Surgical Techniques for Extrahepatic Biliary Tract Cancers

Junichi Shindoh, Giuseppe Zimmitti, and Jean-Nicolas Vauthey

Contents

J. Shindoh · G. Zimmitti · J.-N. Vauthey (✉)
The University of Texas, MD Anderson Cancer Center, Texas, USA
e-mail: jvauthey@mdanderson.org

Abstract

For patients with extrahepatic biliary tract cancer, surgical resection is the only therapeutic option offering a chance of cure. However, with its specific location surrounded by multiple viscera and major vascular structures, surgical resection for biliary tract cancer frequently requires advanced surgical techniques. To secure the safety of radical surgery in high risk patients, optimization of the condition of patient and adequate selection of surgical procedure is necessary.

1 Introduction

Complete surgical resection is the single most effective treatment for patients diagnosed with extrahepatic biliary tract cancer [38, 40, 55]. However, because of its specific location surrounded by multiple viscera and complex vascular structures, resection of extrahepatic biliary cancer frequently requires combined hepatic resection or Whipple procedure to secure the surgical margin. In addition, extrahepatic biliary cancers are often complicated by jaundice and impaired hepatic function due to obstruction of the biliary tract. Therefore, meticulous preoperative assessment and preparations are needed to achieve this 'high-risk' surgical resection. In this chapter, surgical strategies and technical refinements to improve the treatment outcomes of extrahepatic biliary cancer will be described.

2 Anatomic Basis for the Surgical Resection of Extrahepatic Biliary Cancer

2.1 Variations in Biliary Anatomy

In 1957, Couinaud [10] described major variations of biliary anatomy in adult liver (Fig. 1). One of the most important observations in his work is that the left hepatic duct is

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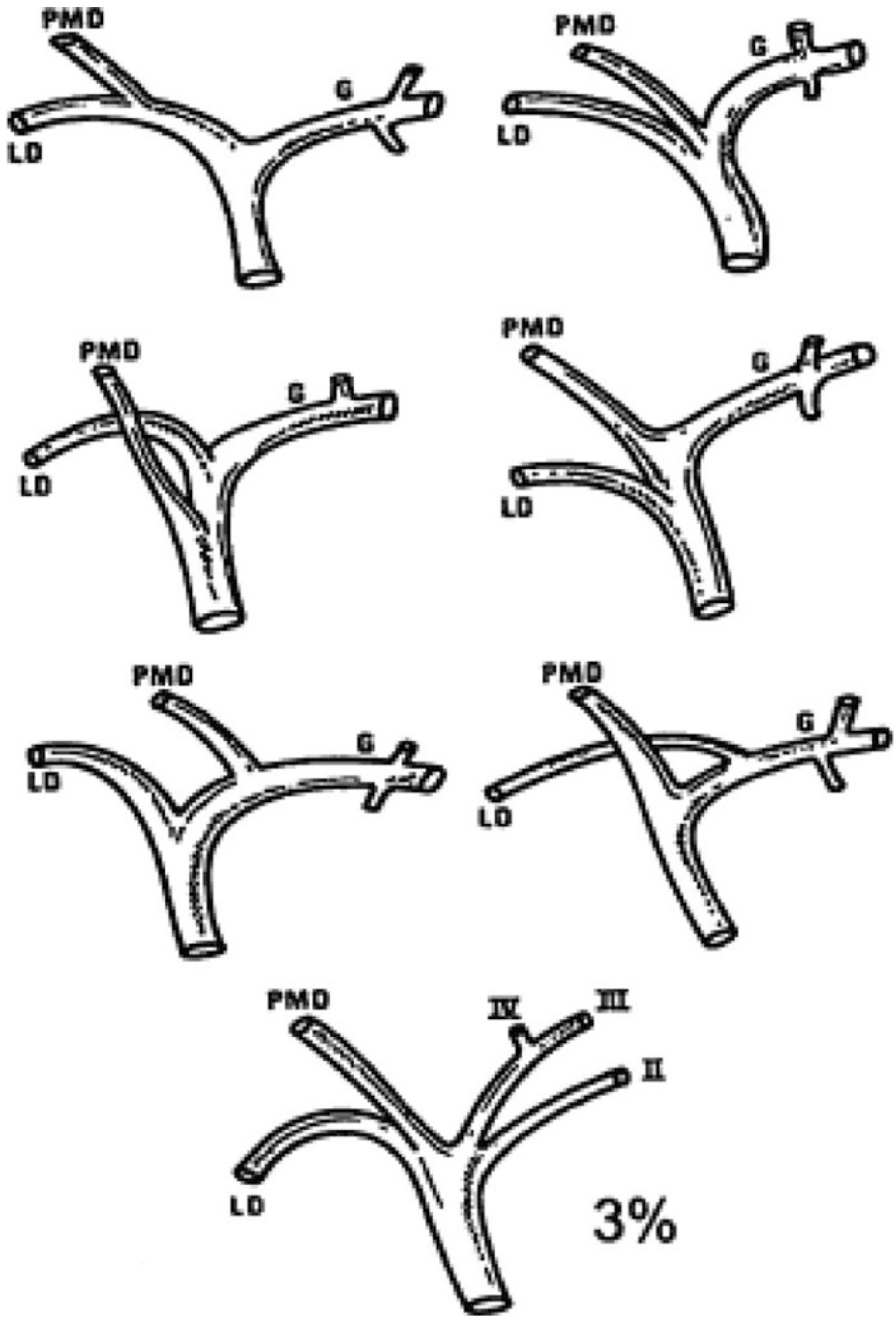

Fig. 1 **Variations in biliary anatomy**. The left hepatic duct is long and present in 97 % of patients. In types I, II, and IIIa hilar cholangiocarcinomas, an extended right hepatectomy permits placement of a safe and single anastomosis away from the confluence, minimizing the probability of positive margins. *G left*; *LD right lateral* ; *PMD* right paramedian (from [10] pp 469–479, with permission.)

present in 97 % of patients, while the biliary branches for the right side of the liver vary considerably. It is also noteworthy that the left hepatic duct is mostly extrahepatic, located strategically at the base of Segment IV, and extends to the left for a length of 1–5 cm. These characteristics aid in the extension of the resection toward the left, away from the biliary confluence, with minimizing the likelihood of positive margins and facilitating the biliary reconstruction [61].

2.2 Three-dimensional Relationship between the Extrahepatic Biliary Tract and Surrounding Vascular Structures

Figure 2 shows a typical three-dimensional relationship among the biliary tract, the portal vein, and the hepatic artery at the hepatic hilum. The common hepatic duct bifurcates into the right and left branches at the very cephalad part of the hepatoduodenal ligament, and these

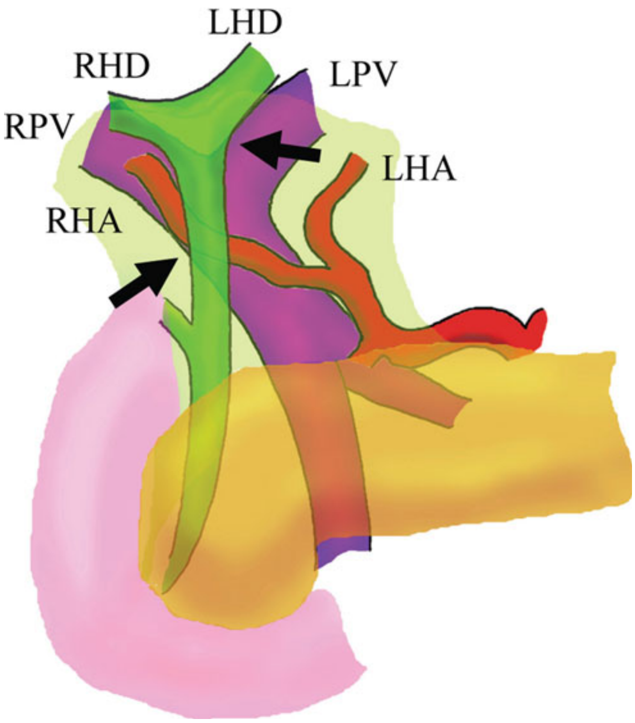

Fig. 2 **Vascular anatomy at the hepatic hilum**. Right hepatic artery and portal bifurcation are located just behind the extrahepatic biliary tract, and they are subjected to invasion by extrahepatic biliary cancers at these points (*arrows*). *LHA* left hepatic artery; *LHD* left hepatic duct; *LPV* left portal vein; *RHA* right hepatic artery; *RHD* right hepatic duct; *RPV* right portal vein

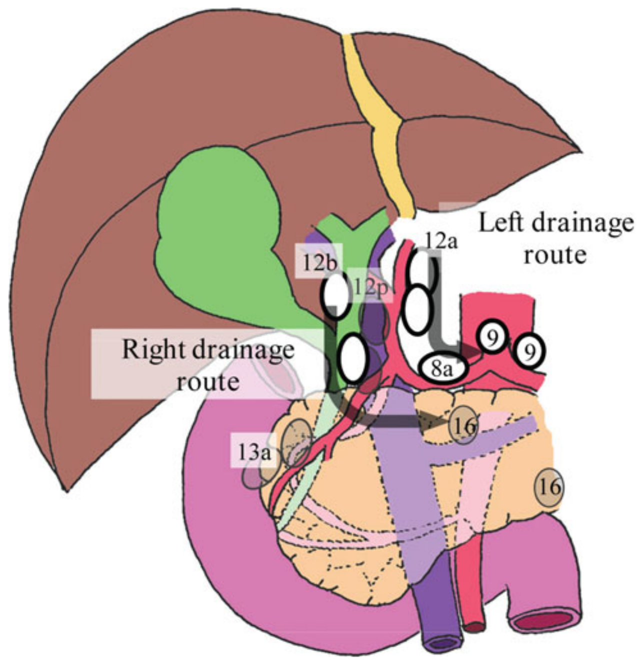

Fig. 3 Schematic drawing of the biliary lymphatic system and supposed major drainage routes (Adapted from [29])

branches run within the dense connective tissue called *hilar plate* before entering the hepatic parenchyma. Two oncologically important anatomic features regarding the three-dimensional vascular relationship are that (1) the right hepatic artery runs just behind the common hepatic duct and (2) the portal bifurcation is located very close to the confluence of the hepatic ducts. Because these structures are prone to invasion by extrahepatic biliary cancers, right-sided hepatic resection is preferred in most of the surgical resection for hilar cholangiocarcinoma.

2.3 Peribiliary Lymphatic Systems

Patterns of peribiliary lymphatic drainage have been actively investigated, and two major lymphatic drainage routes have been described [34, 78]: the right-sided route from biliary/portal nodes (No. 12b/12p) to para-aortic nodes (No. 16) and the left-sided route from hepatic arterial nodes (No. 12a) to para-aortic nodes (No. 16) via common hepatic arterial nodes (No. 8a) and celiac nodes (No. 9) (Fig. 3). Although the detailed anatomy in biliary lymphatic systems has not been fully understood, groups of regional lymph node have been defined and lymphadenectomy has been recommended according to each location of tumor [39, 68].

3 Assessment of Tumor Extension and Surgical Planning

3.1 Diagnosis and Assessment of Tumor Extension

For diagnosis of extrahepatic malignancy, histologic assessment is required to rule out other benign cause for biliary obstruction. Extent of disease is assessed using several imaging modalities including computed tomography (CT), magnetic resonance imaging/cholangiopancreatography (MRI/MRCP), endoscopic ultrasonography (EUS), fluorodeoxyglucose positron emission tomography, or direct cholangiography via endoscopic or percutaneous routes. Among these, direct contrast cholangiography may yield the most important anatomic data regarding the location and morphologic characteristics of biliary obstruction. However, cholangiography may place the patients at risk for cholangitis and hepatic abscess by introducing enteric/cutaneous flora to the biliary system. Also, subsequently placed biliary stent would interfere with further evaluation of resectability by the other imaging modalities. Aloia et al. [3] have reported that the use of high-resolution CT is an

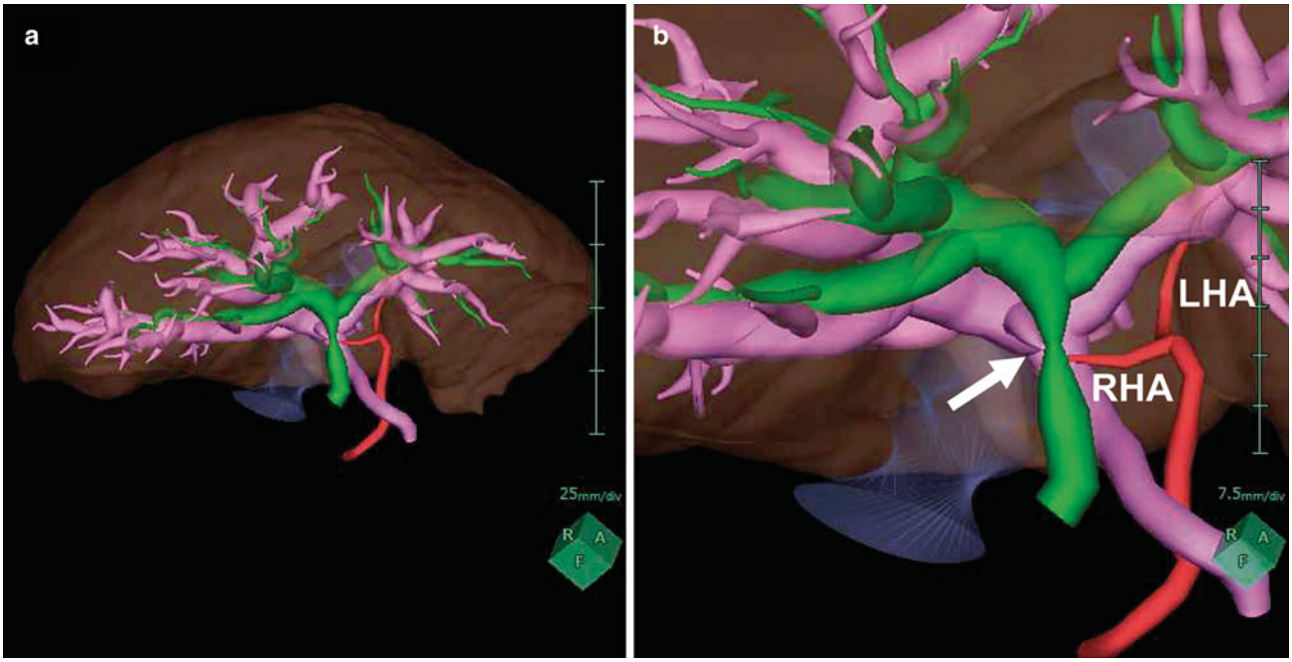

Fig. 4 3-D visualization of anatomic structures for surgical planning of hilar cholangiocarcinoma (courtesy to Dr. Yoshihiro Mise). **a** 3-D intrahepatic vascular structures (*pink* portal vein; *green* biliary tract; *red* hepatic artery). **b** Magnified view of hepatic hilum. Cancerous stricture of the common hepatic duct (*arrow*) and its relation with the right hepatic artery are clearly visualized. *RHA* right hepatic artery; *LHA* left hepatic artery

oblique coronal plane with three-dimensional reformation that accurately predicts resectability of hilar cholangiocarcinoma with sensitivity of 94 % and specificity of 79 %. Thin-slice high-resolution CT scan with an adequate enhancement protocol may offer sufficient anatomic and oncological data for surgery non-invasively. It may also enable simultaneous assessment of distant metastasis through single scanning from thorax to pelvis.

3.2 Surgical Planning with Advanced Imaging Modalities

Recently, a novel three-dimensional (3-D) simulation technique has been introduced and broadly used in anatomic confirmation and/or surgical planning for complex hepatobiliary surgery [45, 64, 65, 72]. The major advantages of this technique are individualized inflow/outflow analysis and accurate volume calculation that enables surgical planning through various virtual hepatectomies simulated on a computer. For surgical planning of extrahepatic biliary cancer, a 3-D simulator offers accurate visualization of 3-D vascular relationships and it may help to avoid misunderstandings of complex anatomy and secure surgical margin (Fig. 4).

4 Preparation for Safe Surgical Resection

4.1 Biliary Drainage

Because biliary obstruction and jaundice have been reported to impair hepatic function, [16, 25, 35], biliary drainage either by endoscopic or percutaneous approach is preferable for patients with small future liver remnant. Empirically, portal vein embolization and surgical resections can be safely performed when serum bilirubin levels reach less than 5 mg/dL and less than 2 mg/dL, respectively [41, 71]. However, biliary drainage may also increase the risk of cholangitis or hepatic abscess due to introduction of enteric/cutaneous flora. Therefore, adequate management of drainage tubes (e.g., checking the patency of the stent by daily counting drainage volume) and close monitoring of signs of cholangitis are required to minimize preoperative cholangitis and optimize surgical outcome.

4.2 Portal Vein Embolization

Portal vein embolization (PVE) is a safe and minimally invasive procedure that leads to atrophy in the liver to be resected and compensatory hypertrophy of the future liver

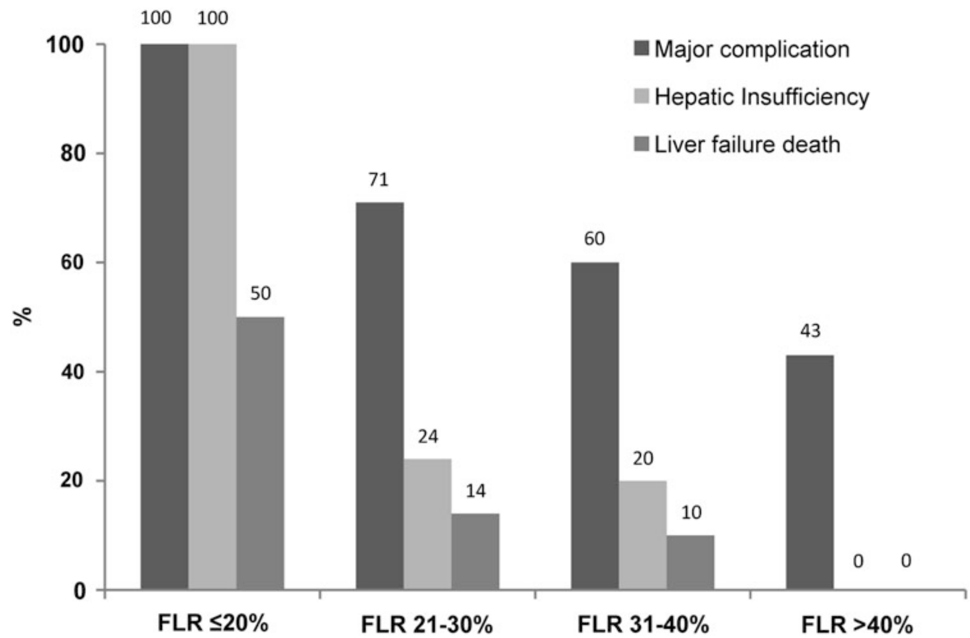

Fig. 5 Incidences of major complication, hepatic insufficiency, and liver failure death after resection of hilar cholangiocarcinoma (MD Anderson Cancer Center 1997–2011, $n = 47$)

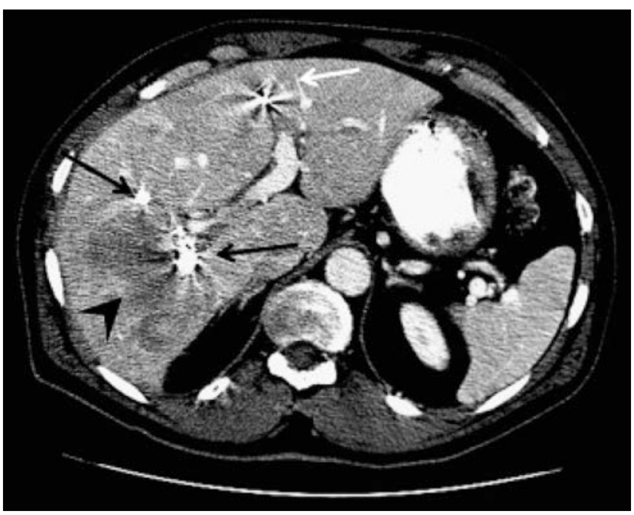

Fig. 6 CT image after right PVE + Segment IV embolization. Note that major S4 branches, in addition to right portal vein branches, were distally embolized (*white arrow*). *Black arrows*, coils used to embolized right portal vein branches; *black arrowhead*, tumor (From [37], with permission)

remnant (FLR). Although proposed minimum requirement of FLR volume in patients with normal liver varies among the authors and optimal FLR volume for extrahepatic biliary cancer is still controversial, [25, 35, 36, 53, 71, 81], many patients have complications such as jaundice, cholangitis, or malnutrition before surgery, and therefore, at least 30–40 % of FLR volume may be needed especially in patients with hilar cholangiocarcinoma [35, 53, 71] (Fig. 5).

To maximize regeneration of the FLR in PVE, selection of embolic materials [44] and concurrent embolization of Segment IV portal veins [37, 52] have been recommended. Our previous work comparing right PVE with and without Segment IV embolization revealed significant difference in volume increase rates in Segment II + III (median, 26 % vs. 54 %; $p = 0.021$) [37] (Fig. 6). Recently, European groups have introduced associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) approach consisting of right portal vein ligation and in situ splitting of the liver at the umbilical fissure, and reported rapid and significant regeneration of FLR after the procedure. However, considering the very high morbidity and mortality rates of current ALPPS approach, [70], routine use of this technique should be avoided in patients with extrahepatic biliary cancer who are at high risk of postoperative hepatic insufficiency.

5 Surgical Principles for Hilar Cholangiocarcinoma

5.1 Classification and Surgical Approach

Surgical procedure for hilar cholangiocarcinoma is selected according to the Bismuth–Corlette classification (Fig. 7) [6]. For types I, II, and IIIa hilar cholangiocarcinoma, an extended right hepatectomy is usually performed, whereas for type IIIb hilar cholangiocarcinoma, a left or extended left hepatectomy is performed. In both surgical approaches, Segment IV must be completely or partially resected because most hilar cholangiocarcinomas extend to involve the base of Segment IV. Isolated bile duct resections or central resections for these tumors are not recommended

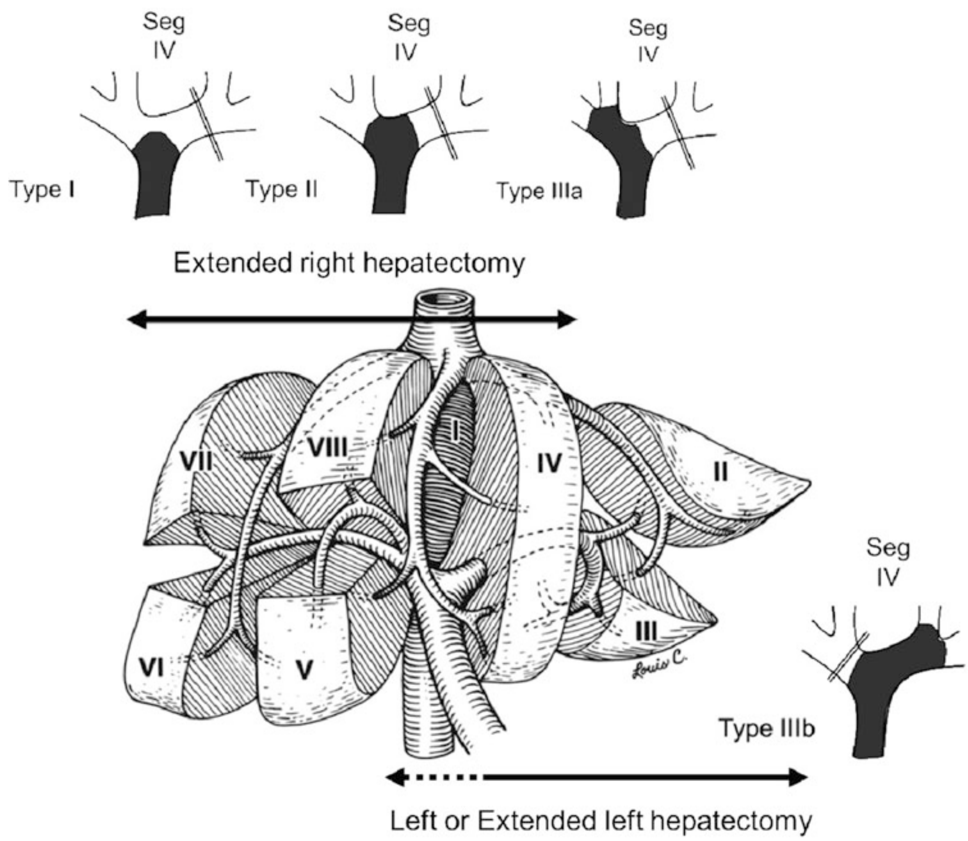

Fig. 7 Extent of hepatic resection according to Bismuth–Corlette classification of hilar cholangiocarcinoma (adapted from [62] with permission)

because of the limited margins and multiple bile duct anastomoses, both of which increase the risk of bile leaks and recurrences [61].

5.2 Significance of Caudate Lobe Resection

Mizumoto et al. [49] first emphasized the importance of resection of the caudate lobe based on their observation that 11 out of 26 patients had tumor invasion to the caudate lobe or its biliary branches and that curative resection rate was higher in patients with combined caudate lobectomy. Sugiura et al. [74] indicated that the survival rate was superior in patients with combined caudate lobectomy in a multi-institutional study. Type I or II hilar cholangiocarcinoma can theoretically be resected without hepatectomy. However, caudate branches usually drain into proximal part of the hepatic ducts, and prognostic superiority of hepatectomy with combined caudate lobectomy for types I and II hilar cholangiocarcinoma has also been reported [24].

Anatomic structure of the caudate lobe and distribution of its biliary ducts are rather complex. However, in some cases, partial preservation of the caudate lobe can be feasible especially on the left side (Spiegel lobe) as long as tumor invasion to this part or to its biliary branch can be excluded (Fig. 8). Couinaud [11] reported that Spiegel branch drains into left hepatic duct in 90 % of the cases, while drainage patterns of right caudate branch vary considerably. If the Spiegel duct is sufficiently distant from the biliary bifurcation and drains into left hepatic duct, Spiegel lobe can be preserved in extended right hepatectomy.

5.3 Role of Vascular Resection

Due to proximity to major vascular structures (Fig. 2), portal bifurcation is often involved and combined resection is required for R0 resection in some cases. Recently, with introduction of vascular surgery techniques, relatively favorable outcomes in *en bloc* portal vein resection have been reported [54, 56, 57]. However, morbidity/mortality rates associated with this procedure is relatively high (Table 1), and its prognostic impact is still controversial. Therefore, vascular resection should be considered only in patients with definite vascular invasion.

5.4 Long-term Surgical Outcomes

Surgical outcomes of hilar cholangiocarcinoma reported from high-volume centers during the last decade have shown that 3- and 5-year overall survival rates ranged from

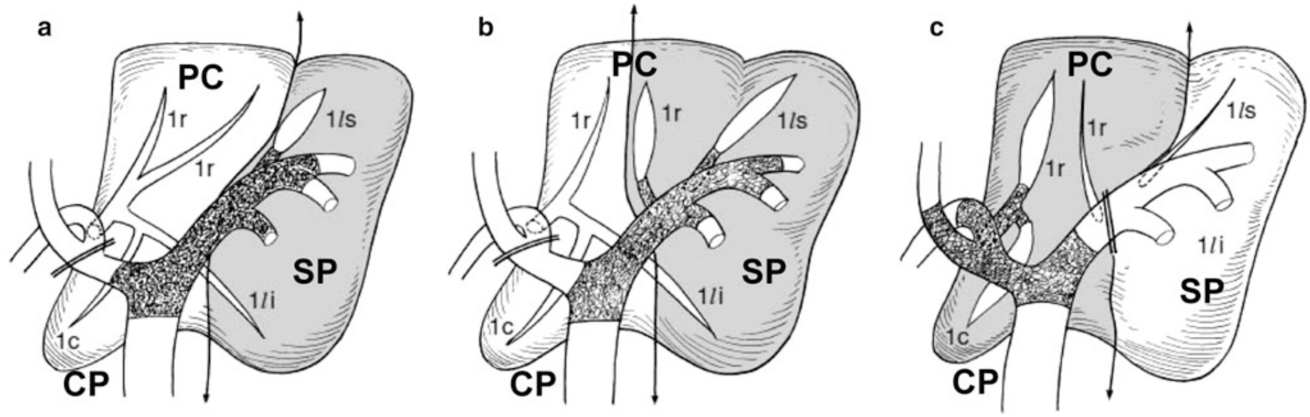

Fig. 8 Partial preservation of the caudate lobe based on the biliary anatomy and tumor invasion (Adapted from [59] Tan-to-sui 26:309–314 with permission). **a** Preservation of right caudate lobe in extended left hepatectomy for type IIIb tumor without invasion to 1r and 1c. **b** Partial preservation of right caudate lobe in extended left hepatectomy for type IIIb tumor with suspected invasion to one of right caudate branch (1r). **c** Preservation of the Spiegel lobe in extended right hepatectomy for type IIIa tumor without invasion to Spiegel branches. Areas with *black dot* represent tumor invasion. *Gray* areas represent part of the caudate lobe to be resected. *SP* Spiegel lobe; *PC* paracaval portion; *CP* caudate process; 1r, right caudate branch; 1c, caudate process branch; 1/s, left superior branch; 1/I left inferior branch

Table 1 Curative resection rate and operative mortality in patients who underwent vascular resection

Authors	Year	*N*	R0 resection (%)	Mortality (%)
Nimura et al. [57]	1999	29	–	17.2
Neuhaus et al. [56]	1999	23	60.9	17.4
Ebata et al. [14]	2003	52	–	9.6
Miyazaki et al. [47]	2007	41	55.9	8.8
Hirano et al. [20]	2009	64	96.9	4.7
Nagino et al. [54]	2010	50	66.7	2.0
Hemming et al. [18]	2011	42	–	5.0

37 to 60 % and 20 to 42 %, respectively [2, 5, 8, 13, 17, 19, 21, 23, 26, 32, 43, 48, 51, 56, 58, 67, 71, 77, 80, 86]. A recent report from Japanese Biliary Tract Cancer Statistics Registry revealed that the overall 3- and 5-year survival rates after curative surgery for hilar cholangiocarcinoma ($n = 255$) were 47 and 39 %, respectively [46].

6 Surgical Principles for Distal Bile Duct Cancer

6.1 Tumor Distribution and Selection of Surgical Procedure

Distal bile duct cancer comprises 20–30 % of all cholangiocarcinoma [1]. Because of its specific location at the terminal part of the biliary tract, most patients present jaundice at relatively early stage of the disease, and accordingly, resection rate of distal bile duct cancer is usually higher than hilar cholangiocarcinoma.

Pancreaticoduodenectomy (PD), including pylorus-preserving PD (PPPD) coupled with lymphadenectomy, is the standard treatment of choice for the complete removal of distal bile duct cancer. Simple extrahepatic bile duct resection is feasible only in 10 % of patients [15, 82]. For patients with distal bile duct cancers, PPPD has been investigated with the expectation of functional preservation of the stomach. However, randomized controlled trial and meta-analysis have revealed that PD and PPPD provide equal short-term and long-term outcomes for pancreaticobiliary malignancies. Therefore, selection of surgical procedure should depend on the results of preoperative assessment including potential nodal involvement and/or extent of tumor invasion.

6.2 Long-term Surgical Outcomes

The overall 3- and 5-year survival rates after surgical resection of distal bile duct cancer ranged from 33 to 63 % and 16 to 52 %, respectively [2, 4, 9, 12, 22, 28, 31, 33, 42,

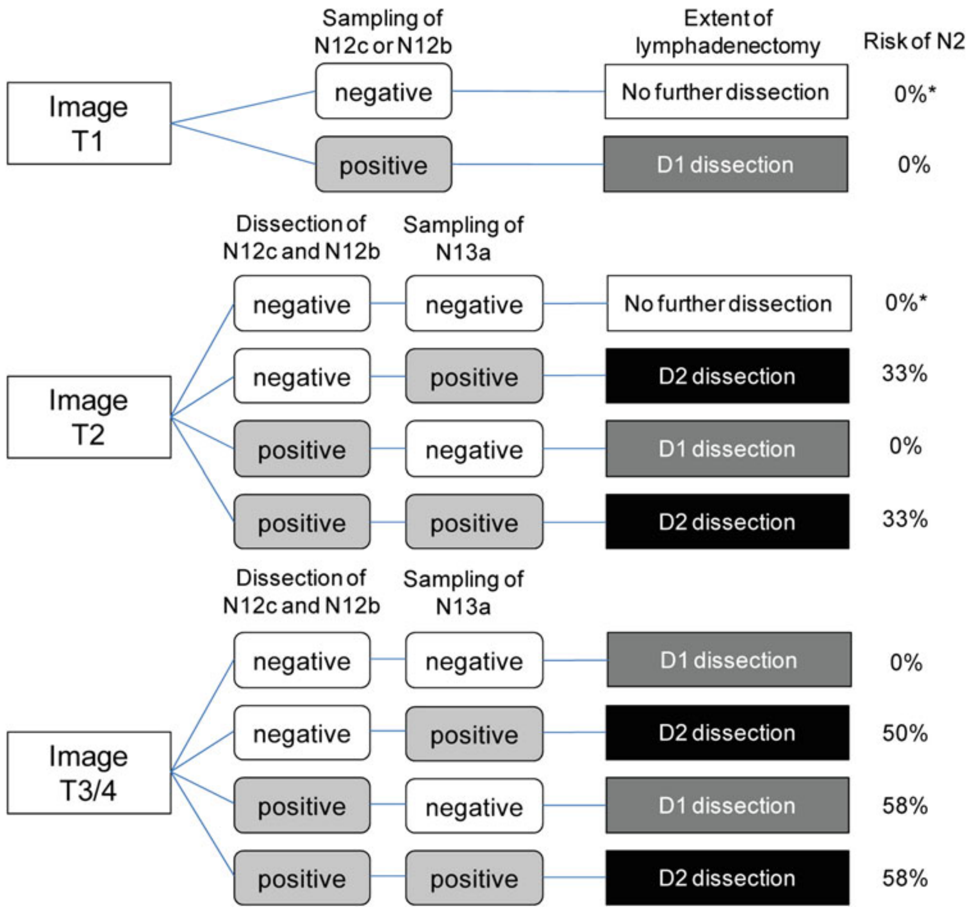

Fig. 9 Algorithm for the extent of lymph node dissection based on preoperative diagnosed T factor (Image T) and intraoperative frozen section of key lymph nodes. (Adapted from [39] with permission). D1 dissection, lymphadenectomy of first-echelon lymph nodes (N12c and N12b); D2 dissection, lymphadenectomy of second-echelon lymph nodes (N12p, N12a, N13a, N8a, and N8p). Number of lymph node is based on the classification of Japanese Society of Biliary Surgery [29]. N12c, cystic nodes; N12b, pericholedochal nodes, N12p, portal nodes; N12a, nodes along the proper hepatic artery; N13a, superior retropancreatic nodes; N8a, anterior nodes along the common hepatic artery; N8p, posterior nodes along the common hepatic artery. * Risk of N1, 0 %

50, 60, 66, 69, 75, 84, 85]. The latest report from Japanese Biliary Tract Cancer Statistics Registry revealed that the overall 3- and 5-year survival rates after PD or PPPD for distal bile duct cancer ($n = 779$) were 58 and 44 %, respectively [46].

7 Surgical Principles for Gallbladder Cancer

7.1 Selection of Surgical Procedure Based on the Clinical Outcomes

Various surgical procedures have been indicated for gallbladder cancer according to the extent of the disease. However, precisely preoperative staging remains difficult. Therefore, surgical approach should be adopted systematically based on the previous clinical outcomes. In surgical treatment of gallbladder cancer, R0 resection is needed to achieve extended survival [73]. To achieve this surgical outcome, various surgical approaches have been attempted.

7.1.1 Lymphadenectomy

Effectiveness of lymphadenectomy has been well documented [39, 73, 79]. Also, assessment of lymph node status is recommended for risk stratification after surgery [27]. Although there still remain controversies in optimal extent of lymphadenectomy, incidence of lymph node metastases is well correlated with depth of tumor invasion. Kokudo et al. [39] investigated the accuracy of preoperative image studies in predicting T stage of gallbladder cancer and proposed algorithms for stepwise lymphadenectomy based on the risk and incidence of lymph node involvement (Fig. 9).

7.1.2 Hepatic Resection

When direct invasion of gallbladder cancer to the liver or the bile duct is evidenced or suspected, gallbladder bed or further extensive hepatic resection, or combined bile duct resection is performed. However, optimal extent of resection remains controversial.

7.1.3 Pancreaticoduodenectomy and Combined Resection of Surrounding Organs

En bloc resection is required to achieve R0 resection according to the patterns of tumor invasion in advanced gallbladder cancer. In selected patients with advanced tumor, prognostic advantage of pancreaticoduodenectomy-combined major hepatectomy has been reported if R0 resection is feasible [83].

7.2 Additional Resection and Lymphadenectomy for Incidentally Diagnosed Gallbladder Cancer after Cholecystectomy

When gallbladder cancer is incidentally diagnosed in resected specimen by cholecystectomy, additional resection is required in some patients. For patients with T1 tumor, additional resection or lymphadenectomy is unnecessary because of the very low incidence of lymph node metastasis. However, when the depth of tumor is reaching subserosal layer (i.e., T2 or higher), additional resection with lymphadenectomy is required due to higher chance of lymph node metastasis as indicated in Fig. 9.

7.3 Long-term Surgical Outcomes

When R0 resection is feasible, long-term survival can be expected especially in early-stage gallbladder cancer. A five-year overall survival rate is of 41.6 % after curative resection in a large cohort of patients with gallbladder cancer ($n = 1{,}094$) [46]. Because the reported 5-year survival of Stage III gallbladder cancer (41.8 %) was higher than Stage III hilar or distal cholangiocarcinoma (30.5 %), systematic approach for R0 resection is important to achieve long survival.

8 Effectiveness of Adjuvant Therapy for Extrahepatic Biliary Tract Cancer

Extrahepatic biliary tract cancer has a propensity to recur locally or regionally [30], and it is the leading cause of morbidity and tumor-related mortality. For this reason, various adjuvant therapies have been attempted especially in advanced biliary cancers. However, there have been only two prospective studies [63, 76] on the effectiveness of adjuvant chemotherapy or radiotherapy for extrahepatic biliary cancer, and no prognostic advantages have been shown. In addition, our group previously investigated the efficacy of adjuvant chemoradiotherapy for extrahepatic biliary tract cancer. Although time to local recurrence tended to be longer in patent treated with postoperative chemoradiotherapy, total relapse-free survival and overall survival rates were not improved by adding additional chemoradiotherapy after surgery [7]. Therefore, there has been no established adjuvant therapy for extrahepatic biliary cancer, and accordingly, surgery plays a central role in treatment for extrahepatic biliary cancer.

9 Conclusion

Because the extrahepatic biliary tract is in a critical anatomic location surrounded by complex vascular structures and multiple organs, surgical resection of a biliary malignancy often requires resection of adjacent organs. In addition, because of jaundice caused by biliary obstruction and very small future liver remnant in extended hepatic resection for biliary cancer, careful preparations including biliary drainage and portal vein embolization are needed prior to extensive resections. However, surgical resection is the only therapeutic option offering a chance of cure for patients with extrahepatic biliary tract cancers. Thus, optimization of the condition of the patient and selection of appropriate surgical procedure are needed to achieve favorable surgical outcomes.

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