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Original Article

Short-term and Long-term Clinical Outcomes of Combined Caudate Lobectomy for Intrahepatic Cholangiocarcinoma Involving the Hepatic Hilus: A Propensity Score Analysis

Di Zeng[1,2], Yaoqun Wang[1,2], Ningyuan Wen[1,2], Bei Li[1,2], Nansheng Cheng[1,2], Jiong Lu[1,2]

[1]Division of Biliary Tract Surgery, Department of General Surgery, West China Hospital, Sichuan University, Chengdu, China;
[2]Research Center for Biliary Diseases, West China Hospital, Sichuan University, Chengdu, China

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Corresponding Author
Nansheng Cheng
ORCID https://orcid.org/0000-0002-9334-5715
E-mail nanshengcheng@yeah.net

Jiong Lu
ORCID https://orcid.org/0009-0002-8669-5634
E-mail lujiong@scu.edu.cn

Background/Aims: Extended hepatectomy combined with caudate lobe resection has been approved for the radical resection of hilar cholangiocarcinoma. There was a lack of credible research on the clinical value of caudate lobectomy (CL) for intrahepatic cholangiocarcinoma involving the hepatic hilus when combined with hepatectomy. We aimed to compare the short-term and long-term outcomes of the combined procedure with those of only CL for curative resection of intrahepatic cholangiocarcinoma involving the hepatic hilus.

Methods: This single-center retrospective cohort study of patients with hilar cholangiocarcinoma was conducted from January 2007 to December 2021. Patients who underwent radical resection were enrolled in this study. The short-term and long-term clinical outcomes of the groups were compared before and after propensity score matching (PSM).

Results: A total of 282 patients were included. There were no statistically significant differences in perioperative clinical outcomes between the CL group and the non-CL group before and after PSM. Compared to patients in the non-CL group, patients in the CL group had significantly longer overall survival before and after PSM (p=0.007 before PSM, p=0.033 after PSM). Moreover, compared to the non-CL group, the CL group had longer disease-free survival before and after PSM (p<0.001 before PSM, p=0.019 after PSM).

Conclusions: The postoperative complications of the CL group were comparable to those of the non-CL group. CL improved the long-term survival of patients with intrahepatic cholangiocarcinoma involving the hepatic hilus when combined with hepatectomy. Therefore, hepatectomy combined with caudate lobe resection should be performed for patients with hilar cholangiocarcinoma. **(Gut Liver, 2025;19:438-453)**

Key Words: Intrahepatic cholangiocarcinoma; Hepatectomy; Postoperative complications; Propensity score

INTRODUCTION

Cholangiocarcinoma is a diverse group of rare malignancies that can arise from any part of the biliary epithelium,[1] and is anatomically classified as intrahepatic cholangiocarcinoma (ICC), perihilar cholangiocarcinoma, and distal cholangiocarcinoma.[2] As the second most common primary liver cancer following hepatocellular carcinoma, the global incidence of ICC is gradually increasing.[3,4] The clinical outcome of cholangiocarcinoma patients with ICC is unfavorable, with 5-year survival ranging from 15% to 45%, depending on tumor stage.[5,6] ICC is frequently diagnosed as an advanced disease with bulky locoregional involvement and/or distant metastases and a complete surgical resection is only feasible in 30% to 40% of patients.[7] ICC has been categorized as arising from small intrahepatic bile ducts or major intrahepatic bile ducts, including the hilum.[8,9] Originating from an intrahepatic lesion, some ICC grows down towards the hilum and may eventually involve the hilum, which can be defined as ICC involv-

ing the hepatic hilum (hICC).[8,10] More specifically, hilar cholangiocarcinoma (HC) originates from the epithelium of the common hepatic, right, or left hepatic duct, whereas ICC involving the hepatic hilus originates in the intrahepatic bile duct or bile ductules.[11] Discrimination between HC and ICC involving the hepatic hilus is primarily based on the location of the main tumor, as illustrated in Fig. 1. HC is characterized by a tumor originating in the upper common, right, or left hepatic duct.

Surgical resection remains the cornerstone of treatment for patients with cholangiocarcinoma featuring hilar involvement. Given the propensity of hilar tumors to infiltrate biliary branches or directly invade the parenchyma of the caudate lobe, several studies have demonstrated a survival advantage associated with aggressive surgical approaches incorporating complete caudate lobe excision. This practice is now widely acknowledged as the standard surgical approach in the management of HC.[12,13] Nevertheless, the necessity of concomitant caudate lobectomy (CL), in hICC remains uncertain due to distinct clinicopathological characteristics, more aggressive biological behaviors, diverse prognostic factors, and poorer prognosis compared to HC.

For hICC patients, extended hepatectomy, combined with caudate lobe resection, maximizes the likelihood of achieving negative margins.[14] However, due to the proximity of the caudate lobe to the inferior vena cava and the portal vein confluence, it presents a challenge to expose. Performing a total CL poses challenges, including the need for meticulous exposure and the risk of substantial intraoperative bleeding during the resection of the caudate lobe.[15] Therefore, the clinical value of combined resection of caudate lobe in hICC remains controversial and few studies have been published by surgical experts worldwide on this clinical topic. The present study hypothesized that

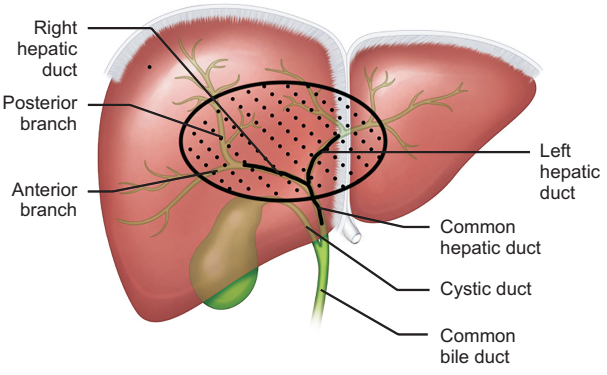

Fig. 1. Differentiation between hilar cholangiocarcinoma and hICC: tumors in the black pasted area were categorized as hilar cholangiocarcinoma, while those in the dotted area were classified as hICC. hICC, intrahepatic cholangiocarcinoma involving the hepatic hilum.

hICC patients with combined CL would be associated with improved disease-free survival (DFS) and overall survival (OS). Simultaneously, the cumulative postoperative complications of CL group would be comparable with that of non-CL group. To test these hypotheses, we performed this single-center retrospective PSM-based study. Propensity score matching (PSM) analysis was utilized to reduce the bias due to lack of randomization,[16] and so far, no study has conducted PSM analysis on this topic.

MATERIALS AND METHODS

1. Setting

We retrospectively collected patients with hICC who underwent curative-intent resection at West China Hospital (Sichuan University, Chengdu, China) from January 2007 to December 2021. This study was approved by the Ethics Committee of the West China Hospital of Sichuan University (approval number: 2022-1774). The requirement for informed consent was waived by the Ethics Committee considering the retrospective design of the study. The primary criterion used to differentiate between hICC and HC was the location of the main tumor, as illustrated in Fig. 1. hICC was defined as cholangiocarcinoma predominantly located in the liver parenchyma with involvement of the adjacent hilar duct, while HC was defined as cholangiocarcinoma which arose from the main lobar hilar bile ducts. The types of cholangiocarcinoma, whether the tumor was hICC or HC, were prudently confirmed by both pathologic and radiologic reviews. When the original tumor location was difficult to identify, we would turn to pathologist and radiologists to reach a consensus.

The preoperative diagnosis of hICC is based on the European Society for Medical Oncology clinical practice guideline for biliary tract cancer in 2023[17] and patients were staged according to the TNM classification for IHC (8th edition).[18] Absolute contraindications for curative-intent hepatectomy include American Society of Anesthesiologists III, ascites, unresectable vascular tumor infiltration, extrahepatic metastases and future remnant liver <40%.[19] The decision to combine caudate lobe resection for hICC is on the basis of two main factors: the invasion of malignancy and the intraoperative decision of the surgeon in charge.

2. Inclusion and exclusion criteria

Patients who met the following criteria were included: (1) male or female patients >18 years of age; (2) patient without contraindication for hepatectomy; (3) patients who underwent curative-intent resection at West China

Hospital, Sichuan University; (4) hICC confirmed by pathological examination and imaging studies; and (5) since ICC manifests in three primary macroscopic growth patterns–mass-forming, periductal-infiltrating, and intraductal–it is essential to clarify that our study exclusively enrolled patients with the mass-forming subtype. Other subtypes of ICC were not considered in this investigation.

Patients meeting the following criteria were excluded: (1) patients with no intrahepatic tumor component and diagnosed as HC; (2) patients who underwent palliative resection (R2) or hilar bile duct resection; (3) history of any other primary malignancy except ICC; (4) severe dysfunction of heart, kidney or other vital organs; and (5) other subtypes of ICC that are not mass-forming subtype.

3. Basic characteristics assessment of patients

The preoperative assessment includes the basic information of the patient, clinical laboratory indicators, medical imaging indicators, and preoperative treatment. The basic information of the patient includes gender, age, and any other comorbidities (e.g., cardiovascular or respiratory diseases). Preoperative clinical laboratory indicators include serum carbohydrate antigen 19-9, total bilirubin, direct bilirubin, serum albumin, aspartate aminotransferase, and alanine aminotransferase, etc. The indicators of medical imaging examination (contrast-enhanced ultrasound, computed tomography, magnetic resonance imaging, etc.) include: the size, number, adjacent invasion of the malignancy and the Bismuth type of HC. In addition, information on preoperative treatment including preoperative biliary drainage and portal vein embolization were collected. When the imaging examination was inconsistent with the pathological examination, the diagnosis was based on the pathological examination.

4. Surgical technique

To date, available evidence supports the recommendation that hepatic resection with negative margins should be the goal of surgical therapy in potentially resectable ICC.[20,21] The caudate lobe resection encompasses the Spigelian lobe, the portion adjacent to the vena cava, and the caudate process. The specific extent of liver resection is further determined according to the Bismuth type. R0 resection should be accompanied by standardized regional lymph node (LN) dissection, including the N1 and N2 stations (N1: LN within the porta hepatis [12h], LN adjacent to the bile duct [12b], LN adjacent to the cystic duct [12e], LN behind the portal vein [12p], and LN adjacent to the proper hepatic artery [12a]; N2: LN behind the head of the pancreas [13a] and LN along the common hepatic artery [8a, 8p]).[22] Vascular invasion is associated with unfavorable prognosis, but not an absolute contraindication for surgery.[23] The decision to perform combined vascular resection was made by the attending physician team after assessing the patient's condition.

5. Postoperative pathological examination

The pathological evidence of cancer was determined by paraffin sections. All cases of ICC included in this study underwent histopathological confirmation by experienced pathologists. TNM stage, tumor differentiation, tumor diameter, full-thickness bile duct wall invasion, LN metastasis, liver parenchymal invasion, liver capsule invasion, and nerve invasion were all examined pathologically. An R0 resection was defined as the absence of macroscopic or microscopic disease at the surgical margin, while an R1 resection was classified as microscopic presence of tumor.[24] Tumors were staged according to the American Joint Committee on Cancer classification (8th edition).

6. Short-term outcomes

Surgery-related short-term clinical outcomes included: total blood loss recorded in surgical records, information about blood transfusions and operation time. Liver function and blood routine examinations were performed on the 1st, 3rd, 5th, and 7th days after the operation to check if postoperative liver failure, jaundice, postoperative hemorrhage, or infection occurred. For patients with postoperative infection symptoms, ultrasonography and abdominal computed tomography were used to further investigate the cause of infection (e.g., pulmonary infection, abdominal infection, or biliary-enteric anastomotic fistula). Daily physical examination was performed to check for biliary leakage, ascites, pleural effusion, gastrointestinal obstruction, and incision infection. In addition, we also recorded the occurrence of rare complications in patients, including pulmonary insufficiency, acute renal insufficiency, and acute left heart failure. The incidence of secondary surgical procedures during hospitalization as well as the length of hospital stay were collected.

In this study, the standard of postoperative liver failure conforms to "50-50 criteria."[25] The occurrence of postoperative ascites was defined according to the daily abdominal drainage volume (>500 mL per day over a period of 3 days) after operation. Post-hepatectomy hemorrhage was defined as a sheer decrease in postoperative hemoglobin level, which exceeded the limit of 30 g/L.[26] If the bilirubin level of the peritoneal drainage fluid exceeded 3 times that of the serum in 3 days consecutively after the operation, bile leakage was considered to have occurred.

7. Follow-up program and long-term outcomes

Within 1 year after discharge, the patients were followed up every 3 months in the first year, and every 6 months afterwards. The follow-up mainly included blood routine, liver and kidney function, serum tumor markers, and medical imaging examination (whole abdominal enhanced computed tomography, magnetic resonance imaging, etc.). The main clinical outcomes of this study were OS and DFS. OS was defined as the time from the end of surgery to death. DFS was defined as the time from the end of surgery to recurrence.

8. Statistical analysis

Patient data were retrospectively collected, and statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). We found baseline characteristics mismatching between the two groups after patient grouping, and to reduce the bias resulting from non-randomized grouping, we employed PSM analysis. The variables selected for the propensity score model is shown in Table 1. We have meticulously chosen variables for PSM, including age, gender, Bismuth staging, TNM staging, carbohydrate antigen 19-9, tumor diameter, bilirubin levels, liver invasion, comorbidities, and surgical factors. This comprehensive selection aims to account for all relevant confounders, enhancing the study's internal validity. These variables are linked to postoperative prognosis in cholangiocarcinoma; for example, carbohydrate antigen 19-9 levels have been associated with poorer outcomes.[27] By including these variables, we mitigated potential bias and ensured a robust analysis of the surgical approach's impact on patient outcomes. After analysis, we chose a caliper value of 0.2 to balance accuracy and feasibility, avoiding an increased number of unmatched subjects with stricter criteria like 0.1, while also preventing the introduction of more heterogeneity with looser criteria. If the quantitative variables had a normal distribution, they are reported as mean (standard deviation), otherwise they are expressed as median and range. Absolute values and percentages are used to display qualitative characteristics. Normally distributed continuous data were compared by means of the Student t-test, and the Mann-Whitney U-test was used to compare skewed-distributed data. The chi-square test or Fisher exact test was used to compare ordinal data. Survival was described using the Kaplan-Meier method and differences between subgroups were reviewed with the log-rank test. The multivariate analysis for prognostic factors used a Cox proportional hazards model to analyze variables with p<0.05 in the univariate analyses. Two-sided p-values <0.05 were defined to be statistically significant. Meanwhile, we conducted subgroup analysis according to

Table 1. Baseline Characteristics of Patients with Intrahepatic Cholangiocarcinoma Involving the Hepatic Hilum before and after Propensity Score Matching

Variable	Before matching (n=282)			After matching (n=178)			
	Non-caudate lobectomy (n=176)	Caudate lobectomy (n=106)	p-value	Non-caudate lobectomy (n=89)	Caudate lobectomy (n=89)	Mean difference	p-value
Sex (female:male)	84:92	49:57	0.903	45:44	43:46	0.023	
Age, yr	60.50 (53.00–66.00)	59.00 (52.00–63.00)	0.147	61.00 (52.00–66.00)	59.00 (52.00–65.00)	2.000	0.881
Hypertension	27 (15.3)	22 (20.8)	0.317	16 (18.0)	13 (14.6)	0.034	0.477
Diabetes	8 (4.5)	5 (4.7)	>0.999	4 (4.5)	4 (4.5)	0.000	0.685
COPD	6 (3.4)	3 (2.8)	>0.999	3 (3.4)	3 (3.4)	0.000	>0.999
History of cardiovascular accident	3 (1.7)	2 (1.9)	>0.999	2 (2.2)	2 (2.2)	0.000	>0.999
Serum CA19-9, IU/L	281.15 (72.92–926.20)	241.95 (59.56–998.18)	0.870	272.10 (57.62–1,000)	234.80 (52.39–992.70)	37.300	>0.999
Total bilirubin, μmol/L	167.10 (47.42–266.38)	159.65 (44.48–222.95)	0.237	165.20 (36.00–252.50)	160.10 (45.60–229.70)	5.100	0.664
Direct bilirubin, μmol/L	143.65 (36.15–224.00)	144.45 (35.30–189.75)	0.364	142.20 (19.80–207.30)	144.90 (37.40–192.60)	–2.700	0.764
Albumin, g/L	38.20 (34.60–40.70)	38.00 (34.90–40.58)	0.836	37.67 (35.13–40.52)	37.68 (34.49–40.07)	–0.010	0.845
ALT, IU/L	109.50 (61.00–191.25)	97.50 (54.25–167.75)	0.288	106.00 (55.00–177.00)	96.00 (50.00–167.00)	10.000	0.990
AST, IU/L	92.50 (57.75–165.00)	79.00 (44.50–126.25)	0.044	81.00 (53.00–135.00)	79.00 (43.00–131.00)	2.000	0.652
Preoperative biliary drainage	31 (17.6)	19 (17.9)	>0.999	16 (18.0)	15 (16.9)	0.011	0.581

Table 1. Continued

Variable	Before matching (n=282)			After matching (n=178)			
	Non-caudate lobectomy (n=176)	Caudate lobectomy (n=106)	p-value	Non-caudate lobectomy (n=89)	Caudate lobectomy (n=89)	Mean difference	p-value
Bismuth staging			0.007				>0.999
I	0	0		0	0	0.000	
II	26 (14.8)	4 (3.8)		9 (10.1)	3 (3.4)	0.067	
IIIa	26 (14.8)	13 (12.3)		11 (12.4)	12 (13.5)	−0.011	
IIIb	52 (29.5)	47 (44.3)		28 (31.5)	40 (44.9)	−0.135	
IV	72 (40.9)	42 (39.6)		41 (46.1)	34 (38.2)	0.079	
TNM staging			0.679				0.954
I	22 (12.5)	14 (13.2)		13 (14.6)	12 (13.5)	0.011	
II	62 (35.2)	35 (33.0)		24 (27.0)	29 (32.6)	−0.056	
IIIA	30 (17.0)	19 (17.9)		17 (19.1)	16 (18.0)	0.011	
IIIB	31 (17.6)	24 (22.6)		22 (24.7)	20 (22.5)	0.022	
IIIC	28 (15.9)	14 (13.2)		13 (14.6)	12 (13.5)	0.011	
IVA	3 (1.7)	0		0	0	0.000	
Differentiation			0.685				0.757
High	67 (38.1)	37 (34.9)		32 (36.0)	35 (39.3)	−0.034	
Medium or low	109 (61.9)	69 (65.1)		57 (64.0)	54 (60.7)	0.034	
Tumor diameter, cm	2.80 (2.10–4.00)	3.05 (2.20–4.50)	0.196	2.90 (2.20–4.20)	3.00 (2.10–4.20)	−0.100	0.980
Invasion of the whole bile duct	127 (72.2)	70 (66.0)	0.342	61 (68.5)	59 (66.3)	0.023	0.873
Liver parenchymal invasion	83 (47.2)	59 (55.7)	0.208	46 (51.7)	46 (51.7)	0.000	>0.999
Liver capsule invasion	25 (14.2)	26 (24.5)	0.043	17 (19.1)	18 (20.2)	−0.011	>0.999
Nerve invasion	83 (47.2)	50 (47.2)	>0.999	45 (50.6)	40 (44.9)	−0.011	0.548
ASA PS classification			0.518				0.777
I	2 (1.1)	2 (1.9)		1 (1.1)	2 (2.2)	−0.011	
II	102 (58.0)	64 (60.4)		53 (59.6)	55 (61.8)	−0.022	
III	72 (40.9)	39 (36.8)		35 (39.3)	32 (36.0)	0.034	
IV	0	1 (0.9)		0	0	0.000	
R0 resection	134 (76.1)	92 (86.8)	0.044	73 (82.0)	75 (84.3)	−0.023	0.841
Vasculectomy	56 (31.8)	43 (40.6)	0.173	38 (42.7)	33 (37.1)	0.056	0.540
Postoperative adjuvant chemotherapy	155 (80.0)	91 (85.9)	0.697	80 (89.9)	78 (87.6)	2.000	0.893
Capecitabine monotherapy	54 (30.7)	30 (28.3)		27 (30.3)	30 (33.7)	−3.000	
Gemcitabine + cisplatin	45 (25.6)	25 (23.6)		22 (24.7)	20 (22.5)	2.000	
Capecitabine + oxaliplatin	23 (13.1)	14 (13.2)		12 (13.5)	13 (14.6)	−1.000	
5-Fluorouracil + oxaliplatin	33 (18.8)	22 (20.8)		19 (21.3)	17 (19.1)	2.000	

Data are presented as median (range) or number (%).

COPD, chronic obstructive pulmonary disease; CA19-9, carbohydrate antigen 19-9; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ASA PS, American Society of Anesthesiologists physical status.

gender, age, TMN staging, Bismuth staging, tumor grade, tumor size, marginal status, whether to perform preoperative bile duct drainage and the extent of tumor invasion. The data of each subgroup are summarized in the forest plot.

RESULTS

1. Baseline characteristics

A total of 282 patients diagnosed with ICC involving the hepatic hilus, and who underwent curative treatment at our hospital, were evaluated retrospectively from January 2007 to December 2021. According to the surgical technique adopted, patients were divided into two subgroups (106 in the CL subgroup and 176 in the non-CL subgroup). Baseline characteristics in term of Bismuth staging, aspartate aminotransferase level, liver capsule invasion and R0 resection rate showed significant difference before matching (Table 1). After 1:1 matching, 79 patients in the CL subgroup were meticulously matched with 79 patients in the non-CL subgroup. All baseline characteristics were balanced between patient groups after matching. Table 1 shows the detailed baseline characteristics of pre-PSM group and post-PSM group.

2. Short-term clinical outcomes in CL and non-CL groups

Table 2 shows the short-term clinical outcomes (surgery-related outcomes and postoperative complications) of patients in CL group and non-CL group before and after PSM matching. As for the incidence of postoperative complications which includes postoperative infection, postoperative organ insufficiency and postoperative bile leakage, no difference existed between the two groups, either before or after PSM. Clavien-Dindo grade, length of hospital stays, and intensive care unit treatment time were comparable between the two groups. Regarding surgery-related outcomes, none showed a statistically significant difference between the two groups, except for operation time. Although the combined CL group had a longer operation time than the non-combined group before PSM (420.00 minutes [range, 346.25 to 508.75] vs 377.50 minutes [range, 298.75 to 460.00], p<0.001), the significant difference in operation time between the two groups was eliminated after PSM (420.00 minutes [range, 345.00 to 510.00] vs 401.00 minutes [range, 300.00 to 470.00], p=0.063).

3. Long-term clinical outcomes in CL and non-CL groups before and after PSM

Before PSM, the median follow-up time was 36.6 months. Two hundred and twenty-nine patients (81.2%) experienced postoperative tumor recurrence, 208 patients (73.8%) died during the follow-up period, and only 45 patients (16.0%) survived for more than 5 years. Patients who received CL had significantly longer OS and DFS compared to those in the non-CL group. The median OS and median DFS for patients receiving CL were 35.7 months (95% confidence interval [CI], 31.33 to 40.20) and 20.0 months (95% CI, 17.19 to 23.02), respectively, while, these two metrics were only 19.7 months (95% CI, 14.68 to 23.67) and 12.4 months (95% CI, 9.44 to 16.13), respectively, in patients who did not receive CL (p=0.007 in OS and p=0.001 in PFS) (Fig. 2).

After PSM, the median follow-up time was 36.1 months. One hundred and forty-four patients (80.9%) experienced postoperative tumor recurrence, 126 patients (72.5%) died during the follow-up period, and only 28 patients (15.7%) survived for more than 5 years. Patients who underwent caudate lobe resection had significantly longer OS and DFS compared to those who did not get their caudate lobe resected. The median OS and median DFS for patients receiving CL were 34.5 months (95% CI, 29.24 to 30.06) and 19.4 months (95% CI, 15.46 to 22.65), respectively, while, these two metrics were only 18.5 months (95% CI, 13.50 to 23.60) and 13.0 months (95% CI, 9.46 to 16.65), respectively, in patients who did not receive CL (p=0.033 in OS and p=0.019 in DPF) (Fig. 3).

In addition to the 1-year and 5-year recurrence rates, we conducted a comparative analysis of postoperative recurrence rates between the CL and non-CL groups after PSM. For the 1-year recurrence rate, we observed that 46.1% of patients in the CL group experienced postoperative recurrence, compared to 69.6% of patients in the non-CL group. The non-CL group exhibited a higher odds ratio (OR) of 2.688 (95% CI, 1.454 to 4.971; p=0.002). Similarly, for the 5-year recurrence rate, we found that 66.3% of patients in the CL group experienced postoperative recurrence, compared to 83.1% of patients in the non-CL group. In terms of 5-year recurrence rates, the non-CL group had a higher OR of 2.508 (95% CI, 1.236 to 5.092; p=0.011).

4. Sensitivity analysis of CL effects on OS and DFS in R0 subgroup

We conducted an additional comparative sensitivity analysis, specifically focusing on the R0 subgroup. The results revealed that within the R0 group, both OS and DFS are significantly better in the CL group (OS, 34.39; 95% CI, 28.95 to 39.83 and DFS, 22.41; 95% CI, 16.81 to 28.02; p=0.045) compared to the non-CL group (OS, 20.24; 95% CI, 15.23 to 25.26 and DFS, 15.13; 95% CI, 11.22 to 19.04; p=0.029). This analysis enriches our evaluation by specifi-

Table 2. Short-term Clinical Outcomes of Patients with Intrahepatic Cholangiocarcinoma Involving the Hepatic Hilum before and after Propensity Score

Variable	Before matching (n=282)			After matching (n=178)		
	Non-caudate lobectomy (n=106)	Caudate lobectomy (n=176)	p-value	Non-caudate lobectomy (n=89)	Caudate lobectomy (n=89)	p-value
Intraoperative hemorrhage, mL	600 (400–1,000)	600 (400–1,000)	0.112	600 (400–900)	600 (400–1,000)	0.075
Intraoperative transfusion	84 (47.7)	48 (45.3)	0.783	38 (42.7)	40 (44.9)	0.880
Operation time, min	377.50 (298.75–460.00)	420.00 (346.25–508.75)	0.001	401.00 (300.00–470.00)	420.00 (345.00–510.00)	0.063
Second surgery during hospitalization	15 (8.5)	6 (5.7)	0.514	8 (9.0)	5 (5.6)	0.565
Postoperative infection	13 (7.4)	6 (5.7)	0.753	8 (9.0)	6 (6.7)	0.781
Pulmonary infection	12 (6.8)	4 (3.8)	0.421	5 (5.6)	4 (4.5)	>0.999
Abdominal infection	20 (11.4)	19 (17.9)	0.171	7 (7.9)	13(14.6)	0.235
Incisional infection	5 (2.8)	1 (0.9)	0.520	3 (3.4)	1 (1.1)	0.613
Sepsis	2 (1.1)	0	0.712	0	0	-
Liver abscess	1 (0.6)	0	>0.999	0	0	-
Abdominal effusion	19 (10.8)	0	0.516	15 (16.9)	12 (13.5)	0.676
Pleural effusion	14 (8.0)	6 (5.7)	0.626	8 (9.0)	4 (4.5)	0.370
Bile leakage	36 (20.5)	16 (15.1)	0.334	16 (18.0)	12 (13.5)	0.537
Postoperative hemorrhage	11 (6.2)	5 (4.7)	0.785	7 (7.9)	3 (3.4)	0.329
Biliary-enteric anastomotic fistula	2 (1.1)	0	0.712	2 (2.2)	0	0.477
Gastrointestinal obstruction	2 (1.1)	2 (1.9)	>0.999	2 (2.2)	2 (2.2)	>0.999
Postoperative hepatic insufficiency	11 (6.2)	5 (4.7)	0.785	4 (4.5)	4 (4.5)	>0.999
Postoperative pulmonary insufficiency	2 (1.1)	0	0.712	0	0	-
Postoperative renal insufficiency	2 (1.1)	1 (0.9)	>0.999	0	1 (1.1)	>0.999
Postoperative cardiac insufficiency	0	2 (1.9)	0.273	0	1 (1.1)	>0.999
Clavien-Dindo grade			0.593			0.683
I	15 (8.5)	4 (3.8)		7 (7.9)	3 (3.4)	
II	39 (22.2)	22 (20.8)		21 (23.6)	19 (21.3)	
IIIa	21 (11.9)	16 (15.1)		10 (11.2)	12 (13.5)	
IIIb	4 (2.3)	2 (1.9)		3 (3.4)	2 (2.2)	
IV	12 (6.8)	5 (4.7)		5 (5.6)	3 (3.4)	
Length of hospital stay, day	18.50 (14.00–24.00)	17.50 (14.00–23.75)	0.450	18.00 (14.00–24.00)	17.00 (14.00–23.00)	0.270
Postoperative hospital stay, day	13.00 (9.00–17.00)	11.00 (10.00–15.00)	0.711	13.00 (9.00–16.00)	11.00 (10.00–15.00)	0.636
ICU treatment time, day	1.00 (0.00–2.00)	1.00 (0.00–2.00)	0.602	1.00 (0.00–2.00)	1.00 (0.00–2.00)	0.893

Data are presented as median (range) or number (%).
ICU, intensive care unit.

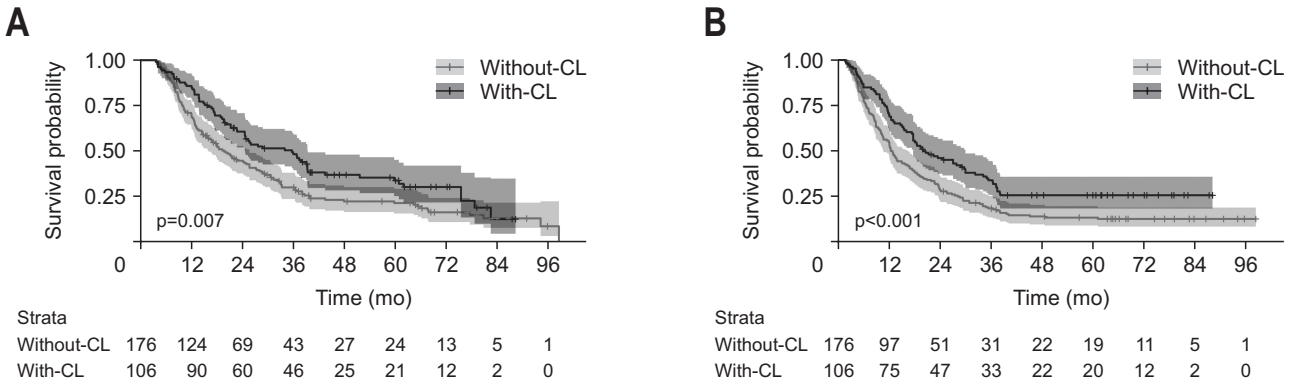

Fig. 2. Before propensity score matching. (A) Overall survival and (B) disease-free survival for patients in the caudate lobectomy (CL) group and the non-CL group (n=282).

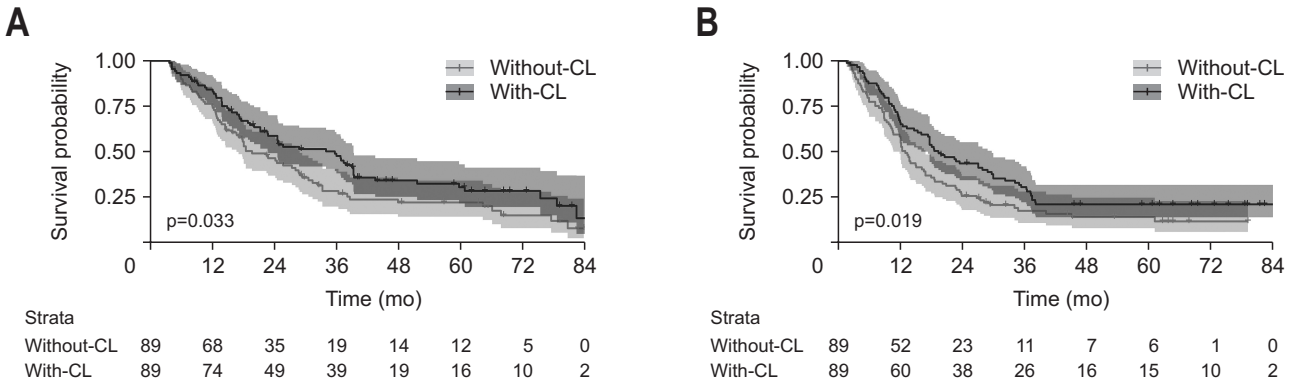

Fig. 3. After propensity score matching. (A) Overall survival and (B) disease-free survival for patients in the caudate lobectomy (CL) group and the non-CL group (n=178).

cally targeting cases with R0 resections, thereby offering a more precise understanding of outcomes within this subgroup.

5. Prognostic factors on OS for patients with hICC

Univariable and multivariable Cox regression analysis of OS for patients involved is shown in Table 3. Before PSM, the results showed that CL (hazard ratio [HR], 0.711; 95% CI, 0.530 to 0.953; p=0.023) and R0 resection (HR, 0.634; 95% CI, 0.450 to 0.894, p=0.009) were associated with better OS on pre-PSM multivariable analysis, while invasion of liver parenchyma (HR, 1.358; 95% CI, 1.024 to 1.802; p=0.034), postoperative pulmonary infection (HR, 2.804; 95% CI, 1.627 to 4.831; p=0.000) and poor tumor differentiation (HR, 1.402; 95% CI, 1.221 to 1.603; p=0.018) were associated with inferior OS on multivariable analysis. Invasion of the whole bile duct (HR, 1.549; 95% CI, 1.128 to 2.218; p=0.007) was related to worse OS on univariable analysis but was not significantly related to worse OS due to the outcome of multivariable analysis (HR, 1.190; 95% CI, 0.851 to 1.665; p=0.308).

After PSM, the results of multivariable analysis showed that CL (HR, 0.697; 95% CI, 0.492 to 0.988; p=0.042) was associated with better OS. Preoperative bile duct drainage (HR, 1.591; 95% CI, 1.030 to 2.456; p=0.036), invasion of liver parenchyma (HR, 1.737; 95% CI, 1.211 to 2.493; p=0.004) and poor tumor differentiation (HR, 1.594; 95% CI, 1.103 to 2.305; p=0.013) were associated with inferior OS on multivariable analysis. Cardiovascular accident (HR, 2.973; 95% CI, 1.085 to 8.141; p=0.034) was related to worse OS on univariable analysis but was not significantly related to worse OS due to the outcome of multivariable analysis (HR, 2.634; 95% CI, 0.939 to 5.218, p=0.059).

6. Prognostic factors on DFS for patients with hICC

Univariable and multivariable Cox regression analysis of DFS for patients involved is shown in Table 4. Before PSM, multivariable Cox regression analysis show that CL (HR, 0.684; 95% CI, 0.515 to 0.909; p=0.009) and R0 resection (HR, 0.754; 95% CI, 0.621 to 0.956; p=0.018) contributed to longer OS for patients. Invasion of liver parenchyma (HR, 1.356; 95% CI, 1.089 to 1.697; p=0.042)

Table 3. Univariable and Multivariable Cox Regression Analysis of OS for Patients with Intrahepatic Cholangiocarcinoma Involving the Hepatic Hilum

Variable	OS before PSM				OS after PSM			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Caudate lobectomy	0.673 (0.505–0.898)	0.007	0.711 (0.530–0.953)	0.023	0.687 (0.485–0.972)	0.033	0.697 (0.492–0.988)	0.042
Combined vesse1 resection	1.093 (0.821–1.456)	0.542			1.174 (0.824–1.671)	0.374		
Gender male	0.776 (0.486–1.241)	0.290			1.013 (0.561–1.831)	0.966		
Vascular invasion	1.096 (0.826–1.454)	0.524			1.171 (0.823–1.667)	0.381		
Hypertension	1.150 (0.805–1.644)	0.442			1.277 (0.806–2.024)	0.298		
Cardiovascular accident	1.732 (0.712–4.212)	0.226			2.973 (1.085–8.141)	0.034	2.634 (0.939–5.218)	0.059
Diabetes	0.919 (0.471–1.793)	0.804			0.939 (0.414–2.134)	0.881		
COPD	1.190 (0.587–2.415)	0.630			1.698 (0.746–3.861)	0.207		
Arrhythmia	0.905 (0.401–2.039)	0.809			0.520 (0.128–2.112)	0.361		
Preoperative bile duct drainage	1.346 (0.950–1.906)	0.095			1.629 (1.055–2.515)	0.028	1.591 (1.030–2.456)	0.036
Poor differentiation	1.515 (1.130–2.030)	0.005	1.402 (1.221–1.603)	0.018	1.594 (1.103–2.305)	0.013	1.478 (1.076–1.898)	0.021
Tumor diameter	1.201 (0.919–1.569)	0.181			1.156 (0.835–1.601)	0.382		
Invasion of the whole bile duct	1.549 (1.128–2.128)	0.007	1.190 (0.851–1.665)	0.308	1.422 (0.969–2.087)	0.072		
Invasion of liver parenchyma	1.494 (1.130–1.974)	0.005	1.358 (1.024–1.802)	0.034	1.901 (1.328–2.720)	0.000	1.737 (1.211–2.493)	0.004
Peritoneal invasion of the liver	0.937 (0.651–1.349)	0.728			1.092 (0.704–1.692)	0.695		
Nerve invasion	1.117 (0.849–1.469)	0.429			1.219 (0.862–1.724)	0.264		
ASA classification	0.808 (0.427–1.525)	0.510			0.583 (0.264–1.286)	0.181		
Intraoperative hemorrhage	1.053 (0.928–1.196)	0.424			1.067 (0.896–1.270)	0.467		
Intraoperative transfusion	1.236 (0.940–1.624)	0.129			1.287 (0.911–1.818)	0.153		
Operation time	0.870 (0.632–1.197)	0.391			0.777 (0.509–1.186)	0.242		
Second surgery	1.177 (0.694–1.996)	0.546			1.290 (0.652–2.551)	0.465		
Length of hospital stay	1.119 (0.890–1.407)	0.335			1.061 (0.795–1.416)	0.687		
Postoperative hospital stay	1.155 (0.942–1.415)	0.166			1.092 (0.842–1.417)	0.505		
ICU treatment time	1.037 (0.898–1.198)	0.618			1.087 (0.910–1.299)	0.359		
Total postoperative infection	1.358 (0.772–2.387)	0.288			1.052 (0.513–2.159)	0.889		
Pulmonary infection	2.890 (1.698–4.919)	0.000	2.804 (1.627–4.831)	0.000	2.018 (0.983–4.145)	0.056		
Abdominal infection	0.956 (0.645–1.416)	0.821			0.840 (0.482–1.464)	0.538		
Incisional infection	2.037 (0.834–4.977)	0.118			2.650 (0.829–8.474)	0.100		
Sepsis	3.489 (0.858–14.193)	0.081			NA	NA	NA	NA
Liver abscess	2.765 (0.385–19.857)	0.312			NA	NA	NA	NA
Abdominal effusion	0.893 (0.583–1.367)	0.602			0.991 (0.614–1.601)	0.972		
Pleura effusion	1.201 (0.710–2.032)	0.495			1.066 (0.541–2.100)	0.854		
Bile leakage	1.220 (0.866–1.719)	0.256			0.832 (0.511–1.356)	0.461		
Post operative hemorrhage	1.032 (0.561–1.900)	0.919			0.963 (0.424–2.190)	0.928		
Biliary fistula	1.165 (0.162–8.354)	0.879			1.277 (0.177–9.219)	0.809		
Gastrointestinal obstruction	2.416 (0.765–7.628)	0.133			2.665 (0.833–8.526)	0.099		

Table 3. Continued

Variable	OS before PSM				OS after PSM			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Hepatic insufficiency	1.443 (0.863–2.413)	0.162			1.883 (0.914–3.881)	0.086		
Pulmonary insufficiency	3.136 (0.773–12.730)	0.110			NA	NA	NA	NA
Renal insufficiency	2.043 (0.651–6.409)	0.221			1.267 (0.176–9.095)	0.814		
Cardiac insufficiency	0.440 (0.062–3.140)	0.413			1.015 (0.142–7.284)	0.988		
R0 resection	0.618 (0.443–0.864)	0.005	0.634 (0.450–0.894)	0.009	0.818 (0.516–1.297)	0.393		

OS, overall survival; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; ICU, intensive care unit; NA, not available.

Table 4. Univariable and Multivariable Cox Regression Analysis of DFS for Patients with Intrahepatic Cholangiocarcinoma Involving the Hepatic Hilum

Variable	DFS before PSM				DFS after PSM			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Caudate lobectomy	0.634 (0.482–0.835)	0.001	0.684 (0.515–0.909)	0.009	0.676 (0.486–0.939)	0.020	0.708 (0.508–0.986)	0.041
Combined vesse1 resection	1.020 (0.777–1.338)	0.887			0.765 (0.546–1.072)	0.120		
Gender male	0.860 (0.552–1.341)	0.506			0.914 (0.522–1.598)	0.752		
Vascular invasion	1.007 (0.770–1.317)	0.960			0.785 (0.560–1.100)	0.160		
Hypertension	1.085 (0.774–1.523)	0.635			1.334 (0.872–2.041)	0.185		
Cardiovascular accident	1.458 (0.601–3.539)	0.405			2.660 (0.979–7.229)	0.055		
Diabetes	0.815 (0.432–1.537)	0.528			1.132 (0.555–2.311)	0.733		
COPD	1.123 (0.554–2.273)	0.748			0.738 (0.302–1.803)	0.505		
Arrhythmia	0.658 (0.271–1.597)	0.355			0.932 (0.231–3.770)	0.922		
Preoperative bile duct drainage	1.363 (0.982–1.892)	0.064			1.618 (1.067–2.454)	0.023	1.517 (0.998–2.305)	0.051
Poor differentiation	1.313 (1.000–1.723)	0.051			1.436 (1.019–2.023)	0.039	1.329 (0.940–1.881)	0.108
Tumor diameter	1.166 (0.904–1.503)	0.238			0.924 (0.653–1.306)	0.654		
Invasion of the whole bile duct	1.274 (0.951–1.707)	0.104			1.048 (0.740–1.485)	0.792		
Invasion of liver parenchyma	1.454 (1.118–1.892)	0.005	1.356 (1.089–1.697)	0.042	1.076 (0.775–1.493)	0.662		

Table 4. Continued

Variable	DFS before PSM				DFS after PSM			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Peritoneal invasion of the liver	0.965 (0.688–1.353)	0.835			0.914 (0.601–1.390)	0.674		
Nerve invasion	1.132 (0.874–1.468)	0.347			0.961 (0.692–1.334)	0.812		
ASA classification	0.727 (0.396–1.333)	0.302			1.228 (0.587–2.567)	0.586		
Intraoperative hemorrhage	1.058 (0.936–1.195)	0.366			0.962 (0.806–1.147)	0.664		
Intraoperative transfusion	1.111 (0.857–1.440)	0.425			1.211 (0.871–1.684)	0.254		
Operation time	0.708 (0.525–0.955)	0.024			1.065 (0.692–1.640)	0.774		
Second surgery	1.296 (0.801–2.097)	0.292			1.160 (0.627–2.147)	0.637		
Length of hospital stay	1.082 (0.871–1.345)	0.477			0.899 (0.687–1.176)	0.437		
Postoperative hospital stay	1.132 (0.933–1.374)	0.210			0.976 (0.760–1.252)	0.846		
ICU treatment time	0.948 (0.824–1.091)	0.456			0.884 (0.739–1.057)	0.176		
Total postoperative infection	1.644 (1.014–2.664)	0.044	1.305 (0.700–2.432)	0.402	1.354 (0.765–2.398)	0.298		
Pulmonary infection	2.594 (1.555–4.329)	0.000	2.180 (1.255–3.788)	0.006	1.032 (0.604–1.762)	0.909		
Abdominal infection	0.937 (0.647–1.355)	0.728			0.796 (0.253–2.506)	0.696		
Incisional infection	2.331 (1.031–5.273)	0.042	1.807 (0.633–5.165)	0.269	2.037 (0.834–4.977)	0.118		
Sepsis	3.779 (0.930–15.353)	0.063			NA		NA	
Liver abscess	2.504 (0.349–17.968)	0.361			NA		NA	
Abdominal effusion	1.026 (0.695–1.515)	0.897			1.167 (0.741–1.839)	0.504		
Pleura effusion	1.233 (0.762–1.995)	0.394			1.008 (0.513–1.981)	0.981		
Bile leakage	1.186 (0.858–1.640)	0.301			1.124 (0.714–1.771)	0.614		
Post operative hemorrhage	1.238 (0.707–2.167)	0.455			1.079 (0.549–2.119)	0.825		
Biliary fistula	2.204 (0.545–8.923)	0.268			1.193 (0.294–4.838)	0.804		
Gastrointestinal obstruction	2.721 (1.003–7.381)	0.049	2.263 (0.787–6.507)	0.130	2.301 (0.848–6.243)	0.102		
Hepatic insufficiency	1.110 (0.634–1.943)	0.716			1.627 (0.796–3.327)	0.182		
Pulmonary insufficiency	3.837 (0.944–15.594)	0.060			NA		NA	
Renal insufficiency	2.048 (0.654–6.417)	0.219			0.833 (0.116–5.965)	0.855		
Cardiac insufficiency	0.337 (0.047–2.403)	0.278			1.396 (0.194–10.021)	0.740		
R0 resection	0.609 (0.445–0.834)	0.002	0.754 (0.621–0.956)	0.018	1.251 (0.794–1.971)	0.334		

DFS, disease-free survival; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists; ICU, intensive care unit; NA, not available.

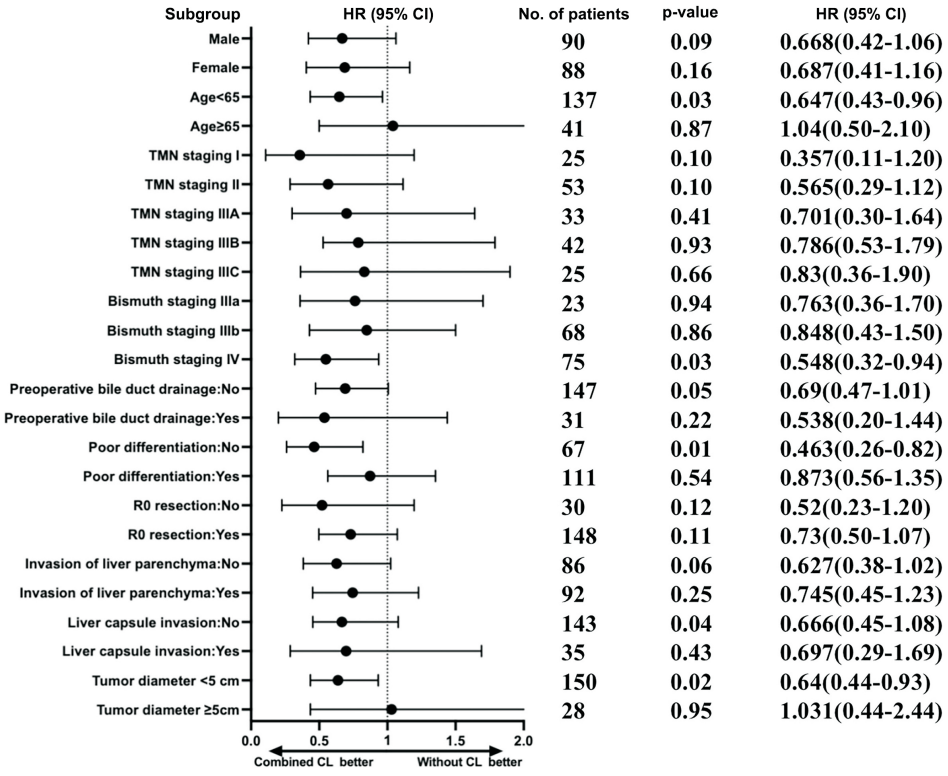

Fig. 4. Forest plot showing the results of the subgroup analysis of overall survival in the propensity score matching cohort. HR, hazard ratio; CI, confidence interval; CL, caudate lobectomy.

and pulmonary infection (HR, 2.180; 95% CI, 1.255 to 3.788; p=0.006) contributed to poorer DFS for patients. Total postoperative infection (HR, 1.644; 95% CI, 1.014 to 2.664; p=0.044), postoperative pulmonary infection (HR, 2.594; 95% CI, 1.555 to 4.329; p<0.001), postoperative incisional infection (HR, 2.331; 95% CI, 1.031 to 5.273; p=0.042) and gastrointestinal obstruction were identified by univariable analysis as independent predictors that contributed to inferior DFS. When multivariable analysis was utilized to analyze these factors, only pulmonary infection remained statistically significant (HR, 2.180; 95% CI, 1.255 to 3.788; p=0.006). After PSM, CL (HR, 0.708; 95% CI, 0.508 to 0.986; p=0.041) were contributed to longer DFS on multivariable Cox regression analysis. Poor tumor differentiation (HR, 1.436; 95% CI, 1.019 to 2.023; p=0.039) and preoperative bile duct drainage (HR, 1.618; 95% CI, 1.067 to 2.454; p=0.023) were only associated with shorter DFS on univariable analysis.

7. Subgroup analysis of the usefulness of CL

To evaluate the association between CL utilization and OS among different patient subgroups, Cox regression models using the post-PSM cohort were examined following stratification based on gender, age, TMN staging, Bismuth staging, tumor histological grade, tumor size, resection margin status, whether to perform preoperative bile duct drainage and features of tumor invasion. Analysis of Bismuth stage I and Bismuth stage II was excluded due to insufficient patient data, and the results of subgroup analysis were presented by a forest plot (Fig. 4). Notably, in the case of combined CL, some subgroups were more significantly associated with improved OS, including age <65 years (HR, 0.65; 95% CI, 0.43 to 0.96; p=0.03), well differentiated tumor (HR, 0.463; 95% CI, 0.26 to 0.82; p=0.01), Bismuth stage IV (HR, 0.55; 95% CI, 0.32 to 0.94; p=0.03), and tumor diameter <5 cm (HR, 0.64; 95% CI, 0.44 to 0.93; p=0.02). Apart from the mentioned subgroups, almost all subgroups showed combined CL to be a better choice than without caudate resection in terms of OS, although the results of these subgroups did not reach statistical significance.

DISCUSSION

It is generally accepted that surgical resection is the only potentially curative therapy for patients with ICC. For patients undergoing resection of ICC, R1 margin status was associated with an inferior long-term outcome,[24] and margin-negative resection (R0) to was the strongest predictor of survival after surgical resection, independent of disease stage.[28] Therefore, extended liver resection with or without vascular or biliary reconstructions is often required to obtain R0 margins, especially in cases of voluminous lesions

or multifocal tumors, which account for 50% to 70% of all ICC cases.[13,29] However, it may be more complicated to reach R0 resection when ICC progressed and involved hepatic hilum.

Typically, hICC exhibits an infiltrative growth pattern extending into the hepatic parenchyma, perihilar structures, and adjacent vascular systems. The caudate lobe consists of three main parts: the Spiegel lobe, paracaval portion, and caudate process portion.[30] The Spiegel lobe is situated to the left of the caudate lobe, adjacent to the left side of the inferior vena cava and the Arantius tube (the ligament of the umbilical vein), and dorsally to the omentum. The paracaval portion occupies the middle area of the caudate lobe, located on the right side of the Arantius tube and partially encircling the inferior vena cava on the abdominal side, extending to the root of the secondary porta of the liver. Its upper right boundary merges with the right posterior lobe of the liver without a distinct demarcation, and its lower right boundary connects to the caudate process through the right posterior branch of the portal vein. The caudate process, positioned in the right part of the caudate lobe, may merge with the right posterior lobe of the liver or exist as an independent mastoid structure on its right side. Due to the position of the caudate lobe, it is closely connected with the hilar bile duct, and tumors can easily invade the caudate lobe,[31] resulting in implantable metastasis of the hepatic caudal lobe. Therefore, combined CL is more conducive to achieving R0 resection.[32] However, owing to its proximity to the portal vein, inferior vena cava, and hepatic vein, caudate lobe resection poses a risk of injury to these structures and associated bleeding. Apart from the acute issues resulting from blood loss and subsequent hypovolemia, blood transfusion has been associated with worse all-cause and oncologic outcomes for patients undergoing major oncologic surgeries.[33] In addition, because the caudate lobe is connected to the right posterior lobe of the liver without obvious boundary, complete removal of the caudate lobe is particularly difficult.[34] Specifically, the left side of the caudate lobe is free and has an Arantius tube as an anatomical marker, making the resection line on the left side easily determined.[35] However, there is no obvious boundary between the right side (especially the paracaval portion) and the right posterior lobe of the liver, so the right boundary is difficult to judge.[36] Therefore, it is challenging to completely remove the caudate lobe while retaining the right lobe of the liver. One method to address this is to establish an ischemic line by ligating all the blood vessels of the caudate lobe during anterograde resection to find the boundary with the right posterior lobe.[37] Other surgical techniques require further exploration and study by hepatobiliary surgeons. Although aggressive surgical approach including extended liver resection and complete excision of the caudate lobe have been widely accepted as standard surgical practice for HC,[38,39] controversy persists regarding the curative resection of ICC. The justification for incorporating caudate lobe resection in common hepatic duct cancer lies in the susceptibility of the caudate lobe duct to invasion. This reasoning extends to hICC, supporting the inclusion of caudate lobe resection in its treatment approach. Available studies have demonstrated that hICC, in comparison with HC, shows distinct clinicopathological features, including more aggressive biological behaviors, different prognostic factors, and worse prognosis. Therefore, it is vital to discover whether combine CL can benefit hICC patient in the way of longer OS and DFS. As a result, uncertainty persists about the impact of caudate lobe resection on perioperative morbidity and postoperative survival. We therefore performed this propensity score analysis to further explore the impact of combined caudate lobe resection on the short-term clinical outcomes and long-term prognosis of patients with hICC.

Based on data from the current study, patients in CL group had a better long-term survival (OS and DFS) than those in non-CL group before and after PSM (Fig. 2A and B). We conducted an analysis of the potential reasons for the better OS and DFS in the CL group compared to the non-CL group and identified the following mechanisms. First, the CL group may have had better OS and DFS due to better surgical margins. We analyzed the postoperative resection margin status of all patients after PSM. Our analysis revealed that the non-CL group had a significantly higher probability of R1 resection margins compared to the CL group, with an OR of 2.333 (95% CI, 1.127 to 4.831). This aligns with previous research findings. For example, a 2014 meta-analysis on prognostic factors for ICC clearly indicated that R1 resection is associated with poor prognosis.[40] Second, the CL group may have better OS and DFS due to the more effective removal of microscopic disease. This can be directly evidenced by the postoperative recurrence rates.[28] The CL group's 1-year and 5-year recurrence rates were significantly lower than those of the non-CL group. The non-CL group exhibited a higher OR of 2.688 (p=0.002) for the 1-year recurrence rate. Similarly, for the 5-year recurrence rate, we found that 66.3% of patients in the CL group experienced postoperative recurrence, compared to 83.1% of patients in the non-CL group. In terms of 5-year recurrence rates, the non-CL group had a higher OR of 2.508 (p=0.011). Higher postoperative recurrence rates clearly indicate poorer prognosis, suggesting that the CL group may be more effective in removing microscopic disease, thereby reducing recurrence, and achieving better

OS and DFS compared to the non-CL group.

Patients undergoing resection that combined caudate lobe had no statistically significant difference compared to those undergoing caudate-sparing resection in perioperative clinical outcomes or the incidence of complications, either before or after PSM. According to the results of subgroup analysis, CL is more recommended for patients with following characteristics: age <65 years, well-differentiated tumor, Bismuth stage IV and tumor diameter <5 cm. As for other patients, combined caudate resection generally leads to a better prognosis than no resection of the caudate lobe.

Currently, postoperative complications have been a crucial factor in surgical decision making for surgeons.[41] It has been elaborated that postoperative complications can lead to inferior prognosis of cancer patients in multiple ways, such as postoperative hemorrhage, malnutrition, muscle depletion, and local or general infection. For patients with malignancies undergoing surgical treatment, long-term survival can be affected by major postoperative complications, which has been demonstrated in tumors of many sites.[42-44] Therefore, the impact of complications after combined caudate resection on the prognosis of patients with ICC involving the hepatic hilus should be meticulously assessed when deciding the surgery approach. In this study, we found that the overall postoperative complications of patients combined CL do not differ from that of non-CL group, indicating the tumor itself and resection margin status are the primary determinant of long-term prognosis, rather than postoperative complications. Hence, as curative R0 resection is the only means by which clinical cure can be achieved, more aggressive surgery strategy including resection of the caudate lobe is requisite.

This study is the only study that used propensity score-matched analysis to evaluate the prognostic impact of combined caudate lobe resection on the prognosis of patients with ICC involving the hepatic hilus. Apart from focusing on the long-term survival outcomes of patients, we also focused on the impact of short-term clinical outcomes after curative-intent surgery. Meanwhile, PSM on the two groups of patients was performed to minimize the impact of the bias due to retrospective study on the conclusions. This study can provide new evidence for clinical diagnosis and surgical treatment of hICC.

However, several limitations of this study should be carefully considered when interpreting the results. First, this study was retrospective, which means there are inevitable limitations in its design. As a result, some clinical bias was inevitable. Secondly, due to the rarity of hICC and the screening by propensity score, the final sample size was relatively small. This resulted in our ability to only divide patients into two groups based on whether the caudate lobe was resected, preventing further subdivision of the CL group into partial or complete caudate lobe resection subgroups. Third, this study was a single-center study, which may lead to certain restriction on the application of the conclusion. Therefore, future randomized controlled studies and large-scale multicenter prospective cohort studies are warranted for further verification.

In summary, this study is unique in employing propensity score-matched analysis to assess the prognostic implications of combined CL for patients with ICC affecting the hepatic hilum. The findings indicate that combined caudate lobe resection may enhance long-term survival in such patients. Moreover, there were no statistically significant differences in postoperative complications between the CL group and the non-CL group. Thus, the study suggests that combined caudate lobe resection should be considered a proactive approach in the management of patients with hICC.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Study concept and design: D.Z., N.W. Data acquisition: D.Z. Data analysis and interpretation: D.Z., N.W. Drafting of the manuscript: D.Z. Critical revision of the manuscript for important intellectual content: D.Z., N.W., Y.W. Statistical analysis: D.Z., N.W. Obtained funding: N.C., J.L. Administrative, technical, or material support; study supervision: B.L., J.L. Approval of final manuscript: all authors.

ORCID

Di Zeng	https://orcid.org/0009-0001-4587-9421
Yaoqun Wang	https://orcid.org/0000-0003-0122-122X
Ningyuan Wen	https://orcid.org/0000-0003-0608-464X
Bei Li	https://orcid.org/0009-0004-7114-2994
Nansheng Cheng	https://orcid.org/0000-0002-9334-5715
Jiong Lu	https://orcid.org/0009-0002-8669-5634

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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