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Prognostic impact of lymph node and surgical margin in patients with perihilar cholangiocarcinoma

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Abstract

Background The study aimed to assess the prognostic impact of lymph node (LN) metastasis combined with surgical margin status on the 5-year overall survival (OS) of patients after radical resection perihilar cholangiocarcinoma (PHCC).

Methods Clinicopathological data of patients with PHCC who underwent curative resection between June 2014 and June 2022 were analyzed retrospectively. Cox regression analyses were performed to evaluate the risk factors for OS and LN metastasis. Kaplan–Meier method with log-rank test was performed for OS curves.

Results 71 patients were enrolled and the 5-year OS rate was 52.4%. Poor differentiation grade, R1/2 resection, and the presence of LN metastasis were the independent prognostic factors of poor OS. In patients without LN metastasis, the 5-year OS rate was significantly higher in patients with negative surgical margin than patients with positive surgical margin. In LN metastasis positive patients, a comparable 5-year OS rate was found between patients with and without positive surgical margin ($P=0.185$).

Conclusions In patients with curatively resected for PHCC, R1 resection margin does not influence OS in patients with LN metastasis even when radical resection was achieved. Consequently, the risk of highly invasive procedures aimed at achieving R0 margins should be judiciously weighed against potential morbidity risk in patients with LN metastasis, as aggressive surgical strategies may not translate to survival benefits.

Keywords Perihilar cholangiocarcinoma, Klatskin tumor, Lymph node, Surgical margin, Overall survival

Introduction

Perihilar cholangiocarcinoma (PHCC), accounting for 50–60% of all cholangiocarcinoma, arises at or near the confluence of the right and left hepatic ducts to the junction of the cystic duct and the common bile duct [1]. Surgical radical resection combined with regional lymphadenectomy remains the only potential treatment for patients suffered PHCC, with reported 5-year overall survival (OS) rates ranging from 20 to 40% [2, 3].

To date, lymph node (LN) metastasis and surgical margin status have been widely recognized as the well-established prognostic factors in PHCC [4]. Despite significant advances in aggressive surgical techniques and postoperative adjuvant treatment, the 5-year OS for

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patients with positive LN remains below 20%, compared to 55% in LN-negative patients [4–6]. Prior studies have highlighted that the quantity rather than location of positive LN provides a better discriminatory capacity in prognosis, which formed the basis of adjustments in American Joint Committee on Cancer (AJCC) 8th pN stage [7–10]. The retrospective study conducted by Hosokawa et al. further demonstrated that positive ductal margin status is associated with poor survival in resected PHCC significantly [4]. With evolving treatment strategies for PHCC, the role of extended resection aimed at achieving curative margins in LN-positive patients warrants further investigation. However, the independent prognostic significance of LN metastasis and surgical margin status as well as their interplay on long-term OS remains unclear.

This ambiguity complicates the evaluation of survival benefits derived from extended resection to achieve negative margins in patents with LN metastasis, particularly when weighed against the risks of increased morbidity and mortality. Therefore, this study aims to evaluate the impact of LN metastasis and surgical margin status on 5-year OS in patients undergoing radical resection for PHCC.

Material and methods

Patients

Between June 2014 and June 2022, a total of 106 consecutive patients with PHCC were treated in the Drum Tower Hospital of Nanjing University Medical School. Of these, 26 patients (24.5%) were deemed inoperable due to locally advanced disease (with or without distant metastasis), performance status, and/or poor hepatic function. One patient who received neoadjuvant chemotherapy and/or radiotherapy, one patient with Clavien–Dindo grade V postoperative complication and 7 patients with incomplete clinical data were excluded. The final cohort comprised 71 patients who underwent curative resection (hepatectomy and/or extrahepatic bile duct resection). Among these, R0 resection (microscopically negative margins) was achieved in 57 patients (80.3%), while lymph node (LN) metastasis was histologically confirmed in 32 patients (45.1%) (Fig. 1). The study was approved by the Health Research Ethics Board of Drum Tower Hospital of Nanjing University Medical School (2023-214-01).

Surgical procedures and perioperative management

All patients underwent a standardized preoperative clinical evaluation. Briefly, laboratory tests, multiphase contrast-enhanced multidetector-row computed tomography (MDCT) and magnetic resonance cholangiopancreatography (MRCP) were performed routinely for assessing the resectability of tumor. Endoscopic nasobiliary drainage (ENBD) served as the primary method for preoperative biliary drainage (PBD), with percutaneous transhepatic cholangiodrainage (PTCD) reserved for cases when ENBD failed.

Hemihepatectomy combined total caudate lobectomy was performed as the basic surgical approach for PHCC [4, 11]. Portal vein and/or hepatic artery resection and reconstruction were performed for patients with tumor invasion. Preoperative planning incorporated three-dimensional anatomical analysis, evaluation of tumor extent (longitudinal and vertical dimensions), and future liver remnant (FLR) volume assessment. Portal vein embolization (PVE) was performed preoperatively in patients with insufficient future liver remnant

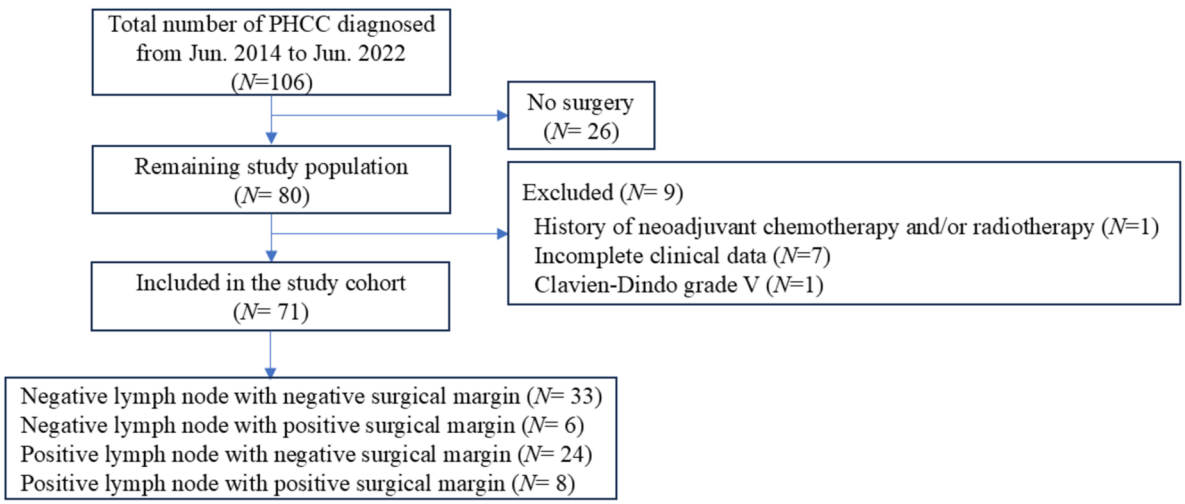

Fig. 1 Flow chart of the study population. PHCC, perihilar cholangiocarcinoma

(FLR) < 40% of the total liver volume, and ICGK-F ≥ 0.05 was served as the safety threshold for proceeding with hepatectomy of PHCC [12]. Intraoperative frozen-section examination for all intraoperative biliary margins was conducted routinely. In locally advanced cases, R0 resection is sought through three types of extended radical surgery: right/left trisectionectomy, hepato-pancreaticoduodenectomy, and combined arterial resection for reconstruction. Regional LN dissection was performed routinely according to the Japanese rules after sampling of the para-aortic LN [5, 13].

Bile reinfusion combined with enteral nutrition was conducted as the core of perioperative management of PHCC [14]. A nasoduodenal catheter, which is used for bile reinfusion and enteral nutrition, was inserted at the same time as ENBD drainage before surgery. During surgery, the ENBD catheter was removed, while the nasoduodenal catheter remained in situ to facilitate postoperative enteral nutritional support. For prevention of postoperative infections complications, preoperative bacteriological monitoring of drained bile was performed regularly and sensitive antibiotics were selected as surgical prophylactic antibiotics based on antimicrobial susceptibility [15].

Clinicopathological variables and definition of complication

Demographic and surgical variables (age, gender, preoperative biliary drainage, type of liver resection, combined resection, operating time, volume of blood loss and transfusion) were collected. The pathological details included Bismuth classification, differentiation grade, microscopic perineural invasion, microvascular invasion (MVI), macrovascular invasion (defined as tumor involvement of the portal vein and/or hepatic artery), tumor classification, LN metastasis, tumor stage according to the 8th AJCC stage, resection margin status. Three or more segments of the Couinaud liver resection were defined as major hepatectomy, with minor hepatectomy was defined as fewer than three segments resection [16]. R0 resection was defined as the microscopic absence of residual cancer at all surgical margins [17]. The occurrence of postoperative complications was collected within 30 days after surgery. The severity of postoperative complications was classified according to the Clavien–Dindo classification, with major complications being defined as grade ≥ III [18]. Surgical site infection (SSI) which includes incisional and organ/space SSI was diagnosed with the Centers for Disease Control and Prevention (CDC) guidelines [19]. Posthepatectomy liver failure (PHLF) and bile leakage (BL) were recognized by the International Study Group of Liver Surgery (ISGLS) [20, 21]. The definitions established by the International Study Group of Pancreatic Surgery (ISGPS) were used to make definite diagnoses of clinically relevant postoperative pancreatic fistula (CR-POPF), chyle leakage [22, 23].

Patient follow-up

Fluorouracil analogs (capecitabine or S-1) served as the first-line adjuvant chemotherapy regimen following curative resection. For patients with high-risk recurrence factors, such as LN metastasis, R1/2 resection and AJCC stage III or IV, adjuvant chemotherapy was initiated within 3 months postoperatively using the aforementioned agents. All patients were followed up in outpatient manner after curative surgery regularly. Routine laboratory tests (biochemical, coagulation, and tumor-related parameters), MDCT or MRCP were performed every 3 months for the first and second year after surgery, then once every 6 months from the third to the fifth year. OS was defined as the time from the date of surgery until death of any causes or the last follow-up.

Statistical analysis

The continuous variables with normal distribution were analyzed using independent *t*-test and reported as mean ± standard deviation (SD). For non-normally distributed clinical data, Mann–Whitney *U* test which express as median (interquartile range, IQR) were conducted. The categorical variables were compared via χ^2 test or Fisher's exact test, as appropriate, and presented as absolute frequencies (percentages). Univariable and multivariable logistic regression analysis were performed to identify potential independent predictors of lymph node (LN) metastasis. OS curves were generated using the Kaplan–Meier method and compared via log-rank test. The variables with $P < 0.1$ in univariable analysis were incorporated into the multivariable Cox proportional hazards regression model. Hazard ratio (HR) and 95% confidence intervals (95%CI) were calculated appropriately. The two-sided P value < 0.05 was considered as statistics significantly. Statistical analyses were performed by SPSS 26.0 software for Windows (SPSS Inc.) and survival curves were displayed using GraphPad Prism 8.

Results

Baseline characteristics

The baseline characteristics of study patients are summarized in Table 1. A total of 71 qualified patients with resected PHCC from 2014 to 2022 were enrolled, comprising 50 (70.4%) males and 21 (29.6%) females, with a mean age of 62.5 ± 9.7 years. A total of 63 (88.7%) underwent PBD with 61 (85.7%) received ENBD. The most common Bismuth–Corlette classification was III

Table 1 Baseline characteristic of all patients

Characteristic	Total(n = 71)
Age (mean ± SD), years	62.5 ± 9.7
Gender, n (%)	
Male	50 (70.4%)
Female	21 (29.6%)
PBD, n (%)	63 (88.7%)
ENBD	61 (85.9%)
PTCD	2(2.8%)
Intraoperative blood loss (median, IQR), ml	1000.0 (600.0–1400.0)
Intraoperative blood transfusion (median, IQR), ml	1000.0 (400.0–1300.0)
Operative time (median, IQR), min	570.0 (495.0–670.0)
Type of liver resection, n (%)	
S1,4,5,6,7,8	7 (9.9%)
S1,5,6,7,8	23 (32.4%)
S1,2,3,4,5,8	6 (8.5%)
S1,2,3,4	31 (43.7%)
S1,4b,5/S4b,5/S1	2 (2.8%)
Without hepatectomy	2 (2.8%)
Combined resection, n (%)	
Pancreaticoduodenectomy	7 (9.9%)
Portal vein resection	17 (23.9%)
Hepatic artery resection	6 (8.5%)
Bismuth classification, n (%)	
I/II	9 (12.7%)
III	41 (57.7%)
IV	21 (29.6%))
Differentiation grade, n (%)	
Poor	21 (29.6%)
Moderate/Well	50 (70.4%)
Microscopic perineural invasion, n (%)	59 (83.1%)
Microvascular invasion, n (%)	12 (16.9%)
Macrovascular invasion, n (%)	44 (61.9%)
Tumor classification, n (%)	
0	1 (1.4%)
1	7 (9.9%)
2a/b	19 (26.8%)
3	27 (38.0%)
4	17 (23.9%)
Node classification, n (%)	
0	39 (54.9%)
1/2	32 (45.1%)
Stage, n (%)	
0	1 (1.4%)
I	6 (8.5%)
II	12 (16.9%)
IIIA/IIIB	44 (61.9%)
IVA	4 (5.6%)
IVB	4 (5.6%)
Resection margin, n (%)	
R0	57 (80.3%)
R1/2	14 (19.7%)
Postoperative complication, n (%)	
PHLF	5 (7.0%)
BL	24 (33.8%)
Major postoperative complication	17 (23.9%)
Organ/space SSI	38 (53.5%)
Incisional SSI	7 (9.9%)
Abdominal hemorrhage	3 (4.2%)
DGE	7 (9.9%)
CR-POPF	5 (7.0%)
CL	10 (14.1%)
Relaparotomy	5 (7.0%)
Hospital stay (median, IQR), day	21.0 (18.0–31.0)
Postoperative adjuvant chemotherapy, n (%)	58 (81.7%)

ENBD Endoscopic nasobiliary drainage, *PTCD* percutaneous transhepatic cholangiodrainage, *PHLF* posthepatectomy liver failure, *BI* biliary leakage, *SSI* surgical site infection, *DGE* delayed gastric emptying, *CR-POPF* Clinically relevant postoperative pancreatic fistula, *CL* chyle leakage, *IQR* interquartile range, *SD* standard deviation

(57.7%) and IV (29.6%). According to AJCC 8th staging system, 27 (38.0%) patients had T3 tumors and 17 (23.9%) patients had T4 tumors. Approximately one-thirds (29.6%) of the tumors were poorly differentiated.

Organ/space SSI was the most common type of complication after surgery, accounting for 31.2%. 5 (7.0%) patients developed PHLF, 24 (33.8%) patients underwent BL and 17 (23.9%) occurred major postoperative complication (Clavien–Dindo grade ≥ III). 81.7% patients received adjuvant chemotherapy after surgery.

Overall survival in all patients with resected PHCC

Out of the 71 patients, the 3- and 5-year OS rates were 71.7% and 52.4%, respectively. The median OS duration for the full cohort was 49 months (Fig. 2a). Six parameters were identified as likely to influence OS in patients with resected PHCC ($P < 0.1$, Table 2): combined portal vein and/or hepatic artery resection, Bismuth classification, differentiation grade, LN metastasis, surgical margin, and tumor stage. On multivariate analysis, poor differentiation grade (HR = 3.229, 95%CI 1.433–7.274, $P = 0.005$), positive surgical margin (HR = 2.799, 95%CI 1.174–6.675, $P = 0.020$), and presence of LN metastasis (HR = 2.405, 95%CI 1.053–5.43, $P = 0.037$) were the independent prognostic factors of poor OS (Table 2).

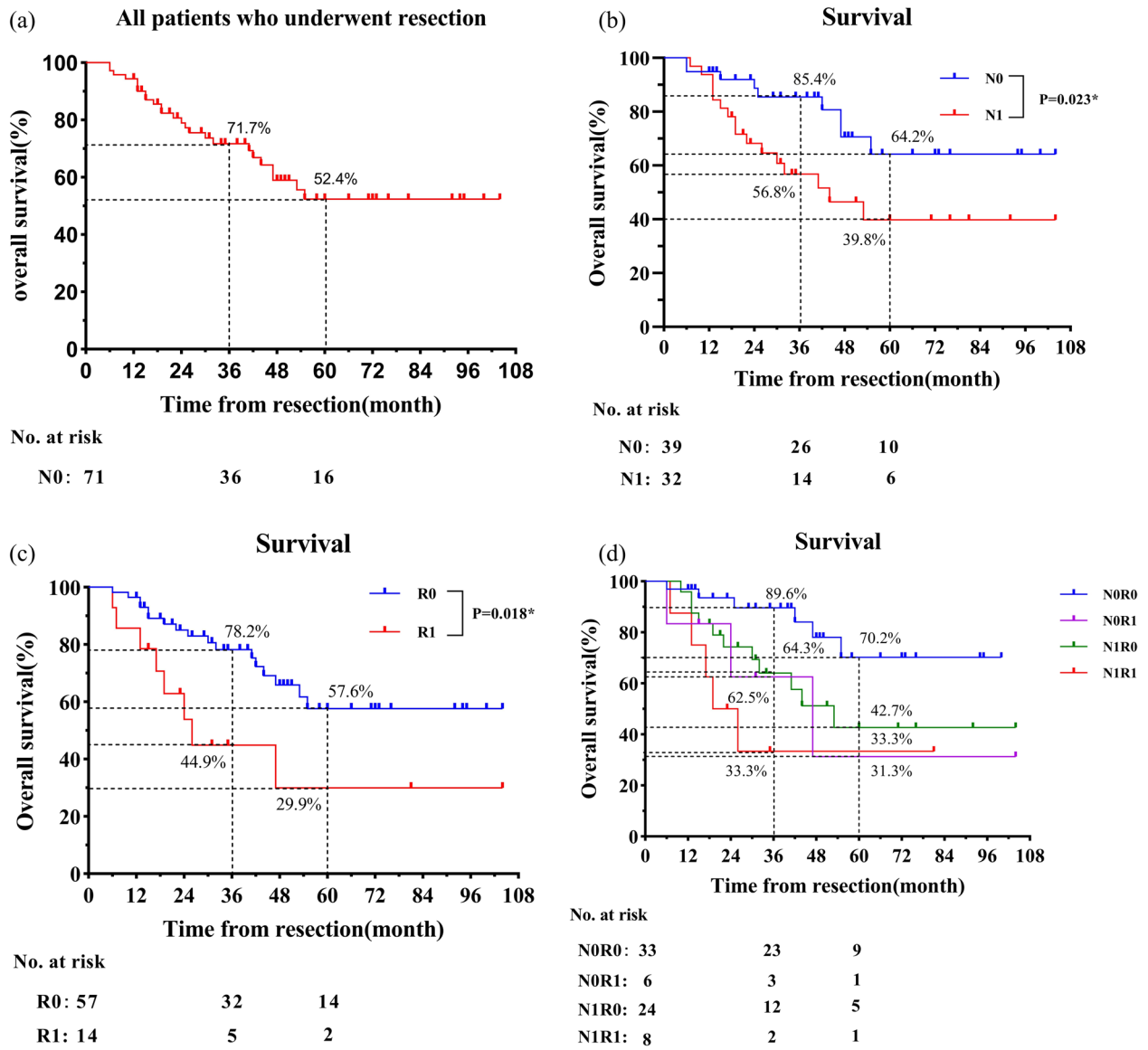

Fig. 2 **a** Overall survival curve for all enrolled patients. **b** Overall survival curve of negative lymph node (N0) and positive lymph node (N1) patients. **c** Overall survival curve of negative surgical margin (R0) and positive surgical margin (R1) patients. **d** Overall survival curve of patients with negative lymph node and negative surgical margin (N0R0), negative lymph node and positive surgical margin (N0R1), positive lymph node and negative surgical margin (N1R0), positive lymph node and positive surgical margin (N1R1)

Overall survival according to lymph nodes metastasis, surgical margin

Figure 2b showed survival curves according to nodal status. The 3-year and 5-year OS of negative LN patients were 85.4% and 64.2%, which was significantly better than patients with LN metastasis (OS: 56.8% at 3 years, 39.8% at 5 years, $P=0.023$). As LN metastasis was identified as one of the independent prognostic factors of OS, we further investigated factors likely to influence OS in patients with LN metastasis. Poor differentiation grade (HR = 3.930, 95%CI 1.446–10.679, $P=0.007$) was identified as the only independent factor in the prognosis of patients with LN metastasis (Table 3). Compared to patients with negative LN, microvascular invasion (OR = 4.873, 95%CI 1.139–20.846, $P=0.033$) and macrovascular invasion (OR = 2.942, 95%CI 1.016–8.519, $P=0.047$) were significantly relate to the presence of LN metastasis (Table 4).

Figure 2c showed survival curves according to surgical margin. The 3-year and 5-year OS of patients with

Table 2 Uni- and multivariate analysis for overall survival in all patients

Variables	n	Survival Rate (%)		Univariate *P*	Multivariate	*P*
		3-year	5-year		HR (95%CI)	
Age						
< 65	32	71.0	57.0	0.920		
≥ 65	39	72.4	45.3			
Gender						
Male	50	71.0	54.2	0.901		
Female	21	73.4	42.8			
PBD						
Yes	63	69.9	52.6	0.477		
No	8	87.5	58.3			
Type of hepatectomy						
Major hemihepatectomy	67	69.8	54.4	0.774		
Minor hepatectomy	4	75.0	50.0			
Combined PD						
Absent	64	70.2	48.1	0.184		
Present	7	85.7	85.7			
Combined PV and/or HA						
Absent	54	77.0	58.7	0.050		
Present	17	55.2	30.7			
Blood transfusion						
Absent	15	84.4	65.7	0.238		
Present	56	68.2	48.1			
Bismuth classification						
Type I–III	50	79.5	59.7	0.018		
Type IV	21	54.5	34.0			
Differentiation grade						
Moderate/well	21	79.0	61.0	0.007	1	0.005
Poor	50	53.3	22.2		3.229 (1.433–7.274)	
Microscopic perineural invasion						
Absent	59	76.7	54.2	0.106		
Present	12	45.5	45.5			
Microscopic perineural invasion						
Absent	12	85.7	53.6	0.284		
Present	59	65.9	52.4			
R						
0	57	78.2	57.6	0.018	1	0.020
1/2	14	44.9	29.9		2.799 (1.174–6.675)	
N						
Absent	39	85.4	64.2	0.023	1	0.037
Present	32	56.8	39.8		2.405 (1.053–5.493)	
Stage						
0–2	27	92.0	73.3	0.004		
3–4	44	57.7	37.1			

PBD preoperative biliary drainage, *PD* pancreaticoduodenectomy, *PV* portal vein, *HA* hepatic artery, *CI* confidence intervals, *HR* hazard ratio

R0 margin were 78.2% and 57.6%, which was significantly better than patients with R1 margin (OS: 44.9% at 3 years, 29.9% at 5 years, $P=0.018$).

Overall survival according to the combination of surgical margin and lymph node status

The patients were stratified by surgical margin status

Table 3 Uni- and multivariate Cox regression analysis for overall survival in patients with lymph node metastasis

Variables	n	Survival Rate (%)		Univariate *P*	Multivariate	
		3-year	5-year		HR (95%CI)	*P*
Age						
< 65	18	58.5	41.8	0.969		
≥ 65	14	55.0	27.5			
Sex						
Male	20	51.3	36.7	0.676		
Female	12	65.6	49.2			
PBD						
Yes	29	53.5	40.8	0.901		
No	3	66.7	33.3			
Combined PD						
Absent	30	57.3	38.2	0.813		
Present	2	50.0	50.0			
Combined PV and/or HA						
Absent	23	67.5	52.5	0.033		
Present	9	29.6	–			
Blood transfusion						
Absent	6	80.0	53.3	0.376		
Present	26	52.0	36.4			
Bismuth classification						
Type I-III	20	67.8	47.5	0.192		
Type IV	12	41.7	27.8			
Differentiation grade						
Moderate/well	22	69.8	54.3	0.004	1	0.007
Poor	10	26.7	13.3		3.930 (1.446–10.679)	
Microscopic perineural invasion						
Absent	23	66.0	45.3	0.080		
Present	9	33.3	–			
Microscopic perineural invasion						
Absent	2	–	–	0.950		
Present	30	54.1	41.7			
R						
0	24	64.0	42.7	0.185		
1/2	8	33.3	–			

PBD preoperative biliary drainage, *PD* pancreaticoduodenectomy, *PV* portal vein, *HA* hepatic artery, *CI* confidence intervals, *HR* hazard ratio

and LN metastasis into the following four subgroups: 33 (46.5%) patients with N0R0, 6 (8.4%) patients with N0R1, 24 (33.8%) patients with N1R0, 8 (11.3%) patients with N1R1. Based on both surgical margin and lymph node status (N0R0, N0R1, N1R0 and N1R1), the median and 5-year OS were undefined and 70.2%, 47 months (95%CI 11.6–82.4) and 31.3%, 53 months (95%CI 33.5–72.5) and 42.7%, and 19 months (95%CI 8.3–29.7) and 33.3%, respectively. The comparison per status was as follows: N0R0 vs. N1R0: $P=0.035$, N0R1 vs. N1R1: $P=0.559$, N1R0 vs. N1R1: $P=0.185$, N0R0 vs. N0R1: $P=0.065$ (Fig. 2d).

Discussion

In the current study, the 3- and 5-year OS rates for the entire cohort were 71.7% and 52.4%, respectively, consistent with prior studies [24, 25]. We further investigated the prognostic significance of LN metastasis and surgical margin status in patients undergoing curative resection for PHCC, and identified that LN metastasis and R1 surgical margin were independent prognostic indicators of poor prognosis. Notably, the adverse prognostic impact of LN metastasis persisted independently of margin status. Additionally, the poor differentiation grade was identified as an independent risk factor for reduced

Table 4 Factors associated with positive lymph nodes on uni- and multivariable logistic regression analysis

Variables	Univariate analysis		Multivariate analysis	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Age	0.960 (0.914–1.010)	0.113		
Gender	2.067 (0.737–5.795)	0.168		
PBD	1.381 (0.304–6.274)	0.676		
Bismuth classification				
I/II	Reference			
III	1.360 (0.298–6.198)	0.691		
IV	2.667 (0.521–13.655)	0.239		
Number of resected LN	1.010 (0.944–1.080)	0.774		
Differentiation grade	1.918 (0.432–3.323)	0.728		
Microscopic perineural invasion	5.690 (1.159–27.921)	0.032		
Microvascular invasion	4.826(1.182–19.698)	0.028	4.873 (1.139–20.846)	0.033
Macrovascular invasion	3.000 (1.090–8.254)	0.033	2.942 (1.016–8.519)	0.047
Resection margin	1.889 (0.580–6.150)	0.291		

PBD preoperative biliary drainage, *LN* lymph node, *OR* odds ratio, *CI* confidence interval

survival in both the overall cohort and LN-positive subgroups. These findings suggest that radical or extended resection confers limited long-term survival benefit for tumors with aggressive biological behavior such as LN metastasis.

Nowadays, radical surgery with R0 margin remains the first goal for patients suffered PHCC to acquire long-time survival. The R0 resection rate in current study was as high as 80.3%, aligning with outcomes from previous reports from high volume centers [5, 26]. This may be due to dramatic advances in the invasive surgery in last decades, such as trisectionectomy, combined vascular resection and hepatopancreatoduodenectomy. However, such aggressive operations always accompanied by relatively high morbidity and mortality rates, making it imperative to weigh the risks to the patients and its oncology benefits.

Multivariable analysis confirmed LN metastasis as a robust predictor of poor survival, correlating with microvascular and macrovascular invasion, which were widely accepted as hallmarks of aggressive tumor biology. Consequently, accurate and timely evaluation of nodal status is of enormous clinical value. Nowadays, the status of LN can be diagnosis—preoperatively or intraoperatively—according to MDCT [27], diffusion-weighted magnetic resonance [13], positron emission tomography [4] and intraoperative frozen-section examination. Nimura et al. [5] demonstrated that for patients with negative LN, radical resection improved long-term survival, whereas its impact is attenuated in LN-positive cohorts. Meanwhile, the systematic review conducted by Kambakamba et al. reported that LN count ≥ 15 do not enhance diagnostic sensitivity for LN metastasis of PHCC. Thus, comprehensive histopathological evaluation of LN is imperative to avoid understaging and to identify high-risk patients with anticipated poor survival who may benefit from preoperative adjuvant therapies. Concurrently, intraoperative frozen-section analysis should be performed routinely and mandatorily to identify LN metastasis, thereby avoiding unnecessary extended radical resection which may increase the surgical risk of postoperative morbidity and mortality.

R0 surgical margin is recognized as an important indicator for the poor prognosis of PHCC, consistent with the current study showed. Shinohara et al. [28] pointed that both radial and ductal bile duct margin positivity significantly impair survival in curatively resected patients. In clinical practice, intraoperative frozen-section analysis was performed for real-time assessment of ductal margin status which guide to the subsequent surgical procedure. Sometimes, to achieve negative margins, extended radical surgery, such as trisectionectomy, hepatectomy combined with vascular resection, and hepatopancreatoduodenectomy, may be employed. Although the clinical significance of additional resection for patients with positive intraoperative ductal margins remains controversial [29, 30], it remains an effective way for obtaining negative margins. The current study showed a comparable 5-year OS rate between N0R1 and N1R1 subgroups, whereas patients with N0R0 had significantly higher 5-year OS rate than patients with N1R0. These results align with the recent European multicenter registry data demonstrating that LN metastasis independently predicts poor survival and recurrence, irrespective of margin status. Notably,

Hosokawa et al. conducted a retrospective study and identified that the proximal ductal status does not influence survival in patients with LN metastasis [4], a conclusion consistent with our findings. The 5-year OS rate of N0R0 patients in this study was higher than that of N0R1 patients, but there was no statistical difference between the two groups. This may due to the small sample size of the N0R1 group.

The present study must be viewed with some limitations. First, it was a single center retrospective study accompanied by selection bias, further multicenter and prospective study are indispensable to validate the present results. Second, adjuvant chemotherapy was not included in current study due to the fact that most patients received adjuvant chemotherapy which has not changed drastically. Additionally, the study period was relatively long, during which there may have been newer iterations of surgical techniques and perioperative management practices. Thus, the enrolled patients who underwent curative resection between June 2014 and June 2022 during which the treatment strategy for PHCC was consistent.

Conclusions

The findings of the current study confirm that LN metastasis and surgical margin status serve as independent prognostic factors in patients undergoing curative resection for PHCC. Notably, the resection margin does not influence OS in patients with positive LN, even when radical resection was achieved. Consequently, in cases with LN metastasis, the risk of highly invasive procedures aimed at achieving R0 margins should be judiciously weighed against potential morbidity risk, as aggressive surgical strategies may not translate to survival benefits.

Abbreviations

PHCC	Perihilar cholangiocarcinoma
LN	Lymph node
AJCC	American Joint Committee on Cancer
OS	Overall survival
ENBD	Endoscopic nasobiliary drainage
PTCD	Percutaneous transhepatic cholangiodrainage
PVE	Portal vein embolization
FLR	Future liver remnant
MVI	Microvascular invasion
SSI	Surgical site infection
PHLF	Posthepatectomy liver failure
BL	Bile leakage
ISGLS	The International Study Group of Liver Surgery
CR-POPF	Clinically relevant postoperative pancreatic fistula

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Author contributions

Study concept and design: Xu Fu, Liang Mao; Data acquisition: Yifei Yang, Jianjie Sheng, Ailixier Aibaidula; Data analysis and interpretation: Yifei Yang, Chenglin Lu; Drafting of the manuscript: Yifei Yang, Jianjie Sheng; Critical revision of the manuscript for important intellectual content: Liang Mao, Yudong Qiu; Statistical analysis: Yifei Yang, Xu Fu; Final approval of manuscript: all authors.

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Availability of data and materials

All data generated or analyzed during this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Health Research Ethics Board of Drum Tower Hospital of Nanjing University Medical School (2023-214-01), and written informed consent was obtained from all the patients included in the study.

Consent for publication

Written informed consent for publication was obtained from all participants.

Competing interests

The authors declare no competing interests.

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