

Resection of Perihilar Cholangiocarcinoma



Hermien Hartog, MD, PhD^a, Jan N.M. Ijzermans, MD, PhD^a,
Thomas M. van Gulik, MD, PhD^b, Bas Groot Koerkamp, MD, PhD^{a,*}

KEYWORDS

- Perihilar cholangiocarcinoma • Hepatectomy • Caudate lobectomy
- Staging laparoscopy • Vascular reconstruction

KEY POINTS

- Staging laparoscopy avoids unnecessary laparotomy in 1 out of 4 patients with perihilar cholangiocarcinoma (PHC) scheduled for potential resection.
- Key anatomic features essential to recognize for resection of PHC:
 - Proximity of the biliary confluence to the right hepatic artery, except in cases of aberrant right hepatic artery.
 - The relation of the umbilical fissure and the confluence of the segment II and III bile ducts.
 - The relation of the right posterior bile duct and the right portal vein branches.
- Arterial involvement, lobar atrophy, and proximal biliary involvement together determine the feasibility of a complete resection and the optimal extent of resection.
- Portal venous resection may be required for a complete resection. Experts disagree whether arterial reconstructions should be considered in selected patients.
- Concomitant caudate lobectomy is the standard of care for resections of PHC based on level 2 evidence of increasing R0 resection rates.

INTRODUCTION

Perihilar cholangiocarcinoma (PHC) is located at the confluence of the left and right hepatic ducts. It is distinguished from distal cholangiocarcinoma by arising proximal to the cystic duct confluence.¹ Intrahepatic cholangiocarcinoma typically involves large liver tumors arising proximal to the second-order bile ducts.¹ The location of

^a Division of HPB and Transplant Surgery, Department of Surgery, Erasmus MC, Postbus 2040, 3000 CA Rotterdam, The Netherlands; ^b Department of Surgery, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands

* Corresponding author. Department of Surgery, Erasmus MC, Postbus 2040, Rotterdam 3000 CA, The Netherlands.

E-mail address: b.grootkoerkamp@erasmusmc.nl

PHC at the biliary confluence near the bifurcation of the portal vein and the right hepatic artery explains why surgical resection is challenging.

The incidence of PHC is about 1 to 2 patients per 100,000 in Western countries. Patients typically present at an advanced stage with jaundice, weight loss, and abdominal discomfort.²⁻⁴ Up to 65% of patients have unresectable or metastatic disease at time of presentation or surgical exploration and are ineligible for surgical resection.^{3,5} Surgery for PHC is complex low-volume surgery, and therefore mainly performed in tertiary referral centers. The role of surgery for palliation is limited. Palliative treatment involves endoscopic and percutaneous biliary drainage and systemic chemotherapy.⁶⁻⁸

Most patients with resectable PHC require a major liver resection, which may entail complex biliary and vascular reconstruction. Over the past decades, the safety of major liver resections has increased because of improvements in perioperative management, resulting in a postoperative mortality of 1% to 3% in Eastern series.⁹ However, 90-day postoperative mortality after resection of PHC was about 10% in 2 large nationwide Western series.^{10,11} The main challenge in the preoperative management for patients with PHC is biliary drainage. A major liver resection may result in liver failure without prior biliary drainage of the future liver remnant (FLR). However, biliary drainage itself may cause cholangitis and liver failure.

This article gives an overview of current standards in surgical treatment of PHC and a description of signature strategies to PHC. Updates of twenty-first century management and outcomes have been published by all major groups and are summarized in this article ([Appendix 1](#), [Table 1](#)).

PREOPERATIVE STAGING AND MANAGEMENT

Classification

Several tumor-staging systems have been developed to classify PHC for resectability and prognosis. The Bismuth-Corlette system¹² describes the extent of involvement of the biliary tree, but is insufficient to determine resectability and poorly predicts survival ([Fig. 1B](#)). The Blumgart/Memorial Sloan Kettering Cancer Center (MSKCC) system added portal vein involvement and lobar atrophy to the biliary extent of the tumor.⁵ This addition led to a 3-stage system that is associated with both resectability and survival (see [Fig. 1B-D](#)).¹³

The seventh edition of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control staging system requires histopathologic data that become available only after surgical resection.¹ The recently proposed Mayo staging system is based on imaging features, performance status, and cancer antigen 19.9 level.¹⁴ The AJCC and the Mayo staging are not useful to determine resectability in the preoperative setting.

Preoperative Staging

Staging of PHC typically starts with an abdominal and chest computed tomography (CT) scan to rule out stage IV disease. Both distant metastases and lymph node involvement beyond the hepatoduodenal ligament (ie, N2 nodes) are considered stage IV disease.¹ Suspicious lymph nodes beyond the hepatoduodenal ligament (ie, celiac or periaortic) may be assessed by endoscopic ultrasonography and fine-needle aspiration. Biliary extent of the tumor (Bismuth classification), portal vein and hepatic artery involvement, and anatomic variants are also addressed by multiphase contrast-enhanced liver CT. Magnetic resonance cholangiopancreatography is recommended if surgical decision making requires more detail of the biliary extent of

the tumor. With high suspicion of malignancy on imaging, pathologic confirmation of PHC before surgery is not imperative. A negative brush or biopsy does not rule out cancer. Series of resection for PHC typically find a benign cause in about 10%.^{15–17}

Anatomy

Several anatomic relations may determine resectability and the extent of liver resection (see **Fig. 1A**):

- The biliary confluence is located eccentrically to the right side of the hepatoduodenal ligament. The right portal vein and right hepatic artery are at higher risk of tumor involvement even in tumors mainly involving the left hepatic duct.
- The right hepatic duct and portal vein divide early into second-order branches. Consequently, complete resection with a wide margin and reconstruction of bile ducts and portal vein can be difficult. The left hepatic duct and portal vein have a longer extrahepatic course before branching.
- The left hepatic artery is rarely involved because it runs at the left periphery of the porta hepatis before entering the umbilical fissure.
- Segment I bile ducts enter the main bile ducts near the confluence of the left and right hepatic duct superior to the portal bifurcation and are therefore typically involved by direct tumor spread.¹⁸
- Biliary obstruction and portal vein involvement may cause lobar atrophy as shown by a shrunken lobe without regeneration capacity.⁵

Several prevalent anatomic variations may further affect the surgical strategy for liver resections:

- About 10% of patients have an infraportal right posterior duct compared with a supraportal course (**Fig. 2**). This variation allows a wider right posterior and anterior sectoral bile duct margin with a left hemihepatectomy.¹⁹
- About 10% of patients have a replaced or accessory right hepatic artery arising from the superior mesenteric artery.²⁰ Because this artery courses at the right and dorsal side of the hepatoduodenal ligament, it evades its normal close proximity to the biliary confluence.

Resectability

Centers in the Western and Eastern hemispheres disagree whether patients with stage IV PHC should undergo a resection. In Eastern series, patients with stage IVb PHC typically represent up to 10% of patients undergoing a resection.^{19,21} Because survival of these patients is poor, most Western centers do not consider a resection for stage IV disease.

The goal of surgery is to completely remove all tumor tissue (R0 resection) maintaining an adequate FLR. An incomplete (R2) resection is probably futile and any potential benefit too small to justify the surgical risk. The biliary extent of PHC should allow an R0 resection and permit technically feasible biliary-enteric anastomoses. An adequate FLR includes at least 2 contiguous liver segments with arterial and portal inflow and venous outflow. An adequate FLR is typically defined as representing at least 25% of the total liver volume. However, the size of an adequate FLR also depends on the FLR function, which is determined by preexisting liver disease and biliary obstruction. Preoperative cholestasis and cholangitis are risk factors for postoperative liver failure and may require a larger FLR (ie, 30%–40%). PHC is unresectable if an R0 resection or an adequate FLR is not anticipated. In some patients a curative-intent resection is only possible with an arterial reconstruction. Clinicians at most Western centers think that

Table 1
Recent Eastern and Western patient series of resected PHC

Author	Accrual	N	Median Survival (mo)	Morbidity (%)	Mortality (%)	CL (%)	R0 (%)	L/R	Tri/Hemi/Min
Eastern Series									
Nagino et al ⁴⁴	2001–2010	386	36	47	2	100	78	219/148	121/245/20
Lee ⁷⁸	2000–2008	302	28–47	43	2	100	71	94/163	14/243/45
Song et al ³⁶	1995–2010	230	39	9	4	44	77	41/132	80/93/54
Shimizu et al ²¹	1984–2008	224	±34	40	2–10	100	63–69	88/84	13/159/26
Esaki et al ²⁶	2000–2011	214, incl. IHC	38–45	56	3	100	53–72	119/46	30/182/2
Natsume et al ¹⁹	2001–2010	201	24	33–59	1	100	70–85	—	86/115/—
Matsumoto et al ²⁷	2001–2012	174	±36	27–45	0–4	100	85 vs 82	—/174	33/141/—
Cheng et al ³³	2001–2010	171	29	26	3	80	78	122/41	28/131/12
Chen et al ³¹	2000–2007	138	38	30	0	83	89	26/19	—/45/93
Kow et al ³⁴	1995–2010	127	35–64	6	3	55	88	34/83	45/72/—
Unno et al ⁷⁹	2001–2008	125	27	49	8	100	63	51/74	10/115/—
Hosokawa et al ²⁸	2001–2012	61	25–42	51	3	100	72	61/0	18/43/—
Xiong et al ⁴⁷	2005–2012	52	13–45	34–70	4	85	65–100	14/6	—/20/32
Lim et al ⁴⁶	2000–2012	52	19–23	31	0	100	73–100	6/13	1/18/26
Tamoto et al ⁴³	2005–2009	49	21	63	4	NR	82	0/49	49/—/—

Western Series									
Nuzzo et al ¹⁰	1992–2007	440, MC	NR	48	10	78	77	182/172	106/248/86
Farges et al ¹¹	1997–2008	366, MC	NR	67	11	Usually	NR	182/184	NR
De Jong ⁸⁰	1984–2010	305, MC	NR	NR	12	NR	65	95/114	68/141/96
Wahab et al ³⁵	1995–2010	159	36	52	6	50	55	104/55	—/159/—
Matsuo et al ¹³	1991–2008	157	39	59	8	43	76	53/72	64/61/31
Neuhaus et al ⁴²	1990–2004	100	24–60	NR	8–9	100	NR	27/73	83/17/—
Hemming ⁸¹	1999–2010	95	38	35	5	100	84	29/66	74/11/—
Ribero et al ³²	1989–2010	82	25	65	10	95	89	33/39	29/44/9
van Gulik et al ⁵⁰	2008–2010	41	NR	46	7	78	92	13/18	29/2/10
Total, n%/median, range	—	4251	34 (13–64)	42 (6–70)	5 (0–12)	100 (43–100)	78 (53–100)	1393/1825 43 vs 57%	981/2305/542 26/60/14%

Search strategy: PubMed: (hilar OR perihilar) AND (cholangio*). Limits: English, humans. Case series published before 2008 or with fewer than 5 patients per year were excluded.

Abbreviations: CL, caudate lobectomy; Hemi, hemihepatectomy; IHC, intrahepatic cholangiocarcinoma; L/R, left-sided and right-sided liver resections; MC, multicenter study; Min, minor resection, including central liver resections and extrahepatic bile duct resections; NR, not reported; R0, R0 resection rate; Tri, trisectionectomy.

Data from Refs. [10](#), [11](#), [13](#), [19](#), [21](#), [26–28](#), [31–36](#), [42–44](#), [46](#), [47](#), [50](#), [78–81](#)

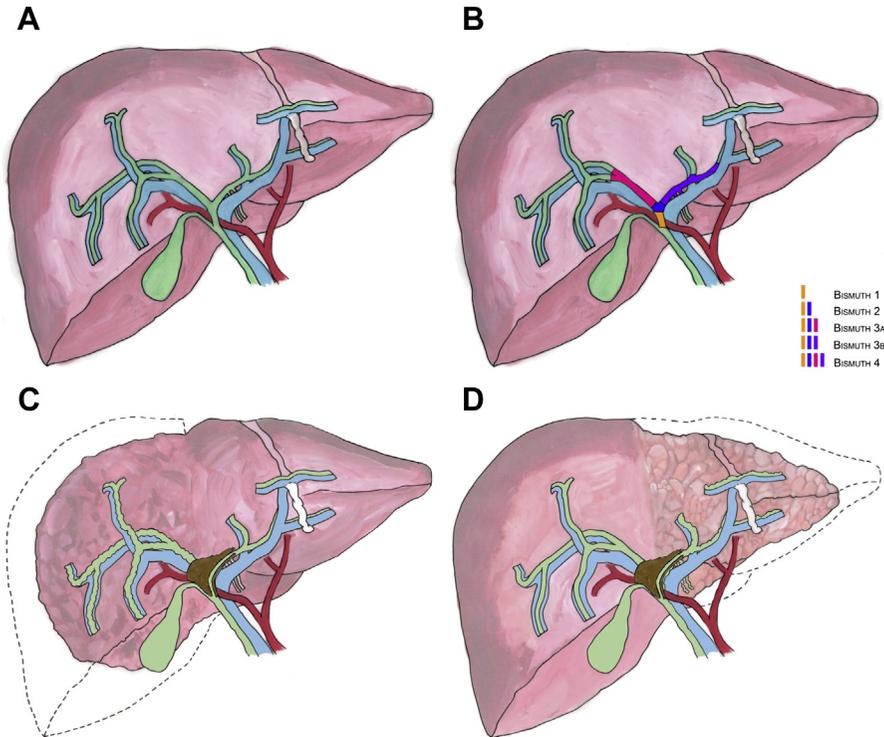


Fig. 1. Classification of PHC. (A) Key anatomic features. (B) Bismuth-Corlette staging system. Blumgart/Memorial Sloan Kettering Cancer Center (MSKCC) stage T1: tumor involving bile duct bifurcation and/or unilateral extension into second-order bile ducts. (C) Blumgart/MSKCC stage T2, with unilateral vascular involvement and/or unilateral lobar atrophy. (D) Blumgart/MSKCC stage T3, with bilateral/contralateral involvement of second-order bile ducts, vascular involvement, and/or lobar atrophy. *Original artwork by Mrs. Elsbeth Leeffers.*

the increased postoperative mortality risk without proven survival benefit does not justify arterial reconstruction.²²

Preoperative Biliary Drainage

Endoscopic or percutaneous biliary drainage of the FLR facilitates restoration of FLR function and regeneration. The contralateral lobe needs to be drained only in case of cholangitis. Whether biliary drainage should be pursued in each jaundiced patient with resectable PHC is still subject to debate, as is the optimal route of decompression. Risk of cholangitis caused by instrumentation of the bile ducts should be weighed against improvement of liver function and regeneration with biliary drainage. Most centers currently recommend preoperative biliary decompression with bilirubin levels greater than 2 mg/dL.²³ Eastern centers typically prefer nasobiliary decompression.⁹ Western centers perform both endoscopic and percutaneous drainage. A phase III trial is currently recruiting patients to compare endoscopic and percutaneous drainage for patients with resectable PHC.²⁴

Portal Vein Embolization

When the FLR is smaller than 40% of the total liver volume, portal vein embolization (PVE) of the contralateral portal vein is recommended to induce hypertrophy of the

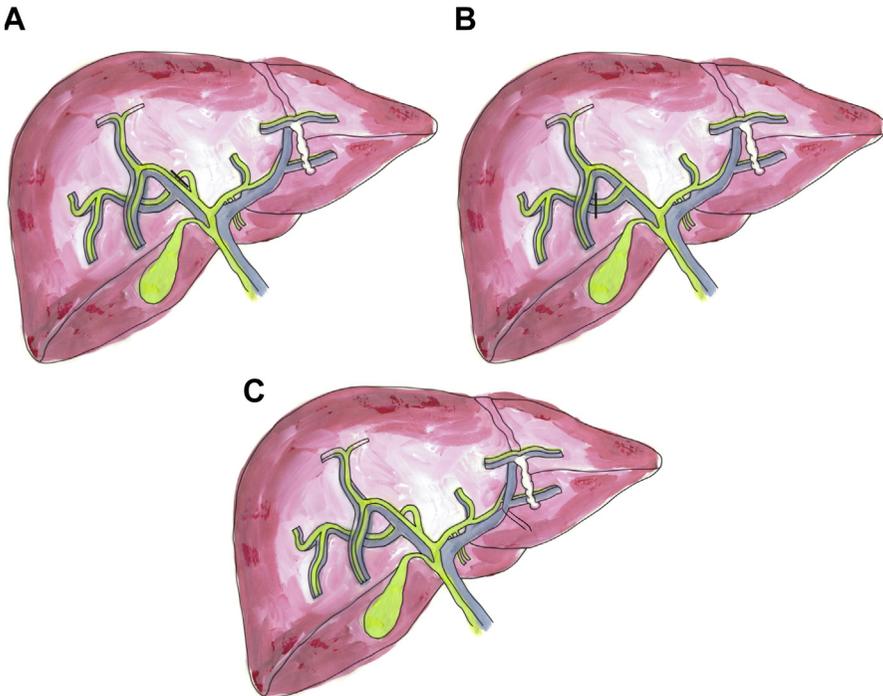


Fig. 2. Relation of the sectoral bile ducts to portal vein branches. (A) Supraportal course of right posterior bile duct. (B) Infraportal course of right posterior bile duct. (C) The umbilical portion of the left portal vein can be mobilized to the left, allowing transection of the bile ducts to segments II and III on the left side of the umbilical fissure. *Original artwork by Mrs. Elsbeth Leeffers.*

FLR.²⁵ Regenerative capacity of the liver is affected by bilious congestion, and biliary drainage of the FLR should therefore be performed before PVE. A downside of PVE is that the surgeon has to commit to a right-sided or left-sided resection. The preferred side for liver resection may change during exploratory laparotomy when the extent of the tumor differs from preoperative imaging (eg, contralateral hepatic artery involvement).

EXTENT OF LIVER RESECTION

Left or Right Hemihepatectomy

In patients eligible for resection, a choice should be made between a right-sided and a left-sided hepatectomy. Typically, the side of the liver with more extensive biliary disease (ie, involvement of second-order bile ducts or lobar atrophy) is resected. Both a left-sided and right-sided resection are possible in patients without lobar atrophy, second-order bile duct involvement, or right hepatic artery involvement. However, biliary drainage of the FLR and PVE of the resected liver regularly require that the decision between left-sided and right-sided resection is made before exploratory laparotomy.

In recent patient series, right-sided hepatectomies were performed slightly more often (58%) than left-sided resections (see [Table 1](#)). Three groups from Japan compared patients with left-sided and right-sided resections.^{19,21,26,27} No difference was found in R0 resection rates, 5-year survival, and rate of portal vein reconstruction.

However, significantly more hepatic artery reconstructions were needed with a left hemihepatectomy (odds ratio [OR], 0.14; 95% confidence interval [CI], 0.06–0.31, $P < .001$) (Appendix 2: Fig. S1). The close anatomic relation of the right hepatic artery to the bile duct bifurcation may require more dissection near the tumor in left-sided approaches. One study accordingly found more positive periductal margins in left hemihepatectomies.²¹

A right-sided resection seems to allow for a wider margin because of the longer extrahepatic course of the left hepatic duct. However, detailed pathology study found small differences in the length of the resected right hepatic duct in left hemihepatectomy specimens (13.7 mm) and the left duct in right hemihepatectomy specimens (14.5 mm).^{19,28}

In left-sided resections, wider margins can be obtained by extending the resection into the segmental ducts of the right anterior and posterior sector. However, in most patients (85%), the supraportal course of the right posterior sectoral duct limits the extent of bile duct resection: the right posterior sectoral duct quickly disappears behind the right anterior portal vein (see Fig. 2A).^{29,30} In patients with a variant infra-portal course of the right posterior sectoral duct (15%), a wide margin on the bile duct is facilitated with left hemihepatectomy (see Fig. 2B).¹⁹ Theoretic advantages of left-sided and right-sided resections are summarized in Table 2.

In centers that do not commit to arterial reconstructions for PHC, establishing involvement of the right hepatic artery is a first crucial step before committing to a left hemihepatectomy. Left hepatic artery involvement is rare. Fig. 3 presents a flow-chart to guide selection of the type of liver resection in patients with PHC.

Trisectionectomy

A trisectionectomy is required if a hemihepatectomy may result in an incomplete resection. In patients with unilateral involvement of the second-order bile ducts (ie, Bismuth III) a trisectionectomy is required in the presence of contralateral atrophy or arterial involvement. For example, a right trisectionectomy can be considered for a patient with a Bismuth IIIb PHC and involvement of the right hepatic artery.

In patients with bilateral involvement of the second-order bile ducts (ie, Bismuth IV) a trisectionectomy is almost always required for a complete resection. One potential exception is patients with a variant infraportal course of the right posterior sectoral duct (15%), facilitating a wide margin when transecting the right sectoral ducts with a left hemihepatectomy (see Fig. 2B).¹⁹

Extended resections encompass 28% of resections for PHC in recent series (see Table 1). Four recent patient series studied the additional benefit of trisectionectomy versus hemihepatectomy in patients with PHC. Three studies included only left-sided resections and 1 study only right-sided resections. Pooled analysis showed that extended resections could be performed with no apparent additional risk of mortality

Table 2

Advantages and disadvantages of left-sided and right-sided liver resections

	Left-sided Resection	Right-sided Resection
FLR	Larger ⁷⁸	Smaller
Achieving negative bile duct margins	May be more difficult	May be more feasible
Portal vein reconstructions	More complex	Less complex
Arterial reconstruction required	More frequent	Rare
Trisectionectomy	More complex	Less complex

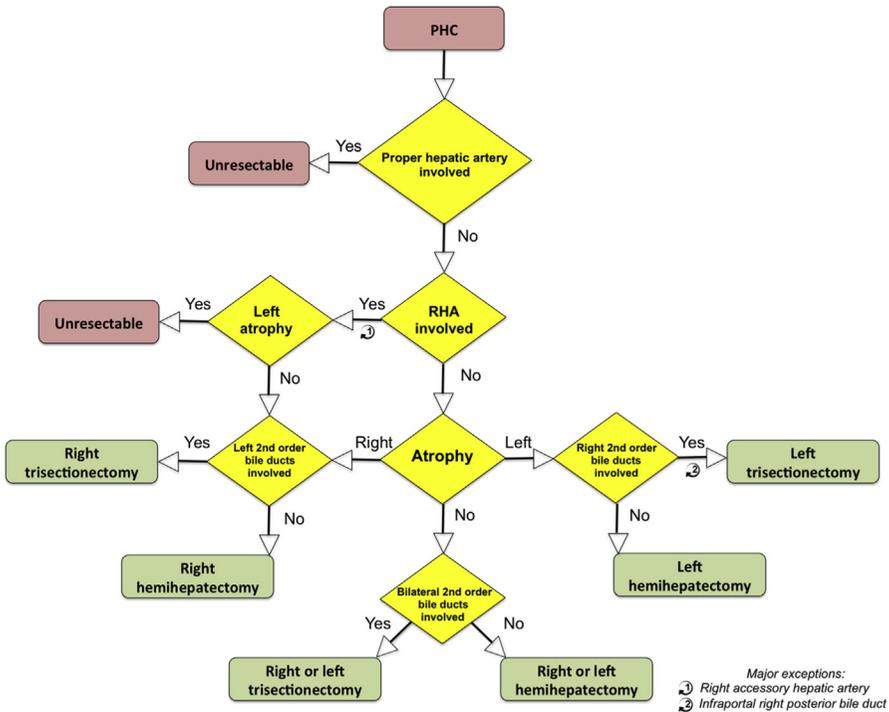


Fig. 3. Flowchart for surgical resection in PHC. RHA, right hepatic artery.

(2%–3%; OR, 0.65; 95% CI, 0.15–2.85; $P = .6$). However, a 2-fold increase in morbidity rate was found (up to 80%; OR, 2.37; 95% CI, 1.40–4.0; $P = .001$). These studies are all from Asian centers and may not be applicable to Western centers, which generally report higher mortalities.^{10,11} Pooled analysis showed an increase in R0 resection rate with trisectionectomy (OR, 1.86; 95% CI, 1.18–2.94; $P = .008$) (Appendix 2: Fig. S2). No survival benefit was shown, although the trisectionectomy group contained more patients with advanced tumors.

Trisectionectomy seems justified to improve R0 resection rates in selected patients with PHC who are fit for major surgery with an anticipated adequate FLR (recommendation B2).

Caudate Lobectomy

The anatomic rationale for caudate lobectomy (CL) is that the segment I bile ducts enter the main bile ducts near the confluence of the left and right hepatic duct and are therefore prone to becoming involved by direct tumor spread. CL may increase the chance of an R0 resection by clearance of the caudate bile duct branches and surrounding hilar plate tissue. In 1990, Nimura and colleagues¹⁸ first described a case series of caudate lobe resection combined with partial hepatectomy. This report showed microscopic tumor involvement in the caudate branches in 44 out of 45 patients with PHC (98%). Two other reports show a much lower rate of involvement of 22% and 34%.^{31,32}

In an analysis of 4 studies, representing 580 patients with Bismuth III to IV PHC, 61% underwent a concomitant CL. A 5-fold increased R1 rate was found when CL was

omitted (OR, 0.20; 95% CI, 0.09–0.45; $P = .003$) (Appendix 2: Fig. S3).^{33–36} CL was not an independent prognostic factor for overall survival in any individual study, and no increase in perioperative morbidity or mortality was reported.

CL can be technically challenging. The caudate lobe lies between the portal vein and the vena cava, beneath the gastrohepatic ligament. Caudate branches arising from the left and right hepatic arteries and portal vein are ligated and divided to control inflow to the caudate lobe. Transection of the lesser omentum exposes the caudate lobe. In right-sided resections an aberrant or accessory left hepatic artery should be preserved.

In right-sided resections, the right hepatic lobe is then mobilized and the retrohepatic veins are ligated and divided. The caudate lobe is now completely detached from the inferior vena cava (IVC), allowing division of the right hepatic vein. Next, at parenchymal transection the dorsal aspect of the middle hepatic vein is exposed, and the caudate lobe is pulled ventrally and detached from the left liver.

In left-sided resections, the retrohepatic veins are ligated and divided with a left-sided and inferior approach. Division of the ligamentum venosum exposes the common trunk of the left and middle hepatic veins, which is encircled and divided. The caudate lobe is then completely detached from the IVC en bloc with the left liver. Mobilization of the caudate lobe from the right side may be avoided to preserve the outflow vessels of the remnant liver. In these cases, an anterior approach (with hanging maneuver) can be considered to facilitate parenchymal transection with preservation of the outflow vessels of the remnant liver.^{37,38}

En-bloc CL is recommended for resection of PHC (recommendation B1).

Extensive Resections

Several strategies have been proposed to decrease the risk of incomplete (R1 or R2) resections by extended hepatectomies or routine portal vein resections. A trade-off should be made between the oncological benefit of more extensive resection and the associated increased postoperative mortality.

Neuhaus and colleagues^{39,40} (Berlin, Germany) proposed a hilar en-bloc resection involving a right trisectionectomy with en-bloc portal vein bifurcation, right hepatic artery, and extrahepatic bile ducts. The portal vein resection is performed in all patients without dissection near the tumor to determine involvement of the portal vein or right hepatic artery. The right hepatic artery is transected at its origin from the common hepatic artery. The left portal branch is isolated at the base of the umbilical portion, without dissecting out the portal bifurcation. After cross-clamping of the main and left portal veins, the portal vein is transected followed by an end-to-end reconstruction. In addition, the parenchyma is transected along the right side of the umbilical fissure. A similar technique was described by Hirano and colleagues⁴¹ (Sapporo, Japan), combining routine portal vein resection with a right hemihepatectomy. This strategy is particularly appealing for patients with a high risk of portal vein involvement. In a retrospective study, this approach in 50 patients was compared with 50 conventional liver resections without routine portal vein resection.⁴² The hilar en-bloc resection with routine portal vein resection conferred a survival benefit in R0 resected patients with similar postoperative mortality. However, a recent study failed to confirm the survival benefit associated with hilar en-bloc resection.⁴³ Therefore, routine portal vein resection is not recommended by consensus guidelines (recommendation C2).²³

Nagino and colleagues⁴⁴ (Nagoya, Japan) introduced the anatomic right trisectionectomy. This approach extends the transection of the segmental bile ducts to the left side of the umbilical fissure to decrease the risk of a positive bile duct margin. In a right trisectionectomy, most surgeons divide the liver just to the right of the

umbilical fissure to avoid injury to the blood supply and biliary drainage of segment II and III. Instead, with this strategy the branches to segment IV are divided within the umbilical fissure. Subsequently, the umbilical portion of the left portal vein can be pulled to the left, allowing transection of the bile ducts to segments II and III on the left side of the umbilical fissure (see [Fig. 2C](#)). With this approach, on average a 1-cm additional length of bile duct is resected.²⁷ This strategy is appealing in particular for patients with left-sided second-order bile duct involvement who require a right-sided resection. Rela and colleagues⁴⁵ (London, United Kingdom) introduced the Rex recess approach by combining the previous 2 strategies and adding a venous interposition graft for portal venous reconstruction.

Central Hepatectomy

Extended liver resections have a high incidence of postoperative liver failure and death. Consequently, a parenchymal-sparing central hepatectomy has been proposed. This partial hepatectomy involves anatomic or nonanatomic resection of only segments I and IV with en-bloc extrahepatic bile duct resection. The left bile duct is transected at the origin of the umbilical portion and at the right bile duct at the bifurcation of the anterior and posterior right bile ducts.^{31,46} Multiple biliary-enteric reconstructions are typically required.

In 3 studies, a total of 150 patients undergoing central liver resection were compared with 91 patients with comparable tumor characteristics undergoing conventional major liver resection.^{31,46,47} Most patients had Bismuth 1 or 2 tumors, and meta-analysis of the 3 studies showed more R0 resections with conventional major liver resection, although the OR was not statistically significant (OR, 0.20; 95% CI, 0.03–1.20; $P = .08$) ([Appendix 2: Fig. S4](#)). Infrequent concomitant CL may have biased these results toward lower R0 resection rates in central hepatectomies. Complication rates were 3-fold lower with central hepatectomies (OR, 0.35; 95% CI, 0.20–0.62; $P < .001$).

As in other resections for PHC, a central hepatectomy involves transection of the distal common bile duct and skeletonizing the portal vein and hepatic artery.^{31,46,48,49} The caudate lobe is dissected free and its segmental arterial, portal, and retrohepatic branches are ligated and divided. Intraoperative ultrasonography guides the nonanatomic parenchymal resection of segment 4b a few centimeters away from the tumor. Alternatively, a wider dome-shaped central hepatectomy is performed, referred to as Taj Mahal resection ([Fig. 4](#)). This central hepatectomy consists of a base formed between the left side of the right hepatic vein and the medial side of the middle hepatic vein. At the liver dome the resection line narrows down toward the Cantlie line, which can be visualized by temporary vascular clamping.^{48,49} The left hepatic duct is transected at the umbilical fissure and the right hepatic duct at or beyond the confluence of the right anterior and posterior bile ducts.

Central liver resections with CL can be considered for PHC with caution (recommendation B2). The main advantage is the reduced risk of postoperative liver failure and death. The main disadvantages are the concern for incomplete resection and the increased risk of biliary complications with multiple bilioenteric anastomoses. Alternative parenchymal-sparing techniques concern preservation of segment IVa and/or segment VIII with (extended) hemihepatectomies.⁵⁰ The decision to preserve segment IVa in a right trisectionectomy depends on the level where the segment IV sectoral duct enters the left hepatic duct.

Liver Transplantation

If a positive margin or inadequate FLR is anticipated, a total hepatectomy with liver transplant should be considered for PHC. A published multicenter study from the

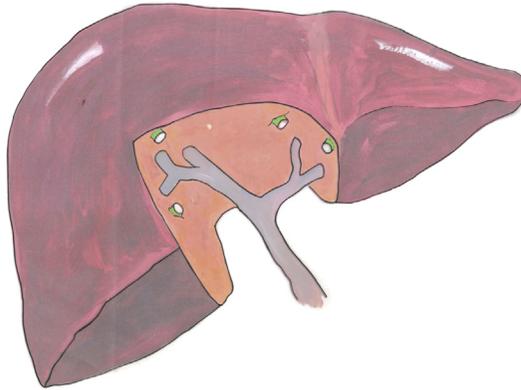


Fig. 4. Central liver resection including CL for PHC. *Original artwork by Mrs. Elsbeth Leeffers.*

United States presented a large cohort of 216 patients who underwent liver transplant for PHC after neoadjuvant (external beam) radiotherapy and chemotherapy.⁵¹ Patients had unresectable early stage (I or II) PHC or underlying primary sclerosing cholangitis (63%). Posttransplant 5-year recurrence-free survival was 65%. Other groups have shown long-term survival in 30% to 45% of patients.^{52,53} At present, PHC is an accepted indication for liver transplant in several countries worldwide, performed in study protocols with or without neoadjuvant therapy.⁵⁴

INTRAOPERATIVE DECISION MAKING

Staging Laparoscopy

Up to 65% of patients who proceed to surgery for a curative-intent resection are found to have metastasis or unresectable tumors at surgical exploration.^{55–58} Staging laparoscopy can avoid a laparotomy when peritoneal or liver metastases are found. In a pooled analysis ([Appendix 2: Fig. S5](#)) of 6 studies representing 546 patients with PHC, the authors found that the yield of staging laparoscopy was 27% (95% CI, 17%–37%).^{55–60} However, the actual yield may be lower because of selection bias and improvement in preoperative imaging. After a negative staging laparoscopy an additional 1 out of 4 patients are found to harbor metastasis or are unresectable at exploratory laparotomy. Moreover, staging laparoscopy typically fails to detect nodal metastases beyond the hepatoduodenal ligament (N2) or unresectable disease because of biliary extent or vascular involvement.⁶¹

Laparoscopic examination for metastatic disease includes inspection of the peritoneum (including the diaphragm, falciform ligament, hepatoduodenal ligament, lesser sac, and pelvis), the liver (including the undersurface of segments 2/3 and 4b/5/6), and the greater omentum. The lesser omentum is opened to inspect the celiac lymph nodes. Enlarged lymph nodes may be sampled using a biopsy forceps.

Staging laparoscopy avoids unnecessary laparotomy in 1 out of 4 patients with PHC who are adequately staged by preoperative imaging techniques. It should be performed in all patients with PHC before exploratory laparotomy.

Frozen Sections

The risk of an R1 resection was about 25% in recent series of patients undergoing a curative-intent resection for PHC (see [Table 1](#)). Longitudinal tumor extension in bile

ducts is difficult to assess with preoperative imaging as well as intraoperative ultrasonography. Frozen sections of the proximal and distal bile duct resection margins can ascertain tumor clearance. A pancreatoduodenectomy should be considered if a positive margin at the distal common bile duct is found and obtaining an additional margin is infeasible. Obtaining an additional proximal bile duct margin is often technically possible. Whether obtaining additional margins results in a survival benefit for patients with PHC has not been proved.^{32,62,63} However, patients with a negative proximal bile duct margin after an initial positive frozen section have a better survival than those with an additional positive margin.⁶⁴ Frozen sections are tempting and performed by most liver surgeons, but probably do not improve survival. A positive margin is more likely a reflection of an advanced tumor than poor surgical judgment or technique.⁶⁵

Intraoperative Assessment of Resectability

About 1 out of 6 patients with PHC with resectable disease on preoperative imaging is found to have (locally advanced) unresectable disease at exploratory laparotomy.⁵ The most common findings precluding a curative-intent resection are the extent of bile duct involvement and unexpected involvement of the right hepatic artery. Preoperative imaging is imperfect in determining the biliary extent of the tumor. PHC is unresectable if a negative bile duct margin is not anticipated intraoperatively.

Unexpected involvement of the right hepatic artery may also preclude a resection; for example, in patients with left lobar atrophy. The right hepatic artery runs posterior to the common hepatic duct in 85% of patients. In this position posterior to the bile duct, extensive dissection in the liver hilum is required to evaluate involvement of the right hepatic artery. Early transection of the distal bile duct has been proposed to avoid dissection near the tumor and facilitate clearance of all tissue in the hepatoduodenal ligament.⁶⁶ The disadvantage of this strategy is that unresectable disease may be ascertained only after transecting the distal common bile duct.

Portal Vein Resection and Reconstruction

About 40% of patients with PHC have unilateral portal vein involvement.⁶⁴ In many patients, the involved left or right portal vein can be transected without vascular reconstruction. Portal vein reconstruction is required in patients with tumor involvement of the bifurcation or contralateral portal vein involvement. Reconstruction depends on the extent of resection: primary closure of a wedge resection, end-to-end anastomosis of a short segmental resection, and rarely reconstruction requiring patches or interposition grafts. In general, a left-sided hepatectomy requires a more complex portal vein reconstruction than right-sided hepatectomy, because of a shorter branch.⁶⁷ Portal vein reconstruction can be done before or after parenchymal transection. Several Eastern studies found no increase in morbidity and mortality with portal vein resections in patients with PHC.^{22,68,69}

Lymphadenectomy

Regional lymph node metastases (N1) include nodes along the cystic duct, common bile duct, hepatic artery, and portal vein.^{1,70,71} Involvement of periaortic, pericaval, and celiac nodes constitutes N2 and stage IV disease.¹ Lymphadenectomy of the hepatoduodenal ligament is recommended for all resections for PHC.⁷² Lymphadenectomy is performed by skeletonizing the main portal vein and hepatic artery within the hepatoduodenal ligament. All lymphatic tissue can be resected en bloc with the extrahepatic bile duct.

A survival benefit of lymphadenectomy has not been shown. Lymphadenectomy is mainly useful for accurate staging. Lymph node status is the strongest independent

prognostic factor in patients with PHC. In a series of 79 patients undergoing a resection for node-positive PHC, all patients eventually died of PHC.⁷³ No randomized controlled trial has been performed to investigate the benefit of extended lymphadenectomy for PHC. However, for pancreatic cancer, 5 randomized controlled trials found no benefit of extended lymphadenectomy.⁷⁴ A recent systematic review of the literature found that a lymph node count of more than 6 is adequate for prognostic staging of PHC.⁷⁵

OUTCOMES OF CURATIVE-INTENT RESECTION FOR PERIHILAR CHOLANGIOMATOSIS

A review of recent case series, representing more than 4000 patients with PHC who underwent surgery with curative intent, showed a median overall survival of 34 months. The aggregated morbidity and hospital mortality were 42% and 5%, respectively (see [Table 1](#)). These analyses include Eastern series with patients who underwent incomplete (R2) resections and resections for stage IV disease. Two large multicenter nationwide Western studies found a postoperative mortality of about 10%.^{10,11}

Several prognostic factors may identify subgroups of patients with better survival. In patients with R0 resection median overall survival rates of 60 to 65 months are reported.^{34,42,73} In addition, a negative lymph node status, lymph node count of more than 3, well-differentiated tumor grade, and papillary phenotype are independent predictors of favorable survival.^{73,76} Lymph node metastases, present in 30% to 50% of patients, invariably lead to recurrence, with recurrence rates approaching 80% at 3-year follow-up and 100% at 7-year follow-up.^{73,77} Despite these poor outcomes, a resection may still improve life expectancy and quality of life in patients with positive lymph nodes.

SUMMARY

Patients with stage IV disease (distant metastases or N2 nodal disease) and those unfit to tolerate major surgery are not eligible for surgical resection of PHC. Moreover, PHC is unresectable if an R0 resection with an adequate functional liver remnant is not feasible. Bilateral involvement of second-order bile ducts (ie, Bismuth IV) does not preclude an R0 resection. Patients requiring a hepatic artery reconstruction are considered unresectable in most Western centers. Selected patients with unresectable early stage tumors should be considered for liver transplant.

Preoperative decision making regarding biliary drainage and PVE is difficult. Preoperative biliary drainage of the FLR is intended to decrease the risk of postoperative liver failure. However, drainage may also cause cholangitis, which is strongly associated with postoperative death. PVE can increase the FLR volume beyond a minimum of 25% to 40%, but commits the surgeon to a left-sided or right-sided resection before exploratory laparotomy.

Lobar atrophy, involvement of the right hepatic artery, and involvement of second-order bile ducts guide the choice between left-sided and right-sided hepatectomies. The main advantages of a right-sided resection are less need for dissection near the tumor and the long left hepatic duct to avoid an incomplete resection. The main advantage of a left-sided resection is the larger size of the right posterior sector. A trisectionectomy may be required for a complete resection, but is associated with a substantial risk of liver failure and postoperative mortality. Resection for PHC should always include a CL.

A staging laparoscopy before exploratory laparotomy has a yield of about 1 in 4 patients with occult metastatic disease. The use of frozen section probably bears little

significance on outcome, as does lymphadenectomy. However, adequate lymphadenectomy including at least 6 lymph nodes is recommended for proper staging.

Future studies should focus on reducing the high postoperative mortality in Western centers and finding better adjuvant treatments to reduce the high recurrence rate.

ACKNOWLEDGMENTS

The authors acknowledge the contribution from Mrs Elsbeth Leeffers for her excellent artwork.

REFERENCES

1. Edge S, Byrd DR, Compton CC, et al. *AJCC Cancer Staging Manual*. 7th edition. New York: Springer; 2010.
2. Bengmark S, Ekberg H, Evander A, et al. Major liver resection for hilar cholangiocarcinoma. *Ann Surg* 1988;207:120.
3. Gazzaniga GM, Filauro M, Bagarolo C, et al. Surgery for hilar cholangiocarcinoma: an Italian experience. *J Hepatobiliary Pancreat Surg* 2000;7:122.
4. Konstadoulakis MM, Roayaie S, Gomatos IP, et al. Aggressive surgical resection for hilar cholangiocarcinoma: is it justified? Audit of a single center's experience. *Am J Surg* 2008;196:160.
5. Jarnagin WR, Fong Y, DeMatteo RP, et al. Staging, resectability, and outcome in 225 patients with hilar cholangiocarcinoma. *Ann Surg* 2001;234:507.
6. Kambakamba P, DeOliveira ML. Perihilar cholangiocarcinoma: paradigms of surgical management. *Am J Surg* 2014;208:563.
7. Valle J, Wasan H, Palmer DH, et al. Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *N Engl J Med* 2010;362:1273.
8. Parodi A, Fisher D, Giovannini M, et al. Endoscopic management of hilar cholangiocarcinoma. *Nat Rev Gastroenterol Hepatol* 2012;9:105.
9. Nagino M, Ebata T, Yokoyama Y, et al. Evolution of surgical treatment for perihilar cholangiocarcinoma: a single-center 34-year review of 574 consecutive resections. *Ann Surg* 2013;258:129.
10. Nuzzo G, Giuliante F, Ardito F, et al. Improvement in perioperative and long-term outcome after surgical treatment of hilar cholangiocarcinoma: results of an Italian multicenter analysis of 440 patients. *Arch Surg* 2012;147:26.
11. Farges O, Regimbeau JM, Fuks D, et al. Multicentre European study of preoperative biliary drainage for hilar cholangiocarcinoma. *Br J Surg* 2013;100:274.
12. Bismuth H, Corlette MB. Intrahepatic cholangioenteric anastomosis in carcinoma of the hilus of the liver. *Surg Gynecol Obstet* 1975;140:170.
13. Matsuo K, Rocha FG, Ito K, et al. The Blumgart preoperative staging system for hilar cholangiocarcinoma: analysis of resectability and outcomes in 380 patients. *J Am Coll Surg* 2012;215:343.
14. Chaiteerakij R, Harmsen WS, Marrero CR, et al. A new clinically based staging system for perihilar cholangiocarcinoma. *Am J Gastroenterol* 2014;109:1881.
15. Corvera CU, Blumgart LH, Darvishian F, et al. Clinical and pathologic features of proximal biliary strictures masquerading as hilar cholangiocarcinoma. *J Am Coll Surg* 2005;201:862.
16. Juntermanns B, Kaiser GM, Reis H, et al. Klatskin-mimicking lesions: still a diagnostic and therapeutic dilemma? *Hepatogastroenterology* 2011;58:265.
17. Kloek JJ, van Delden OM, Erdogan D, et al. Differentiation of malignant and benign proximal bile duct strictures: the diagnostic dilemma. *World J Gastroenterol* 2008;14:5032.

18. Nimura Y, Hayakawa N, Kamiya J, et al. Hepatic segmentectomy with caudate lobe resection for bile duct carcinoma of the hepatic hilus. *World J Surg* 1990; 14:535.
19. Natsume S, Ebata T, Yokoyama Y, et al. Clinical significance of left trisectionectomy for perihilar cholangiocarcinoma: an appraisal and comparison with left hepatectomy. *Ann Surg* 2012;255:754.
20. Hiatt JR, Gabbay J, Busuttill RW. Surgical anatomy of the hepatic arteries in 1000 cases. *Ann Surg* 1994;220:50.
21. Shimizu H, Kimura F, Yoshidome H, et al. Aggressive surgical resection for hilar cholangiocarcinoma of the left-side predominance: radicality and safety of left-sided hepatectomy. *Ann Surg* 2010;251:281.
22. Abbas S, Sandroussi C. Systematic review and meta-analysis of the role of vascular resection in the treatment of hilar cholangiocarcinoma. *HPB (Oxford)* 2013;15:492.
23. Mansour JC, Aloia TA, Crane CH, et al. Hilar Cholangiocarcinoma: expert consensus statement. *HPB (Oxford)* 2015;17:691.
24. Wiggers JK, Coelen RJ, Rauws EA, et al. Preoperative endoscopic versus percutaneous transhepatic biliary drainage in potentially resectable perihilar cholangiocarcinoma (DRAINAGE trial): design and rationale of a randomized controlled trial. *BMC Gastroenterol* 2015;15:20.
25. Ebata T, Yokoyama Y, Igami T, et al. Portal vein embolization before extended hepatectomy for biliary cancer: current technique and review of 494 consecutive embolizations. *Dig Surg* 2012;29:23.
26. Esaki M, Shimada K, Nara S, et al. Left hepatic trisectionectomy for advanced perihilar cholangiocarcinoma. *Br J Surg* 2013;100:801.
27. Matsumoto N, Ebata T, Yokoyama Y, et al. Role of anatomical right hepatic trisectionectomy for perihilar cholangiocarcinoma. *Br J Surg* 2014;101:261.
28. Hosokawa I, Shimizu H, Yoshidome H, et al. Surgical strategy for hilar cholangiocarcinoma of the left-side predominance: current role of left trisectionectomy. *Ann Surg* 2014;259:1178.
29. Shimizu H, Sawada S, Kimura F, et al. Clinical significance of biliary vascular anatomy of the right liver for hilar cholangiocarcinoma applied to left hemihepatectomy. *Ann Surg* 2009;249:435.
30. Govil S, Reddy MS, Rela M. Surgical resection techniques for locally advanced hilar cholangiocarcinoma. *Langenbecks Arch Surg* 2014;399:707.
31. Chen XP, Lau WY, Huang ZY, et al. Extent of liver resection for hilar cholangiocarcinoma. *Br J Surg* 2009;96:1167.
32. Ribero D, Amisano M, Lo Tesoriere R, et al. Additional resection of an intraoperative margin-positive proximal bile duct improves survival in patients with hilar cholangiocarcinoma. *Ann Surg* 2011;254:776.
33. Cheng QB, Yi B, Wang JH, et al. Resection with total caudate lobectomy confers survival benefit in hilar cholangiocarcinoma of Bismuth type III and IV. *Eur J Surg Oncol* 2012;38:1197.
34. Kow AW, Wook CD, Song SC, et al. Role of caudate lobectomy in type III A and III B hilar cholangiocarcinoma: a 15-year experience in a tertiary institution. *World J Surg* 2012;36:1112.
35. Wahab MA, Sultan AM, Salah T, et al. Caudate lobe resection with major hepatectomy for central cholangiocarcinoma: is it of value? *Hepatogastroenterology* 2012;59:321.
36. Song SC, Choi DW, Kow AW, et al. Surgical outcomes of 230 resected hilar cholangiocarcinoma in a single centre. *ANZ J Surg* 2013;83:268.

37. Nanashima A, Tobinaga S, Abo T, et al. Left hepatectomy accompanied by a resection of the whole caudate lobe using the dorsally fixed liver-hanging maneuver. *Surg Today* 2011;41:453.
38. Hwang S, Lee SG, Lee YJ, et al. Modified liver hanging maneuver to facilitate left hepatectomy and caudate lobe resection for hilar bile duct cancer. *J Gastrointest Surg* 2008;12:1288.
39. Neuhaus P, Jonas S. Surgery for hilar cholangiocarcinoma—the German experience. *J Hepatobiliary Pancreat Surg* 2000;7:142.
40. Neuhaus P, Jonas S, Settmacher U, et al. Surgical management of proximal bile duct cancer: extended right lobe resection increases resectability and radicality. *Langenbecks Arch Surg* 2003;388:194.
41. Hirano S, Kondo S, Tanaka E, et al. No-touch resection of hilar malignancies with right hepatectomy and routine portal reconstruction. *J Hepatobiliary Pancreat Surg* 2009;16:502.
42. Neuhaus P, Thelen A, Jonas S, et al. Oncological superiority of hilar en bloc resection for the treatment of hilar cholangiocarcinoma. *Ann Surg Oncol* 2012;19:1602.
43. Tamoto E, Hirano S, Tsuchikawa T, et al. Portal vein resection using the no-touch technique with a hepatectomy for hilar cholangiocarcinoma. *HPB (Oxford)* 2014;16:56.
44. Nagino M, Kamiya J, Arai T, et al. “Anatomic” right hepatic trisectionectomy (extended right hepatectomy) with caudate lobectomy for hilar cholangiocarcinoma. *Ann Surg* 2006;243:28.
45. Rela M, Rajalingam R, Shanmugam V, et al. Novel en-bloc resection of locally advanced hilar cholangiocarcinoma: the Rex recess approach. *Hepatobiliary Pancreat Dis Int* 2014;13:93.
46. Lim JH, Choi GH, Choi SH, et al. Liver resection for Bismuth type I and Type II hilar cholangiocarcinoma. *World J Surg* 2013;37:829.
47. Xiong J, Nunes QM, Huang W, et al. Major hepatectomy in Bismuth types I and II hilar cholangiocarcinoma. *J Surg Res* 2015;194:194.
48. Kawarada Y, Isaji S, Taoka H, et al. S4a + S5 with caudate lobe (S1) resection using the Taj Mahal liver parenchymal resection for carcinoma of the biliary tract. *J Gastrointest Surg* 1999;3:369.
49. Miyazaki M, Kimura F, Shimizu H, et al. Extensive hilar bile duct resection using a transhepatic approach for patients with hepatic hilar bile duct diseases. *Am J Surg* 2008;196:125.
50. van Gulik TM, Ruys AT, Busch OR, et al. Extent of liver resection for hilar cholangiocarcinoma (Klatskin tumor): how much is enough? *Dig Surg* 2011;28:141.
51. Darwish Murad S, Kim WR, Harnois DM, et al. Efficacy of neoadjuvant chemoradiation, followed by liver transplantation, for perihilar cholangiocarcinoma at 12 US centers. *Gastroenterology* 2012;143:88.
52. Sudan D, DeRoover A, Chinnakotla S, et al. Radiochemotherapy and transplantation allow long-term survival for nonresectable hilar cholangiocarcinoma. *Am J Transplant* 2002;2:774.
53. Robles R, Figueras J, Turrion VS, et al. Spanish experience in liver transplantation for hilar and peripheral cholangiocarcinoma. *Ann Surg* 2004;239:265.
54. DeOliveira ML. Liver transplantation for cholangiocarcinoma: current best practice. *Curr Opin Organ Transplant* 2014;19:245.
55. Weber SM, DeMatteo RP, Fong Y, et al. Staging laparoscopy in patients with extrahepatic biliary carcinoma. Analysis of 100 patients. *Ann Surg* 2002;235:392.

56. Connor S, Barron E, Wigmore SJ, et al. The utility of laparoscopic assessment in the preoperative staging of suspected hilar cholangiocarcinoma. *J Gastrointest Surg* 2005;9:476.
57. Ruys AT, Busch OR, Gouma DJ, et al. Staging laparoscopy for hilar cholangiocarcinoma: is it still worthwhile? *Ann Surg Oncol* 2011;18:2647.
58. Barlow AD, Garcea G, Berry DP, et al. Staging laparoscopy for hilar cholangiocarcinoma in 100 patients. *Langenbecks Arch Surg* 2013;398:983.
59. Tillemann EH, de Castro SM, Busch OR, et al. Diagnostic laparoscopy and laparoscopic ultrasound for staging of patients with malignant proximal bile duct obstruction. *J Gastrointest Surg* 2002;6:426.
60. Goere D, Wagholikar GD, Pessaux P, et al. Utility of staging laparoscopy in subsets of biliary cancers : laparoscopy is a powerful diagnostic tool in patients with intrahepatic and gallbladder carcinoma. *Surg Endosc* 2006;20:721.
61. Jarnagin WR, Bodniewicz J, Dougherty E, et al. A prospective analysis of staging laparoscopy in patients with primary and secondary hepatobiliary malignancies. *J Gastrointest Surg* 2000;4:34.
62. Shingu Y, Ebata T, Nishio H, et al. Clinical value of additional resection of a margin-positive proximal bile duct in hilar cholangiocarcinoma. *Surgery* 2010;147:49.
63. Endo I, House MG, Klimstra DS, et al. Clinical significance of intraoperative bile duct margin assessment for hilar cholangiocarcinoma. *Ann Surg Oncol* 2008;15:2104.
64. Groot Koerkamp B, Wiggers JK, Gonen M, et al. Survival after resection of perihilar cholangiocarcinoma-development and external validation of a prognostic nomogram. *Ann Oncol* 2015;26:1930.
65. Cady B. Basic principles in surgical oncology. *Arch Surg* 1997;132:338.
66. Blumgart LH, Benjamin IS. Liver resection for bile duct cancer. *Surg Clin North Am* 1989;69:323.
67. Nagino M, Nimura Y, Nishio H, et al. Hepatectomy with simultaneous resection of the portal vein and hepatic artery for advanced perihilar cholangiocarcinoma: an audit of 50 consecutive cases. *Ann Surg* 2010;252:115.
68. Chen W, Ke K, Chen YL. Combined portal vein resection in the treatment of hilar cholangiocarcinoma: a systematic review and meta-analysis. *Eur J Surg Oncol* 2014;40:489.
69. Song GW, Lee SG, Hwang S, et al. Does portal vein resection with hepatectomy improve survival in locally advanced hilar cholangiocarcinoma? *Hepatogastroenterology* 2009;56:935.
70. Tsuji T, Hiraoka T, Kanemitsu K, et al. Lymphatic spreading pattern of intrahepatic cholangiocarcinoma. *Surgery* 2001;129:401.
71. Kitagawa Y, Nagino M, Kamiya J, et al. Lymph node metastasis from hilar cholangiocarcinoma: audit of 110 patients who underwent regional and paraaortic node dissection. *Ann Surg* 2001;233:385.
72. Razumilava N, Gores GJ. Cholangiocarcinoma. *Lancet* 2014;383:2168.
73. Groot Koerkamp B, Wiggers JK, Allen P, et al. Recurrence rate and pattern of perihilar cholangiocarcinoma after curative intent resection. *J Am Coll Surg* 2015;221(6):1041–9.
74. Dasari BV, Pasquali S, Vohra RS, et al. Extended Versus Standard Lymphadenectomy for Pancreatic Head Cancer: Meta-Analysis of Randomized Controlled Trials. *J Gastrointest Surg* 2015;19:1725.
75. Kambakamba P, Linecker M, Slankamenac K, et al. Lymph node dissection in resectable perihilar cholangiocarcinoma: a systematic review. *Am J Surg* 2015.

76. Popescu I, Dumitrascu T. Curative-intent surgery for hilar cholangiocarcinoma: prognostic factors for clinical decision making. *Langenbecks Arch Surg* 2014; 399:693.
77. Kobayashi A, Miwa S, Nakata T, et al. Disease recurrence patterns after R0 resection of hilar cholangiocarcinoma. *Br J Surg* 2010;97:56.
78. Lee SG, Song GW, Hwang S, et al. Surgical treatment of hilar cholangiocarcinoma in the new era: the Asan experience. *J Hepatobiliary Pancreat Sci* 2010;17:476.
79. Unno M, Katayose Y, Rikiyama T, et al. Major hepatectomy for perihilar cholangiocarcinoma. *J Hepatobiliary Pancreat Sci* 2010;17:463.
80. de Jong MC, Marques H, Clary BM, et al. The impact of portal vein resection on outcomes for hilar cholangiocarcinoma: a multi-institutional analysis of 305 cases. *Cancer* 2012;118:4737.
81. Hemming AW, Mekeel K, Khanna A, et al. Portal vein resection in management of hilar cholangiocarcinoma. *J Am Coll Surg* 2011;212:604.
82. Bismuth H. Revisiting liver anatomy and terminology of hepatectomies. *Ann Surg* 2013;257:383.
83. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ* 2008;336:1049.
84. Open source software. Available at: http://www.cebm.brown.edu/open_meta/index.html. Accessed March 23, 2015.

APPENDIX 1: METHODS FOR LITERATURE REVIEW SECTIONS

A literature search was conducted in PubMed, using search terms “(hilar OR perihilar) AND (cholangio*),” including only human studies, written in English. A total of 1226 references were screened based on title and abstract and relevant selections filed into subtopics (eg, case series, staging laparoscopy, lymphadenectomy, frozen section, and liver transplantation). Case series published before 2008 or with fewer than 5 patients per year were excluded. In case series diluted with cases of intrahepatic or distal cholangiocarcinoma, data pertaining to patients with PHC were extracted. Meta-analysis was performed for case series reporting results of right versus left hemihepatectomy, trisectionectomy versus hemihepatectomy, and concomitant versus no CL. Quality assessment of studies was performed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation [short GRADE] Working Group) tool.^{82,83} Data are presented as ORs or proportions. Meta-analysis was performed using OpenMeta [Analyst] 10.10⁸⁴ and random-effects model (DerSimonian Laird) was used.

APPENDIX 2: SUPPLEMENTARY FIGURES

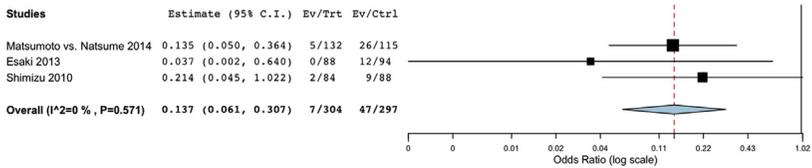


Fig. S1. Forest plot for proportion of hepatic artery reconstructions in right versus left hemihepatectomy. OR less than 1 favors right hemihepatectomy.

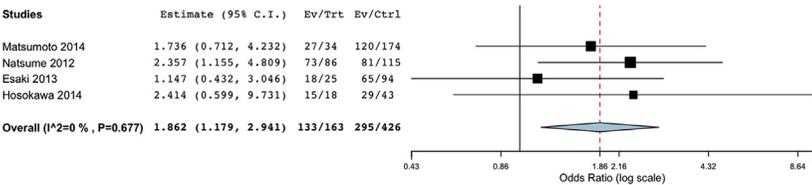


Fig. S2. R0 resection rate in trisectionectomies versus hemihepatectomies. OR greater than 1.0 favors trisectionectomies.

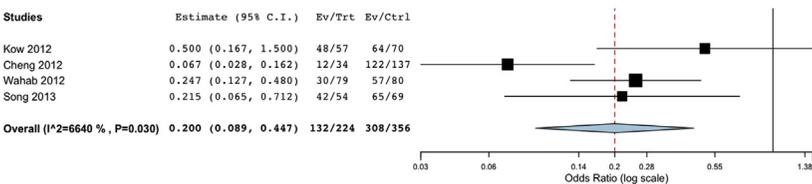


Fig. S3. Forest plot caudate lobectomies. OR for obtaining negative resection margins (R0). OR less than 1.0 favors CL.

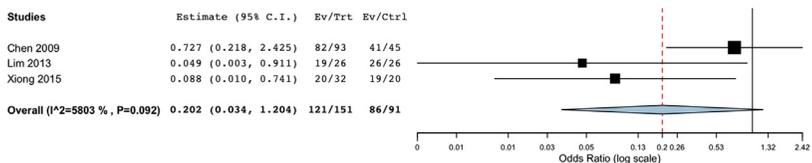


Fig. S4. R0 resection rates in major liver resection (MLR) versus central liver resections. OR less than 1.0 favors MLR.

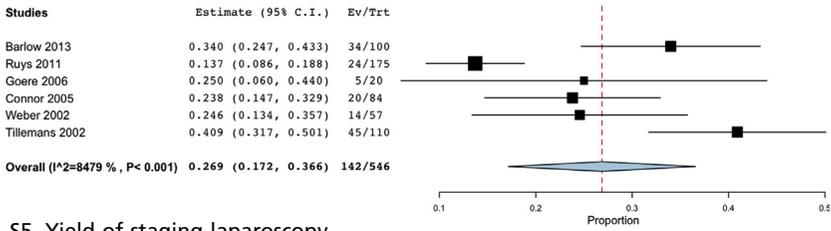


Fig. S5. Yield of staging laparoscopy.