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Major complications and mortality after resection of intrahepatic cholangiocarcinoma: A systematic review and meta-analysis

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A R T I C L E I N F O

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A B S T R A C T

Background: Evaluation of morbidity and mortality after hepatic resection often lacks stratification by extent of resection or diagnosis. Although a liver resection for different indications may have technical similarities, postoperative outcomes differ. The aim of this systematic review and meta-analysis was to determine the risk of major complications and mortality after resection of intrahepatic cholangiocarcinoma.
Methods: Meta-analysis was performed to assess postoperative mortality (in-hospital, 30-, and 90-day) and major complications (Clavien-Dindo grade ≥III).
Results: A total of 32 studies that reported on 19,503 patients were included. Pooled in-hospital, 30-day, and 90-day mortality were 5.9% (95% confidence interval 4.1–8.4); 4.6% (95% confidence interval 4.0–5.2); and 6.1% (95% confidence interval 5.0–7.3), respectively. Pooled proportion of major complications was 22.2% (95% confidence interval 17.7–27.5) for all resections. The pooled 90-day mortality was 3.1% (95% confidence interval 1.8–5.2) for a minor resection, 7.4% (95% confidence interval 5.9–9.3) for all major resections, and 11.4% (95% confidence interval 6.9–18.7) for extended resections ($P = .001$). Major complications were 38.8% (95% confidence interval 29.5–49) after a major hepatectomy compared to 11.3% (95% confidence interval 5.0–24.0) after a minor hepatectomy ($P = .001$). Asian studies had a pooled 90-day mortality of 4.4% (95% confidence interval 3.3–5.9) compared to 6.8% (95% confidence interval 5.6–8.2) for Western studies ($P = .02$). Cohorts with patients included before 2000 had a pooled 90-day mortality of 5.9% (95% confidence interval 4.8–7.3) compared to 6.8% (95% confidence interval 5.1–9.1) after 2000 ($P = .44$).
Conclusion: When informing patients or comparing outcomes across hospitals, postoperative mortality rates after liver resection should be reported for 90-days with consideration of the diagnosis and the extent of liver resection.

Introduction

Cholangiocarcinoma is a heterogenous group of malignancies in the biliary tree and accounts for 3% of all gastrointestinal cancers worldwide.[1,2] Intrahepatic cholangiocarcinoma (iCCA) arises from the epithelial cells of the peripheral bile ducts proximal to the second-order bile ducts.[3] Intrahepatic cholangiocarcinoma represents around 20% of all cholangiocarcinoma and its incidence in Western countries is 1 to 2 per 100,000.[4,5] The incidence of cholangiocarcinoma in Asian countries exceeds that in Western countries, up to >6 per 100,000.[6] Treatment and diagnosis of patients with iCCA entails many challenges. Patients with iCCA are initially asymptomatic and 20% of patients are diagnosed in the absence of symptoms.[7] When symptomatic, most patients present with unresectable disease due to locally advanced or metastatic disease.

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About 20% of patients are eligible for complete surgical resection.[8] Five-year overall survival (OS) rate after curative-intent resection of iCCA is about 30% and median OS about 30 months after surgery.[9–11] Resection usually involves a major hepatectomy (82%) (3 segments or more) and sometimes resection of the (common) bile duct (23%) requiring an additional hepatico-jejunostomy.[12] In addition, most patients have underlying liver disease or postcholestatic liver dysfunction. Therefore, these extensive resections come with substantially higher risks than for instance resections for colorectal metastasis. The most frequent postoperative complications are liver failure, biliary leakage, and intra-abdominal abscess.[11,13,14] Postoperative morbidity and mortality rates vary in the literature. Postoperative major complication risks vary from 18% to 52%,[15,16] whereas overall 90-day postoperative mortality ranges from 2% to 11%.[16,17]

The evaluation of morbidity and mortality after hepatic resection often lacks stratification by the extent of resection or diagnosis. Although a hepatectomy for different indications may have technical similarities, postoperative outcomes differ.[18] Due to the low incidence of iCCA, postoperative morbidity and mortality rates are mainly derived from observational cohort studies or case series. Therefore, the aim of this systematic review and meta-analysis was to determine the risk of postoperative major complications and mortality after resection of iCCA. With subgroup analyses for the extent of liver resection, region, and time period.

Methods

This systematic review and meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses statement.[19]

Literature search

A librarian was consulted to perform a systematic search on February 19, 2021. Databases of MEDLINE, Embase, the Cochrane Library, and Web of Science were queried. A combination of keywords and Medical Subject Headings terms were used for the search: bile duct neoplasms, intrahepatic cholangiocarcinoma, hepatectomy, postoperative morbidity, postoperative mortality and variations thereof. No restriction on date, language, or publication type was applied in the search. The complete search strategy is presented in Supplementary Table S1. Two independent authors (A.K. and S.B.) screened the title and abstract of each identified publication for eligibility. Publications that seemed eligible for inclusion were retrieved for full text reading by A.K. Discrepancies at any stage were resolved by a third author (P.B.O.).

Eligibility criteria

All studies that reported on complications and mortality after resection of iCCA were eligible for inclusion. Non-English and non-original publications such as reviews, case reports, letters, editorials, or conference abstracts were excluded. Studies including patients who underwent a resection before 1990 were excluded. Studies that reported a combined study population (eg, intrahepatic- and extrahepatic cholangiocarcinoma) were only included if outcomes were presented separately for iCCA. If a population had mixed pathology (eg, iCCA and hepatocellular carcinoma), the study was excluded. Studies that lacked data on the outcomes of interest were excluded, as well as studies that reported on treatments other than initial complete resection of iCCA (eg, associating liver partition and portal vein ligation for staged hepatectomy and resection of recurrences). In case of overlapping cohorts, the largest or the most recent series was included. Studies with <50 patients were excluded.

Data collection

The extracted data included study characteristics (ie, author, year of publication, inclusion period, and number of patients), patient characteristics (ie, age, sex, and American Society of Anesthesiologists classification [ASA]), preoperative characteristics (ie, portal vein embolization), operative characteristics (ie, type of resection, vascular reconstruction, and biliary reconstruction), and postoperative details (ie, major complications and mortality). Authors from some studies were contacted for lacking data. The primary outcome was postoperative mortality, defined as in-hospital, 30-day, or 90-day mortality. The secondary outcome was major complications (Clavien-Dindo grade ≥III). Subgroup analyses were prespecified for 90-day mortality and major complications in relation to the extent of liver resection (ie, minor, major, and extended), period (ie, start of inclusion period before or after 2000), and region (ie, Asian or Western studies). A study was classified as Asian or Western if the origin of the participating centers originated for at least 80% from Asian or Western countries. A minor hepatectomy was defined as resection of <3 Couinaud segments, a major hepatectomy was defined as resection of ≥3 Couinaud segments, and an extended hepatectomy was defined as resection of ≥5 Couinaud segments.

Quality assessment

Risk of bias was assessed by the Joanna Briggs Institute checklist that is specifically designed for case series.[20] The checklist consists of 10 predefined items that can be specified to questions particularly relevant for the interest of this systematic review, which can be answered with ‘yes,’ ‘no,’ and ‘unclear or not applicable’ (Supplementary Table S2).

Statistical analysis

The categorical values are presented as numbers and percentages. Continuous data are presented as mean with SD. Studies were pooled separately for in-hospital, 30-day, and 90-day mortality. Studies were pooled for postoperative morbidity if they reported major complications (Clavien-Dindo grade ≥III). The I^2 statistic was used to quantify the heterogeneity across studies. An I^2 value >50% indicated significant heterogeneity. A random-effects model was used for all analyses. Pooled analyses were visualized with forest plots. Statistical analyses were performed using R version 4.1.1 (http://www.r-project.org; R Foundation for Statistical Computing, Vienna, Austria).

Results

The search and screening process of the literature search is presented in Figure 1. A total of 9,821 records were identified through database searching. The duplicate records were removed. The title and abstract of 7,076 records were screened for eligibility. This led to full-text assessment of 184 studies, of which 32 were included in the meta-analysis.

Study characteristics

The 32 included studies reported on 19,503 patients who underwent resection of iCCA between 1990 and 2018. The main characteristics of the included studies are presented in Table I. Fourteen studies had a multicenter design,[11,15,21–32] of which 4

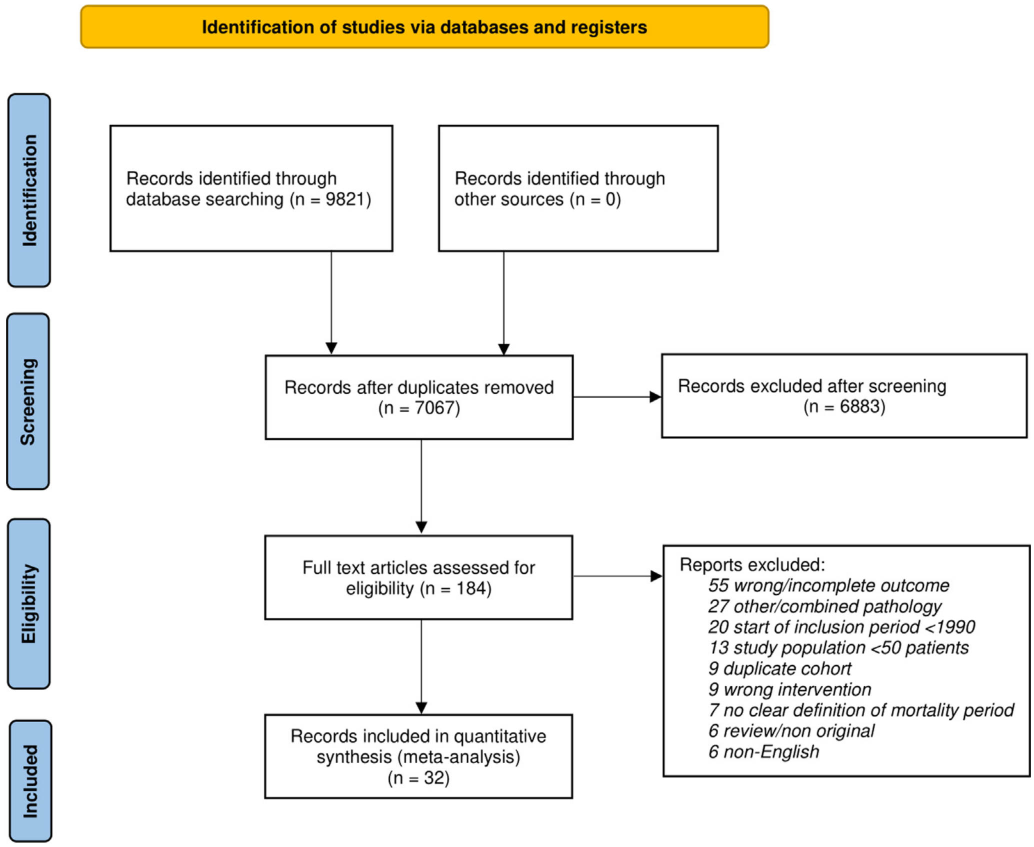

Figure 1. Preferred Reporting Items for Systematic Review and Meta-Analyses flowchart of the study selection process.

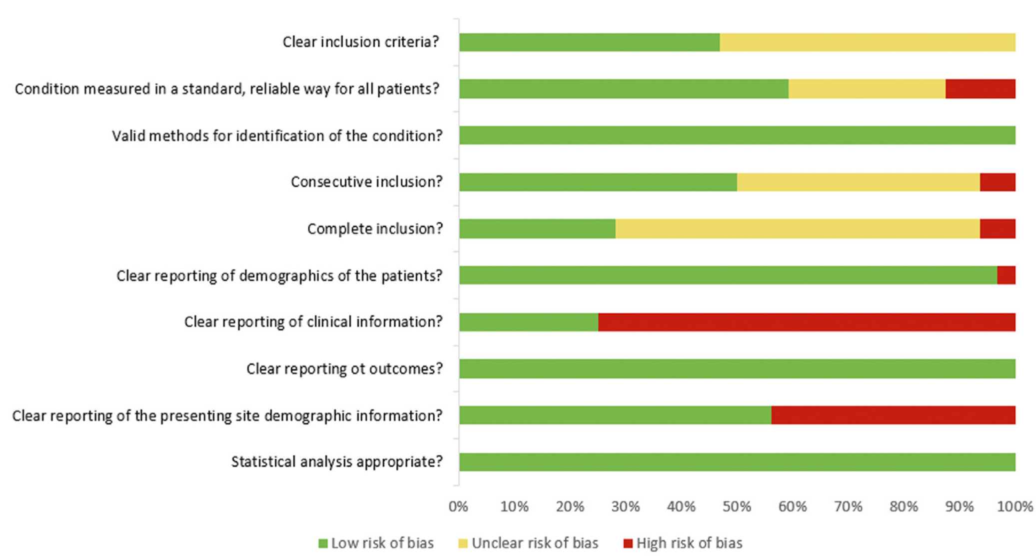

Figure 2. Risk of bias graph according to the Joanna Briggs Institute checklist.

studies queried nationwide databases.[29–32] Of the 14 multicenter studies, 5 studies were multinational.[15,24–27] None of these studies presented the results separately per center or per country. Twenty-two studies originated from Western countries,[11,15,16,18,21,22–39] whereas 10 studies originated from Asian countries.[13,22,40–47] Western countries included the USA,[29–31] Germany,[23,32–35,38,39] France,[16,36] Italy,[11,21,37] Spain,[18] and the Netherlands.[28] Asian countries included Japan,[22,43,45] China,[13,41,42,44,46,47] and the Republic of Korea.[40] All studies had a retrospective design.

Patient characteristics

Twenty-nine studies (representing 16,199 patients) had a pooled minor hepatectomy proportion of 25.9% (95% CI 18–35.7).[11,13,15,16,18,21–29,31–35,37–43,45–47] Thirty studies (representing 16,306 patients) had a pooled major hepatectomy (including extended hepatectomies) proportion of 72.8% (95% CI 62.5–81.1).[11,13,15,16,18,21–29,31–43,45–47] As a subgroup of major hepatectomies, 22 studies (representing 13,007 patients) had a pooled

Table 1
Study characteristics

Author	Country	Inclusion period	Liver resections	Male, *n* (%)	Median age (y)	ASA 3-4 *n* (%)	Resection type (LH/RH/ELH/ERH)	Bile duct *n* (%)	Vascular resections *n* (%)	PVE *n* (%)
Asian studies										
An[47]	China	2004-2013	114	66 (58)	56	-	14/10/1/1	-	-	-
Cho[40]	Korea	2001-2007	63	41 (65)	61.4	-	8/21/13/5	3 (5)	-	-
Li[41]	China	2001-2009	144	91 (63)	-	-	72/16/25/9	-	-	-
Luo[42]	China	2007-2011	1281	912 (68)	-	-	-	-	-	-
Ma[13]	China	1991-2013	107	59 (55)	61	-	11/13/9/21	15 (14)	V: 4 (4)	-
Miyata[43]	Japan	2002-2016	60	14 (23)	-	-	-	5 (8)	-	-
Morimoto[22]	Japan	1991-2000	51	27 (53)	-	-	13/6/7/8	16 (31)	V: 2 (4)	-
Si[44]	China	2006-2010	702	428 (61)	-	-	-	-	-	-
Yoh[45]	Japan	1993-2014	144	85 (59)	-	-	-	49 (34)	-	-
Zhu[46]	China	2012-2017	83	51 (61)	-	8 (10)	28/17/0/0	-	-	-
Western studies										
Bartsch[33]	Germany	2008-2018	150	73 (49)	64.2	86 (57)	10/25/22/26	-	A: 0 (0), V: 18 (12)	-
Beetz[34]	Germany	1996-2018	269	134 (50)	62	-	85/41/31/64	51 (19)	-	-
Bektas[35]	Germany	1996-2010	158	84 (53)	61	-	-	2 (1)	-	-
Bergeat[36]	France	1997-2013	107	82 (77)	-	-	-	10 (9)	A: 3 (3), V: 7 (7)	14 (13)
Buettner[4]	Multinational	1990-2017	1013	540 (55)	59	348 (34)	-	-	-	-
Conci[21]	Italy	1995-2015	270	137 (51)	68	-	-	-	V: 15 (6)	-
Filmann[32]	Germany	2010-2015	4667	-	-	-	984/827/-/-	-	-	-
Guglielmi[37]	Italy	1990-2007	52	32 (62)	-	-	17/9/2/5	-	V: 2 (4)	-
Hobeika[16]	France	2000-2016	115	57 (50)	-	19 (17)	-	-	-	11 (10)
Jutric[31]	USA	1998-2011	881	392 (45)	-	-	140/140/39/51	-	-	-
Lee[29]	USA	2004-2014	2256	1046 (46)	-	-	-	-	-	-
Liu[30]	USA	2005-2012	2089	1436 (69)	-	-	-	-	-	-
Lurje[38]	Germany	2011-2016	71	34 (48)	-	42 (59)	-	-	-	8 (11)
Merath[27]	Multinational	1993-2015	687	370 (54)	61	268 (39)	-	-	-	-
Nickkholgh[39]	Germany	2001-2015	190	107 (56)	63	-	45/41/21/34	-	-	4 (2)
Olthof[50]	Netherlands	2014-2017	97	53 (55)	67	26 (27)	24/12/5/13	-	-	13 (13)
Rafecas[17]	Spain	1996-2017	67	45 (67)	66	-	20/11/4/4	-	-	4 (6)
Reames[26]	Multinational	1990-2016	1087	594 (55)	-	438 (40)	218/179/107/140	190 (18)	V: 98 (9)	-
Ribero[11]	Italy	1990-2008	434	243 (56)	65	-	-/-/19/65	84 (19)	V: 14 (3)	-
Schnitzbauer[23]	Germany	2004-2013	488	250 (51)	67	-	-	-	-	-
Spolverato[25]	Multinational	1990-2013	583	302 (52)	59.9	-	-	-	-	-
Zhang[15]	Multinational	1990-2016	1023	569 (56)	59	-	202/161/99/128	177 (17)	-	-

A, hepatic artery reconstruction; *ASA*, American Society of Anesthesiologists; *ELH*, extended left hemihepatectomy; *ERH*, extended right hemihepatectomy; *LH*, left hemihepatectomy; *PVE*, portal vein embolization; *RH*, right hemihepatectomy; *V*, portal vein reconstruction.

extended hepatectomy proportion of 22.8% (95% CI 17.3–29.4).[11,13,15,18,22,26,28,29,31–42,45,47] Six studies (representing 647 patients) had a pooled rate of preoperative portal vein embolization of 8.2% (95% CI 5.0–13.1) (Supplementary Figure S1, *A*).[16,18,28,36,38,39] The pooled rate of a vascular resection was 10.2% (95% CI 6.7–15.3) and involved mostly a portal vein reconstruction (Supplementary Figure S1, *B*).[13,15,16,21,26,28,33–36,39,45]

Critical appraisal and risk of bias

The individual score of risk-of-bias per study is given in Supplementary Table S3. The overall risk of bias for each item on the Joanna Briggs Institute checklist is presented in Figure 2. Incomplete reporting of clinical information (ASA classification, extent of resection) occurred in 75% (24/32) of the studies. Incomplete reporting of the demographic information occurred in 43.8% (14/32) of the studies. No multicenter studies presented the individual results of each center. Follow-up data were unclear or incomplete in 71.9% (23/32) of the studies.

Postoperative mortality

Supplementary Table S4 presents the mortality rates per study. In-hospital mortality was reported by 8 studies (representing 7,639 patients) and ranged from 1.6% (1/63) to 11% (513/4,667) across studies.[22,23,30,32,35,37,38,40] The pooled in-hospital mortality was 5.9% (95% CI 4.1–8.4) (Figure 3, *A*). Eleven studies (representing 6,847 patients) described 30-day mortality rates ranging from 0% (0/83) to 8% (12/150) across studies.[13,15,26,27,29,31,33,34,39,46,47] The pooled 30-day mortality was 4.6% (95% CI 4.0–5.2) (Figure 3, *B*). Sixteen studies (representing 8,607 patients) reported on 90-day mortality ranging from 1.5% (1/67) to 11.3% (13/115) across studies.[11,13,15,16,18,21,23–26,29,33,34,36,41,43,44] The pooled 90-day mortality of these studies was 6.1% (95% CI 5.0–7.3; Figure 3, *C*). Six studies reported both on 30- and 90-day mortality.[13,15,26,29,33,34] The pooled difference between 30- and 90-day mortality was 2.5% (95% CI 1.6–3.8) (Supplementary Figure S2, *A*). Six studies (representing 16 patients) reported the proportion in which liver failure was the cause of mortality, for which the pooled proportion was 29.1% (95% CI 18.7–42) (Supplementary Figure S2, *B*).[22,33–36,47]

Major complications

Twenty studies (representing 8,213 patients) reported on major complications after resection of iCCA, ranging from 4% (51/1,281) to 52.2 (60/115) across studies.[11,13,15,16,21,23–26,28,33-38,42–45] The pooled major complication rate after resection of iCCA (Clavien-Dindo grade ≥III) was 22.2% (95% CI 17.7–27.5; Figure 3, *D*).

Major complications and mortality in relation to the extent of resection

Ninety-day mortality rates were reported for minor resections in 2 studies (representing 452 patients),[15,33] major resections in 4

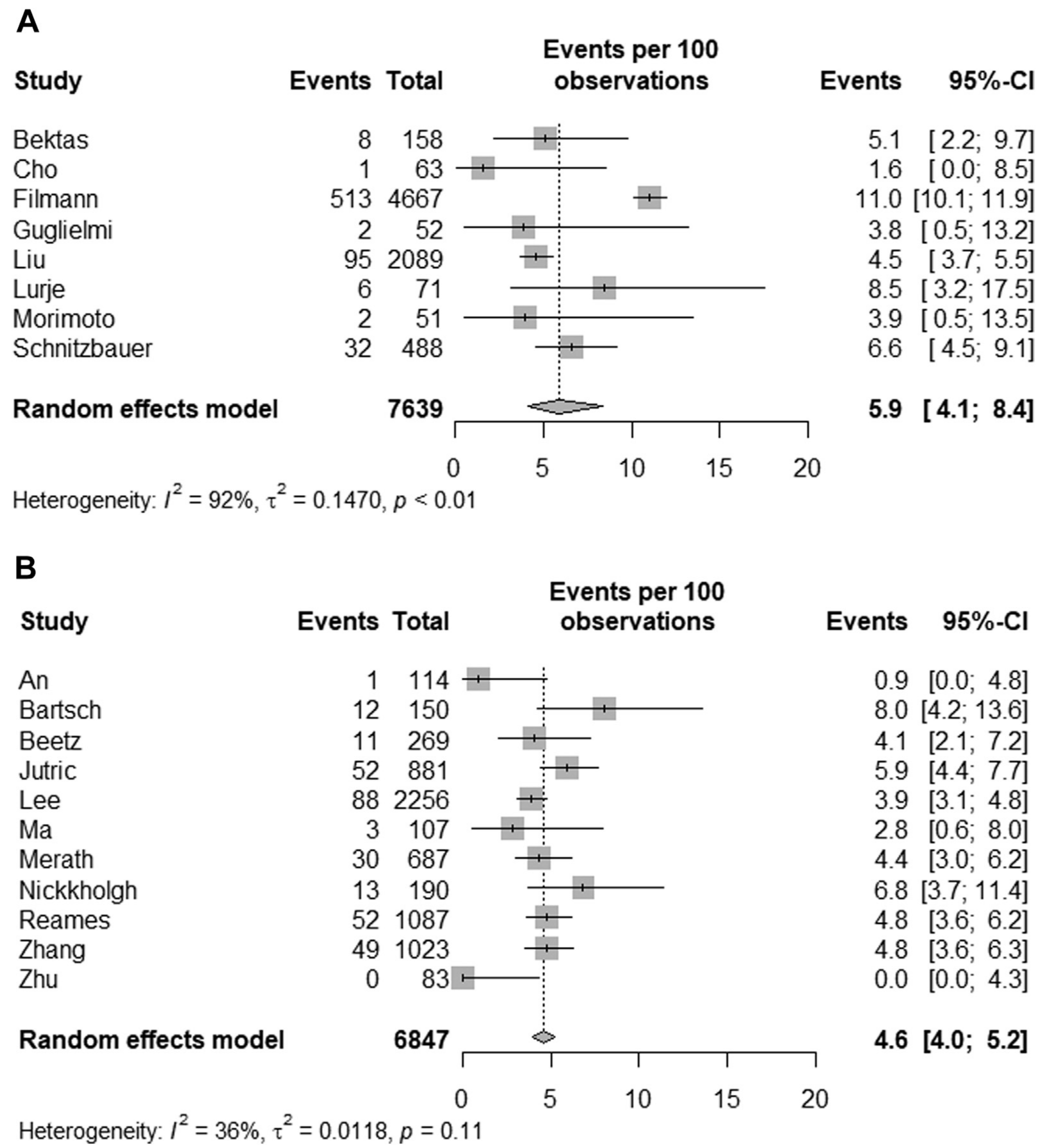

Figure 3. Forest plots of postoperative mortality and morbidity rates after resection of intrahepatic cholangiocarcinoma. (A) in-hospital mortality, (B) 30-day mortality, (C) 90-day mortality, and (D) major complications (Clavien-Dindo grade ≥III) after resection of intrahepatic cholangiocarcinoma.

studies (representing 892 patients),[15,33,36,41] and extended resections in 2 studies (representing 114 patients).[33,36] The subgroup analysis revealed a pooled 90-day mortality of 3.1% (95% CI 1.8–5.2) for a minor hepatectomy, 7.4% (95% CI 5.9–9.3) for all major hepatectomies, and 11.4% (95% CI 6.7–18.7) after an extended hepatectomy (*P* = .001) (Figure 4, *A*).

Six studies (representing 932 patients) reported on major complications specifically after a major hepatectomy, which ranged from 25.6% (10/39) to 59.3% (16/27) across studies.[15,16,28,33,36,43] Two studies (representing 452 patients) reported on major complications after a minor hepatectomy, which ranged from 7.2% (30/415) to 21.6% (8/37) across studies.[15,33] The pooled major complication rate after a major hepatectomy was 38.8% (95% CI 29.5–49) compared to 11.3% (95% CI 5.0–24) after a minor hepatectomy (*P* = .001; Figure 4, *B*).

Mortality in relation to Asian versus Western studies

Ten studies (representing 2,749 patients) originated from Asian centers and 22 studies (representing 16,754 patients) originated from Western centers. The pooled in-hospital mortality was 2.6% (95% CI 0.9–7.8) in Asian studies and 6.5% (95% CI 4.1–8.4) in Western studies (*P* = .12; Supplementary Figure S3, *A*). The pooled 30-day mortality was 1.3% (95% CI 0.4–4.3) in Asian studies and 4.8% (95% CI 4.2–5.5) in Western studies (*P* = .03; Supplementary Figure S3, *B*). The pooled 90-day mortality was 4.4% (95% CI 3.3–5.9) in Asian studies and 6.8% (95% CI 5.6–8.2) in Western studies (*P* = .02; Figure 4, *C*).

Mortality in relation to inclusion period

Ninety-day mortality risks were reported by 9 studies (representing 4,690 patients) that started the inclusion period before the year 2000,[11,13,15,24–26,34,36,39] and 7 studies (representing 3,917 patients) that started the inclusion period after the year 2000.[16,23,29,33,41,43,44] The pooled 90-day mortality was 6.8% (95% CI 5.1–9.1) for studies that started the inclusion period after 2000, and 5.9% (95% CI 4.8–7.3) for studies that started the inclusion period before 2000 (*P* = .44; Figure 4, *D*).

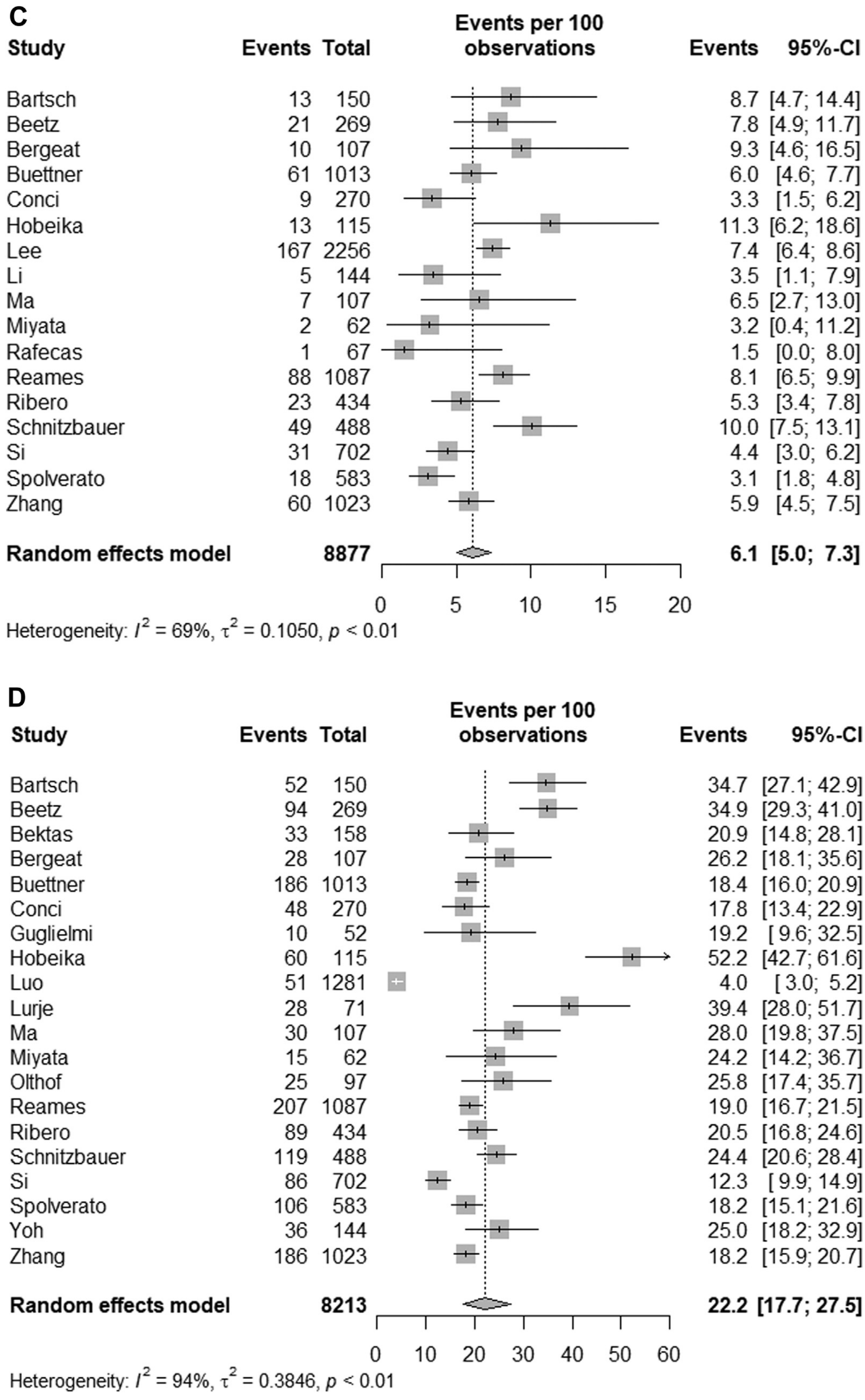

Figure 3. (*continued*).

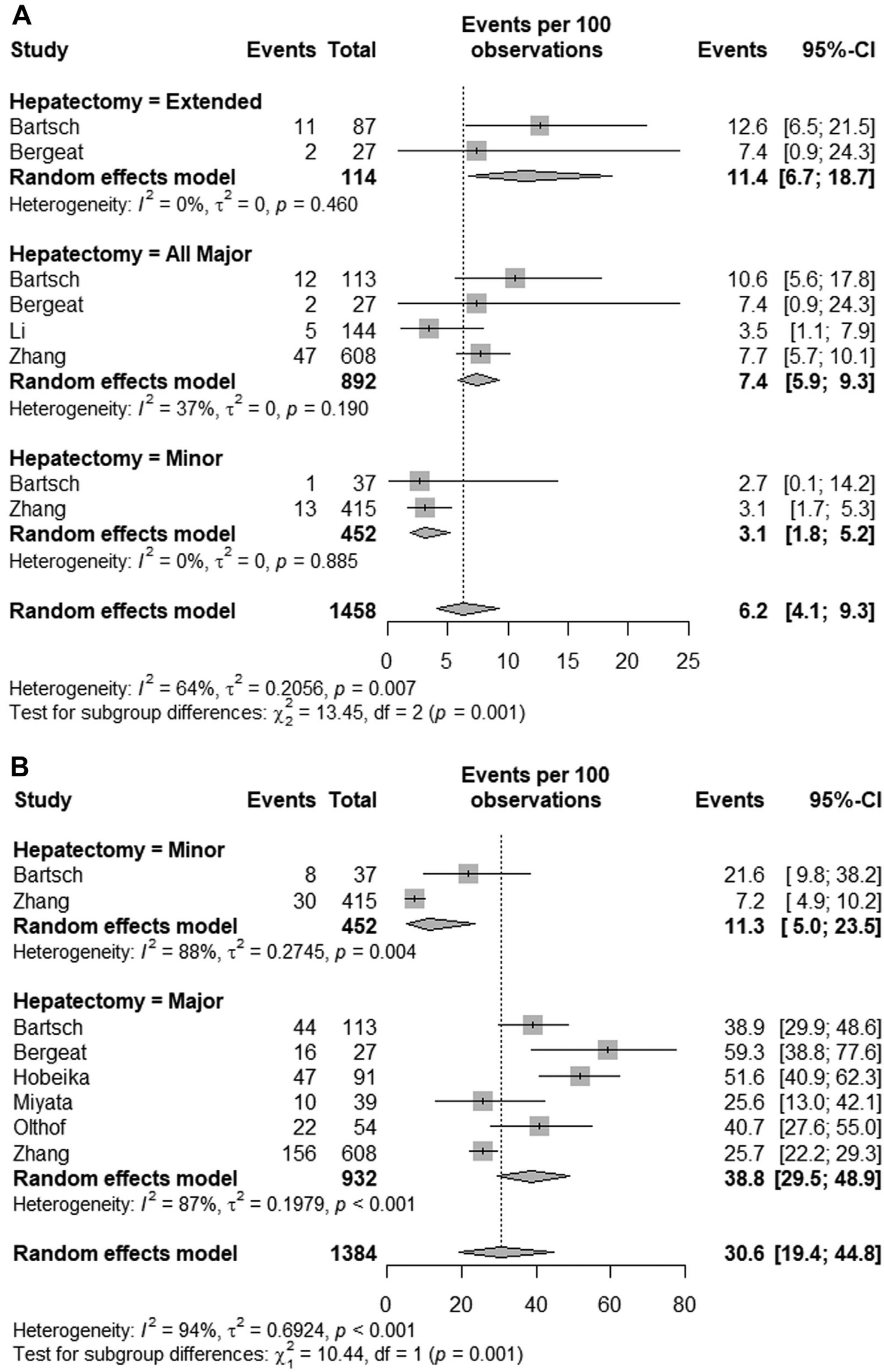

Figure 4. Forest plots of subgroup analyses. (A) 90-day mortality after a minor, major, or an extended hepatectomy (subgroup of major); (B) major complications (Clavien-Dindo grade ≥III) after a minor and major hepatectomy; (C) 90-day mortality in Asian studies and Western studies; and (D) 90-day mortality for studies that started their inclusion period before or after the year 2000.

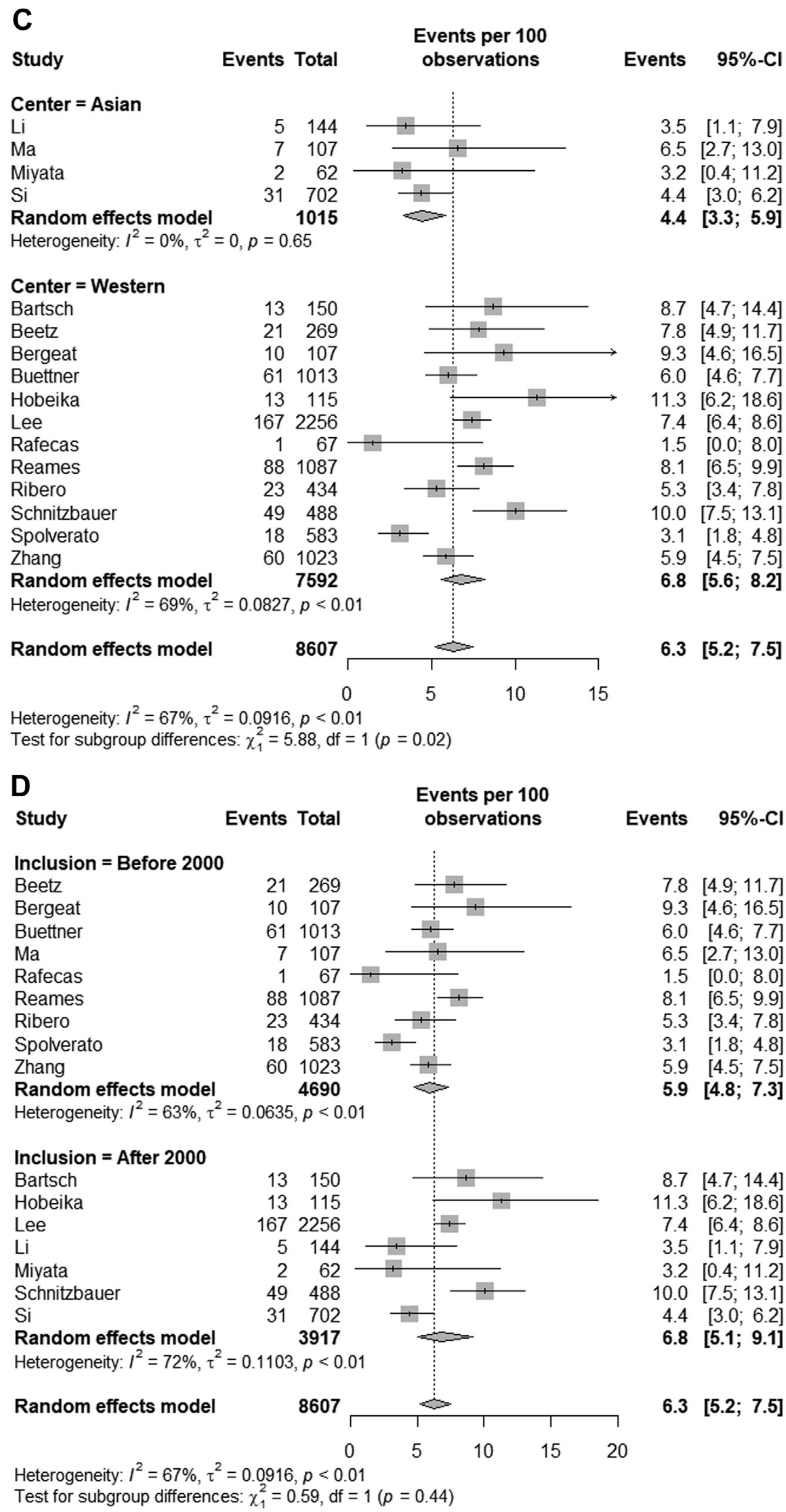

Figure 4. (*continued*).

Discussion

This systematic review and meta-analysis on postoperative major complications and mortality after resection of iCCA included 32 studies that reported on 19,503 patients. The pooled in-hospital mortality was 5.9%, the 30-day mortality 4.6%, and the 90-day mortality 6.1%. The major complication (Clavien-Dindo grade ≥III) risk after resection of iCCA was 22.2%. Differences were found for 90-day mortality in relation to the extent of resection: the pooled 90-day mortality was 3.1% for minor resections, 7.4% for major resections, and 11.4% for extended resections ($P = .001$). The major complication rate was higher after a major hepatectomy when compared to a minor hepatectomy (38.8% vs 11.3%; $P = .001$). The pooled 90-day mortality was lower for Asian studies when compared to Western studies (4.4% vs 6.8%; $P = .02$). Studies with patients included before 2000 had a similar pooled 90-day mortality as after 2000 (5.9% vs 6.8%; $P = .44$).

Liver resections for different indications are associated with different mortality rates, despite technical similarities.[28] Shubert et al suggested that outcomes after hepatectomy should be stratified by the diagnosis, by showing differences in mortality for different indications using National Surgical Quality Improvement Program data of >7,000 patients.[18] The highest 30-day mortality rates were observed for cholangiocarcinoma (8.2% for intrahepatic and perihilar combined) and hepatocellular carcinoma (5.2%), which were classified as 'high risk' diagnoses. These were followed by lower risk diagnoses such as metastatic disease (1.3%), gallbladder cancer (1%), and benign neoplasms (0.5%). This study could not be included in the current review because mortality was not reported for intrahepatic cholangiocarcinoma alone. A large cohort of >100,000 liver resections in Germany for all indications between 2010 and 2015 also found substantial difference in mortality rates depending on the diagnosis.[32] In-hospital mortality was 5.5% for colorectal liver metastases, 7.1% for gallbladder cancer, 9.3% for hepatocellular carcinoma, and 11% for iCCA. A fair comparison of postoperative mortality after liver resection requires consideration of diagnosis.

Mortality outcomes should not only be stratified according to diagnosis, but also by the extent of the resection. In the same German cohort, in-hospital mortality (including liver resections for all diagnoses) was 3.8% for a segmental resection, 9.1% for a major hepatectomy, and 16.2% for an extended hepatectomy. The in-hospital mortality of an extended hepatectomy for iCCA ($n = 709$) was 21.8%, which is higher than the 11.4% in the pooled analysis for 90-day mortality in the present study.[32] A study on >1,000 liver resections for iCCA found that 30-day mortality was 5 times higher and 90-day mortality was 2.5 times higher after a major compared to a minor liver resection.[15]

Thirty-day mortality has been used as a benchmark to assess the quality of major surgical procedures. In the present study, the pooled difference between 30-day and 90-day mortality was 2.5%, indicating that surgery related death may be underestimated at 30 days, postoperatively. Posthepatectomy liver failure (PHLF) is a major cause of death after liver resection, and 25% of patients die from PHLF >30 days after resection.[48] Posthepatectomy liver failure requires complex treatment at the intensive care unit, which prolongs hospital stay and may result in slow physical deconditioning and death eventually. Truant et al found a median time to postoperative mortality of 31 days for patients undergoing an extended hepatectomy.[49] Twenty-two out of 26 patients (ie, 84.6%) died from PHLF, often after >30 days.[49] Therefore, 90-day postoperative mortality is a better outcome measure when reporting outcomes of liver resection.

A difference was found in postoperative mortality rate between Asian studies and Western studies for the 90-day mortality risk (4.4% vs 6.8%; $P = .02$). A lower mortality risk in Asian studies was also found for perihilar cholangiocarcinoma.[50] The patient characteristics differ among regions, and a higher incidence of obesity is observed in Western populations. This adds to co-morbidity scores and increases the surgical risk. It remains unclear to what extent the higher postoperative mortality in Western studies is explained by differences in baseline patient and tumor characteristics or differences in patient care.

Intrahepatic cholangiocarcinoma patients often present with multifocal disease, for which guidelines recommend palliative chemotherapy rather than surgical resection.[51–54] Hepatic arterial infusion pump (HAIP) has been investigated for patients with unresectable iCCA confined to the liver. The HAIP delivers high doses of chemotherapy with floxuridine directly in the hepatic artery via a surgically implantable pump. A recent study found that patients with multifocal iCCA had a similar median OS after HAIP floxuridine chemotherapy compared to surgical resection, whereas major complication (6% vs 25%) and postoperative 30-day mortality (1% vs 6%) were lower in the HAIP group.[55] These results suggest consideration of HAIP instead of surgical resection in patients with multifocal iCCA, in particular in patients with an increased surgical risk.

Several limitations should be addressed for this systematic review and meta-analysis. First, the included studies were all retrospective studies that are prone to selection bias and information bias with underreporting of postoperative complications. A high risk of bias was detected at the level of 'clear reporting of clinical information.' This was mainly because most studies (24/32) lacked details on the ASA classification. However, resection type was specified in most studies (24/32), which was relevant for the subgroup analyses. Postoperative morbidity and mortality are increased in patients with a poor future liver remnant function and volume. The results of the included studies were too heterogeneous for analyzing such risk factors. Furthermore, many studies include patients over a long inclusion period because of the rarity of the disease, of which some included patients from the 1990s. Since 1990, many advancements in technique and surgical management were introduced over time. The year of surgery was not reported in any of the included studies. A subgroup analysis, however, found that mortality was similar in studies with only patients after 2000. However, a difference in postoperative mortality could not be demonstrated. Finally, some of the pooled analyses included a smaller number of studies and patients resulting in wider 95% CIs.

In conclusion, the best estimate for the 90-day postoperative mortality after resection of iCCA is 6.1% with a major complication rate of 22.2%. Ninety-day postoperative mortality rates were lower in Asian studies compared to Western centers (4.4% vs 6.8%). When informing patients or comparing outcomes across hospitals, postoperative mortality rates after liver resection should be reported for 90-days due to the significant number of patients that may survive the first 30 days (ie, PHLF) but will succumb within the following 60 days, with consideration of the diagnosis and extent of liver resection.

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Conflict of interest/Disclosure

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