In the last 20 years, surgical management of hilar cholangiocarcinoma has evolved due to improvements in preoperative imaging and an enhanced appreciation of tumor growth characteristics [5]. Unfortunately, despite these surgical advances, a significant proportion of hilar cholangiocarcinoma were deemed unresectable because of the locally aggressive nature of the disease, and survival rates after surgery have not substantially changed over the past 20 years. In a recent review of 25 studies on surgical resection for hilar cholangiocarcinoma published from 1990 to 2008, the resectability for hilar cholangiocarcinoma was 28–95 %, with a median resectability of 70 %. The curative resection rates ranged between 14 and 95 %. The 5-year survival rates varied from 25 to 40 % in recent series (Table 19.1) [5]. As complex biliary and hepatic resections are required to obtain complete resection, the risks of perioperative morbidity and mortality are significant. The median morbidity and mortality rates are 47 % (14–76 %) and 8 % (0–19 %), respectively. Perioperative morbidity includes bleeding, biliary fistula, liver failure, and infectious complications including cholangitis, liver abscess, intra-abdominal abscess, wound infection, and pneumonia. Of these, postoperative hepatic failure was particularly common, and mortality has been associated with the extent of liver resection [5].

Hilar cholangiocarcinoma is a relatively slow growing tumor and is usually tiny at clinical presentation. There is no effective screening for hilar cholangiocarcinoma and most patients with unresectable disease die within 4–8 months of diagnosis [6]. Palliative biliary drainage by stents or prostheses appears to confer a survival benefit of only a few months [7]. Treatment for hilar cholangiocarcinoma has remained challenging because of the lack of effective adjuvant treatment, the close proximity of the tumor to vital biliary and vascular structures as well as to other organs, and a limited ability to achieve complete resection owing to the locally advanced nature of the tumor at presentation [3]. The operative management of hilar cholangiocarcinoma has evolved since its first description by Durand-Fardel in 1840, and surgical resection is the only therapeutic option with a chance of cure. The goals of surgical resection should be complete excision of tumor with negative margins and reconstruction of biliary-enteric continuity. The ability to completely excise the tumor with negative margins is usually limited by its infiltrative and longitudinal spread pattern and its close proximity to the hepatic artery and portal vein. Furthermore, surgical therapy is dictated by the location of the tumor and the presence of underlying liver disease. Surgical therapy for hilar cholangiocarcinoma in the early 1970s was primarily palliative or it involved only bile duct resection and

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Table 19.1 Results of surgical resection for hilar cholangiocarcinoma

Authors	Published year	Resections (n)	Resectability (%)	Morbidity (%)	Mortality (%)	5-year survival rate (%)
Hadjis et al.	1990	27	NA	NA	7	22
Nimura et al.	1990	55	83	41	6	41[a]
Nakeeb et al.	1996	109	56	47	4	11
Su et al.	1996	49	28	47	10	15
Klempnauer et al.	1997	151	45	NA	10	28
Miyazaki et al.	1998	76	NA	33	13	26
Burke et al.	1998	30	43	NA	6	45
Neuhaus et al.	1999	80	NA	55	8	22
Kosuge et al.	1999	65	73	37	9	33
Launois et al.	2000	131	35	NA	19	NA
Gerhards et al.	2000	112	NA	65	18	NA
Nimura et al.	2000	142	80	49	9	26[b]
Todoroki et al.	2000	101	89	14	4	28
Jarnagin et al.	2001	80	50	64	10	26
Kawarada et al.	2002	65	89	28	2.3	26
Capussotti et al.	2002	36	NA	47	3	27
Kawasaki et al.	2003	79	75	14	1.3	22
Seyama et al.	2003	87	94	43	0	40
Rea et al.	2004	46	NA	52	9	26
Kondo et al.	2004	40	95	48	0	NA
IJitsma et al.	2004	42	NA	76	12	19
Hemming et al.	2005	53	50	40	9	35
Jarnagin et al.	2005	106	70	62	8	NA
Dinant et al.	2006	99	NA	62	15	27
Ito et al.	2008	38	55	32	0	33

NA indicates data not available
[a]Data from the patients who underwent curative resection
[b]Data from the patients who underwent hepatectomy

hepaticojejunostomy. The high rates of disease recurrence and poor survival outcomes after bile duct resection alone had led surgeons to pursue a more radical approach. Early experience using combined liver resection in hilar cholangiocarcinoma resulted in a low R0 resection rate with significantly high perioperative morbidity and mortality [8]. The development and evolution of liver surgery and perioperative care in the past 20 years has significantly improved the surgical management of hilar cholangiocarcinoma. At present, a combined radical bile duct resection and partial hepatectomy is the accepted surgical approach for hilar cholangiocarcinoma. Concomitant liver resection is one of the most important elements of the surgical procedure to achieve negative resection margins. In a report from the Memorial Sloan-Kettering Cancer Center negative margins could be achieved in 84 % of patients who received partial hepatectomy as compared to 56 % of patients who did not have hepatectomy. The 5-year survival in the liver resection group in this series was 39 %, while none of the patients who did not have liver resection survived for 5 years [9]. A recent study demonstrated that the R0 resection rate and patient survival significantly improved over time after the addition of partial hepatectomy to bile duct resection [10]. There was a positive correlation between the rates of R0 resection and partial hepatectomy in surgical therapy for hilar cholangiocarcinoma [11]. Moreover, surgical adjuvant strategies such as portal vein embolization have resulted in increased rates of major liver resections and negative resection margins as well as improved rates in recurrence-free survival [12, 13].

19.2 Major Liver Resection

Surgeons from Japan and the West have performed major liver resection in order to increase the curative resection rate. Neuhaus et al. advocated the inclusion of portal vein resection and showed increased resectability and survival rates [14, 15]. Some centers routinely include hepatic segment 1 resection because of the proximity of the caudate lobe duct to the hilar bifurcation to achieve tumor clearance [16, 17]. Unfortunately, the prognosis of these patients after such extensive surgery has not been significantly improved further and this approach increased the 5-year survival rate to less than 50 % only in one reported series up to the present time [18]. These unsatisfactory results have been attributed largely to the high operative morbidity (40–71.2 %) and mortality

(6.9–17 %) rates after major liver resection in patients with an obstructed biliary system [10, 19–28]. Specifically, in patients with cirrhotic livers or impaired liver function or both, the minimal required amount of functional liver volume in the remnant liver after liver resection increases. Liver failure is one of the main causes of postoperative morbidity and it is directly associated with mortality. In the majority of cases, the liver remnant consists only of 2–3 segments, posing a great risk for postoperative small-for-size syndrome and liver failure. Although a few authors reported that major hepatectomy can be carried out without liver failure or mortality by using preoperative portal vein embolization (PVE) together with preoperative biliary drainage (BD), high mortality rates up to 6.9–17 % after major liver resection have been reported by most authors, with the main causes of death due to insufficient functional liver remnant and liver failure.

19.3 Liver Transplantation

Because of the limitations of surgical resection, orthotopic liver transplantation (OLT) was initially proposed as an optimal solution. Complete hepatectomy followed by transplantation addressed all the problems related to resection margins and the underlying liver disease such as primary sclerosing cholangitis, a primary risk factor for hilar cholangiocarcinoma. Unfortunately, the experience with liver transplantation for hilar cholangiocarcinoma was uniformly disappointing, with a high incidence of disease recurrence and subsequent mortality. In a recent review, Meyer et al. reported the results of liver transplantation for cholangiocarcinoma in 207 patients: the 2- and 5-year survival rates were 48 and 23 %, but >50 % of patients had a recurrence within 2 years, with a median time from transplantation to recurrence of 9 months and a median time between recurrence and death of 2 months [29]. The Spanish liver transplant centers reported a similar result of 30 % 5-year survival and a 53 % tumor recurrence rate for 36 patients with nondisseminated, unresectable hilar cholangiocarcinoma [30]. Recently, the so-called "Mayo protocol" has been developed with the intent of treating a highly selected group of patients with hilar cholangiocarcinoma with a strict regimen of preoperative staging and neoadjuvant treatment followed by OLT [31]. Patients eligible for OLT under this protocol have locally advanced tumors but no pathologic nodal disease. Furthermore, the prolonged course of neoadjuvant therapy, staging laparotomy, and time on the OLT waiting list provide an opportunity to exclude patients demonstrating disease progression. This highly rigorous selection bias in favor of patients with biologically favorable disease is reflected in the early outcomes published from the Mayo group. In 38 patients who received this protocol, a 5-year survival of 82 % was reported (as compared with a 5-year survival of 21 % after resection, which included patients with nodal disease, $P = 0.022$) [32]. The patients who ultimately underwent OLT were generally young (mean age 48 years). Pathologic analysis of the resected specimens confirmed N0 and R0 status in all patients. Later outcomes on 65 patients who received this protocol showed a 1-year survival of 91 % and a 5 year survival of 76 % (mean follow-up 32 months) [33]. Another study by Wu et al. used *en bloc* total hepatectomy-pancreaticoduodenectomy-orthotopic liver transplantation (OLT-Whipple) to achieve a complete eradication of early-stage cholangiocarcinoma (CC) complicating primary sclerosing cholangitis (PSC). Between 1988 and 2001, CC was detected in 8 of 42 PSC patients who were followed-up according to a surveillance protocol, 6 of whom underwent OLT-Whipple. Of these 6 patients, 4 had stage I CC, and 2 had stage II CC. All 6 OLT-Whipple patients received combined external-beam and brachytherapy radiotherapy. One patient died 55 months post-transplant of an unrelated cause, without tumor recurrence. The other 5 were well and without recurrence at 5.7, 7.0, 8.7, 8.8, and 10.1 years. The authors concluded that, for patients with an early-stage hilar CC complicating PSC, broad and lesion-focused radiotherapy combined with OLT-Whipple to remove the biliary epithelium *en bloc* offered promising long-term, tumor-free survival [34]. However, these data originated from a single centre with specialized interest in this disease; the generalizability of this experience remains untested. Thus, OLT in the setting of hilar cholangiocarcinoma is controversial and deserves more studies.

19.4 Central Lobectomy

19.4.1 Anatomic Basis and Rationale

A reduction in morbidity and mortality after liver resection is the key strategy for improving the results of surgical treatment of hilar cholangiocarcinoma. Central lobectomy is a way to resolve this problem. Central lobectomy, a segment-oriented procedure, preserves more functional liver tissue than either extended left or right hepatectomy. More than 30 years ago, McBride and Wallace described central liver resection for a centrally located tumor in a child [35]. This procedure has been referred to by different authors as central hepatectomy, central bi-/trisegmentectomy, middle lobectomy and middle hepatic segments resection. With this form of resection, later named as mesohepatectomy, the central liver segments 4 and/or 5, and 8 ± 1 are removed and the lateral sections remain intact (Fig. 19.1) [36]. This technique requires access to the right anterior portal pedicle and resects the area drained by the middle hepatic vein [37]. Depending on the size of the right and left lateral sections, parenchymal loss with central lobectomy can be up to 35 % less than with

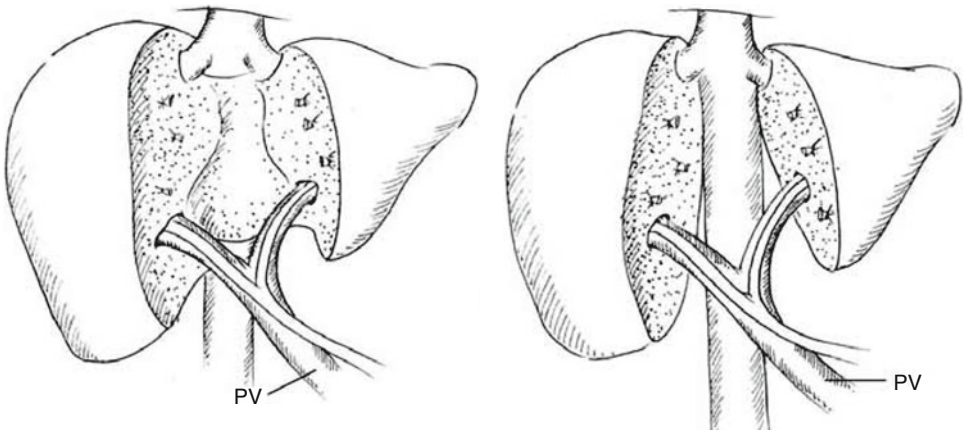

Fig. 19.1 Mesohepatectomy without excision of the caudate lobe (*left*) and with excision of the caudate lobe (*right*). *PV* portal vein

an extended right/left liver resection. Preserving more functional liver tissue is crucial for preventing postoperative liver failure. However, central lobectomy has not been widely applied, perhaps partly because of its complexity and partly because of the difficulties in bile duct reconstruction.

19.4.2 Assessment for Resectability

The American Joint Committee on Cancer (AJCC) TNM staging system is most commonly used to stage hilar cholangiocarcinoma. However, this system is based on pathologic criteria and does not provide information on the potential for resectability. The Bismuth-Corlette classification stratifies patients based on the extent of biliary involvement by tumor, which has been used to predict resectability and to assess the extent of resection [38]. In brief, Type I: tumors below the confluence of the left and right hepatic ducts; Type II: tumors reaching the confluence; Type IIIa and IIIb: tumors occluding the common hepatic duct and either the right or the left hepatic duct, respectively; and Type IV: tumors involving the confluence and both the right and left hepatic ducts [11]. Although it does not incorporate radial tumor extension, it provides a useful preoperative terminology to describe the extent of hepatic resection that will be necessary to encompass the longitudinal intraductal extension of hilar cholangiocarcinoma.

19.4.3 Surgical Principle

We determined the extent of liver resection in central lobectomy based on the Bismuth-Corlette classification of the tumor. Segment IVb resection is performed for type I tumors; segment IVb/extended IVb combined with segment I resection for type II tumors; segment IVb/extended IVb plus V/extended V combined with segment I resection for type IIIa and IIIb tumors without invasion of the right or left branches of the hepatic artery or portal vein; right/extended right hepatectomy combined with segment I resection for type IIIa tumors with invasion of the right branch of the portal vein or type IV tumors; and left/extended left hepatectomy combined with segment I resection for type IIIb tumors with invasion of the left branch of portal vein. On occasions, the extent of liver resection has to be modified during surgery to suit an individual patient. For tumors with invasion of both branches of the portal vein or the main portal vein, resection is not performed. Routine porta hepatis lymph node dissection is carried out with skeletonization of the portal vein and hepatic artery, and nodal clearance up to the celiac origin and around the head of pancreas. Where possible, gross resection margins of 1 cm is achieved for intrahepatic ducts.

19.5 Operative Procedures

19.5.1 Central Lobectomy

An incision is made 2 cm below the right costal margin extending from the midline to the right flank. A thorough exploration followed by intraoperative ultrasonography (IOUS) is performed.

The extent of resection depends on the extent of tumor in the bile duct, and whether the branches of the hepatic artery or portal vein are involved as determined before surgery on medical imaging and during operation by gross examination and IOUS. After porta hepatis lymph node dissection starting from the celiac plexus and the retropancreatic region, and with skeletonization of the hepatic artery and portal vein, the common bile duct is divided at the upper border of the pancreas. The gallbladder is dissected from its bed and the extrahepatic biliary tree dissected up to the hepatic hilum. The tumor is freed from the vessels if they have not been invaded by the tumor. The amount of liver to be resected is determined and the appropriate feeding vessels are ligated and divided. The liver is fully mobilized and the caudate lobe dissected from the inferior vena cava for combined segment

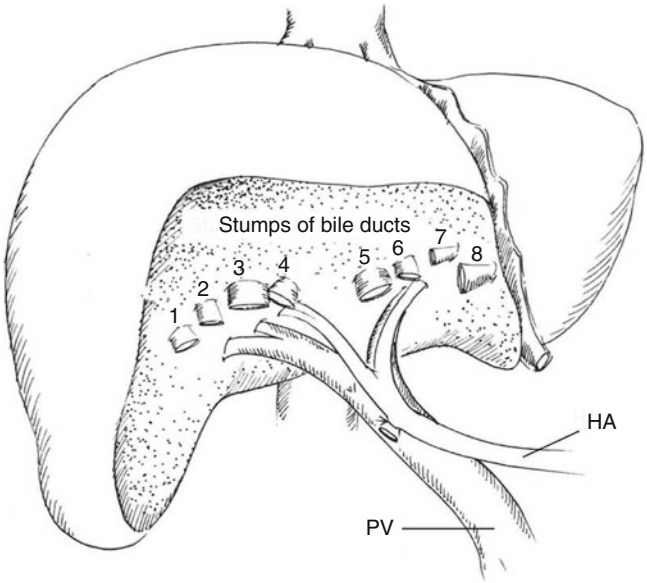

Fig. 19.2 Intrahepatic ductal openings on the remnant liver. *1–8* Stumps of bile duct, *PV* portal vein, *HA* hepatic artery

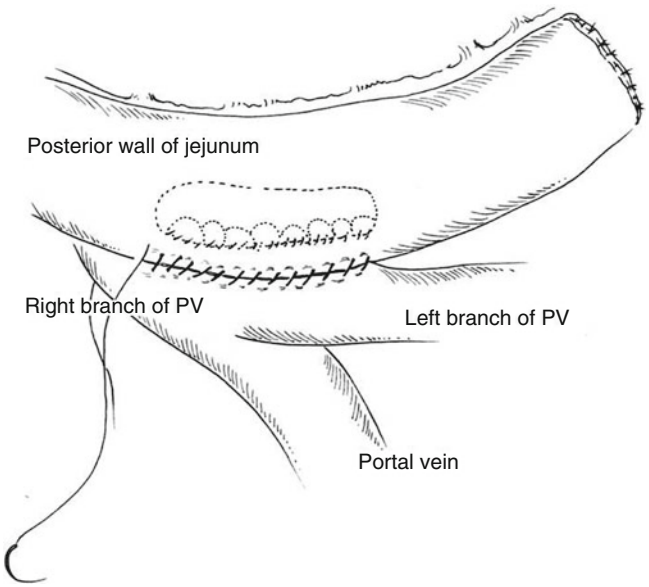

Fig. 19.3 Operative diagram showing anastomosis involving the posterior wall of jejunum: a continuous 4/0 polypropylene suture was used to sew the seromuscular layer of the posterior wall of jejunum to the wall of the right and left branches of the portal vein. *PV* portal vein, *R* right branch of portal vein, *L* left branch of portal vein

I resection. Under IOUS guidance, the line of liver transection is marked on the surface of the liver by diathermy 1 cm away from the margin of the tumor. The liver parenchyma and intrahepatic bile ducts are transected and the specimen is removed *en bloc* with the extrahepatic duct and the gallbladder. There are usually three to five divided openings for right intrahepatic ducts and two to four divided openings for left intrahepatic ducts; the diameter of these openings varied from 0.2 to 1 cm (Fig. 19.2).

19.5.2 Hepaticojejunostomy

Hepaticojejunostomy is made in an end-to-end fashion for patients who have resection of segment IVb with or without segment I, and in an end-to-side fashion in patients who have resection of segments IVb, V and I. First, adjacent hepatic ducts are sutured together to form a single large duct for anastomosis. Mucosal to mucosal anastomosis is then made between a Roux-en-Y loop of jejunum and the bile duct using continuous 4/0 polypropylene. When it is not possible to join the intrahepatic bile ducts because their openings are too far away from one another, the jejunum is sutured to the adjacent liver around the bile duct openings with intermittent 3/0 polypropylene U sutures. When the intrahepatic ducts are small and thin walled, the seromuscular layer of the posterior wall of the jejunum is anastomosed to the adjacent walls of the portal venous branches with continuous 4/0 polypropylene sutures (Fig. 19.3) to ensure stability of the anastomosis. The anterior wall of the anastomosis is made between the jejunum and the liver adjacent to the bile duct openings with intermittent U sutures (Fig. 19.4).

Transhepatic tubes are not used. A drainage tube is placed inside the Roux-en-Y jejunal loop next to the hepatojejunal anastomosis to monitor postoperative bile secretion and to reduce pressure within the loop, thus helping the anastomosis to heal. The tube is brought out from the loop 10 cm away from the anastomosis. Abdominal drainage tubes are placed on either side of the hepatojejunal anastomosis, and brought to the outside through separate stab incisions in the abdominal wall.

19.6 Feasibility and Safety of Central Lobectomy

Mehrabi et al. [36] reviewed and analyzed all reported cases of mesohepatectomy found in the PubMed database between 1972 and April 2008. There were no restrictions on the number of reported patients, although some articles reported on a mixed population of patients who underwent different types of resection. The data of 859 patients (including 48 patients reported by the authors) were analyzed. In 658 patients with available data, the three most common indications for mesohepatectomy were HCC (82.7 %, n = 544), liver metastasis (11.1 %, n = 73), and hilar cholangiocarcinoma(3.4 %, n = 22). The recorded data of 636 patients showed 27.8 % (n = 177) had complications after mesohepatectomy. The majority of these complications were pleural effusion or pneumonia (12.6 %, n = 80), ascites (4.1 %, n = 26), bilioma or bile leakage (3.5 %, n = 22), wound infection (1.1 %,

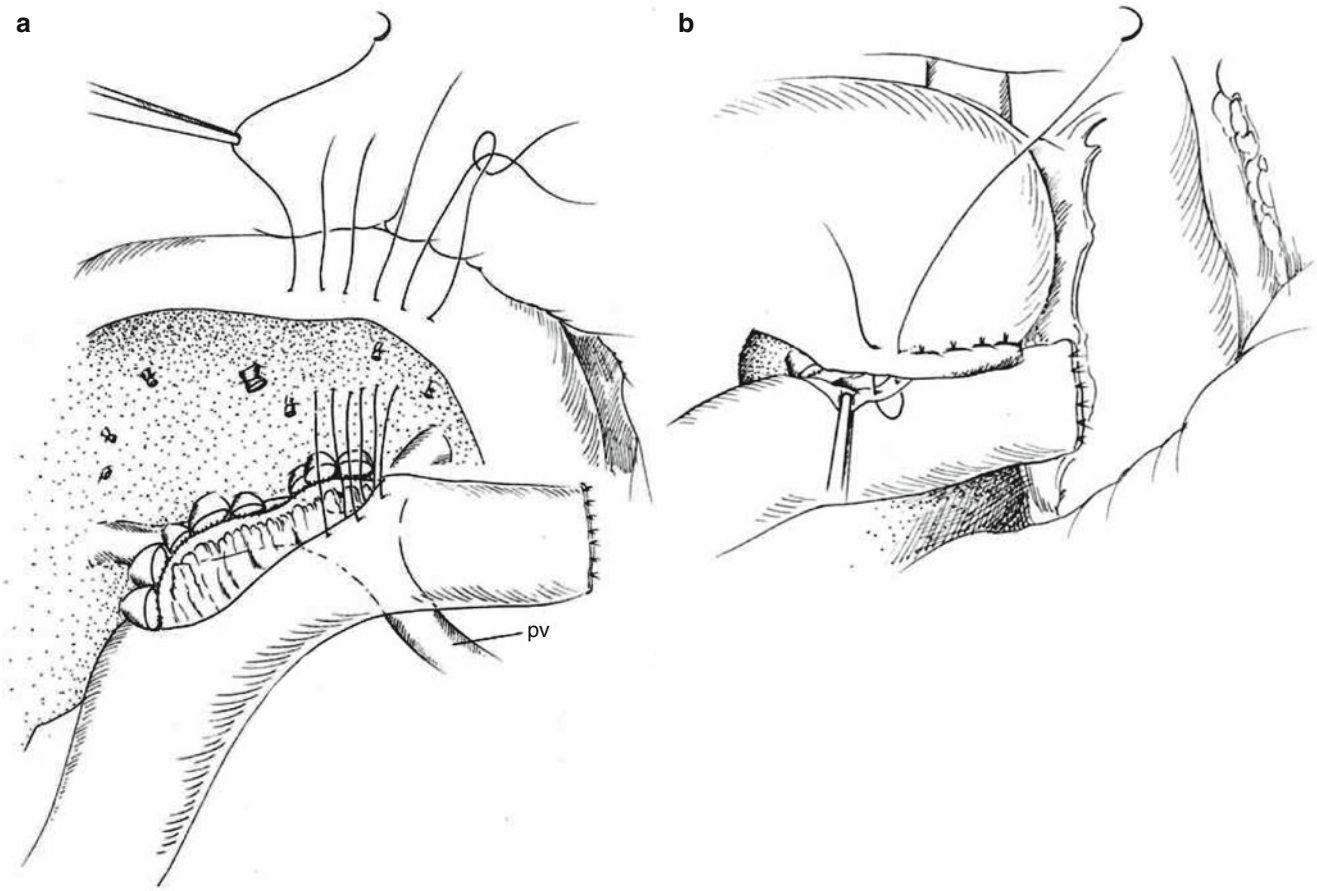

Fig. 19.4 (**a**) Start of the anterior anastomosis: the anterior edge of the jejunal opening was sutured to the edge of the liver adjacent to the bile duct opening. (**b**) Anterior anastomosis almost completed. *PV* portal vein

n=7), intraabdominal/subphrenic abscess (1.1 %, n=7), temporary renal insufficiency (0.6 %, n=4), and hemorrhage/hematoma (0.6 %, n=4). Interestingly, the mortality rate after mesohepatectomy for 756 patients was 1.6 %(n=12) (range 0–6 %), and this was mainly due to liver failure (42 %, 5 of 12) [36]. We previously reported on 256 patients who received mesohepatectomy for hepatocellular carcinoma. The in-hospital mortality rate was 0.4 % and the postoperative morbidity rate was 28.1 % [39]. In another report by us on mesohepatectomy on 93 patients with hilar cholangiocarcinoma, the morbidity and mortality were 22 and 0 %, respectively [40], which were lower than most published reports on extended hepatectomy [5].

19.7 Outcomes of Central Lobectomy for Hilar Cholangiocarcinoma

Between January 2000 and December 2007, 138 (73.8 %) of 187 patients with hilar cholangiocarcinoma who underwent surgical exploration at our centre (the Hepatic Surgery Centre, Tongji Hospital, Wuhan, China) had their tumors resected with an curative intent. There were 86 men and 52 women. The median age was 54 (range 26–72) years. These patients were evaluated before surgery with a baseline history, physical and biochemical examinations. Imaging included ultrasonography, computed tomography (CT) or magnetic resonance cholangiopancreatography, cholangiography through the percutaneous transhepatic or the endoscopic retrograde approach. Preoperative biliary drainage was performed only when jaundice had lasted for more than 4 weeks and the total bilirubin level was 200 μmol/L or higher. Preoperative portal vein embolization was not carried out. The criteria for resectability were absence of peritoneal or liver metastasis, tumor extension beyond the secondary biliary branches bilaterally, or extension to the secondary portal venous branches bilaterally.

With preoperative imaging and intraoperative findings (including IOUS), the Bismuth–Corlette classification of the 138 patients with hilar cholangiocarcinoma was: type I in 11 patients (8.0 %), type II in 34 patients (24.6 %), type IIIa in 43 patients (31.2 %), type IIIb in 35 patients (25.4 %) and type IV in 15 patients (10.9 %). Of the 45 patients who had a major hepatectomy, preoperative biliary drainage was performed in

Table 19.2 Extent of liver resection according to Bismuth–Corlette classification in 138 patients

		Bismuth–Corlette classification				
Extent of liver resection	No. of patients	Type I (n = 11)	Type II (n = 34)	Type IIIa (n = 43)	Type IIIb (n = 35)	Type IV (n = 15)
Segment IVb/extended IVb resection	24	11	13			
Segment IVb/extended IVb + I resection	30		21	7	2	
Segment IVb/extended IVb + V/extended V + Iresection	39			32	7	
Right/extended right hepatectomy[a]	19			4		15
Left/extended left hepatectomy[a]	26				26	

[a]All left or right hepatectomies combined with segment I resection

11 patients who had jaundice for more than 4 weeks (range 4–7 weeks) and a total bilirubin level of 200 μmol/L or greater (range 200–410 μmol/L). Preoperative biliary drainage was not performed in 34 patients with jaundice for less than 4 weeks (range 4 days to 3 weeks); in five of these patients the total bilirubin level was more than 200 μmol/L (range 210–270 μmol/L). Preoperative biliary drainage was not performed in patients undergoing minor hepatectomy. No patient had preoperative portal vein embolization.

Segment IVb/extended IV resection was carried out in 24 patients with Bismuth–Corlette type I and II tumors that did not involve the cranioposterior wall of the hepatic duct bifurcation and the ducts to segment I. Segment IVb/extended IVb + I resection was performed in 30 patients with type II, IIIa and IIIb tumors with caudate lobe invasion but without vascular invasion. Segment IVb/extended IVb + V/extended V + I resection was carried out in 39 patients with type IIIa and IIIb tumors that had not invaded the right or left branches of the hepatic artery or portal vein. Right/extended right hepatectomy was performed in 19 patients with type IIIa tumors that had invaded the right branch of the hepatic artery or portal vein, or with type IV tumors. Left/extended left hepatectomy was undertaken in 26 patients with type IIIb tumors that had invaded the left branch of the hepatic artery or portal vein (Table 19.2). All left or right hepatectomies/extended hepatectomies were combined with caudate lobectomy, because caudate lobe involvement by tumor was common. Operating time ranged from 166 to 322 (median 195) minutes. Blood loss ranged from 100 to 1,260 (median 470) ml. Twenty-three patients received blood transfusion [median 2 (range 1–4) units].

Portal venous invasion was detected macroscopically in 45 patients (32.6 %) during surgery, and documented microscopically in a further 15 patients (10.9 %) after surgery. Hepatic arterial invasion was detected histopathologically in nine patients (6.5 %). The vascular involvement was ipsilateral to the side of the resected liver in all cases. Bile duct resection margins were negative in 123 patients (89.1 %) and positive in 15 (10.9 %). All patients with caudate lobe resection had negative resection margins, although extension of the tumor into the ducts of the caudate lobe was documented histopathologically in 37 (34.9 %) of 106 patients who had combined caudate lobectomy.

Table 19.3 Relationship between recurrence and extent of hepatectomy in patients with Bismuth–Corlette type IIIa and IIIb tumors

Extent of hepatectomy	No. of patients	IIIa/ IIIb	Tumor recurrence (%)
Minor resection	48	39/9	24 (50 %)
Major resection	30	4/26	16 (53 %)

During follow-up, tumor recurrence was detected in 76 (55.1 %) of 138 patients, at a median of 2.4 years. The longest interval to recurrence was 5.8 years. The relationship between tumor recurrence and surgery in patients with Bismuth–Corlette type IIIa and IIIb tumors is shown in Table 19.3. The liver remnant was the most common site of recurrence (23 patients, 33.8 %), followed by the retroperitoneum (17 patients, 25 %), the biliary tract (14 patients, 21 %), the peritoneum (11 patients, 16 %) and other sites (3 patients, 4 %). Some patients had more than one site of recurrence. Intrahepatic recurrence was usually adjacent to the liver transection plane. The rate of distant metastasis with or without local recurrence was found in 47 patients (69 %). An aggressive treatment was offered to the patients with recurrence, if possible, which included radiofrequency ablation in 22, microwave tissue coagulation in 14 and stereotactic radiotherapy in 11 patients. No patient with tumor recurrence was considered suitable for repeat resection with intent for cure. Systemic chemotherapy was not offered to any patient.

The median overall survival was 3.2 years for patients having a minor resection and 2.5 years for those having a major resection ($P = 0.11$). Actuarial 1-, 3- and 5-year survival rates were 87, 54 and 34 % respectively for minor resection and 80, 42 and 27 % for major resection, with no significant difference between the groups ($P = 0.300$) . On univariable

Table 19.4 Cox regression analysis of overall survival in 138 patients with hilar cholangiocarcinoma

Variables	Relative risk (95 % confidence interval)	P value
UICC stage	2.43 (0.29, 5.70)	0.001
Histopathological grade	2.50 (0.34, 4.79)	0.003

UICC International Union Against Cancer

analysis, prognostic factors that impacted significantly on long-term survival were portal vein resection, nodal involvement, vascular invasion, International Union against Cancer (UICC) tumor stage, blood transfusion and histopathological grade. On multivariable analysis, significant factors were UICC tumor stage and histopathological grade (Table 19.4).

Sotiropoulos et al. reported using partial or complete mesohepatectomy combined with resection of the hilar bifurcation to treat three cases of Klatskin tumors [41]. Two men and one woman with a median age of 62 years underwent resection of the hilar bifurcation, cholecystectomy, and lymphadenectomy of the liver hilum for clinically diagnosed Bismuth-Corlette type IV Klatskin adenocarcinoma. The first case entailed complete mesohepatectomy plus caudate lobectomy. Biliary reconstruction comprised 6 hepaticojejunostomies (4 right and 2 left ducts) into a single jejunal Roux-en-Y loop. The second case required resection of the quadrate lobe. To re-establish biliary drainage, 4 bile ducts on the right side and 5 bile ducts on the left side were reconstructed into a right and a left common opening, respectively. Subsequently, each common opening, as well as the caudate lobe duct, was anastomosed onto a single Roux-en-Y jejunal loop. The third case required resection of segment 4a. Biliary reconstruction was achieved with 5 hepaticojejunostomies (3 right and 2 left ducts) onto a single jejunal Roux-en-Y loop. All tumors were moderately differentiated. Histological evaluation of the hilar bifurcation showed Bismuth-Corlette type IV Klatskin carcinomas in the first two cases and type IIIB carcinoma in the third case. There was no lymphatic or hematogenous carcinomatosis, and all resection margins were negative for malignancy (R0 resections). Despite the complexity of the procedures undertaken, all three patients had uneventful post-operative courses. The first patient required reintervention 4 months after the primary surgery to resect a local recurrence on the cut surface of segment 5. No reconstruction of the hepaticojejunostomies was needed. He was alive and well at the time of the reporting, with no evidence of tumor recurrence, 87 months after the initial surgery. The second patient was also alive and tumor free 54 months after surgery. The third patient was diagnosed with tumor recurrence 4 months after the resection and died 8 months later (12 months after surgery).

Miyazaki et al. reported 93 patients with hilar cholangiocarcinoma who underwent surgical treatment (Table 19.5) [42]. The patients were stratified into three groups: the extended hepatectomy (EXH) group (n = 66), the parenchyma-preserving hepatectomy (PPH) group (n = 14), and the local resection (LR) group (n = 13). The EXH group had more extensive hepatectomy than hemihepatectomy, the PPH group had hepatectomy less extensive than hemihepatectomy, and the LR group had extrahepatic bile duct resection without hepatic resection. Surgical curability of the PPH and EXH groups was better than the LR group. Fifty-four percent of patients in the LR group showed positive surgical margins at the hepatic stump of the bile duct, compared with 7 % in the PPH group and 20 % in the EXH group ($P < 0.01$ for each comparison). Surgical morbidity was higher in the EXH group (48 %) than in the LR group (8 %) and the PPH group (14 %) ($P < 0.01$ and $P < 0.05$, respectively). Postoperative hyperbilirubinemia occurred more frequently in the EXH group (29 %) than the LR and PPH groups (0 and 0, respectively, $P < 0.05$ for each comparison). Survival rates after resection were significantly higher in patients who underwent hepatectomy, including PPH and EXH, than patients who underwent LR, 29 % versus 8 % at 5 years, respectively ($P < 0.05$). However, no significant difference in survival was found between the PPH and EXH groups. The authors concluded that curative resection is possible with PPH which improved the outcomes for patients with hilar cholangiocarcinoma localized at the hepatic duct confluence if vascular resection was not required. PPH provided benefits to highly selected patients chosen because of the local extent of the disease or because of liver dysfunction.

Table 19.5 Comparison of outcomes between the extended hepatectomy (EXH) group and the parenchyma-preserving hepatectomy (PPH) group

Extent of hepatectomy	PPH (n = 14) (%)	EXH (n = 66) (%)	P value
R0 resection rate	93	71	>0.05
5-year survival rate	36	27	>0.05
Morbidity	14	48	<0.05
Hyperbilirubinemia rate	0	29	<0.05
Mortality	7	12	>0.05

Data were extracted from reference Miyazaki et al. [42]

19.8 Further Comments

19.8.1 Local Resection Alone for Bismuth Type I and II Tumors?

Bismuth type I and II hilar cholangiocarcinomas appear less advanced on cholangiography and are easier to resect than Bismuth type III and IV tumors. As a consequence, many surgeons have chosen local or hilar resection (resection of the extrahepatic suprapancreatic biliary tract) as the treatment of choice for Bismuth type I and II tumors. Patients who receive such a limited resection frequently suffer from

locoregional recurrence even after a R0 resection, and the prognosis is unexpectedly poor [9, 14, 43]. Neuhaus et al. reported on a dismal outcome after hilar resection in 14 patients with Bismuth type I or II tumors. R0 resection was achieved in only six (42.9 %) patients, and all patients died of recurrence within 5 years [14]. Kondo also reported on a poor prognosis after limited resection. In their series, including 19 patients with Bismuth type I and II tumors, 15 (78.9 %) patients underwent limited resection (bile duct resection in 9, isolated caudate lobectomy in 5, and left hepatectomy in 1). Although R0 resection was achieved in most patients, the 3-year survival rate was approximately 15 % and only one patient survived >3 years [43]. Capussotti et al. analyzed the results of surgery for Bismuth type I and II tumors and found the long-term outcome was markedly worse in the subset of patients who underwent bile duct resection; none survived more than 2 years [44]. These previous reports indicate that local or hilar resection alone is inadequate for Bismuth type I and II tumors.

19.8.2 Major Hepatectomy for Bismuth Type I and II Tumors?

Over the past 20 years, there has been an increase in the use of hepatic resection in patients with hilar cholangiocarcinoma. Major hepatic resection addresses both the problems of direct hepatic invasion and intraductal extension of hilar cholangiocarcinoma to achieve negative radial and longitudinal resection margins. Incorporation of major hepatic resection as a fundamental surgical strategy for this disease has increased the proportion of R0 resections, improved recurrence-free survival outcomes, and decreased the prevalence of hepatic recurrences. There are some authors who recommend right hepatectomy for all Bismuth type I and II tumors. Kawasaki et al. have stressed the importance of performing right hepatectomy with caudate lobectomy in all patients with Bismuth type I, II, IIIa, and IV tumors, and recommended left hepatectomy only in patients with Bismuth type IIIb. They believed that right hepatectomy offers the best chance of cure in Bismuth type I, II, and IV tumors in which the right and left hepatic ducts are involved to a similar extent. Although detailed data were not presented in their report, the mean survival for 17 patients with Bismuth type I and II tumors was reported to be 33.7 months [16]. Seyama et al. also reported on a better prognosis in patients with Bismuth type I and II tumors, who underwent right hepatectomy with caudate lobectomy. In their series, the mean survival for 9 patients with Bismuth type I tumor was 42 months and that for 8 patients with Bismuth type II tumor was 51 months [45]. However, it is still uncertain whether or not major hepatic resection can improve survival for patients with Bismuth and Corlette type I or II hilar cholangiocarcinoma. Ikeyama et al. retrospectively evaluated surgical outcome of 54 patients with Bismuth and Corlette type I and II hilar cholangiocarcinoma, and demonstrated survival benefit from right hepatectomy with caudate lobectomy for nodular and sclerosing tumors, but not for papillary tumors [46]. Others have reported no significant difference in survival between hepatectomy and bile duct resection alone for Bismuth and Corlette type I and II tumors. Besides, major hepatic resection in patients with obstructive jaundice results in high surgical morbidity and mortality [47]. Postoperative hepatic failure and its associated mortality have been associated with the extent of liver resection [5]. In patients with cirrhotic livers or impaired liver function, or both, the minimal required amount of functional liver volume increases. Improving perioperative management of patients with hilar cholangiocarcinoma after extended liver resection does not substantially decrease morbidity and mortality rates associated with this technique. High mortality rates have been reported, with the main cause being liver failure due to insufficient functional liver parenchyma left after liver resection. In the large series reported by Klempnauer et al., an aggressive approach resulted in an operative mortality rate of 17 % [48]. In the study by Nishio and co-workers, the operative mortality rate for left trisectionectomy was 23 % [24].

To reduce the perioperative risk of major liver resection for hilar cholangiocarcinoma, two approaches have been proposed. The first is preoperative biliary drainage of the future hepatic remnant. Reports from the West have shown that preoperative biliary drainage does not reduce perioperative risk, but increases hospital costs as a result of septic complications related to the drainage [49, 50]. The second approach is preoperative portal vein embolization (PVE) of the hepatic segments that are to be resected. Recent reports suggested benefit, but the reduction in postoperative liver failure rate was only 2 % after resection of hilar cholangiocarcinoma [16, 23]. For patients with hilar cholangiocarcinoma, the indications for PVE remain controversial.

19.8.3 Central Lobectomy for Bismuth–Corlette Type I, II and III Tumors Without Vascular Invasion?

Hepatic resection, limited as much as possible to what is necessary for curative resection, might result in fewer postoperative complications, including liver failure, in patients with hilar cholangiocarcinoma. Nimura et al. have also advocated limited hepatic resection according to the tumor extent [42]. Our strategy to reduce perioperative mortality is the use of central lobectomy in selected patients with hilar cholangiocarcinoma, so that a sufficient hepatic mass is preserved.

As the hilar bifurcation of the bile ducts is near to liver segments 4, 5 and 1, adequate liver resection of these segments together with the bile ducts can result in cure. Under intraoperative ultrasonographic guidance, the aim is to resect the liver parenchyma and the bile duct 1 cm away from the tumor. The negative surgical resection margin rate in our hands was 89.1 %, and no serious complications with this operation were encountered. Although there are many arguments for or against central lobectomy for hilar cholangiocarcinoma, our results of 0 mortality, 29.7 % morbidity and 34 % 5-year survival rate are encouraging, and better than the results of other authors. For hilar cholangiocarcinoma that involves the right or left hepatic artery or portal vein, or for Bismuth–Corlette type IV tumors, the only surgical option is to perform a right/extended right or left/extended left hepatectomy.

A negative bile duct resection margin is an important factor, but it is not the only factor that influences prognosis after surgery. Although not all patients with clear surgical resection margins have good prognosis, some of the reported long-term survivors are patients with positive resection margins. Maeno et al. found a 5-year survival rate of 20 % in patients with positive bile duct resection margins (a finding similar to our results of 23 % with R1 resection [40]), and 37 % in patients with clear surgical margins [51]. Kondo et al. reported a 3-year overall survival rate in 40 consecutive patients with hilar cholangiocarcinoma with clear resection margins of only 40 % [43]. Hasegawa and co-workers reported that 60 % of patients with hilar cholangiocarcinoma who had an R0 resection developed tumor metastasis [49]. The 3-year survival rate following liver transplantation for hilar cholangiocarcinoma was 35 % [26]. All of these findings suggest that there are many factors influencing the outcomes of surgical treatment for hilar cholangiocarcinoma [40, 52]. Increasing the extent of liver resection is not necessary. If the tumor can be resected completely, minor liver resection is better in patients with hilar cholangiocarcinoma.

Radical resection of hilar cholangiocarcinoma results in higher morbidity rates (40–71 %) compared with resection of other hepatic tumors; the most common complication is bile leakage, which occurs in about 10 % of patients (range 4–61.9 %) [10, 17, 20, 23, 30, 48, 49, 53]. For this reason, biliary tract reconstruction is the key step in this operation. In minor liver resection for hilar cholangiocarcinoma, the liver has to be transected in two or three planes, leaving behind many intrahepatic bile ductal openings (usually between five and nine). Conventionally, each bile duct opening is anastomosed to the jejunum [54, 55], making the reconstruction very difficult, which is the main disadvantage of this procedure. Using our technique of hepatojejunal anastomosis, the bile leak rate was only 1.4 %.

In conclusion, central lobectomy can be used with good results in selected patients with Bismuth–Corlette type I, II and III tumors without vascular invasion. For type III tumors with vascular invasion and selected type IV lesions, major hepatectomy must be performed.

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