

Acta Chir Croat 2019; 16: 11-15

SURGICAL TREATMENT OF PERIHILAR CHOLANGIOCARCINOMA: 10-YEAR EXPERIENCE AT A SINGLE INSTITUTION

Ivan Romić, Igor Petrović, Ante Zvonimir Golem, Emil Kinda, Tihomir Kekez, Goran Augustin, Hrvoje Silovski, Tomislav Bruketa, Trpimir Morić, Željko Jelinčić

ABSTRACT

Background: Our study evaluates surgical outcomes of patients treated for perihilar cholangiocarcinoma in a single institution and demonstrates postoperative (90 days) morbidity and mortality rates and potential prognostic factors associated with complications.

Methods: Medical records of all patients with a diagnosis of perihilar cholangiocarcinoma (pCC) between 2007 and 2017 who underwent a surgical procedure at the University hospital centre Zagreb, were retrospectively evaluated. Statistical analysis to determine predictors of postoperative mortality was performed using the Chi-square test and Fisher exact probability test where appropriate.

Results: Out of 52 surgically treated patients, 43 underwent radical and 9 palliative procedures. Hilar resection and hilar resection along with right hepatectomy were the most commonly performed procedures in 34 radically treated patients. Overall morbidity and mortality rates were 46% and 5.7%, respectively. Significantly higher morbidity rate was observed in a group of patient with untreated preoperative jaundice and in those aged 70 and over.

Conclusion: Current guidelines favor extension of radicality in treatment of pCC by performing left or right hepatectomy in addition to hilar resection. This may increase R0 resection rates and prolong disease free survival. Our experience shows similar mortality/morbidity rates as reported in other centers and confirms that in selected patients, concomitant hepatectomy for perihilar pCC is a safe and feasible surgical strategy.

Keywords:

Perihilar cholangiocarcinoma, surgical outcome, survival, Klatskin tumor

Introduction

Perihilar cholangiocarcinoma (pHCC) is the second most common primary cancer of the liver with a generally poor prognosis and it represents a difficult challenge for hepatobiliary surgeons not just because of aggressive nature of the cancer, but also because of variable anatomical

relations of hilar structures. Historically, the surgery for this cancer was characterized by high mortality rates but also surgeons were confronted with a low resectability rate (up to 50%) and high recurrence rates (50% to 70%) [1,2].

However, over the last decade, studies suggest some progress in treatment and slight improvement in outcome that have mainly derived from a better understanding of the tumor spread and improved technique of liver parenchymal transection [3].

In addition, it can be also explained by wider indications and adopting more radical surgical procedures that include standard or extended hepatectomies along with resection of extrahepatic biliary ducts and portal vein/hepatic artery if necessary.

Material and Methods

Our paper is a review of 10 years' experience with 574 resections for perihilar cholangiocarcinoma in a tertiary institution. Medical records of all patients with a diagnosis of perihilar cholangiocarcinoma (pCC) between 2007 and 2017 who underwent surgical procedure at our surgical department were retrospectively evaluated.

We demonstrate demographic and baseline patient characteristics, intraoperative factors and outcome in terms of morbidity mortality and 1 year disease free survival. Results are expressed as the medians, range and proportions. Statistical analysis to determine predictors of postoperative mortality was performed using the Chi-square test and Fisher exact probability test where appropriate.

Results

Baseline characteristics of patients are shown in Table 1. Out of 52 patients, 31 were men and the median age was 69 years. In the majority of cases (28) preoperative endoscopic stenting was placed to manage obstructive jaundice. Resection procedures comprised 83% of cases (34 R0, 7 R1 and 2 R2 resections) and 9 included exploration laparotomy and palliative procedure only due to distant metastasis or advanced local disease (Figure 1.)

Bile duct resection alone (hilar resection) was performed in 17 and bile duct resection coupled with right hepatectomy in 12 patient. Other types of hepatectomies, left and extended right, were less commonly done, in 3 and 2 cases, respectively. Portal vein resection and reconstruction was required in 4 cases to achieve adequate radicality. Other procedures included resections of primary tumor and metastasectomy (4 cases), pancreaticoduodenectomy (2 cases), partial gastrectomy and transverse colon resection. In resectable cases, a bilio-digestive anastomosis was constructed by means of hepatico-jejunostomy in 37, and choledocho-jejunostomy in 6 cases. Intraoperative characteristics and outcomes are demonstrated in Table 2. Median operative time was 420 minutes and average blood loss 800ml. Hospital stay ranged from 8 to 51 days with a median of 19 days.

Overall morbidity rate was 46% and posthepatectomy liver failure according to the 50:50 definition was the most common complication followed by intraabdominal sepsis and bile leakage. No intraoperative death was seen and three patients died of complications in a postoperative period (within 90 days from the day of surgery).

Liver failure associated with infectious complications was cause of death in all cases.

We conducted comparative univariate study which identified prognostic factors for severe (grade III or more) postoperative morbidity: age over 70 years, and preoperative jaundice that both showed significant association with outcome. Additional hepatectomy resulted in higher, although not statistically significant, morbidity rate while other variables were not associated with morbidity (Table 3).

Discussion

Despite certain advances in chemotherapy, pCC remains a disease which can be cured only by radical surgical procedure. In the last 2 decades, there was a progress in treatment of pCC which can be attributed to significant decrease in surgical morbidity/mortality and expanded indications for radical procedure [4].

Our results presented here are comparable to those reported in literature and we adopted most recent recommendations in this field of surgery[5]. Thereby, we performed surgery in cases which were considered unresectable 10 years ago. This includes vascular infiltration and cases where combined resections of pancreas, stomach, liver or transverse colon are required.

Most authors agree that the goal of surgical treatment of pCC should be an R0 resection, therefore, radical intervention for type 3 and 4 tumors should include resection of the bile duct with lymphadenectomy of the hepatic hilum and right/left hepatectomy including the caudate lobe. However, treatment of type 1 or 2 tumors

is more controversial and most authors suggest hilar resection alone, while the minority of them favor to add right hepatectomy to ensure adequate radicality[6].

In our research, over the time period studied, there was an increasing trend of performing a hilar resection coupled with hepatectomy especially when last 3 years are compared to the period between 2007 and 2009. Such a trend was reported in other research papers as well, and may be explained by the increasing number of evidence that hepatectomy improves R0 resection rates and yields better oncological outcomes compared to hilar resection alone. In addition, our results as well as relevant literature show that hepatectomy does not have significant negative effect on morbidity and mortality rates[7].

We want to highlight that rate of unresectable disease discovered at laparotomy was low (8%). This confirms evolution of more accurate preoperative investigation such as PET scan, EUS and ERCP. Furthermore, in all unresectable cases, some type of palliative procedure was done.

Liver transplantation for pCC was not performed in our institution and this is still under scientific and professional evaluation, but some excellent results have been reported [8]. Preoperative stent insertion is controversial since some authors argue that it may lead to unacceptable risk of cholangitis. However, we adopt the stance to manage biliary obstruction prior to surgery if technical and organizational capabilities allow it.

Conclusions

In conclusion, surgical treatment for pCC has been evolving and improved surgical technique led to expanded surgical indications, satisfactory morbidity/mortality rates and promising oncologic outcome. The most important goal is to achieve R0 resection and preserve sufficient future liver volume. Considering relatively low incidence of pCC, future studies on larger number of patients are required to establish clear guidelines in management of this malignancy.

CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest.

The patient gave her informed consent prior to her inclusion in case report.

REFERENCES:

- Zhang W, Yan LN. Perihilar cholangiocarcinoma: Current therapy. *World J Gastrointest Pathophysiol.* 2014;5(3):344-54.
- Jarnagin WR, Fong Y, DeMatteo RP, Gonen M, Burke EC, Bodniewicz BS J, Youssef BA M, Klimstra D, Blumgart LH. Staging, resectability, and outcome in 225 patients with perihilar cholangiocarcinoma. *Ann Surg.* 2001;234:507-517; discussion 517-519.
- Ramos E. Principles of surgical resection in perihilar cholangiocarcinoma. *World J Gastrointest Oncol.* 2013;5:139-146.
- Kosuge T, Yamamoto J, Shimada K, Yamasaki S, Makuuchi M. Improved surgical results for perihilar cholangiocarcinoma with procedures including major hepatic resection. *Ann Surg.* 1999;230:663-671.
- Hu HJ, Mao H, Shrestha A, et al. Prognostic factors and long-term outcomes of perihilar cholangiocarcinoma: A single-institution experience in China. *World J Gastroenterol.* 2016;22(8):2601-10.
- Kow AW, Wook CD, Song SC, Kim WS, Kim MJ, Park HJ, Heo JS, Choi SH. Role of caudate lobectomy in type III A and III B perihilar cholangiocarcinoma: a 15-year experience in a tertiary institution. *World J Surg.* 2012;36:1112-1121.
- Lillemoe KD, Cameron JL. Surgery for perihilar cholangiocarcinoma: the Johns Hopkins approach. *J Hepatobiliary Pancreat Surg.* 2000;7:115-121.
- Mantel HT, Westerkamp AC, Adam R, et al. Strict Selection Alone of Patients Undergoing Liver Transplantation for Perihilar Cholangiocarcinoma Is Associated with Improved Survival. *PLoS One.* 2016;11(6):e0156127. Published 2016 Jun 8. doi:10.1371/journal.pone.0156127

Patient, disease and procedural characteristics	
Patient Characteristics	All patients (n=52)
Sex (M/F)	31/21
Age (median, range), years	69 (31-82)
BMI, kg/m ² (median, SD)	32.6 (±3.3)
Child-Pugh (A/B)	44/8
ASA score, median	2
Cirrhosis (yes/no)	5/47
Preoperative biliary stent (yes/no)	28/24
Disease characteristics	All patients (n=48)
Preoperative diagnosis(yes/no)*	41/11
Type of tumor **	
- Type I	5 (9.6%)
- Type II	10 (19.2%)
- Type III	23 (44%)
- Type IV	14 (26.4%)
Curative/Palliative	43/9 (83%/17%)
Type of resection	
R0	34
R1	7
R2	2
Palliative	9
*Preoperative pathohistological confirmation	
** According to Bismuth classification	

Table 1. Baseline demographic and disease data

Operative and outcome results	
	All patients (N=52)
Type of procedure	
- Hilar resection	17
- Hilar resection+ right hepatectomy	12
- Hilar resection+ left hepatectomy	3
- Hilar resection+ right hepatectomy	2
- Palliative bilio-digestive bypass	9
- Combined portal vein resections	4
- Other	8
Intraoperative factors	All patients (N=52)
Operative time (median, min)	420/±112
Estimated blood loss (ml)	800±180
ICU stay (median, range) days	6 (3-42)
Hospital stay (median, range) days	19 (8-51)
Outcomes	
90 days mortality	3(5.7%)
Postoperative morbidity*	24(46%)
1 year disease free survival	38 (74%)
Causes of postoperative morbidity	N=24
- Liver failure	11
- Septic complications	7
- Hemorrhage	2
- Bile leakage	2
- Other	2
Trends in additional hepatectomy**	p value
-2007-2012	4/23
-2012-2017	13/25
*According to Clavien-Dindo classification grade >III	
** Prevalence of hepatectomy in two consecutive 5-year periods for resectable cases	

Table 2. Intraoperative factors and outcome

Predictors of severe morbidity			
Variable	No.patients	Morbidity (%)	<i>P</i> value
Age,years			<i>0.006</i>
<70	27	8 (29.6)	
>70	25	16 (64)	
Preoperative jaundice			<i>0.02</i>
yes	28	17 (60)	
no	24	7 (29)	
Concomitant hepatectomy			<i>0.72</i>
yes	17	11 (64.7)	
no	17	9 (52.9)	
Extent of liver resection			<i>0.9</i>
<50%	11	7 (64)	
>50%	6	4 (66)	
Blood loss (ml)			<i>0.82</i>
<800	29	13 (56)	
>800	23	11 (47)	

Table 3. Univariate analysis of predictors of severe postoperative morbidity

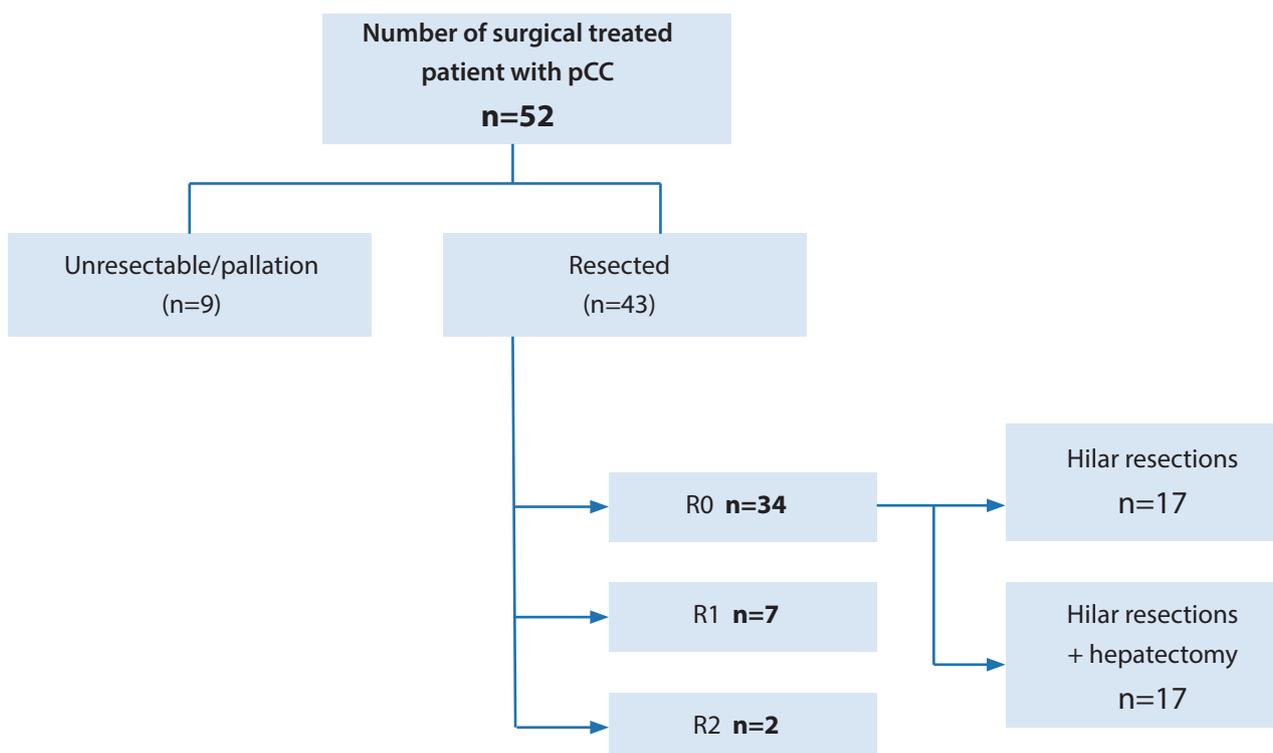


Figure 1. Flowchart of the study

