Int J Clin Exp Med 2016;9(11):21320-21326
www.ijcem.com /ISSN:1940-5901/IJCEM0033806

Original Article

Hepatic artery reconstruction for advanced hilar cholangiocarcinoma: surgical indication expanded

Yi Shao[1], Jiaojiao Feng[2], Qiyi Zhang[1], Weilin Wang[1], Min Zhang[1], Yan Shen[1], Sheng Yan[1], Shusen Zheng[1]

[1]Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, P. R. China; [2]Department of Gynecologic Oncology, Women's Hospital, School of Medicine, Zhejiang University, Hangzhou, P. R. China

Received June 15, 2016; Accepted August 15, 2016; Epub November 15, 2016; Published November 30, 2016

Abstract: *Objective:* To outline our experience with reconstruction of the hepatic artery during radical resection of hilar cholangiocarcinoma, and to discuss the clinical significance of this challenging surgery. *Methods:* We retrospectively reviewed clinical data of 16 patients with advanced hilar cholangiocarcinoma who underwent left hepatectomy with simultaneous resection and reconstruction of the right hepatic artery with or without portal vein reconstruction, focusing on the type of hepatic artery reconstruction and surgical outcome. *Results:* Right hepatic artery was reconstructed with end-to-end anastomosis (n=10), using the autologous greater saphenous vein graft interposition (n=1), the autologous left hepatic artery graft interposition (n=2), the reserved left hepatic artery (n=1), or the gastroduodenal artery (n=2), among which 6 patients underwent portal vein reconstruction simultaneously. Post-operative pathology showed poorly differentiated adenocarcinoma in 6 patients, moderately differentiated adenocarcinoma in 8 and well differentiated adenocarcinoma in 2. R0 resection was achieved in 15 patients. There was no postoperative liver failure, biliary-enteric anastomotic leakage or perioperative deaths. *Conclusions:* Reconstruction of the hepatic artery can improve the radical resection rate of advanced hilar cholangiocarcinoma and control the postoperative complications, which is safe and feasible in selected patients.

Keywords: Bile duct neoplasms, cholangiocarcinoma, hepatic artery, reconstruction

Introduction

Radical tumor resection still remains the optimal choice for the therapy of hilar cholangiocarcinoma. However, achieving negative surgical margins often ends in failure because of vascular invasion. Now portal vein reconstuction has become a routine surgical procedure and been well described in the former researches [1-4]. Hepatic artery reconstruction for advanced hilar cholangiocarcinoma is still the most arduous challenge for hepatobiliary surgeons. Fortunately, in the era of liver transplantation, recent advances in surgical techniques facilitated the performance of hepatic artery reconstruction [5, 6].

In this study, we outlined our surgical experience of left hepatectomy combined with resection and reconstruction of right hepatic artery (RHA) with or without portal vein reconstruction for advanced hilar cholangiocarcinoma, and we also discuss the clinical significance of this challenging surgery.

Patients and methods

Patients

Between August 2008 and August 2015, 16 patients underwent left hepatectomy with simultaneous resection and reconstruction of the right hepatic artery in our center, due to advanced hilar cholangiocarcinoma. There were 10 men and 6 women with a mean age of 59.8 years (38-76 years). All the 16 patients were jaundiced upon admission, with a mean total serum bilirubin concentration of 234 μmol/L (23-427 μmol/L). Percutaneous transhepatic cholangial drainage (PTCD) (n=8) or endoscopic nasobiliary drainage (ENBD) (n=4) was performed in 9 patients to treat segmental cholangitis, to relieve jaundice and to define the anatomy of biliary tree.

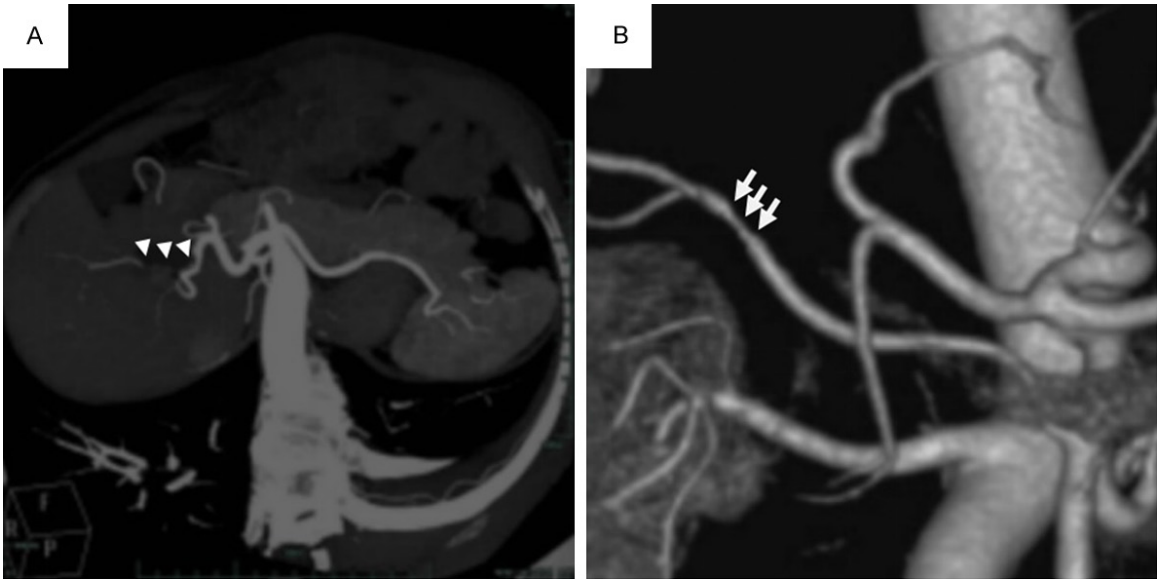

Figure 1. Three-dimensional volume-rendered images. A: Encasement of the right anterior hepatic artery and the bifurcation was found (Δ). This patient underwent left trisectionectomy and caudate lobectomy with right posterior hepatic artery reconstruction. B: Encasement of the variable right hepatic artery coming from the superior mesenteric artery was found (arrow). This patient underwent hepatic artery reconstruction using the gastroduodenal artery.

Table 1. Surgical Procedures for Hilar Cholangiocarcinoma (August 2008-August 2015)

Type of Hepatectomy*	Vascular Resection		
	Total	HA Alone	PV and HA
S2,3,4	4	4	0
S1,2,3,4	7	3	4
S1,2,3,4,5,8	5	3	2
Total	16	10	6

*Expressed as Couinaud's hepatic segment(s) resected. PV indicates portal vein resection; HA, hepatic artery resection.

Vascular invasion was diagnosed using multidetector-row computed tomography (MDCT) angiography preoperatively (**Figure 1**). Multiplanar reformation and 3-dimensional volume-rendered (3DVR) images were generated from arterial, portal and venous phase datas. Multiplanar reformation images were used to estimate the vascular invasion, while vascular resection and reconstruction were planned by 3DVR images (**Figure 1**).

Operative procedures

The type of hepatectomy was summarized in **Table 1**. Left hepatectomy was performed in 4 patients, left hepatectomy with the caudate lobe in 7 and left hepatic trisectionectomy in 5

Figure 2. Completion photography of left trisectionectomy and caudate lobectomy with vascular resection. The right posterior hepatic artery was reconstructed through end-to-end anastomosis with the right hepatic artery (arrow).

(**Table 1** and **Figure 2**). All patients underwent en bloc resection of the hepatic lobe and extrahepatic bile duct. The parenchymal transection was conducted by utilizing cavitron ultrasonic surgical aspirator (CUSA) after separation of the first porta hepatis, under left hemi-hepatic flow occlusion in left hepatectomy and omni-hepatic flow occlusion for 15 minutes at 5-minute intervals in left hepatic trisectionectomy.

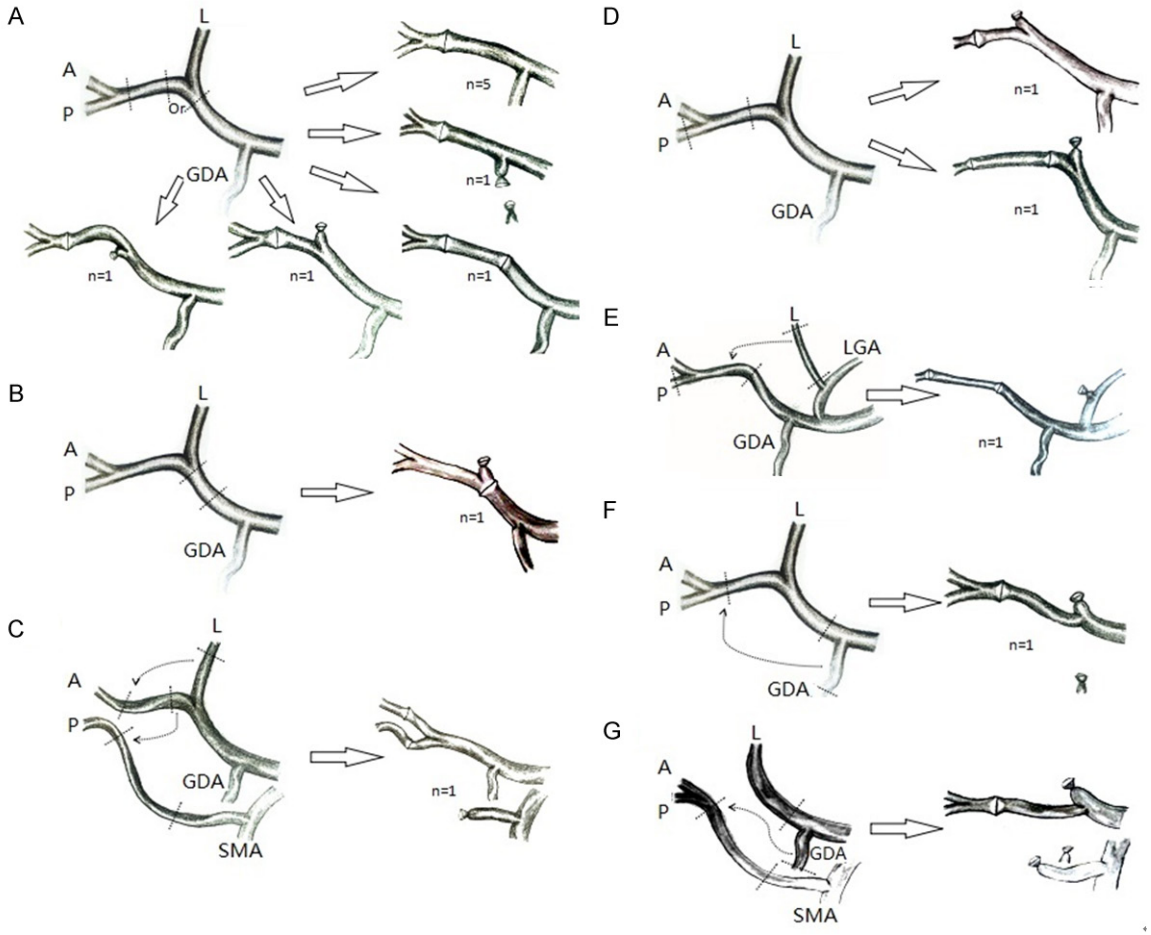

Figure 3. Scheme of hepatic artery resection and reconstruction of all the 16 patients. A: Type of hepatic artery reconstruction with end-to-end anastomosi. B: Proper hepatic artery anastomosed to proper hepatic artery. C: Hepatic artery reconstruction in case of right posterior hepatic artery variation. D, E: Autologous left hepatic artery graft interposition for hepatic artery reconstruction. F, G: Hepatic artery reconstructed with gastroduodenal artery. L indicates left hepatic artery; A, right anterior hepatic artery; P, right posterior hepatic artery; GDA, gastroduodenal artery; SMA, superior mesenteric artery; LGA, left gastric artery.

The vascular resection was carried out only when the vessel could not be detached from the tumor during the skeletonization resection of the hepatoduodenal ligament. Six patients underwent hepatectomy with simultaneous resection and reconstruction of the portal vein and hepatic artery. The portal vein was resected and reconstructed, then was en bloc resection of the tumor, followed by reconstruction of the hepatic artery. The portal vein resections included 4 segmental resections and 2 wedge resections. Reconstruction of the segmental resections was accomplished by end-to-end anastomosis (n=3) or an external iliac vein graft interposition (n=1). In 2 wedge resections, the relatively intact left portal vein patch graft was used to close the defect. All reconstructions of the hepatic artery were performed by hepatobiliary surgeons that had the background of liver transplantation, under magnifying scope, using 8-0 polypropylene. Heparin and papaverine were beneficial and indispensable for topical use during anastomosis to prevent thrombosis and relieve arterial spasm respectively. Intra- or postoperative anticoagulant drugs were not performed in any of the patients.

Ethics approval and consent to participate

Written informed consent was obtained from all participants. This study was approved by the local Ethics Committee at Zhejiang University School of Medicine.

Results

Reconstruction of hepatic artery

RHA was reconstructed with end-to-end anastomosis (n=10, **Figure 3A-C**), using the autolo-

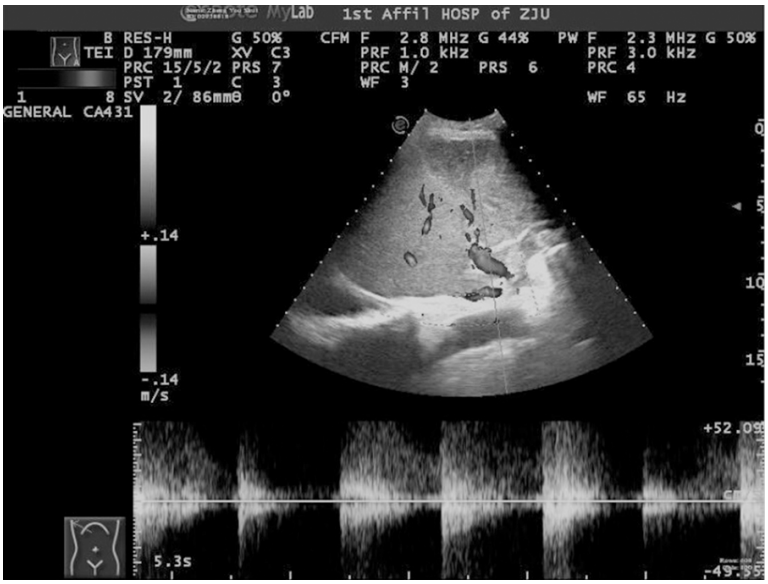

Figure 4. Color-Doppler ultrasound performed postoperatively showed the patency of reconstructed hepatic artery.

gous greater saphenous vein graft interposition (n=1, **Figure 3A**), the autologous left hepatic artery (LHA) graft interposition (n=2, **Figure 3D** and **3E**), the reserved LHA (n=1) (**Figure 3A**), or the gastroduodenal artery (n=2, **Figure 3F** and **3G**).

In 10 patients with end-to-end anastomosis, hepatic arteries were reconstructed through RHA anastomosed to RHA (n=1, **Figure 3A**), RHA anastomosed to proper hepatic artery (PHA) (n=6, **Figure 3A**), right posterior hepatic artery anastomosed to RHA (n=1, **Figures 1A** and **3D**), or PHA anastomosed to PHA (n=1, **Figure 3B**). One patient had the variable right posterior hepatic artery coming from the superior mesenteric artery (SMA), after resection of both right anterior and posterior hepatic artery, the right anterior hepatic artery was anastomosed to the LHA and the right posterior hepatic artery was anastomosed to the proximal RHA (**Figures 3C** and **5B**). The gastroduodenal artery was resected in one patient to reduce anastomotic tension (**Figure 3A**). In two patients who underwent reconstruction with LHA graft interposition, one had the variable LHA coming from the left gastric artery (**Figures 3E** and **5A**), the other had a low hepatic artery bifurcation with relatively long and intact left hepatic artery (**Figure 3D**), so the autologous graft was used. The autologous greater saphenous vein graft was harvested by vascular surgeons.

Pathologic evaluation

Post-operative pathology showed that all of the patients had tubular adenocarcinoma including 6 poorly differentiated adenocarcinomas, 8 moderately differentiated adenocarcinomas and 2 well differentiated adenocarcinomas. Portal vein invasion was confirmed in 5 patients, and the remaining patient had marked fibrosis. All of the 16 patients had hepatic artery invasion demonstrated by histological examination. The distal bile duct margin and proximal bile duct margin were negative for cancer in 15 and 16 patients, respectively. Consequently, R0 resection was achieved in 15 patients.

Surgical outcome

To evaluate the patency of reconstructed hepatic artery, Color-Doppler ultrasound was performed 3 times within 1 week postoperatively (**Figure 4**). MDCT was also done 2 weeks and around 2 months after surgery (**Figure 5**). The monitoring indicated that all reconstructed hepatic arteries were patent.

Of total, 10 patients had good postoperative recovery without any complications, whereas the remaining 6 developed several kinds of complications as moderate ascites (n=5), hepatic cross sectional encapsulated effusion (intra-abdominal abscess) (n=2) and wound infection (n=1). There was no post-operative liver failure, hepatic abscess, biliary-enteric anastomotic leakage, relaparotomy or perioperative death.

Vascular invasion was previously a primary cause for disease irresectability in hilar cholangiocarcinoma. With the development of microsurgical technique, especially the vascular anastomosis technique innovation of the living donor liver transplantation, vascular invasion is no longer the surgical contraindication [1-6]. From the former literatures, portal vein recon-

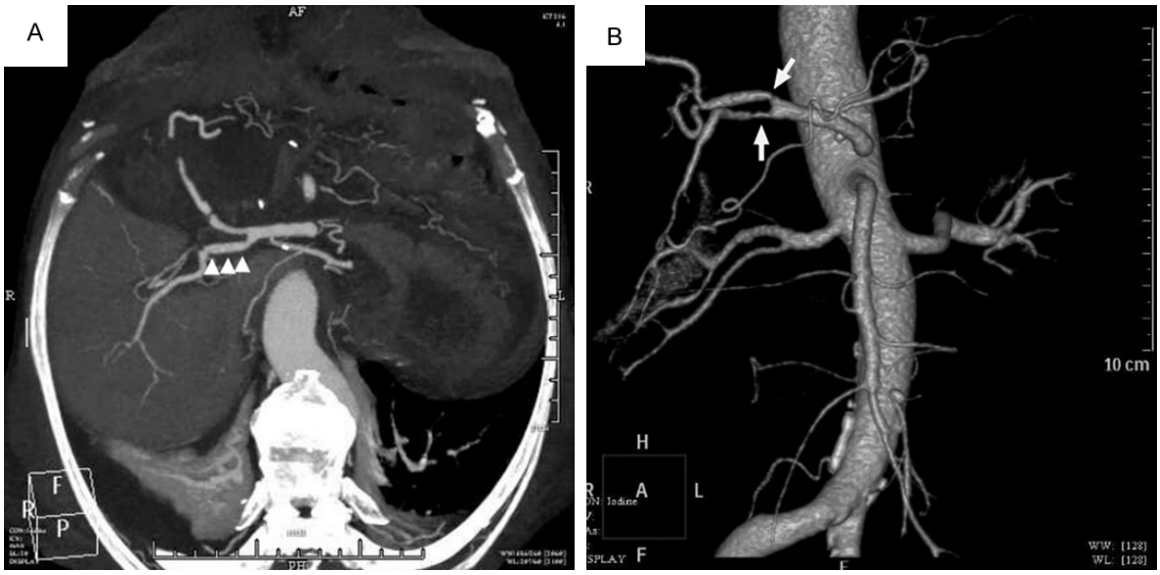

Figure 5. Postoperative three-dimensional volume-rendered images showed patency of the reconstructed hepatic artery. A: The right posterior hepatic artery was reconstructed with autologous left hepatic artery graft interposition (Δ). B: The right anterior hepatic artery was anastomosed to the left hepatic artery and the right posterior hepatic artery was anastomosed to the proximal right hepatic artery (arrow).

struction has been well accepted from an surgical risk viewpoint and might improve survival [1-4]. Whereas, hepatic artery reconstruction cannot be justified [7]. In terms of hepatic artery invasion, in order to ensure en block and radical resection, combined hepatic artery resection is essential and vital. In our series, there was no postoperative liver failure, relaparotomy or perioperative death, though all patients underwent major hepatectomy with hepatic artery reconstruction. This surgical outcome was acceptable. In the first place, our department is skillful in vascular reconstruction and rich-experienced with perioperative managements. Thus no one developed any post-operative complications related to hepatic artery reconstruction. I should touch on, that we have so far performed liver transplantation in more than 1000 patients including 152 cases of living donor liver transplantation [8]. All the surgeons in our group had the background of liver transplantation. This favorable technique is largely responsible for the outstanding results obtained. The last but not the least, intestinal microecological therapy might increase the likelihood of this excellent results.

Since 2004, our center had proceeded hepatectomy combined with portal vein resection and hepatic artery resection in the treatment of local advanced hilar cholangiocarcinoma. In our early reported 2 cases, hepatic artery reconstruction was failed in one case, resulting in hepatic abscess and hepatonecrosis 3 months postoperatively [9]. Therefore we hold the opinion that maintain the double blood supply of the liver and R0 resection have equally significance for the treatment of hilar cholangiocarcinoma. We couldn't destroy the blood supply to achieve R0 resection. That is to say while combined hepatic artery resection is required, it should be reconstructed to reduce operative risk, especially in patients with high serum total bilirubin level preoperatively, extensive hepatectomy intraoperatively, or portal vein resection simultaneously. However in some selected patients with low serum total bilirubin level, young aged, no basic diseases of the liver and limited hepatectomy, the criterion of hepatic artery reconstruction should be loosened.

In this paper we retrospectively analyzed the clinical data, operative procedure and surgical outcome in 16 patients who underwent left hepatectomy with simultaneous resection and reconstruction of the RHA during their radical resection of hilar cholangiocarcinoma. From a functional perspective, left-sided hepatectomy is less risky since the resection volume is small. The LHA runs along the leftmost site of the hepatoduodenal ligament, right-side predominant

hilar cholangiocarcinoma rarely involves the LHA, thus RHA reconstruction is more common in local advanced hilar cholangiocarcinoma [5].

In our experience, if the hepatic artery resection length is within 2-3 cm, directly end-to-end anastomosis is optimal, as after skeletonization resection of the hepatoduodenal ligament the hepatic artery is free, resulting in toilless reconstruction. In case of RHA invasion, while the LHA is intact, the left side ought to be a good choice for reconstruction. However, supposing that directly end-to-end anastomosis is impracticable, reversed gastroduodenal artery is alternative. For cases with large gap and backbreaking to directly anastomose, it is indispensable even to cut off gastroduodenal artery so as to shorten the distance and reduce tension. Otherwise the autogenous greater saphenous vein graft interposition can also be taken into consideration. Besides, in some selected patients we recommended LHA graft interposition for reconstruction, which is citation-free and self-contained. Moreover Nagino et al performed hepatic artery reconstruction using the reversed right gastroepiploic artery, the reversed right gastric artery, or radial artery graft interposition [5]. Liang Y *et al* reported that gastroduodenal artery graft also can be used for hepatic artery reconstruction [10].

For my part, vascular transplantation should not be as the preferred solution, it increased the number of anastomotic and extended the operation time. When direct arterial reconstruction is impossible, arterioportal shunting might be beneficial to maintain the arterial blood supply [11]; or preoperative embolization of the proper hepatic artery could be performed to promote the collateral circulation [12]. We hold the opinion that arterioportal shunting and preoperative embolization are only reported in small amount of cases, the safety of these procedures require further assessment in a large series. Also retain the perihepatic ligament is advantageous for postoperative collateral circulation establishment in patients without arterial reconstruction [9]. Do not simultaneously resect hepatic artery and portal vein to engender a long-drawn-out time of the residual liver ischemia. As portal flow is dominant and portal vein reconstruction is relatively facile and fast, in order to shorten the ischemia time, we advocate portal vein reconstruction first, yet individual plan should be designed based on specific condition of each case. Hence, sufficiently preoperative evaluation to define the status of hepatic artery invasion is crucial, we suggest that computed tomography angiography (CTA) or magnetic resonance angiography (MRA) should be routinely taken in patients that vascular invasion was suspected.

Radical resection with negative surgical margins provides the only chance of cure and long-term survival. Hepatic arterial reconstruction can improve the rate of radical resection of local advanced hilar cholangiocarcinoma and decrease the occurrence of serious complications after operation, which will lead to an expanded surgical indication and improved survival for patients with this horrible disease, is safe and feasible. However, our series are lack of long-term follow-up, and the number of cases is limited; the effect of the operation on the long-term prognosis needs further follow-up and evidentiary support from large scale clinical samples.

Acknowledgements

National Natural Science Fundation of China (81372626); Foundation for Innovative Research Groups of the National Natural Science Foundation of China (81421062).

Disclosure of conflict of interest

None.

Authors' contribution

YS and JJF analyzed the data and wrote the manuscript. QWZ, SY and SSZ commented on and revised the manuscript. WLW, MZ, YS, SY and SSZ built the patient database. All authors read and approved the final manuscript.

Abbreviations

CTA, Computed tomography angiography; CUSA, Cavitron ultrasonic surgical aspirator; ENBD, Endoscopic nasobiliary drainage; LHA, Left hepatic artery; MDCT, Multidetector-row computed tomography; MRA, Magnetic resonance angiography; PHA, Proper hepatic artery; PTCD, Percutaneous transhepatic cholangial drainage; RHA, Right hepatic artery; SMA, Superior mesenteric artery; 3DVR, 3-dimensional volume-rendered.

Address correspondence to: Drs. Sheng Yan and Shusen Zheng, Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, P. R. China. Tel: +86 571 87236112; Fax: +86 571 87236678; E-mail: shengyan@zju.edu.cn (SY); Tel: +86 571 87236567; Fax: +86 571 87236678; E-mail: shusenzheng@zju.edu.cn (SSZ)

References

[1] Nimura Y, Hayakawa N, Kamiya J, Maeda S, Kondo S, Yasui A, Shionoya S. Combined portal vein and liver resection for carcinoma of the biliary tract. Br J Surg 1991; 78: 727-731.

[2] Kondo S, Katoh H, Hirano S, Ambo Y, Tanaka E, Okushiba S. Portal vein resection and reconstruction prior to hepatic dissection during right hepatectomy and caudatelobectomy for hepatobiliary cancer. Br J Surg 2003; 90: 694-697.

[3] 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: 720-727.

[4] Hemming AW, Kim RD, Mekeel KL, Fujita S, Reed AI, Foley DP, Howard RJ. Portal vein resection for hilar cholangiocarcinoma. Am Surg 2006; 72: 599-604; discussion 604-5.

[5] Nagino M, Nimura Y, Nishio H, Ebata T, Igami T, Matsushita M, Nishikimi N, Kamei Y. Hepatectomy with simultaneous resection of the portal vein and hepatic artery for advanced perihilar cholangiocarcinoma: an audit of 50 consecutive cases. Ann Surg 2010; 252: 115-23.

[6] de Santibañes E, Ardiles V, Alvarez FA, Pekolj J, Brandi C, Beskow A. Hepatic artey reconrstruction first for the treatment of hilar cholangiocarcinoma bismuth type IIIB with contralateral arterial invasion: a novel technical strategy. HPB (Oxford) 2012; 14: 67-70.

[7] Konstadoulakis MM, Roayaie S, Gomatos IP, Labow D, Fiel MI, Miller CM, Schwartz ME. Aggressive surgical resection for hilar cholangiocarcinoma: is it justified? Audit of a single center's experience. Am J Surg 2008; 196: 160-169.

[8] Sun Z, Yu Z, Yu S, Chen J, Wang J, Yang C, Jin M, Yan S, Zhang M, Zhang M, Zheng S. Postoperative complications in living liver donors: a single-center experience in China. PLoS One 2015; 10: e0135557.

[9] Wang WL, Tang XF, Yao MY, Liang TB, Jin J, Jiang ZJ, Zheng SS. Safety and efficiency of left hemihepatectomy combined with hepatic artery resection for hilar cholangiocarcinoma with artery infiltration: report of 2 cases. Can J Surg 2008; 51: 305-307.

[10] Liang Y, Wang J, Shi X, Dong J, Gu W. Application of a gastroduodenal artery graft for reconstruction of the hepatic artery during radical resection of hilar cholangiocarcinoma. Gastroenterol Res Pract 2015; 2015: 934565.

[11] Kondo S, Hirano S, Ambo Y, Tanaka E, Kubota T, Katoh H. Arterioportal shunting as an alternative to microvascular reconstruction after hepatic artery resection. Br J Surg 2004; 91: 248-251.

[12] Yasuda Y, Larsen PN, Ishibashi T, Yamashita K, Toei H. Resection of hilar cholangiocarcinoma with left hepatectomy after pre-operative embolization of the properhepatic artery. HPB (Oxford) 2010; 12: 147-152.