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SURGICAL TREATMENT OF THE PERIHILAR CHOLANGIOCARCINOMA WITH PORTAL VEIN INVASION

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Abstract

Background. Perichilar cholangiocarcinoma is a rare type of malignant neoplasm and is 3-7 cases per 100,000 population. Surgical method is the only radical method of treatment, allowing to improve long-term survival results. One of the important and characteristic features of perihilar cholangiocarcinoma is tumor invasion to the area of the portal vein bifurcation, which occurs in 30–45% of cases**.** Portal vein invasion is the one of the main causes of perihilar cholangiocarcinoma irresectability. However, innovative surgical technologies allow resection of the liver with resection and reconstruction of the portal vein with acceptable mortality.

The aim. The aim of our study was to asses results of surgical treatment of perihilar cholangiocarcinoma with (Group 1) and without (Group 2) portal vein invasion.

Materials and methods. From 2003 to January 2023 in the Department of Surgery and Liver Transplantation of the Ukrainian National Institute of Surgery and Transplantation,

208 patients with perihilar cholangiocarcinoma underwent major extended liver resections. We compared 93 (46%) patients who received extended liver resection with portal vein resection (Group 1) with 115 (54%) patients who underwent liver resections without vascular reconstructions (Group 2). The average Ca 19–9 in the group 1 was 288 (8 – 1000) U/ml, in the group 2 –262 (10 – 612) U/ml. The level of total bilirubin in patients of the group 1 was 312 (43 – 621) mcmol/l, in the group 2 – 267 (10 – 612) mcmol/l. In view of this, in the preoperative period, 190 (91,3%) patients underwent decompression of the bile ducts, using percutaneous transhepatic cholangiostomy (PTBD) or retrograde endobiliary stenting. For patients with small remnant liver volume less than 40 %, in 80(38,5%) cases we did preoperative PVE of a resected part of the liver. In 9 cases we made simultaneous PVE and PTBD. When choosing the volume of surgical intervention, we proceeded from the tumor type of Bismuth-Corlette classification, invasion into the portal vessels and the depth of the liver lesion. The portal vein reconstruction was in all cases performed in an “end-to-end”. In all cases we made extended lymphadenectomy.

Results. All complications were classified according to the Dindo-Clavien classification. Postoperative mortality in the main group was 11.5%. The overall 1, 3, 5-year survival in the group 1 was 96%, 68,3%, 57,4%, respectively. 1, 3, 5-year survival rate in the comparison group 2 was 98,4%, 76,7%, 47,3%, respectively.

Conclusions. Aggressive tactics of surgical treatment of perihilar cholangiocarcinoma provides maximum radicality, allows to increase resectability in case of tumor invasion of the portal vein with acceptable mortality and long-term survival.

Keywords: perihilar cholangiocarcinoma; portal vein invasion; surgical treatment; liver resection; long-term survival; radicality.

Introduction

Cholangiocarcinoma is a malignant tumour originating from the biliary tree epithelium, occupying the second place after hepatocellular cancer, primary malignant liver tumours [1, 2, 3]. Cholangiocarcinoma account for up to 3% of all malignant tumours of the abdominal cavity [2, 4, 5]. Previously, cholangiocarcinoma was anatomically divided into three types – intrahepatic cholangiocarcinoma, hilar cholangiocarcinoma, and distal cholangiocarcinoma [4, 6, 7]. Recently, a lot of authors use the term "perihilar cholangiocarcinoma". In 1965, the American pathologist Gerald Klatskin [8], was the first to describe the clinical features of 13 patients with hilar cholangiocarcinoma. According to TNM classification of International Union Against Cancer (UICC) edition 7, the perihilar

cholangiocarcinoma is taken to mean cholangiocarcinoma with biliary duct lesions of liver portals, i.e. biliary ducts topologically located between the right edge of the umbilical portion of the left branch of the portal vein and the mouth of the right posterior sectional branch of the portal vein, and distally restricted place of entrance of the cystic duct [9]. Thus, in the modern surgical literature, three equally important terms are used, which determine the same localization of cholangiocarcinoma confluence of the bile ducts – the hilar, perihilar and Klatskin tumours. Perihilar cholangiocarcinoma – the most common type, is detected from 50 to 70% of all malignant tumours of the bile ducts [7, 10]. The incidence of intrahepatic and distal cholangiocarcinoma is 6-10% and 25-30%, respectively. One of the important and characteristic features of perihilar cholangiocarcinoma is tumour invasion to the area of the portal vein bifurcation, which occurs in 30–45% of cases [11, 12]. Perihilar cholangiocarcinoma is a complex cancer pathology and its surgical treatment remains one of the difficult problems of surgical hepatology. However, since liver resection surgery is the only radical treatment for perihilar cholangiocarcinoma, many of the world's best clinics have adopted an aggressive approach. Recently, with the development of new methods of pre-operative diagnosis and the use of transplant technologies of liver surgery has led to an increase in radical surgical interventions and long-term survival rates.

Nevertheless, there are still many contradictions in the approaches to the treatment of Klatskin tumor. This is caused by low prevalence rate, relatively small groups of studies in various clinics and the lack of large randomized studies.

Materials and methods

From 2003 to January 2023, 276 patients with perihilar cholangiocarcinoma were examined in the Department of Surgery and Liver Transplantation of the National Institute of Surgery and Transplantation of NAMS of Ukraine. In 68 (24.6%) cases, due to the detection of distant metastases, carcinomatosis, or poor liver function, radical surgical interventions were not performed. 208 patients underwent radical liver resections. In 93 (46 %) cases, due to invasion of the perihilar cholangiocarcinoma in the portal vein confluence, liver resection was supplemented with resection and reconstruction of the latter. These 93 (46 %) patients are included in the main study group 1. The experimental group consisted of 115 (54%) patients who underwent liver resections without vascular reconstructions. 120 (57,7%) patients were male, 88 (42,3%) patients were female. The average age of patients in the main group was 57 (37 – 81) years in the experimental group of 57.1 (26 – 74) years (Table 1).

Table 1. Patient and tumor characteristics in two study group (group 1 – with portal vein resection, group 2 – without portal vein resection)

	Group 1 n-93 (46 %)		Group 2 n-115 (54%)		P-value
	n	%	n	%	
Male/ Female	55/38	61,5/38,5	65/50	62,1/37,9	0.898
Age, y	57 (37 – 81)		57,1(26 – 74)		0,829
Bilirubin (mmol/l)	312 (43 – 621)		267 (10 – 612)		0,063
Ca 19-9	288(8 – 1000)		262 (2,5 – 1200)		0,696
TNM					
T2a	3	1,2	15	10,5	0,771
T2b	7	4,9	31	20	0,003
T3	68	76,8	55	54,8	0,002
T4	15	17,1	14	14,7	0.926
N0	72	78,1	88	77,9	0,865
N1	16	15,8	18	17,9	0,505
N2	5	6,1	8	4,2	0,325
M0	93	100	113	97,9	
M1	-		2	2,3	
Bismuth-Corlette classification					
B1	-		-		
B2	-		10	8,4	
B3a	44	47,6	47	36,8	0,783
B3b	36	40,2	44	41,1	0,973
B4	13	12,2	14	13,7	0346

All patients underwent preoperative examination, including general, biochemical analysis of blood, ultrasound of the abdominal organs, EGD, colonoscopy, echocardiography. Three-phase computed tomography of the abdominal organs and chest was mandatory. According to the spiral computed tomography, damage to the liver parenchyma, invasion of the portal vessels, hepatic veins, the presence of extrahepatic metastases was evaluated and the volume of the remaining part of the liver was calculated (Fig. 1). Magnetic resonance

imaging and cholangiography were performed to assess the lesion of the biliary tree of all patients (Fig. 2).

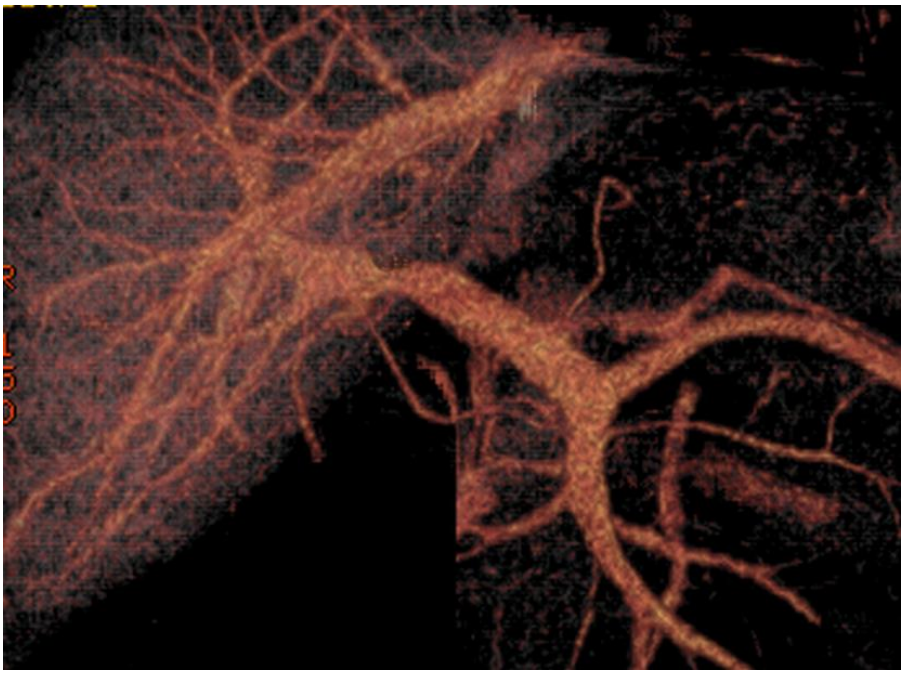

Fig. 1 Spiral computed tomography. Bismuth-Corlette type IIIb perihilar cholangiocarcinoma with portal vein invasion.

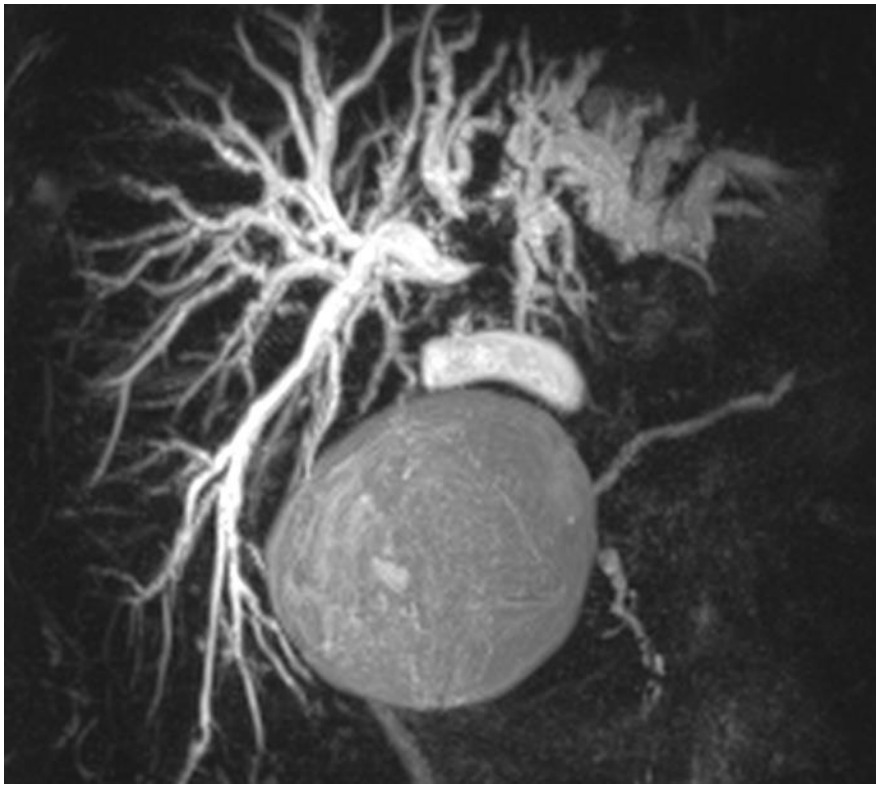

Fig. 2 Magnetic resonance cholangiography. Bismuth-Corlette type IIIb perihilar cholangiocarcinoma.

All patients underwent serological tumour marker tests. The most specific tumour marker in perihilar cholangiocarcinoma was the carbohydrate antigen CA 19-9. The average Ca 19–9 in the main group was 288 (8 – 1000) U/ml, in the experimental group (10 – 612) 262 U/ml. It is known that with an increase in the level of CA 19-9 by more than 180 U/ml, its sensitivity is 79% and specificity – 98% [13, 14, 15].

Obstruction of the bile ducts can lead to bacterial translocation, impaired blood coagulation, renal failure and an increased risk of developing liver failure in the postoperative period [16, 17]. The level of total bilirubin in patients of the main group was 312 (43 – 621) mcmol/l, in the experimental group – 267 (10 – 612) mcmol/l. In view of this, in the preoperative period, 116 (88.5%) patients underwent decompression of the bile ducts, using their external drainage under x-ray or ultrasound control, or retrograde endobiliary stenting (Table 2).

Table 2. Preoperative biliary decompression and portal vein embolization in two study group (group 1 – with portal vein resection, group 2 – without portal vein resection)

	Group 1 n-93 (46 %)		Group 2 n-115 (54%)		p-value
	n	%	n	%	
Without decompression	2	2,6	16	18,2	0.001
PTBD right bile duct	30	34,6	30	30,7	0,413
PTBD left bile duct	29	29,5	32	23,8	0,454
PTBD right and left bile duct	21	24,4	22	19,4	0,432
Endoscopic biliary drainage	7	8,9	8	7,9	0,814
PVE RPV	19	20,5	38	29,6	0,182
PVE RPV + Sg 4	9	7,7	5	4,6	0,395
PVE LL	2	1,3	7	5,7	0,129

Percutaneous transhepatic cholangiostomy (PTBD) of the right lobar duct was performed in 60 (28,8%) cases, the left lobe duct – in 61 (29,3%) cases, the right and left lobe ducts together – in 43 (20,7%) cases. 15 (7,2%) patients underwent retrograde endobiliary stenting. The time from decompression of the biliary tree to the performance of surgery was 50 (13 – 126) days. In the preoperative period, an acceptable level of serum bilirubin was <60 mcmol/l. All patients in the preoperative period had the volume of the remaining part of the liver evaluated with the use of computer volumetry. In cases where the planned hepatic residue was less than 35% of the total liver volume, we performed X-ray endovascular embolication of the portal vein branches (PVE). In 57 (27,4%) cases, patients with Bismuth-

Corlette type IIIa perihilar cholangiocarcinoma underwent embolization of the right lobar branch of the portal vein. In 14 (6,7%) cases, patients with Bismuth-Corlette type IV perihilar cholangiocarcinoma underwent embolization of the right and segmental Sg 4 portal vein branch. In 9 (4,3%) cases, patients with Bismuth-Corlette type IIIb perihilar cholangiocarcinoma underwent occlusion of the left lobar branch of the portal vein. On day 21-28, to assess the degree of liver regeneration, these patients underwent repeated spiral computed tomography with the volumetry of the remaining portion of the liver. With the help of embolization of the corresponding branch of the portal vein, it was possible to reach an increase in the remaining liver residue on average by 25-35%, which made it possible to reduce the manifestations of liver failure in the postoperative period.

Results

During the period from 2003 till January 2023, 208 radical surgical interventions were performed in cases of perihilar cholangiocarcinoma at the National Institute of Surgery and Transplantation. In all cases the first stage included the performance of extended lymph node dissection of lymph nodes of groups 5, 7, 8, 9, 12, 13, 14, 16 and 17 according to the Japanese classification of lymph nodes. When choosing the volume of surgical intervention, we proceeded from the type of biliary tree lesion according to Bismuth-Corlette classification, invasion into the portal vessels and the depth of the liver lesion. Thus in, in case of type IIIa, in 30(31,7%) cases the main group underwent right hemihepatectomy, in 14 (15,8%) cases – right-sided trisectioectomy. In 34 (37,8%) cases with Bismuth-Corlette type IIIb biliary tree lesion, left-sided hemihepatectomy was performed, and in 2 (2,4%) case – left-sided trisectionectomy. In case of type IV, we performed 11 (10,9%) right-sided trisectionectomies and 2 (1.2%) left-sided liver trisectionectomy. Characteristics of surgical interventions are presented in Table 3. The portal vein reconstruction was in all cases performed in an “end-to-end” form between the trunk of the portal vein and the branch of the portal vein of the remaining part of the liver. The average duration of portoplasty was 28.4 (15 – 53) minutes. The duration of the operation in the main group was 518 (325 – 850) minutes, and in the experimental group – 485 (330 – 905) minutes. Intraoperative blood loss was 1133 (100 – 4090) ml in the main group, 700 (250 – 2200) ml.

Histologically, the tumour in the main group in 13 (12,2%) cases was well differentiated, in 71 (78,1 %) cases – moderate differentiated, in 9 (9,7 %) cases – poor differentiated (Table 4). According to a histological study, metastatic lesion of 1-3 regional lymph nodes (N1) was detected in 16 (15,8%) patients, 4 or more (N2) – in 5 (6,1%) patients (Table 1).

Table 3. Types of liver resection depending on Bithmuth-Corlette classification in two study group (group 1 – with portal vein resection, group 2 – without portal vein resection)

Bismuth-Corlette classification	Group 1 n-93 (46 %)		Group 2 n-115 (54%)		p-value
	N	%	n	%	-
B2	-		9	8,4	-
Sg 4,5,8	-		4	4,2	-
RL	-		3	2,1	-
LL	-		3	2,1	-
B3a	44	47,6	45	34,7	0,080
RL	30	31,7	39	29,5	0,727
RTS	14	15,8	6	5,3	0,018
B3b	36	40,2	45	42,1	0,894
LL	34	37,8	38	36,8	0,863
LTS	2	2,4	7	5,3	0,903
B4	13	12,2	145	14,7	0,539
RTS	11	10,9	6	6,3	0,426
LTS	2	1,2	9	8,4	0,051

Table 4. Histologic differentiation and type of tumour growth in two study group (group 1 – with portal vein resection, group 2 – without portal vein resection)

	Group 1 n-93 (46 %)		Group 2 n-115 (54%)		p-value
Histologic differentiation	n.	%	n.	%	
Well differentiated	13	12,2	16	13,7	0,716
Moderate differentiated	71	78,1	91	78,9	0,818
Poor differentiated	9	9,7	7	7,4	0,425
The type of tumour growth					
Periductal infiltrative growth	37	37,8	42	35,8	0,579
Polypoid (intraductal) growth	40	43,9	54	46,3	0,607
Mass-forming or nodular	15	18,3	18	17,9	0,988

The type of tumour growth was also investigated in the main group and the experimental group. Thus, intraductal growth was most often detected in 40 (43,9%) cases, periductal growth – in 37 (37,8%) cases, and the least frequent type of growth was mass-forming or nodular, which was detected in 15 (18,3%) cases.

The incidence of postoperative complications and mortality was not significantly different in both groups. All complications were classified according to the Dindo-Clavien classification (Table 5). In the main group of patients, most frequently in the postoperative period, liver failure was observed in 55 (31,1%) patients, which required a stay in the

intensive care unit. In 23 (12,9%) patients, bile bleeding from the wound surface of the liver was observed, which were drained under ultrasound control. In 6 (3,4 %) patients, there were hepaticojejunostomy leaks, which required relaparotomy with the formation of rehepaticojejunostomy.

Postoperative mortality in the main group was 10,8%. The causes of postoperative mortality in 11 cases were multiple organ failure and sepsis, in 2 case – coagulopathic bleeding, in 5 case – acute cardiovascular insufficiency, in 1 case – thrombosis of the hepatic artery, in 1 case – thrombosis of the portal vein.

Table 5. Postoperative complication in two study group (group 1 – with portal vein resection, group 2 – without portal vein resection)

Grade Dindo-Clavien	Complications	Group 1 n-61 (46,6%)		Group 2 n-70 (53,4%)		p-value
		n	**%**	n	%	
Grade IIIa	Hepatic abcess	2	3,3	-		
	Pleural effusion	3	4,9	6	8,6	0,409
	Bile leak	5	8,2	13	18,6	0,853
Grade IIIb	PV hemorrhage	1	1,6	1	1,4	0,921
	HA hemorrhage	1	1,6	-		
	Biliary fistula	2	3,3	3	4,3	0,764
Grade IVa	Liver failure	10	16,4	6	8,6	0,172
Grade IVb	Sepsis	2	3,3	-		
Grade V	Death	7	11,5	8	11,4	0,993

The overall 1, 3, 5-year survival in the group 1 was 96%, 68,3%, 57,4%, respectively. 1, 3, 5-year survival rate in the comparison group 2 was 98,4%, 76,7%, 47,3%, respectively (Fig. 3).

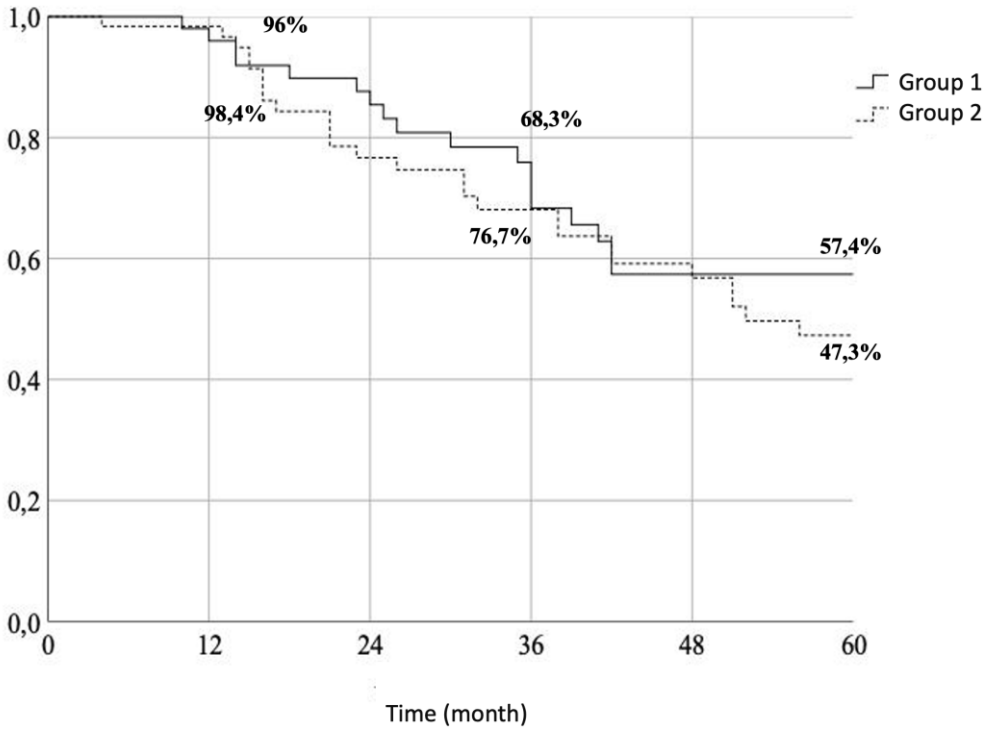

Fig 3. Overall survival in studies group (group 1 – with portal vein resection, group 2 – without portal vein resection)

Discussion

Surgical treatment of perihilar cholangiocarcinoma remains one of the most acute problems of surgical hepatology, connected with the difficulty of performing R0 resection due to frequent invasion of the hepatoduodenal ligament into the vessels.

The initial concept of isolated bile duct resection without liver resection and palliative procedures resulted in local recurrences in the first year in 76% of patients [18]. Miyazaki et al. in their study showed that with isolated resection of the extrahepatic bile ducts, five-year survival is absent, while five-year survival of patients, who underwent liver resection, was 27% [19].

Recent advances in surgical techniques and perioperative patient management, including anesthetic management, reduction of intraoperative blood loss, management of central venous pressure, nutritional support, led to an improvement in the results of surgical treatment of perihilar cholangiocarcinoma [20, 21]. Perioperative mortality decreased from 90% to less than 10%. This development has prompted many leading surgical centers to aggressive treatment of patients with perihilar cholangiocarcinoma. In 1990, Nimura Y. et al. proposed the concept of a routine total caudal lobectomy [22]. This idea is associated with tumour infiltration along the biliary tree and the spreading of the caudate lobe of the liver to

the bile ducts. This approach has led to the possibility of performing R0 liver resections in case of perihilar cholangiocarcinoma and an increase in 5-year survival from 5% to 40% [22, 23, 24]. On the other hand, an aggressive approach and the implementation of extensive liver resections led to an increase in the incidence of postoperative liver failure [25]. However, the development of endovascular technologies and the ability to simulate a hepatic remnant in the preoperative period, by embolization of the portal vein branches, made it possible to reduce postoperative mortality as a result of liver failure to 20%. Thus in 1982, Makuuchi et al. first proposed a method of embolization of the right lobar branch of the portal vein to prevent postoperative liver failure [26]. Ebata T. et al. reported a series of 353 patients with perihilar cholangiocarcinoma who underwent embolization of the portal vein branches of the removed part of the liver before extended hemihepatectomy [27]. In this series, resectability was 83%, postoperative mortality was 4%, and five-year survival increased to 40%. Thus, the use of preoperative decompression of the biliary tree and modelling of the hepatic remnant before liver resection with perihilar cholangiocarcinoma contributes to an increase in resectability with a decrease in postoperative mortality [18, 28, 29].

Invasion of the perihilar cholangiocarcinoma into the portal vein remains the main obstacle to the implementation of surgical interventions. However, the development of hepatobiliary surgery and the introduction of transplantation technologies have made it possible to expand the indications for radical surgical interventions. In their study Ebata T. et al. report that when a perihilar cholangiocarcinoma invades a portal vein, a portal vein resection followed by portoplasty leads to an increase in 5-year survival from 10% to 37% [30].

As the concept of resection of the portal vein developed, Neuhaus P. et al. proposed a new method for achieving a radical surgical treatment of perihilar cholangiocarcinoma [31, 32]. This is the so-called hilar en block resection or non-touch technique, which includes extended right-sided trisectomyectomy (Sg1,4-8), resection of the portal vein bifurcation, resection of the right hepatic artery and extrahepatic bile ducts. The study reported an increase in five-year survival to 58% compared with standard hemihepatectomy (29%). However, the disadvantage of the technique is a high risk of postoperative liver failure, high postoperative mortality, limited use only for Bismuth-Corlette type IIIa and IV perihilar cholangiocarcinoma.

Our approach to the choice of surgical intervention is based on the level of damage to the biliary tree according to Bismuth-Corlette classification. Thus, in case of type IIIa damage to the bile ducts, we perform right-side hemihepatectomy, or right-sided trisectionectomy. In

case of Bismuth-Corlette type IIIb lesion of the biliary tree, we perform left-sided hemihepatectomy or left-sided trisectionectomy. In case of type IV, we performed right-sided trisectionectomy or left-sided liver trisectionectomy. The choice of the volume of the removable part of the liver depended on the level of lesion of the portal vein.

Conclusions

1. Invasion of the perihilar cholangiocarcinoma into the portal vein dictates the need for its resection and reconstruction and is not a contraindication to radical surgical treatment.

2. Aggressive tactics, including resection of the bile ducts, of the corresponding liver parenchyma and necessarily the caudate lobe, with a resection of the portal vein, provides maximum radicalism, allows to increase the resectability of perihilar cholangiocarcinoma.

3. Innovative surgical technologies for the treatment of perihilar cholangiocarcinoma provide satisfactory immediate and long-term results with an acceptable level of mortality and long-term survival.

Author Contribution

Conceptualization, methodology, formal analysis, data curation, writing - O. O. Popov

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Institutional Review Board Statement

This case report did not require IRB approval, patient provided verbal and written consent for publication of this report.

Informed Consent Statement

Written informed consent has been obtained from the patient to publish this paper.

Data Availability Statement

All information is publicly available and data regarding this particular patient can be obtained upon request from corresponding senior author.

Conflicts of Interest

The author declare no conflict of interest.

References

1. Blechacz BR, Gores GJ. Cholangiocarcinoma. Clin Liver Dis. 2008;12(1):131-50, ix.

2. Gatto M, Bragazzi MC, Semeraro R, Napoli C, Gentile R, Torrice A, et al. Cholangiocarcinoma: update and future perspectives. Dig Liver Dis. 2010;42(4):253-60.

3. Sripa B, Pairojkul C. Cholangiocarcinoma: lessons from Thailand. Curr Opin Gastroenterol. 2008;24(3):349-56.

4. Patel T. Cholangiocarcinoma. Nat Clin Pract Gastroenterol Hepatol. 2006;3(1):33-42.

5. Shaib Y, El-Serag HB. The epidemiology of cholangiocarcinoma. Semin Liver Dis. 2004;24(2):115-25.

6. Dondossola D, Ghidini M, Grossi F, Rossi G, Foschi D. Practical review for diagnosis and clinical management of perihilar cholangiocarcinoma. World J Gastroenterol. 2020 Jul 7;26(25):3542-3561.

7. Nakeeb A, Pitt HA, Sohn TA, Coleman J, Abrams RA, Piantadosi S, et al. Cholangiocarcinoma. A spectrum of intrahepatic, perihilar, and distal tumors. Ann Surg. 1996;224(4):463-73; discussion 73-5.

8. Klatskin G. Adenocarcinoma of the Hepatic Duct at Its Bifurcation within the Porta Hepatis. An Unusual Tumor with Distinctive Clinical and Pathological Features. The American journal of medicine. 1965;38:241-56.

9. (UICC) IUAC, editor. TNM classification of malignant tumors. 7th ed. New York2009.

10. Mizuno, Takashi MD*; Ebata, Tomoki MD*; Yokoyama, Yukihiro MD*; et al. Combined Vascular Resection for Locally Advanced Perihilar Cholangiocarcinoma Ann Surg. 2022;275(2) p. 382-390.

11. Wu XS, Dong P, Gu J, Li ML, Wu WG, Lu JH, et al. Combined portal vein resection for hilar cholangiocarcinoma: a meta-analysis of comparative studies. J Gastrointest Surg. 2013;17(6):1107-15.

12. de Jong MC, Marques H, Clary BM, Bauer TW, Marsh JW, Ribero D, et al. The impact of portal vein resection on outcomes for hilar cholangiocarcinoma: a multi-institutional analysis of 305 cases. Cancer. 2012;118(19):4737-47.

13. Yang WL, Zhang XC, Zhang DW, Tong BF. Diagnosis and surgical treatment of hepatic hilar cholangiocarcinoma. Hepatobiliary Pancreat Dis Int. 2007;6(6):631-5.

14. Juntermanns B, Kaiser GM, Reis H, Saner FH, Radunz S, Vernadakis S, et al. Klatskin-mimicking lesions: still a diagnostical and therapeutical dilemma? Hepatogastroenterology. 2011;58(106):265-9.

15. Van Gulik TM, Dinant S, Busch OR, Rauws EA, Obertop H, Gouma DJ. Original article: New surgical approaches to the Klatskin tumour. Aliment Pharmacol Ther. 2007;26 Suppl 2:127-32.

16. Hemming AW, Reed AI, Fujita S, Foley DP, Howard RJ. Surgical management of hilar cholangiocarcinoma. Ann Surg. 2005;241(5):693-9; discussion 9-702.

17. Oussoultzoglou E, Jaeck D. Patient preparation before surgery for cholangiocarcinoma. HPB (Oxford). 2008;10(3):150-3.

18. Nimura Y, Kamiya J, Kondo S, Nagino M, Uesaka K, Oda K, et al. Aggressive preoperative management and extended surgery for hilar cholangiocarcinoma: Nagoya experience. J Hepatobiliary Pancreat Surg. 2000;7(2):155-62.

19. Miyazaki M, Ito H, Nakagawa K, Ambiru S, Shimizu H, Shimizu Y, et al. Aggressive surgical approaches to hilar cholangiocarcinoma: hepatic or local resection? Surgery. 1998;123(2):131-6.

20. Jarnagin WR, Gonen M, Fong Y, DeMatteo RP, Ben-Porat L, Little S, et al. Improvement in perioperative outcome after hepatic resection: analysis of 1,803 consecutive cases over the past decade. Ann Surg. 2002;236(4):397-406; discussion -7.

21. Melendez JA, Arslan V, Fischer ME, Wuest D, Jarnagin WR, Fong Y, et al. Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. J Am Coll Surg. 1998;187(6):620-5.

22. Nimura Y, Hayakawa N, Kamiya J, Kondo S, Shionoya S. Hepatic segmentectomy with caudate lobe resection for bile duct carcinoma of the hepatic hilus. World J Surg. 1990;14(4):535-43; discussion 44.

23. Dinant S, Gerhards MF, Busch OR, Obertop H, Gouma DJ, Van Gulik TM. The importance of complete excision of the caudate lobe in resection of hilar cholangiocarcinoma. HPB (Oxford). 2005;7(4):263-7.

24. Wahab MA, Sultan AM, Salah T, Fathy O, Elebidy G, Elshobary M, et al. Caudate lobe resection with major hepatectomy for central cholangiocarcinoma: is it of value? Hepatogastroenterology. 2012;59(114):321-4.

25. Ellis RJ, Soares KC, Jarnagin WR. Preoperative Management of Perihilar Cholangiocarcinoma. Cancers (Basel). 2022 Apr 24;14(9):2119.

26. Makuuchi M, Thai BL, Takayasu K, Takayama T, Kosuge T, Gunven P, et al. Preoperative portal embolization to increase safety of major hepatectomy for hilar bile duct carcinoma: a preliminary report. Surgery. 1990;107(5):521-7.

27. Ebata T, Yokoyama Y, Igami T, Sugawara G, Takahashi Y, Nagino M. Portal vein embolization before extended hepatectomy for biliary cancer: current technique and review of 494 consecutive embolizations. Dig Surg. 2012;29(1):23-9.

28. Kawasaki S, Imamura H, Kobayashi A, Noike T, Miwa S, Miyagawa S. Results of surgical resection for patients with hilar bile duct cancer: application of extended hepatectomy after biliary drainage and hemihepatic portal vein embolization. Ann Surg. 2003;238(1):84-92.

29. Sano T, Shimada K, Sakamoto Y, Yamamoto J, Yamasaki S, Kosuge T. One hundred two consecutive hepatobiliary resections for perihilar cholangiocarcinoma with zero mortality. Ann Surg. 2006;244(2):240-7.

30. Ebata T, Nagino M, Kamiya J, Uesaka K, Nagasaka T, Nimura Y. Hepatectomy with portal vein resection for hilar cholangiocarcinoma: audit of 52 consecutive cases. Ann Surg. 2003;238(5):720-7.

31. Neuhaus P, Jonas S, Settmacher U, Thelen A, Benckert C, Lopez-Hanninen E, et al. Surgical management of proximal bile duct cancer: extended right lobe resection increases resectability and radicality. Langenbecks Arch Surg. 2003;388(3):194-200.

32. Neuhaus P, Thelen A, Jonas S, Puhl G, Denecke T, Veltzke-Schlieker W, et al. Oncological superiority of hilar en bloc resection for the treatment of hilar cholangiocarcinoma. Ann Surg Oncol. 2012;19(5):1602-8.