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Original Article

Is it time to define the scope of safety for robotic resection in perihilar cholangiocarcinoma surgery? A propensity score matching based analysis of a single center experience

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Backgrounds/Aims: Robotic surgery for perihilar cholangiocarcinoma is in the developmental and exploratory phase. The objective of this study was to compare the short-term outcomes and survival rates of robotic versus open resection for perihilar cholangiocarcinoma in a single center, and to determine the reliable scope of robotic interventions.
Methods: A comparative analysis of outcomes from open and robotic resections at a single center was conducted using propensity score matching (PSM). The balance of covariates was assessed using standardized mean differences, and the robotic resection procedures adhered to the standards of open surgery.
Results: PSM was effectively applied between 41 robotic and 82 open resections. No differences were observed in blood loss, overall and severe morbidity, 90-day mortality, or length of hospital stay. Robotic resections were longer but resulted in better immediate oncological outcomes. Median overall survival for the robotic and open groups was 44 and 30 months ($p = 0.259$) before PSM and 44 and 29 months ($p = 0.164$) after PSM respectively. Conversion was required in 8 cases. A subgroup analysis excluding conversions revealed no differences in immediate and long-term outcomes. All patients undergoing robotic resection for Bismuth types I and II were alive at a mean follow-up of 37 months.
Conclusions: The robotic approach is comparable to open resection regarding immediate outcomes and survival in select patients with perihilar cholangiocarcinoma. For patients with Bismuth type I and II tumors and early (stages I and II) TNM stages, robotic resection is a reliable treatment option when aligned with the principles of open surgery.

Key Words: Perihilar cholangiocarcinoma; Klatskin tumor; Robot surgery; Minimally invasive surgery

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INTRODUCTION

Radical treatment of perihilar cholangiocarcinoma (PHCC) remains one of the most challenging surgical procedures due to the tumor's proximity to major vascular structures and the unpredictability of tumor invasion extent prior to surgery. The integration of laparoscopic technology in managing proximal biliary cancers has been slower compared to other liver and periampullary malignancies, partially due to the tendency of the tumor to invade adjacent tubular structures and metastasize to lymph nodes, significantly increasing surgical complexity.

The robotic and laparoscopic approach in radical surgery for

PHCC is currently in the second stage (development and exploration) according to the IDEAL(idea, development, exploration, assessment, surveillance) paradigm for surgical innovations. The initial series of minimally invasive resection for PHCC predominantly comprised isolated resections of the bile ducts, either without liver resection or with partial liver resections [1]. Over time, the rate of minimally invasive major liver resections for PHCC increased; however, the data remain inconclusive due to heterogeneity in procedures, as clearly demonstrated in a systematic review by Franken et al. [2]. The majority of studies focused on short-term outcomes, which appeared promising in terms of low overall and specific morbidity rates [3-5]. However, these studies had limitations, including a small number of patients and no comparisons with open procedures. Some researchers presented well-designed, transparent comparative studies without survival assessment [4,6]. Data from a few large Eastern studies are insufficient to assess the impact of the technology on long-term outcomes, as 5-year survival rates ranged from 19% to 50% [7,8]. The data from Western studies are inconclusive regarding oncological outcomes, with variations favoring the robotic approach, showing 5-year survival rates of 70% and less than 30% for open resection [9,10]. Comparative studies for the robotic approach did not perform any matching. Given this, it is evident that there is a paucity and heterogeneity of data on the outcomes of robotic resections for PHCC. Consequently, the data available today are inadequate to determine the scope of application of robotic technology, where the expected results should be at least comparable to, if not better than, those of open resections for PHCC.

The objective of the study was to compare short-term outcomes and survival after robotic and open resection for PHCC in a single center, and to identify the area of predictable reliability of robotic technology.

MATERIALS AND METHODS

Ethical statement

The study's protocol was approved by the research ethics committee (4/2024). Informed consent was obtained from all patients before surgery.

Study setting and design

The study was organized at a high-volume tertiary center specialized in hepatobiliary surgery, with expertise in minimally invasive surgery including laparoscopic and robotic liver and bile duct resection. The primary context for the study was the high patient volume with PHCC (more than 20 resections per year). All open procedures were performed by two surgeons, with one performing the robotic procedures. The research was designed as a single center retrospective comparative cohort study.

Data on immediate outcomes and survival estimates were available from a series of patients treated for PHCC between October 2013 and April 2024. The first robotic procedure was performed in 2014. In all included patients, the diagnosis was confirmed by pathological examination. All patients underwent treatment using the da Vinci Si robotic system. The robotic approach was primarily considered for patients without

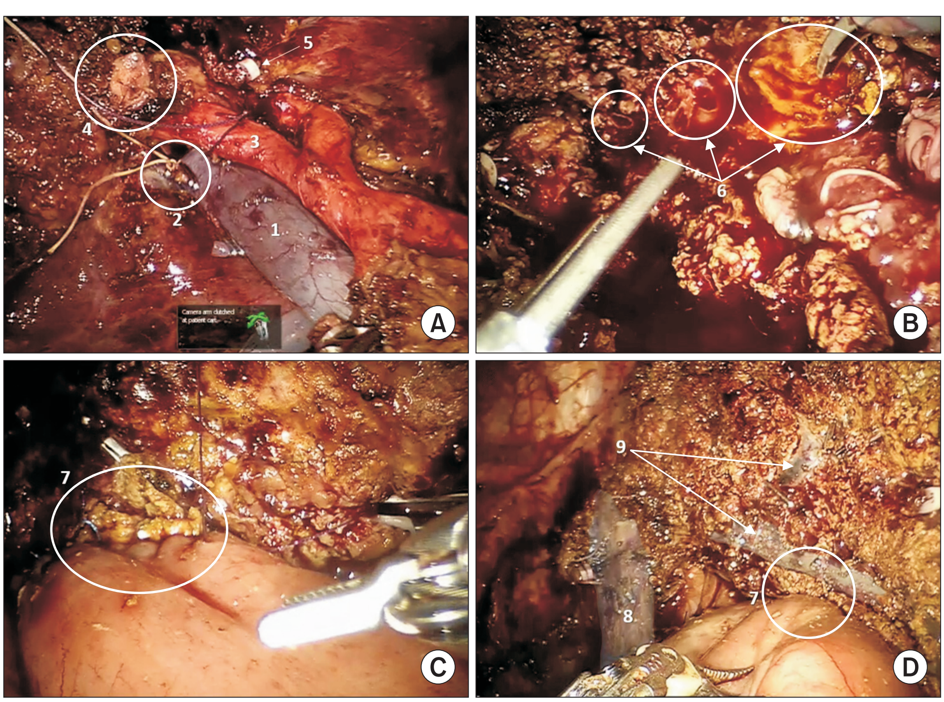

Fig. 1. ALPPS for perihilar cholangiocarcinoma (operation photo). (A) Final view of the resection field after the first stage: (1) portal vein trunk; (2) clipped right portal vein; (3) right hepatic artery; (4) ligated stump of the right hepatic duct; and (5) clipped by hem-o-lok stump of the left hepatic duct. (B–D) Final view of the resection field following right hepatectomy with caudate lobectomy. (B) Three orifices of transected bile ducts to segments 2, 3, and 4 (6); (C) completed hepaticojejunostomy (7); (D) inferior vena cava (8) and middle hepatic vein (9).

evidence of vascular invasion requiring portal vein and/or hepatic artery reconstruction based on preoperative examination. Intolerance to prolonged pneumoperitoneum was also considered a contraindication. Tumor types 3 and 4 according to Bismuth were not contraindications for the robotic approach.

Procedure technique

The volume of robotic resection was comparable to that of the standard open procedure, encompassing extrahepatic bile duct resection with Roux-en-Y hepaticojejunostomy, major liver resections (right, left, or extended hepatectomy), caudate lobectomy, and lymphadenectomy from stations 8a, p; 12a, b, c, p; and 13a, as classified by the Japan Pancreas Society nomenclature. Isolated extrahepatic bile duct resection was performed exclusively for papillary or nodular type I tumors, as classified by Bismuth-Corlette, without vascular invasion and lymph node metastases. A future liver remnant (FLR) volume less than 40% was considered an indication for portal vein embolization (PVE). In one patient, an ALPPS procedure (associated liver partition and portal vein ligation for staged hepatectomy) utilizing the robotic approach at both stages was performed (Fig. 1).

Caudate lobectomy was avoided if it would lead to a potential decrease in the FLR volume to less than 40% after PVE, as well as in the presence of other risk factors for liver failure (cholangitis in the preoperative period, severe jaundice, etc.) in patients with borderline FLR volumes [11].

Data collection and study subjects

Demographic data encompassed age, sex, body mass index, American Society of Anesthesiology (ASA) physiological status classification, Eastern Cooperative Oncology Group (ECOG) performance status estimation, Bismuth type, TNM stage, and history of perioperative chemotherapy.

Morbidity was classified using the Clavien-Dindo scale. A Grade V complication was defined as in-hospital mortality due to any cause. Additionally, the 90-day mortality rate post-surgery for any cause was estimated. The comprehensive complication index (CCI) facilitated the calculation of the cumulative impact of all postoperative adverse outcomes [12]. The Estimation of Physiologic Ability and Surgical Stress (E-PASS) model was employed to predict morbidity and mortality, integrating numerous predictors for an objective comparative analysis of robotic and open resection [13,14]. The comprehensive risk score (CRS) as the resultant scale in the E-PASS model was computed using previously published formulas, incorporating data on age, severe heart and pulmonary diseases, diabetes mellitus, performance status index, ASA score, ratio of blood loss to body weight, duration of operation, and length of skin incision [13].

To determine which component of the CRS most significantly influenced differences between the groups, the CRS was calculated excluding the contribution of skin incision length (equivalent to the approach option). This adjustment allowed for assessment of the approach type on surgical stress tolerance.

Robotic and open resection groups were compared in terms of demographic and perioperative outcomes, and survival rates before and after matching. A subgroup comparative analysis was executed following the exclusion of converted cases to mitigate biases associated with conversion.

Overall survival was defined as the time from resection to disease-specific death, excluding 90-day mortality. Disease-free survival was delineated as the period from resection to either disease relapse at any site or death from any cause. Subgroup survival comparisons were conducted for Bismuth types I and II tumors, where the procedures are technically simpler and the impact of new technologies is less affected by selection biases.

Statistical analysis

The covariates were balanced using propensity score matching (PSM) with a 1:2 nearest neighbor match ratio and a caliper of 0.2. The covariates used for matching included age, Bismuth tumor type, TNM stage, ASA, ECOG, complicated biliary drainage, PVE, FLR < 50%, vascular resection, perioperative chemotherapy, and reconstruction.

The balance of covariates was measured by calculating standardized mean differences (SMD). A balance was deemed good with a SMD < 0.2. Differences corresponding to SMD values of 0.2 to 0.5 were considered small; values between 0.5 and 0.8 were viewed as medium; and SMD values exceeding 0.8 indicated a large difference [14].

Recurrence-free and overall survival were evaluated using Kaplan–Meier curves. Predictors that significantly influenced survival were identified through multivariate Cox regression analysis. The groups undergoing robotic and open resection were compared based on the rate of predictive factors. Continuous data (mean values) were compared using the Mann–Whitney *U* test. Categorical variables were analyzed using either the two-tailed Fisher's exact test or the chi-square test. A p-value of less than 0.05 was considered statistically significant. IBM SPSS version 23.0 (IBM Corp.) and R version 4.3.3 (R Foundation for Statistical Computing), using the MatchIt package, were employed for statistical analysis.

RESULTS

In total, data from 191 patients who underwent open and robotic resection for PHCC were analyzed for study inclusion. After the exclusion of patients with missing data, 180 patients were divided into open (n = 139) and robotic (n = 41) resection groups. Following PSM, 41 and 82 patients in the robotic and open groups were matched respectively. Subgroup analysis was conducted excluding robotic cases that were converted to open procedures, to avoid bias from conversions. The study design's flowchart is presented in Fig. 2.

The demographic and perioperative data after PSM are presented in Table 1.

Comparative analysis of demographic data before PSM revealed significant differences in ECOG physical status between groups: a rate of 0/1 status was 48% in the open group versus 76% in the robotic group. In the open group, Bismuth type IV treatment accounted for 21% of cases, compared to 2% in the robotic group. Biliary drainage was required more frequently in the open group (92% vs 78%), and perioperative chemotherapy was less commonly administered (74% vs 100%). Vascular resection was more frequent in the open group (36% vs 20%), though this difference was not statistically significant. Post-PSM, all demographic differences were resolved, except for the presence of Bismuth type IV tumors. No differences were observed in the rates of type I and II tumors before and after PSM (Table 1). The immediate outcomes pre- and post-PSM are detailed in Table 2.

Despite eliminating significant demographic differences through PSM, disparities in postoperative outcomes that existed prior to PSM persisted after matching. Resection times were longer in the robotic group. The average number of lymph nodes harvested was significantly higher in the robotic group (10 vs 8, $p = 0.011$, SMD = 0.352). A higher rate of R0 resection was achieved in the robotic group (88% vs 66%, $p = 0.010$, SMD = 0.426). This may be partly attributed to the significant differences in the rates of Bismuth IV tumor types (19% vs 2%) between the open and robotic groups, despite prior PSM.

Immediate surgical outcomes, such as morbidity, type of complications, mortality, and length of hospital stay, were comparable between the two groups. The rate of severe morbidity (> II stage, Clavien-Dindo) and the value of the CCI did not differ between the groups. Notably, a CCI greater than 40, indicative of severe comorbidity, also showed no variation between the groups. The rates of specific morbidity, including liver failure (grade A and B according to the International Study Group of Liver Surgery [ISGLS]) and biliary complications, were equivalent regardless of the surgical approach. Biliary complications encompassed all types of biliary fistula and bile collections, with all instances classified as grade A and B in both groups according to the ISGLS classification.

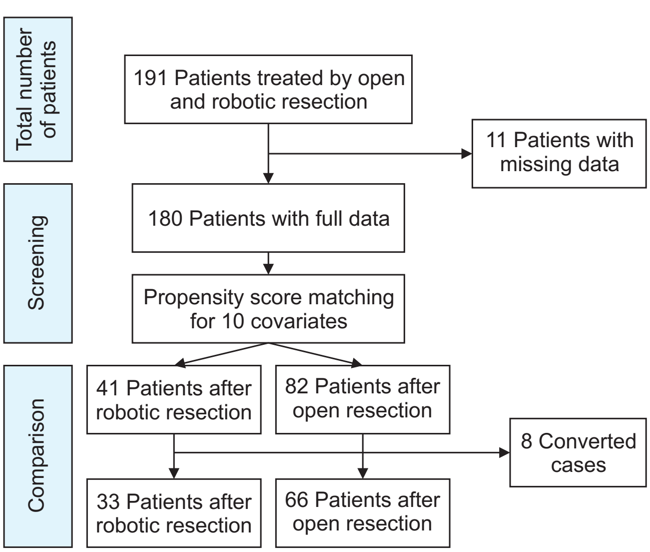

Fig. 2. Flowchart depicting patient selection for comparative analysis.

In the robotic group, patients exhibited a significantly lower CRS. When the effect of the surgical approach was excluded, the CRS values were identical in both groups, suggesting a considerable influence of the surgical approach on the severity of surgical stress in resections for PHCC.

No differences were observed in the duration of intensive care unit (ICU) and hospital stays. The 90-day mortality rate was similar in both groups (5%). In the robotic group, two postoperative deaths occurred: a 79-year-old male succumbed to post-hepatectomy liver failure with a 40% FLR volume, and a 63-year-old female died from a COVID-19 infection.

Before matching, the distribution of patients by the number of ducts included in the hepaticojejunostomy was as follows: one duct was sutured in 7 (18%) patients in the robotic group and 21 (19%) in the open group, 2 ducts in 16 (41%) and 63 (49%) cases, and 3 or more ducts were sutured in 18 (44%) and 55 (40%) patients in the robotic and open groups, respectively. No differences were observed between the groups. Two or more hepaticojejunostomy anastomoses were performed in 19 (46%) patients in the robotic group and 53 (38%) in the open group ($p = 0.346$).

In the robotic group, conversion to open surgery was necessary in 8 patients (19%). Among these, the need for vascular resection and reconstruction to achieve R0 resection prompted conversion in 7 cases. In one case, the conversion was due to lack of surgical progress caused by perivascular fibrosis from multiple abscesses. Given that conversion introduces biases, a subgroup comparison was conducted using matched pairs from the open and purely robotic cases. Demographic data and perioperative outcomes from this subgroup analysis are detailed in Table 3, 4.

In the robotic group, there was a noticeable preference for selecting patients with better-preserved physical status before and after PSM, ($p = 0.074$) after exclusion converted cases. Excluding converted cases significantly increased the difference in the rates of TNM stages 1 and 2 in favor of the robotic approach ($p = 0.037$). Additionally, there was a significant reduction in the rate of biliary drainage within the robotic group ($p = 0.031$), considerably lowering the risk of post-resection complications. Notably, after the exclusion of conversions, most of which involved vascular resections, the rate of vascular resections in the robotic group was considerably reduced ($p = 0.001$).

Excluding conversion cases did not alter the main trends in demographic data and perioperative outcomes. In the robotic group, immediate oncologic outcomes, such as the R0 resec-

Table 1. Demographic and preoperative data before and after PSM

Parameter	Robotic resection (n = 41)[a]	Before PSM		After PSM		
		Open resection (n = 139)	*p*-value	Open resection (n = 82)	*p*-value	d
Age (yr)	61/62 (56–68)	60/61 (52–68)	0.661	59/60 (51–67)	0.451	0.095
Sex (n), female/male	16/25	65/74	0.475	40/42	0.341	–0.202
BMI (kg/m^2)	26/26 (24–28)	25/24 (22–28)	0.400	25/25 (22–27)	0.126	0.215
ASA score			0.187		0.158	
1	1 (3)	12 (9)		8 (10)		–0.287
2	12 (29)	57 (41)		34 (42)		–0.274
3	28 (68)	70 (50)		40 (48)		0.413
ECOG PS			0.019*		0.149	
0	5 (13)	8 (6)		7 (9)		0.128
1	25 (63)	58 (42)		35 (44)		0.388
2	9 (22)	65 (46)		34 (43)		–0.460
3	1 (3)	8 (6)		3 (4)		–0.054
Bismuth-Corlette (type)			0.024*		0.026*	
I	4 (10)	5 (3)		3 (4)		0.237
II	2 (5)	11 (8)		8 (10)		–0.191
IIIa	15 (37)	50 (36)		32 (39)		–0.041
IIIb	19 (46)	44 (32)		23 (28)		0.379
IV	1 (2)	29 (21)		16 (19)		–0.577
Bismuth-Corlette (type I, II)	6 (15)	16 (12)	0.592	11 (13)	> 0.999	0.058
TNM stage			0.122		0.171	
I	3 (7)	13 (9)		7 (9)		–0.074
II	13 (32)	22 (16)		14 (17)		0.354
IIIa	7 (17)	40 (29)		22 (26)		–0.220
IIIb	0 (0)	12 (8)		7 (9)		–0.444
IIIc	12 (29)	33 (24)		19 (23)		0.137
IV	6 (15)	19 (14)		13 (16)		–0.028
TNM stage (I, II)	16 (39)	35 (25)	0.114	20 (24)	0.099	0.327
Total bilirubin before resection (μmol/L)	38/30 (21–39)	39/32 (19–48)	0.911	35/32 (20–43)	0.967	0.127
Preoperative biliary drainage	32 (78)	128 (92)	0.008*	73 (89)	0.051	–0.299
Complicated biliary drainage	13 (32)	58 (42)	0.279	36 (44)	0.242	–0.249
Cholangitis before resection	19 (53)	83 (61)	0.446	50 (63)	0.310	–0.183
PVE	7 (18)	31 (23)	0.519	17 (22)	0.636	–0.100
FLR < 50%	19 (46)	52 (37)	0.364	31 (39)	0.437	0.142
Vascular resection	8 (20)	50 (36)	0.057	28 (34)	0.140	–0.319
Type of liver resection			0.348		0.427	
Right/extended hepatectomy	19 (46)	49 (35)		29 (36)		0.204
Left hepatectomy	18 (44)	73 (53)		42 (51)		–0.141
Partial liver resection	2 (5)	14 (10)		9 (11)		–0.222
Without liver resection	2 (5)	3 (2)		2 (2)		0.163
Major liver resection	39 (95)	135 (97)	0.620	80 (98)	0.600	–0.164
Caudate lobectomy	38 (93)	117 (84)	0.206	69 (84)	0.259	0.285
Perioperative chemotherapy	39 (100)[b]	87 (74)[b]	< 0.001*	80 (100)[b]	> 0.999	0

Values are presented as mean/median (interquartile range) or number (%).
PSM, propensity score matching; BMI, body mass index; ASA, American Society of Anesthesiologists; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PVE, portal vein embolization; FLR, future liver remnant.
[a]As number of patients in robotic group did not change after PSM the only column with data on robotic resection is included in the table. The data on open resection group and outcomes of comparison with robotic group are presented in columns before and after PSM.
[b]Calculation excluding 90-day mortality.
*$p < 0.05$.

Table 2. Postoperative immediate outcomes before and after PSM

Parameter	Robotic resection (n = 41)[a]	Before PSM		After PSM		
		Open resection (n = 139)	p-value	Open resection (n = 82)	p-value	d
Number of lymph nodes retrieved	10/9 (7–13)	8/6 (4–12)	0.002*	8/6 (4–12)	0.011*	0.392
Residual tumor (R1)	5 (12)	40 (29)	0.039*	28 (34)	0.010*	–0.542
Number of bile duct orifices included in anastomosis	2/2 (2–3)	2/2 (2–3)	0.712	2/2 (2–3)	0.830	0
Time of resection (min)	651/625 (570–690)	524/520 (450–600)	< 0.001*	509/510 (450–585)	< 0.001*	1.230
Blood loss (mL)	437/300 (250–500)	485/300 (250–600)	0.628	470/300 (200–500)	0.925	–0.085
Conversion	8 (19)	-	-	NA	-	-
CRS	0.14/0.11 (0.01–0.25)	0.48/0.47 (0.36–0.60)	< 0.001*	0.47/0.45 (0.37–0.59)	< 0.001*	–1.885
CRS without incision contribution	0.14/0.11 (0.01–0.25)	0.14/0.13 (0.02–0.26)	0.665	0.13/0.10 (0.02–0.25)	0.853	–0.026
Severe morbidity (Clavien-Dindo)			0.304		0.525	
IIIa	16 (39)	42 (30)		10 (26)		0.280
IIIb	1 (2)	18 (13)		5 (13)		–0.427
IVa	3 (7)	10 (7)		4 (10)		–0.108
IVb	2 (5)	5 (4)		2 (5)		0
V	2 (5)	16 (11)		1 (3)		0.102
Complication > III (Clavien-Dindo)	8 (20)	31 (23)	0.830	13 (16)	0.622	0.104
CCI	30/26 (21–34)	35/30 (21–42)	0.219	28/26 (21–40)	0.890	0.096
CCI > 40	8 (20)	38 (27)	0.416	18 (22)	0.819	–0.049
Posthepatectomy liver failure	3 (7)	14 (10)	0.766	9 (11)	0.749	–0.140
Biliary complications	17 (42)	47 (34)	0.854	29 (35)	0.556	0.144
Postoperative acute cholangitis	9 (22)	23 (17)	0.486	14 (17)	0.624	0.126
Infected fluid collection	8 (20)	23 (17)	0.633	13 (16)	0.609	0.104
ICU stay (day)	3/2 (1–4)	4/2 (1–5)	0.105	4/2 (1–3)	0.627	–0.198
Hospital stay (day)	22/21 (15–27)	24/20 (14–30)	0.776	25/22 (16–30)	0.558	–0.243
90-day mortality (%)	2 (5)	19 (14)	0.168	2 (2)	> 0.999	0.163

Values are presented as mean/median (interquartile range) or number (%).
PSM, propensity score matching; CRS, comprehensive risk score; CCI, comprehensive complication index; ICU, intensive care unit; NA, not applicable.
[a]As number of patients in robotic group did not change after PSM the only column with data on robotic resection is included in the table. The data on open resection group and outcomes of comparison with robotic group are presented in columns before and after PSM.
*$p < 0.05$.

tion rate and the number of lymph nodes removed, remained significantly better. Even without conversions, the operation duration was still longer and the CRS value lower in the robotic group. After removing incision input from the risk calculation, the CRS values leveled between both groups.

Survival was estimated for 113 patients (94%) after open resection, excluding 19 who died (90-day mortality) and 7 who were lost to follow up. In the robotic group, all 39 patients were included in the survival analysis, excluding two cases of 90-day mortality. The length of the follow-up period ranged from 3 to 84 months (mean 23 ± 21 months) in the robotic group and from 4 to 94 months (mean 30 ± 20 months) in the open group ($p < 0.001$) before PSM. The median overall survival before PSM was 30 months for open resection and 44 months for robotic resection respectively ($p = 0.259$) (Fig. 3A). Median disease-free survival was 17 months for open resection and 26 months for robotic resection respectively ($p = 0.218$).

After PSM, there were no differences in overall and recurrence-free survival between the two groups. Median overall survival post robotic and open resection was 44 and 29 months respectively ($p = 0.164$) (Fig. 3B). Median disease-free survival was 32 and 17 months respectively ($p = 0.310$). After excluding conversion cases, the median overall survival remained the same: 44 and 29 months respectively in the robotic and open groups ($p = 0.173$) (Fig. 3C). Median disease-free survival became 26 and 15 months respectively ($p = 0.195$).

Survival was assessed for Bismuth types I and II in 13 patients in the open group and 6 in the robotic group. The duration of the follow-up period ranged from 9 to 81 months (mean 37 ± 27 months) in the robotic group and from 10 to 94 months (mean 36 ± 27 months) in the open group ($p = 0.869$) before PSM. Median overall survival after robotic resection was not reached before and after PSM, with all patients alive (Fig. 4A). Median overall survival after open resection for Bismuth types

Table 3. Demographic and preoperative data after PSM excluding converted robotic resection

Parameter	Robotic resection (n = 33)	Open resection (n = 66)	*p*-value	d
Age (yr)	61/61 (56–67)	60/62 (53–68)	0.672	0.108
Sex (n), female/male	13/20	32/34	0.521	–0.467
BMI (kg/m^2)	26/26 (24–28)	25/25 (23–28)	0.320	0.196
ASA score			0.205	
1	0 (0)	7 (11)		–0.497
2	11 (33)	27 (40)		–0.210
3	22 (67)	32 (49)		0.541
ECOG PS			0.074	
0	5 (15)	6 (10)		0.173
1	21 (63)	26 (41)		0.451
2	6 (19)	29 (46)		–0.602
3	1 (3)	2 (3)		0
Bismuth-Corlette (type)			0.258	
I	4 (13)	3 (4)		0.327
II	2 (6)	7 (11)		–0.180
IIIa	13 (39)	27 (41)		–0.040
IIIb	13 (39)	20 (30)		0.190
IV	1 (3)	9 (14)		–0.402
Bismuth-Corlette (type I, II)	6 (18)	10 (15)	0.775	0.081
TNM stage			0.060	
I	3 (9)	7 (10)		–0.034
II	12 (37)	8 (12)		0.607
IIIa	6 (18)	18 (27)		–0.217
IIIb	0 (0)	5 (8)		–0.417
IIIc	9 (27)	17 (26)		0.023
IV	3 (9)	11 (17)		–0.240
TNM stage (I, II)	15 (46)	15 (23)	0.036*	0.498
Total bilirubin before resection (μmol/L)	40/32 (21–44)	36/32 (20–46)	0.947	0.161
Preoperative biliary drainage	25 (76)	59 (92)	0.032*	–0.447
Complicated biliary drainage	10 (30)	31 (47)	0.133	–0.354
Cholangitis before resection	15 (52)	41 (64)	0.361	–0.245
PVE	6 (19)	12 (19)	> 0.999	0
FLR < 50%	15 (46)	24 (36)	0.393	0.204
Vascular resection	1 (3)	21 (32)	0.001*	–0.825
Type of liver resection			0.761	
Right/extended hepatectomy	13 (39)	23 (35)		0.083
Left hepatectomy	16 (49)	34 (52)		–0.060
Partial liver resection	2 (6)	7 (11)		–0.180
Without liver resection	2 (6)	2 (3)		0.145
Major liver resection	31 (94)	64 (97)	0.599	–0.145
Caudate lobectomy	30 (91)	55 (83)	0.374	0.240
Perioperative chemotherapy	31 (100)[a]	64 (100)[a]	> 0.999	0

Values are presented as mean/median (interquartile range) or number (%).
[a]Calculation excluding 90-day mortality.
PSM, propensity score matching; BMI, body mass index; ASA, American Society of Anesthesiologists; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PVE, portal vein embolization; FLR, future liver remnant.
*$p < 0.05$.

I and II tumors was 44 months before and after PSM, showing no significant differences compared to robotic cases: $p = 0.123$ and $p = 0.092$ respectively (Fig. 4B).

The marginally improved long-term outcomes in the robotic

Table 4. Postoperative immediate outcomes after PSM excluding converted robotic resection

Parameter	Robotic resection (n = 33)	Open resection (n = 66)	*p*-value	d
Number of lymph nodes retrieved	10/9 (7–13)	8/7 (4–11)	0.023*	0.274
Residual tumor (R1)	4 (12)	23 (35)	0.018*	–0.563
Number of bile duct orifices included in anastomosis	2/2 (2–3)	2/2 (2–3)	0.542	0
Time of resection (min)	644/620 (570–690)	510/510 (450–585)	< 0.001*	0.223
Blood loss (mL)	336/300 (200–450)	439/300 (200–500)	0.295	–0.277
CRS	0.11/0.10 (0.01–0.22)	0.47/0.46 (0.37–0.60)	< 0.001*	–2.435
CRS without incision contribution	0.11/0.10 (0.01–0.22)	0.13/0.12 (0.03–0.26)	0.621	–0.134
Severe morbidity (Clavien-Dindo)			0.341	
IIIa	13 (39)	20 (30)		0.190
IIIb	1 (3)	8 (12)		–0.347
IVa	1 (3)	7 (11)		–0.317
IVb	1 (3)	2 (3)		0
V	2 (6)	1 (2)		0.205
Complication >III (Clavien-Dindo)	4 (12)	11 (17)	0.767	–0.142
CCI	27/26 (21–34)	28/26 (21–42)	0.363	–0.047
CCI > 40	4 (12)	14 (21)	0.408	–0.244
Posthepatectomy liver failure	1 (3)	7 (11)	0.258	–0.317
Biliary complications	14 (42)	19 (29)	0.184	0.274
Postoperative acute cholangitis	7 (21)	11 (17)	0.590	0.102
Infected fluid collection	5 (16)	9 (14)	0.767	0.056
ICU stay (day)	2/1 (1–2)	4/2 (1–3)	0.235	–0.396
Hospital stay (day)	22/20 (15–29)	26/23 (16–31)	0.299	–0.300
90-day mortality	2 (6)	2 (3)	0.599	0.145

Values are presented as mean/median (interquartile range) or number (%).
PSM, propensity score matching; CRS, comprehensive risk score; CCI, comprehensive complication index; ICU, intensive care unit.
*$p < 0.05$.

group may be attributed to the relatively high rate of R1 resection (8/16 vs 0/6, $p = 0.051$) and vascular resection (5/16, $p = 0.266$) in the open group associated with locally advanced tumors (TNM stage III and IV: 9/16 vs 1/6, $p = 0.162$).

In both univariate and multivariate Cox regression analyses, a significantly worsened impact on survival was observed for Bismuth tumor types III and IV, and residual tumors (R1/2) (Table 5).

No differences in survival were observed between the robotic and open resection groups for Bismuth tumor types III and IV. TNM stage, vascular resection, CRS, CCI, and chemotherapy did not influence survival in this series.

DISCUSSION

PHCC surgery is currently one of the most challenging areas in hepatobiliary surgery for the implementation of minimally invasive technologies. This assertion is supported by the considerably lower number of studies on the outcomes of minimally invasive resections for PHCC compared to other complex surgical areas, such as liver resections without reconstruction and pancreatic resections have been widely documented. At the time of this writing, a PubMed search for the keywords "robotic" AND "perihilar cholangiocarcinoma" yielded only 34 articles. Nonetheless, there has been a steady increase in the number of studies demonstrating the successful application of minimally invasive technologies in liver and bile duct resection for PHCC and intrahepatic cholangiocarcinoma over recent years. The initial approach to minimally invasive surgery for PHCC typically involved isolated bile duct resection with or without partial liver resection, suitable for selected patients with Bismuth-Corlette type I and II tumors [15]. In several recently published comparative studies, the extent of minimally invasive resection was comparable to that in patients undergoing open surgery, including routine caudate lobe resection [4,5,16]. Over the past few years, several large clinical series have been evaluated, but most of these studies have not included a comparative analysis with open procedures in terms of assessing immediate and long-term outcomes [9,17,18].

This study is the first to compare short-term outcomes and survival rates between open and robotic liver resections using PSM. To our knowledge, it represents the largest single center Western series to date. The multicenter study by Sucandy et al. (2024) [10] compared the outcomes of 38 robotic resections

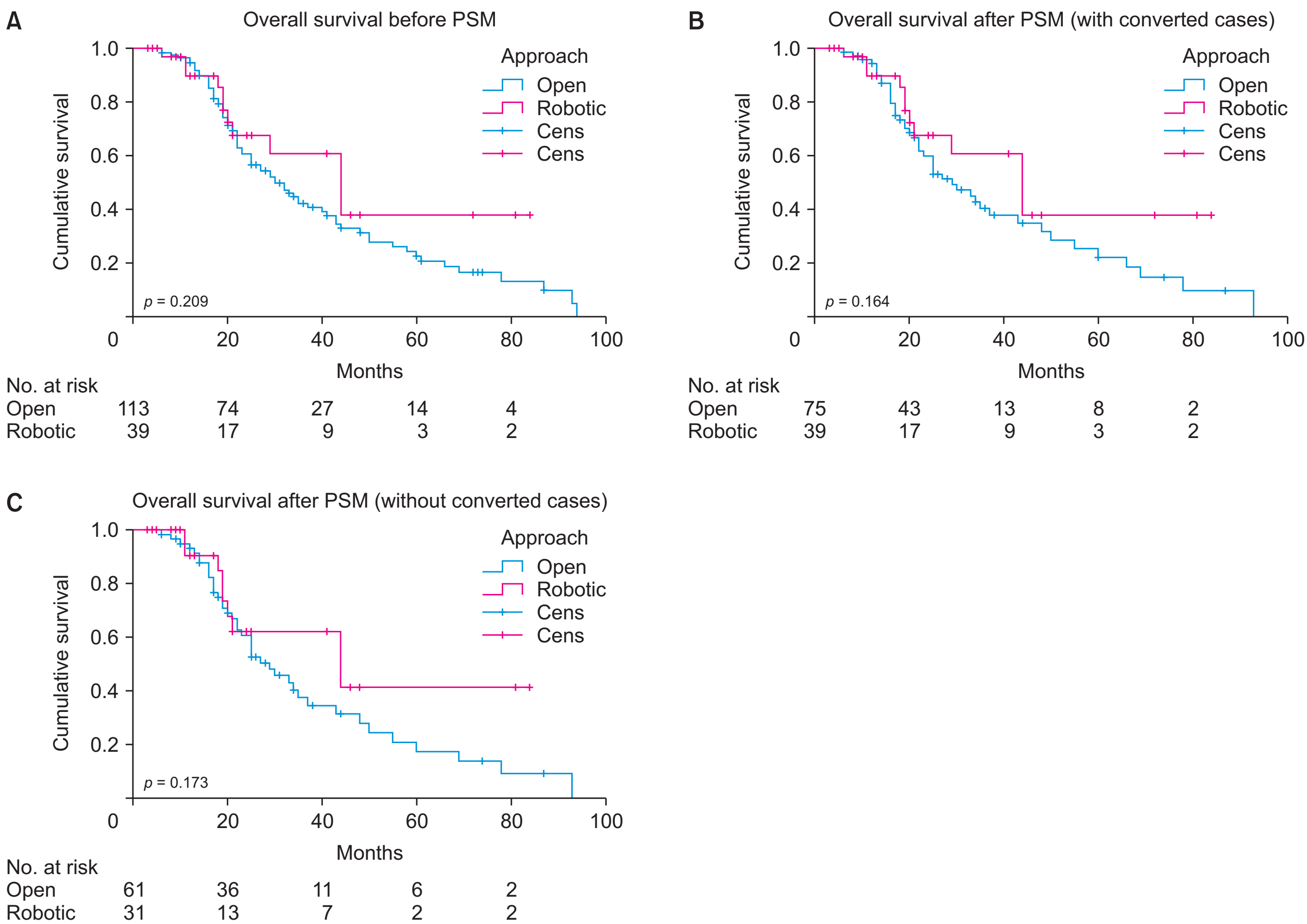

Fig. 3. (A) Group overall survival prior to PSM; (B) group overall survival after PSM with inclusion of converted cases. (C) Group overall survival after PSM excluding conversion cases. PSM, propensity score matching.

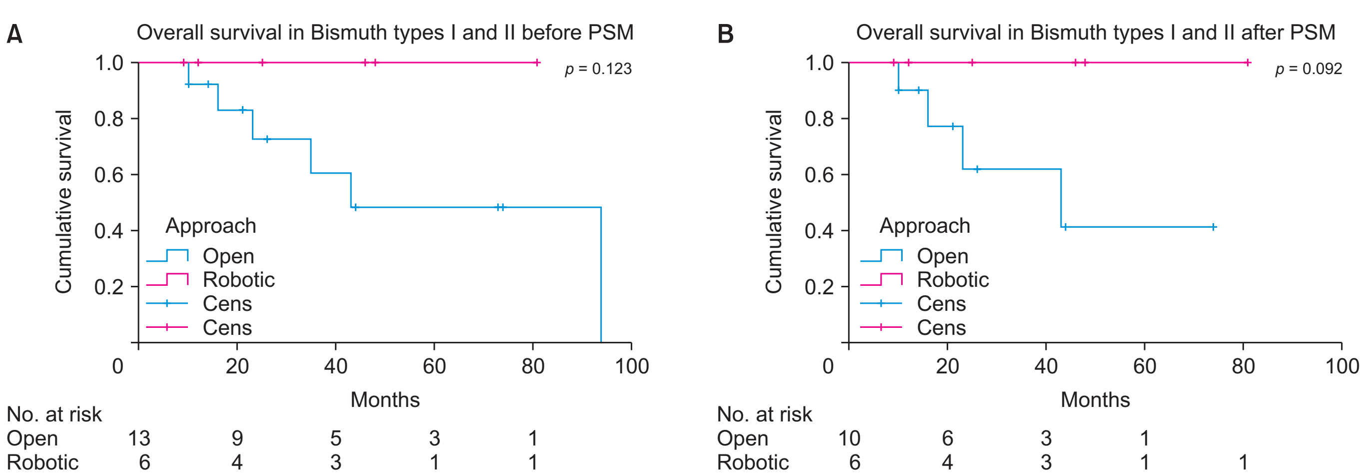

Fig. 4. (A) Overall survival following robotic and open resection in patients with Bismuth types I and II tumors before PSM. (B) Overall survival following robotic and open resection in patients with Bismuth types I and II tumors after PSM. PSM, propensity score matching.

Table 5. Survival predictors according to Cox regression analysis

Predictor	Univariate analysis (p)	Multivariate analysis		
		Hazard ratio	95% CI	p-value
TNM stage > 2	0.235	0.305	0.457–1.512	0.545
Bismuth tumor type (III, IV)	0.039*	0.488	0.108–0.732	0.009*
Comprehensive complication index (CCI)	0.615	-	-	-
Comprehensive risk score (CRS)	0.825	-	-	-
Chemotherapy	0.810	-	-	-
Vascular resection	0.312	-	-	-
Residual tumor (R 1/2)	0.004*	0.231	0.265–0.657	< 0.001*
Number of lymph nodes harvested	0.879	-	-	-

CI, confidence interval.
*$p < 0.05$.

with those of open procedures, without performing matching. Other recent comparative studies included only a small patient cohort and did not evaluate survival [19,20]. Almost all covariates in the present series were well balanced with minimal differences as calculated using SMD. The use of R software for matching enabled retention of the original patient number in the robotic group, which contrasts with other statistical programs that typically reduce the main group's size during the matching process. To increase the control sample size, matching was conducted with a ratio of 1:2.

In the current series, the presence of Bismuth types III and IV in the robotic group was 85%, significantly higher than the rates reported in other large comparative studies, which were 66% (Sucandy et al. [10]), 47% (Wang et al. [6]), and 49% (Qin et al. [8]) for patients with type III and IV. Similarly, the rate of TNM stages 3 and 4 in this study was 61%, while other authors reported rates of 41% (Qin et al. [8]) and 45% (Wang et al. [6]) for TNM stages >II.

The current study identified no significant differences in most immediate outcomes. However, short-term oncological results, such as higher R0 resection rates and a greater number of lymph nodes retrieved, favored the robotic approach. While significant differences were indicated by the p-value, the SMD showed only minor differences between groups. Although these outcomes may reflect selection bias, the clinical significance of these findings demonstrates not merely a hypothetical advantage of the robotic approach, but its non-inferiority in short-term oncological outcomes compared to the open approach. The rate of R0 resection was 88% in the robotic group and 71% in the open group, which is consistent with data presented by other authors. R0 resection rates in the Nagoya experience in open surgery ranged from 74.5% to 77.5%, irrespective of the study period [21]. In series utilizing minimally invasive techniques, R0 resection rates were 81% (Sucandy et al. [10]), 85.2% (Wang et al. [6]), and 91.3% (Qin et al. [8]).

Significant differences were observed in the CRS values. The CRS score, a complex multi-component surgical risk assessment scale, is extremely valuable for predicting in-hospital mortality and the risk of severe morbidity following PHCC treatment [11,13]. Since the approach type, specifically incision length, affects the final CRS value, this variable was omitted from the scoring process to understand the disparities in CRS values across different groups. Once the impact of the surgical approach was excluded, CRS values were found to be comparable between groups, underscoring the significant role of the minimally invasive approach in mitigating the risks associated with surgical interventions in PHCC.

The operative time was longer with the robotic procedure, as anticipated due to the time required for reloading instruments, the challenges in exposing the surgical field during extensive resections, particularly following PVE, and the complexities involved in performing multiple hepaticojejunostomies compared to the open approach.

In discussing the technical elements of minimally invasive resection, it is important to acknowledge the varying opinions of the authors regarding caudal lobectomy. In the reviewed series, caudal lobectomy was executed in 39 (93%) patients. All patients underwent this procedure in the studies by Xu et al. [16] (10 robotic cases) and Ratti et al. [4] (16 laparoscopic cases). The largest comparative studies to date reported caudal lobectomy rates of 45% in the robotic group (Sucandy et al. [10]), 56% (Wang et al. [6]), and 55% (Jingdong et al. [7]). Certain authors have omitted this procedural stage in their reports [3,8]. The criticism of the minimally invasive approach for treating Klatskin tumors, citing the unnecessary omission of segment I excision, began over a decade ago [22]. Recent studies have demonstrated that the immediate outcomes of extensive minimally invasive liver resections with caudal lobectomy are comparable to those of open surgeries, with a tendency toward a shorter hospital stay after the minimally invasive procedures [4,5].

Major hepatectomy remains the standard procedure in open surgery for PHCC, where limited or no liver resection is generally the exception [23]. Major liver resections are advocated for patients diagnosed with Bismuth types I and II [24]. In current series, 40 (95%) patients underwent a robotic major or extended major hepatectomy. The rates of minimally invasive major resections in previously published series are generally lower: 55% (Sucandy et al. [10]), 53% (Wang et al. [6]), and 45% (Jingdong et al. [7]).

A high R0 resection rate is generally achieved through extended hepatectomy [22]. The rate of R0 resection can also be increased to some extent by extensive vessel skeletonization, extending the dissection into segmental ducts, and performing higher duct resections. However, this issue remains controversial [25]. A high level of bile duct resection is characterized by the number of bile duct orifices included in the anastomosis and the number of hepaticojejunostomies performed. In this robotic series, three or more bile ducts were sutured in 44% of cases, and multiple anastomoses were performed in 46% of patients. In the study reported by Sucandy et al. [10], more than one hepaticojejunostomy was conducted in 19% of patients.

In this series, the sole criterion for choosing the robotic approach was the absence of a need for vascular resection and reconstruction. However, in seven patients, R0 resection could only be achieved with vascular resection, which necessitated conversion. In conventional open surgery, portal vein reconstruction does not preclude undergoing the procedure, and the final determination of the extent of vascular invasion typically occurs intraoperatively. The discrepancy between preoperative and intraoperative assessments of portal vein invasion, which is manageable in open surgery, gains significance during robotic resections. Although we do not view this mismatch as a severe limitation of preoperative diagnostics, it has prompted us to be more judicious in selecting patients for the robotic approach, especially considering potential extensive venous invasion.

To eliminate biases associated with conversion, a subgroup analysis was conducted excluding converted cases. The comparison of the parameters after excluding conversions demonstrated identical outcomes for most variables, including the rate of R0 resection and the number of lymph nodes retrieved. The absence of differences in survival outcomes persisted even after the exclusion of converted cases.

Surgery for PHCC often entails a risk of coexisting postoperative morbidities. A CCI was utilized to assess concurrent complications. Neither the absolute nor the critical value of CCI (CCI > 40), indicative of severe morbidity, showed differences between groups. No differences in 90-day mortality were observed. The length of hospital stay remained consistent, despite previous studies demonstrating shorter times to discharge after minimally invasive resection [4,5,10]. One reason for this could be the high prevalence of Bismuth types III and IV in the robotic group (85% before and 82% after excluding converted cases) in the current series. Jingdong et al. [7] identified a correlation between operative time and hospital stay length with tumor type following minimally invasive resection. The length of hospital stay was also influenced by the types of specific complications associated with liver and bile duct resection. Dramatic increases in-hospital stay occurred whenever complications such as bile leakage or liver failure arose, regardless of the surgical approach [3]. The impact of minimally invasive resection on specific morbidity rates remains undetermined.

Despite balanced covariates in perioperative data in the current series, selection biases were mitigated but not eradicated. Patients who underwent robotic surgery presented with less advanced tumors because the selection criteria excluded cases requiring vascular reconstruction for tumor invasion. The inevitability of some selection biases favoring the robotic approach is substantiated by differences in preoperative biliary drainage rates, demonstrated in subgroup analyses after excluding converted cases. Specifically, the robotic group matched the open surgery group in the distribution of Bismuth type I and II tumors, yet the incidence of Bismuth type IV tumors was lower in the robotic group, potentially influencing the higher R0 resection rate in these cases. Bismuth tumor type and R0 resection were predictors of survival in this series. Clear potential selection biases were evident when comparing demographic data after excluding converted cases. A significant trend toward a higher rate of TNM stage I and II after PSM with converted cases was observed. A significantly lower rate of biliary drainage and vascular resection after excluding converted cases confirmed a trend toward treating less advanced tumors in the robotic group.

Patient selection for minimally invasive resection has been consistent across other studies, despite similar resection volumes between open and minimally invasive groups in the latest well-balanced retrospective trials. The primary argument for selection bias is the extended duration necessary for data gathering in many studies, indicating a preferential selection of relatively simple Bismuth types I and II without vascular invasion, particularly in the early stages of the learning curves [3-5,16]. At the same time, the majority of authors did not specify selection criteria [3-5]. Some studies did not regard involvement of vascular structures at the liver hilum as an absolute contraindication [6,7,10]. In a multicenter study by Jingdong et al. [7], surgeon's preference was the sole basis for opting for a minimally invasive approach.

Survival rates after minimally invasive resection for PHCC have been scrutinized in a limited number of studies. Survival estimates are contentious, further complicated by the absence of adequate comparative studies, brief follow-up periods, and thus the challenge of comparing survival across different series [5,16,26]. In a multicenter study analyzing outcomes of 158 minimally invasive resections for PHCC, the overall 3-year and 5-year survival rates were 28.8% and 19.2%, respectively [7].

In the series discussed, despite the PSM, there was a clear trend towards improved survival in the robotic group, though it was not statistically significant. The median overall survival in the robotic group was 44 months, and the 5-year survival rate was 38%. It is crucial to note that in this study, only 15% of patients with type 1 and 2 tumors were included in the robotic group, contrasted with other studies on minimally invasive resection in PHCC, where this figure ranged from 34% to 53% [6-8,10]. In both this series and other studies, Bismuth type was among the few independent predictors of survival [7,8]. In the open group of this series, the proportion of resections for types 1 and 2 was comparable to the robotic group (13% versus 15%), but the proportion of type 4 was higher (19% versus 2%), which could influence survival outcomes in the open group. In studies by Sucandy et al. (2024) [10] and Qin et al. (2023) [8], the median overall survival in the robotic group was not reached, but it is crucial to consider the previously mentioned high proportion of Bismuth tumor types 1 and 2 and the high proportion (61%) of TNM stages 1 and 2 in Qin et al.'s study [8], in contrast to the current study (39%). Another reason for the better survival rate in the robotic group in the Sucandy et al. [10] study was the relatively short average follow-up period of 15 months, with the authors noting that half of the patients were treated in the last two years of the study. Over 50% of participants in the current series had a follow-up period of 3 years or longer, with an average follow-up duration of 23 ± 21 months in the robotic group.

Despite controversy and limited data on survival following minimally invasive resections, the present series, like recently published studies, demonstrates a clear trend towards improved survival outcomes, indicative that robotic and laparoscopic resections do not worsen, but rather enhance survival in selected patients [8,10]. The criteria for such selection may include Bismuth tumor types I and II, and TNM stages I and II. Subgroup survival analysis for Bismuth types I and II in the current series supports the hypothesis that robotic technology is a reliable and safe option for these tumor types when the tumor is at an early stage, as evidenced by all patients being alive. The success of robotic resection hinges on adherence to open surgery principles, namely major resections, caudal lobectomy, and complete lymph node removal at stations 8, 12, and 13. Immediate superior oncological results from robotic resection in the current series provide further support for this hypothesis.

Limitations of the study include a relatively small number of patients who underwent robotic resection, yet the present series offers one of the largest single center Western experiences. Other limitations are the observational and retrospective design of the study, and potential selection biases for the robotic procedure. A limitation of the study is the absence of data regarding readmissions due to difficulties in distinguishing between elective and urgent readmissions retrospectively. PSM was applied to minimize differences between groups by balancing covariates. The study covers the initial phase of the learning curve, which inevitably introduces biases relating to the mastery of technology. The drawback of the subgroup analysis for survival after robotic resection for Bismuth types I and II is the limited number of patients, however, the mean follow-up period was lengthy.

Conclusion

The ongoing series, along with a growing body of pioneering studies assessing early experiences with minimally invasive technology in PHCC treatment, suggests that the robotic approach is at least equivalent to standard open resection in terms of immediate outcomes. The robotic approach not only preserves survival but enhances short-term oncological outcomes, particularly evident in patients with Bismuth types I and II, and early TNM stages I and II, where the robotic technique can be considered a reliable treatment option if it aligns with open surgery principles. This assertion necessitates validation through larger studies. Further investigation including multicenter studies is required to ascertain the safety of robotic surgery in Bismuth types III and IV, particularly in locally advanced cases.

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CONFLICT OF INTEREST

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