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World J Gastroenterol 2017 May 28; 23(20): 3569-3760



EDITORIAL

- 3569 Hepatitis C in injection drug users: It is time to treat
Grassi A, Ballardini G
- 3572 Cyclooxygenase 2 in liver dysfunction and carcinogenesis: Facts and perspectives
Martín-Sanz P, Casado M, Boscá L

REVIEW

- 3581 First quarter century of laparoscopic liver resection
Morise Z, Wakabayashi G
- 3589 Hepatitis A virus infection and hepatitis A vaccination in human immunodeficiency virus-positive patients: A review
Lin KY, Chen GJ, Lee YL, Huang YC, Cheng A, Sun HY, Chang SY, Liu CE, Hung CC
- 3607 Brain changes detected by functional magnetic resonance imaging and spectroscopy in patients with Crohn's disease
Lv K, Fan YH, Xu L, Xu MS
- 3615 Perspectives of traditional Chinese medicine in pancreas protection for acute pancreatitis
Li J, Zhang S, Zhou R, Zhang J, Li ZF

MINIREVIEWS

- 3624 Transition of pediatric to adult care in inflammatory bowel disease: Is it as easy as 1, 2, 3?
Afzali A, Wahbeh G
- 3632 Colorectal cancer population screening programs worldwide in 2016: An update
Navarro M, Nicolas A, Ferrandez A, Lanás A

ORIGINAL ARTICLE

Basic Study

- 3643 Urinary metabolic insights into host-gut microbial interactions in healthy and IBD children
Martin FP, Su MM, Xie GX, Guiraud SP, Kussmann M, Godin JP, Jia W, Nydegger A
- 3655 M2-like Kupffer cells in fibrotic liver may protect against acute insult
Zheng QF, Bai L, Duan ZP, Han YP, Zheng SJ, Chen Y, Li JS

3664 Sonographic appearance of anal cushions of hemorrhoids
Aimaiti A, A Ba Bai Ke Re MMTJ, Ibrahim I, Chen H, Tuerdi M, Mayinuer

3675 Effect of NDC80 in human hepatocellular carcinoma
Ju LL, Chen L, Li JH, Wang YF, Lu RJ, Bian ZL, Shao JG

3684 Animal experimental studies using small intestine endoscope
Liu JH, Liu DY, Wang L, Han LP, Qi ZY, Ren HJ, Feng Y, Luan FM, Mi LT, Shan SM

Retrospective Cohort Study

3690 Radiological response and inflammation scores predict tumour recurrence in patients treated with transarterial chemoembolization before liver transplantation
Nicolini D, Agostini A, Montalti R, Mocchegiani F, Mincarelli C, Mandolesi A, Robertson NL, Candelari R, Giovagnoni A, Vivarelli M

Retrospective Study

3702 Surgical management of liver diseases invading the hepatocaval confluence based on IH classification: The surgical guideline in our center
Li W, Han J, Wu ZP, Wu H

Observational Study

3713 Study on the value of serum miR-106b for the early diagnosis of hepatocellular carcinoma
Shi BM, Lu W, Ji K, Wang YF, Xiao S, Wang XY

Prospective Study

3721 Clinical significance of expression of proliferating cell nuclear antigen and E-cadherin in gastric carcinoma
Hu L, Li HL, Li WF, Chen JM, Yang JT, Gu JJ, Xin L

META-ANALYSIS

3730 Different techniques for harvesting grafts for living donor liver transplantation: A systematic review and meta-analysis
Li H, Zhang JB, Chen XL, Fan L, Wang L, Li SH, Zheng QL, Wang XM, Yang Y, Chen GH, Wang GS

CASE REPORT

3744 Successful treatment of a pancreatic schwannoma by spleen-preserving distal pancreatectomy
Xu SY, Wu YS, Li JH, Sun K, Hu ZH, Zheng SS, Wang WL

3752 Preoperative detection and localization of small bowel hemangioma: Two case reports
Takase N, Fukui K, Tani T, Nishimura T, Tanaka T, Harada N, Ueno K, Takamatsu M, Nishizawa A, Okamura A, Kaneda K

LETTERS TO THE EDITOR

3758 Non-invasive stimulation techniques to relieve abdominal/pelvic pain: Is more always better?

Harvey MP, Watier A, Dufort Rouleau É, Léonard G

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Retrospective Study

Surgical management of liver diseases invading the hepatocaval confluence based on IH classification: The surgical guideline in our center

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Abstract**AIM**

To investigate the short-term outcomes and risk factors indicating postoperative death of patients with lesions adjacent to the hepatocaval confluence.

METHODS

We retrospectively analyzed 54 consecutive patients who underwent hepatectomy combined with inferior vena cava (IVC) and/or hepatic vein reconstruction (HVR) from January 2012 to January 2016 at our liver surgery center. The patients were divided into 5 groups according to the range of IVC and hepatic vein involvement. The patient details, indications for surgery, operative techniques, intra- and postoperative outcomes were compared among the 5 groups. Univariate and multivariate analyses were performed to explore factors predictive of overall operative death.

RESULTS

IVC replacement was carried out in 37 (68.5%) patients

and HVR in 17 (31.5%) patients. Type I2H2 had the longest operative blood loss, operative duration and overall liver ischemic time (all, $P < 0.05$). Three patients of Type I3H1 with totally occluded IVC did not need IVC reconstruction. Total postoperative morbidity rate was 40.7% (22 patients) and the operative mortality rate was 16.7% (9 patients). Factors predictive of operative death included IVC replacement ($P = 0.048$), duration of liver ischemia ($P = 0.005$) and preoperative liver function being Child-Pugh B ($P = 0.025$).

CONCLUSION

IVC replacement, duration of liver ischemia and preoperative poor liver function were risk factors predictive of postoperative death. We should be cautious about IVC replacement, especially in Type I2H2. For Type I3H1, it was unnecessary to replace IVC when the collateral circulation was established.

Key words: Hepatectomy; Inferior vena cava; Hepatic vein; Reconstruction

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Core tip: The proposed IH classification, which divided the patients into 5 groups according to the range of vascular invasion, may be meaningful in selecting procedures for patients with hepatocaval confluence infiltration. Inferior vena cava replacement, duration of liver ischemia and preoperative poor liver function were risk factors predictive of postoperative death for patients with lesions adjacent to the hepatocaval confluence.

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INTRODUCTION

Liver malignancies including hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (ICC) and colorectal liver metastases, combined with liver parasitic diseases like alveolar echinococcosis (AE), often show an infiltrative growth pattern. If major vessels such as the inferior vena cava (IVC) and hepatic vein adjacent to its caval confluence are invaded by these lesions, combined liver and IVC resection followed by IVC and/or hepatic outflow reconstruction with other materials is necessary to achieve R0 resection^[1-3]. As a consequence of recent advances in perioperative management and surgical technique, liver and IVC resection combined with major

vascular reconstruction has become a reasonably safe treatment option with acceptable short- and long-term survival.

Preoperative portal vein embolism, associating liver partition with portal vein ligation for staged hepatectomy (commonly referred to as ALPPS), systemic chemotherapy (mainly for colorectal liver metastases) and other innovative treatments increase the tumor resectability^[4-6]. Total vascular exclusion (TVE) and other vascular exclusion techniques offer chances of resection for tumor with major vascular involvement. *In situ* perfusion technique can be applied in patients with TVE longer than 60 min. Moreover, the utilization of anti-situm and *ex vivo* technique makes it easier to acquire a better operative field and obtain tumor-free surgical margins^[7-9]. Venovenous bypass (VVB) is necessary in some patients under TVE with drastic hemodynamic fluctuations^[7].

Though technically challenging, hepatectomy combined with major vascular resection and reconstruction has been performed in many centers^[7-10]. However, due to the lack of surgical protocols, different standards have been used in different centers. Here, we present our surgical guideline and outcomes for the combined liver and IVC resection in 54 patients with different kinds of liver lesions invading the hepatocaval confluence. The "IH classification" outlined herein was established based on our experience, and was the surgical guideline in our center.

MATERIALS AND METHODS

We retrospectively analyzed 54 consecutive patients who underwent liver resection combined with IVC resection and reconstruction from January 2012 to January 2016 at our liver surgery center at the West China Hospital, Sichuan University. Cases with IVC involvement that could be detached primarily without reconstruction were not included in this study. Patients with tumor thrombus in the IVC or hepatic veins were also excluded. The final diagnoses were confirmed by histopathological examinations after surgery. We have established classifications for this challenging situation based on our experience and the patients were divided into 5 groups according to the classifications (Figure 1). The indications for surgery of these patients are summarized in Table 1. All procedures described in this study were approved by the Ethics Committee of West China Hospital, Sichuan University.

Classifications for liver diseases invading the hepatocaval confluence

Classification based on varying degrees of IVC infiltration:

I1: Less than 50% of IVC circumference is involved and the IVC is not totally occluded; I2: More than 50% of IVC circumference is involved and the IVC is not totally occluded; and I3: The encroached IVC is totally occluded.

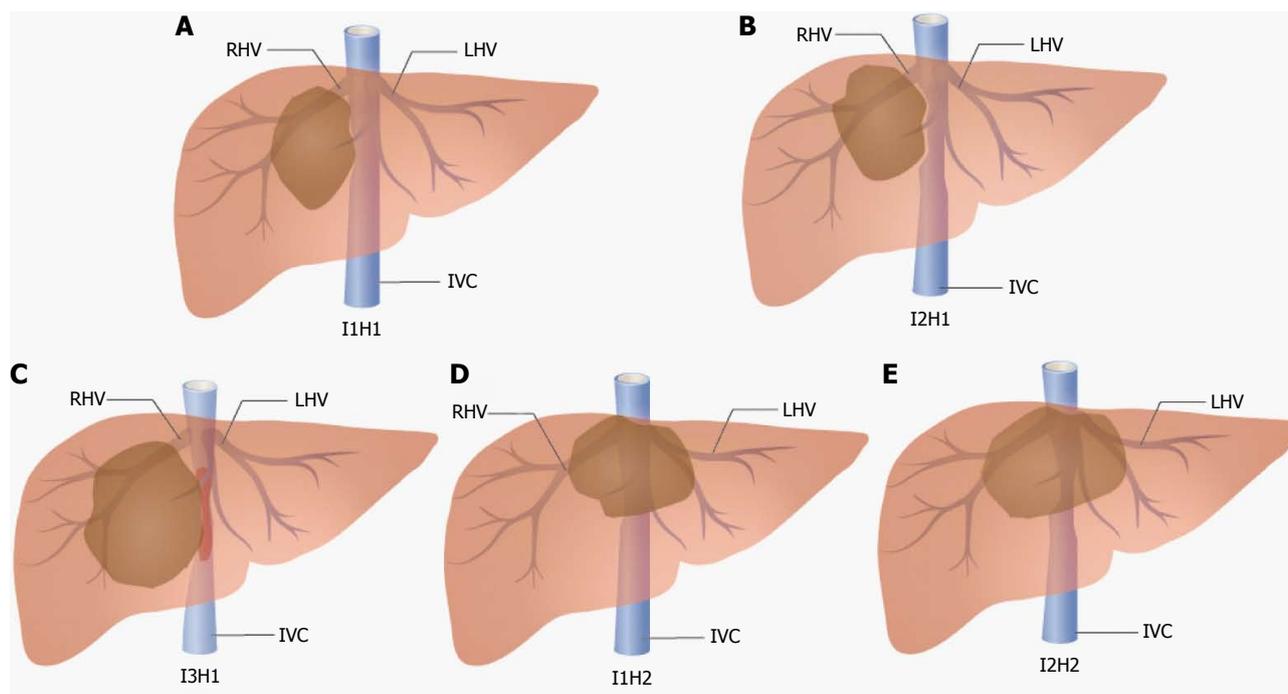


Figure 1 Classifications of liver lesions. A: Type I1H1; B: I2H1; C: I3H1; D: I1H2; E: I2H2. RHV: Right hepatic vein; LHV: Left hepatic vein; IVC: Inferior vena cava.

Table 1 Patients undergoing combined liver and inferior vena cava resection

Indications for surgery	n	Sex (M:F), n	Classifications				
			I1H1	I2H1	I1H2	I2H2	I3H1
Hepatocellular carcinoma	11	6:05	2	5	1	3	0
Cholangiocarcinoma	26	18:08	3	10	4	6	3
Colorectal metastases	8	5:03	1	5	0	1	1
Alveolar echinococcosis	9	5:04	3	3	0	2	1

Classification based on hepatic outflow conditions: H1: The hepatic outflow of the residual liver is not involved; and H2: The hepatic outflow of the residual liver is involved (3 hepatic veins are all infiltrated).

Preoperative management

The ultrasonography and contrast computed tomography (CT) scan or magnetic resonance imaging of the abdomen were performed to evaluate the number and extent of lesions, gross type, liver volume, presence of major vascular infiltration, and regional or distant metastasis. Our standard indication for hepatectomy was Child-Pugh grade A or B, or indocyanine green retention rate at 15 min < 10%. Some patients with metastatic colorectal cancer received systemic chemotherapy after evaluation in the cancer center of our hospital, and all of them underwent colonoscopy before surgery. Our policy for indication of portal vein embolism is when the predicted future liver remnant is less than 40% of the total non-tumorous functional liver volume^[11].

Surgical procedures

The procedures for hepatectomy have been reported elsewhere^[11,12]. Our preferred abdominal incision was J-shaped thoracoabdominal incision. After mobilization, the intraoperative ultrasound was performed routinely to confirm the number and location of lesions as well as to evaluate the relation of tumor to major vessels. The other major procedures before hepatectomy included: portal pedicle division and ligation, exposing and encircling the infra- and supra-hepatic IVC (the supradiaphragmatic IVC was encircled if the diaphragm was invaded), and dividing and ligating the short hepatic veins if possible. Liver parenchyma transaction (Pringle’s maneuver was used if necessary) was carried out with the Kelly crush technique or other instruments including CUSA (Valleylab Corp., Somerville, NJ, United States) or Harmonic scalpel (Johnson & Johnson Corp., Princeton, NJ, United States). The anterior approach was used if bulky lesions resided in the right lobe of the liver.

When the critical remaining parenchyma and vascular structures were exposed, various vascular

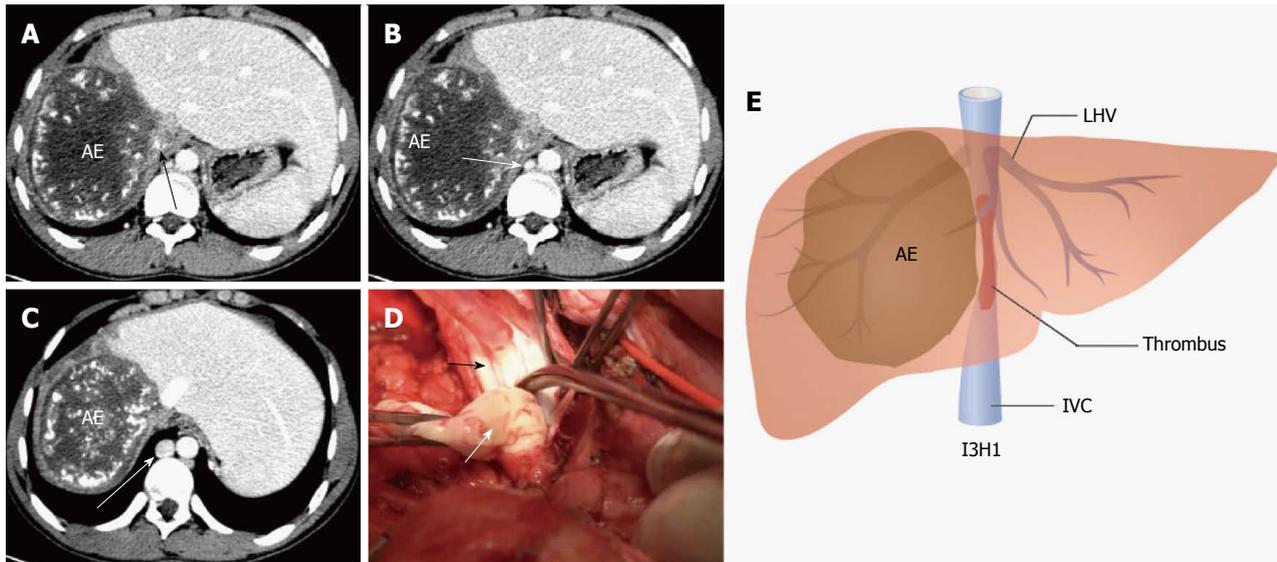


Figure 2 One patient with alveolar echinococcosis in the right lobe of liver. A: The IVC wall was totally occluded (longer black arrow); B and C: The azygos vein was dilated gradually (longer white arrows); D: The retrohepatic IVC was totally occluded, filled with organized thrombus (shorter white arrow). The shorter black arrow: IVC; E: Classification of this patient was I3H1. LHV: Left hepatic vein; IVC: Inferior vena cava; AE: Alveolar echinococcosis.

control techniques were applied. For type I1H1, we clamped the IVC tangentially without IVC exclusion or clamped IVC below the hepatic vein (CIBH) of the remnant liver without hepatic outflow exclusion. In our experience, if IVC involvement was less than 30% of the IVC circumference and 2 cm of the length, the defect was usually sutured transversely after removing the invaded IVC wall. If IVC involvement was 30% to 50% of IVC circumference and longer than 2 cm, we used autogenous veins such as great saphenous vein patches or expanded polytetrafluoroethylene (ePTFE; Gore-Tex, Flagstaff, AZ, United States) patches for IVC repair. As for type I1H2, IVC reconstruction was similar to type I1H1. TVE (clamping the infra-hepatic IVC, portal triad and supra-hepatic IVC sequentially) was utilized for IVC and hepatic vein reconstruction. In this type, 3 hepatic veins were involved, and the remaining stump of hepatic vein was reimplanted directly into the vena cava, or an interposed reinforced ePTFE graft. With respect to type I2H1, we used TVE or CIBH (if there was enough room below the hepatic vein) for blood control. And, if longitudinal infiltration was longer than 3 cm, IVC replacement was performed. Regarding type I2H2, TVE was necessary to complete tumor resection and vascular reconstruction. In this type, vascular reconstruction included hepatic outflow and IVC reconstruction. IVC was replaced with ePTFE tube graft and the hepatic vein was reimplanted into the ePTFE tube graft if it was totally invaded. Otherwise, if hepatic vein of the residual liver was partially involved, we used autogenous vein patches or ePTFE patches for hepatic vein plasty. With respect to I3H1, if collateral circulation including ascending lumbar veins, hemiazygos vein, and azygos vein were dilated and compensated portal hypertension and caval flow effectively, we only performed liver and IVC

resection without IVC replacement (Figure 2).

Ex vivo, in situ perfusion and anti-situm technique

Ex vivo, in situ perfusion and anti-situm technique were predominately used in type I2H2. *In situ* hypothermic perfusion as described by DuBay *et al.*^[13] can be performed when TVE lasts longer than 60 min. When TVE was utilized, the patient's hemodynamic condition was carefully monitored and VVB (installed from the inferior mesenteric vein, and the right femoral vein to the left internal jugular vein) was applied when the patient could not tolerate the hemodynamic fluctuation. *Ex vivo* technique, which we have reported elsewhere^[14], is easier to obtain tumor-free surgical margins and reconstruct the vessels. However, given the higher complications (including bile leakage, bile duct stricture and prosthetic graft infection caused by bile leakage) associated with biliary tract anastomosis^[15,16], *ex vivo* was performed only on patients with the IVC, hepatic vein confluence, and/or portal structures infiltrated extensively. VVB was needed for most of the patients who underwent *ex vivo*. Anti-situm technique, first introduced by Pichlmayr *et al.*^[17] 20 years ago, did not need to divide the portal structures. After cutting off the supra-hepatic IVC, the liver together with the IVC was rotated to the anterior position, away from their anatomic location. Then, hepatectomy could be achieved rather easily with infra-hepatic IVC and the portal triad exclusion, hypothermic hepatic perfusion and percutaneous VVB.

Postoperative management

All patients were treated with low-molecular weight heparin sodium anticoagulation solution (1 mg per kg bodyweight) from 2 d after surgery, with close monitoring. After discharge from hospital, the

patients were given warfarin (2.5 mg, qd, po) for 3 mo. Enhanced abdominal CT or ultrasonography was performed every 7 d in the first mo postoperatively to detect the patency of reconstructed vessels. For hepatitis B virus-infected patients, anti-viral drugs were applied.

Postoperative mortality was defined as death within 90 d of operation. Clavien-Dindo classification was used to classify all general complications occurring at any time during the hospital stay^[18]. Liver failure was defined as peak bilirubin concentration > 7 mg/dL, peak international normalized ratio > 2.0, refractory ascites, or encephalopathy^[19]. Bile leakage was defined as a drain fluid-to-serum total bilirubin concentration ratio \geq 3.0^[20]. Renal insufficiency was defined as increase of serum urea and/or creatinine level (50% above the baseline). Clinically significant ascites was defined when abdominal drainage was more than 500 mL/d for longer than 3 d.

Statistical analysis

The clinicopathologic characteristics and short-term surgical outcomes of these patients were compared among the 5 groups. Categorical variables were expressed as number and tested by chi-square test or Fisher's exact test. Continuous variables were summarized as mean (range) and tested by one-way ANOVA (Student-Newman-Keuls test was used when ANOVA was significant) or Kruskal-Wallis H rank test when necessary. The prognostic significance of the variables in predicting operative death was performed by univariate and multivariate binary logistic regression analysis. All statistical analyses were 2-tailed and *P* values < 0.05 were regarded as statistically significant. All analyses were performed by SPSS 19.0 statistical software (IBM Corp., Armonk, NY, United States).

RESULTS

Fifty-four patients (34 males, 20 females) underwent hepatectomy combined with vascular resection and reconstruction, with a median (range) age of 49.7 (39-72) years. The indications for surgery were: ICC (*n* = 26), HCC (*n* = 11), colorectal metastases (*n* = 8) and AE (*n* = 9) (Table 1). The intra- and postoperative data for the different types of liver lesions treated by hepatectomy combined with IVC and/or HVR are summarized in Table 2. The resection concerned 4.7 liver segments medially (range, 1-6 segments). IVC replacement was performed in 37 (68.5%) patients and HVR in 17 (31.5%) patients.

Type I2H2 had the longest operative blood loss, operation duration and overall liver ischemic time than the other 4 types (all, *P* < 0.05). The other clinical characteristics of the 5 types including tumor size, postoperative liver function, and hospital stay were listed in Table 2 in detail. Type I2H2 had the most complex procedure, which needed IVC replacement

and hepatic vein plasty (*n* = 3; with autogenous vein patches in 2 and ePTFE patches in 1) or reimplantation (*n* = 9; reimplant to ePTFE graft in 5 and to residual IVC in 4). Anti-situm (*n* = 2), *ex vivo* (*n* = 6) and *in situ* perfusion (*n* = 5) were mainly utilized in I2H2. Three patients of type I3H1 with totally occluded IVC did not need IVC reconstruction. The other 2 patients underwent IVC resection and replacement due to the uncompensated collateral circulation. The surgical procedures for the other 3 types were described in Table 2.

Total postoperative morbidity rate was 40.7% (22 patients) and the operative mortality rate was 16.7% (9 patients) (Table 3). Total morbidity and mortality rates of type I2H2 were higher than for type I1H1 (both, *P* < 0.05). Artificial graft infection (*n* = 4; 2 in type I2H2 and 2 in type I2H1), liver failure (*n* = 4; 2 in type I2H1 and 2 in type I2H2) and thrombosis of reconstructed vessels (*n* = 1; 1 in type I2H2) were the main reasons leading to postoperative death. Univariate analysis of factors predictive of death were Child-Pugh B (*P* = 0.004), IVC replacement (*P* = 0.044), duration of ischemia (*P* < 0.001) and duration of operation (*P* < 0.001) (Table 4). Factors predictive of operative death in multivariate analysis included IVC replacement (*P* = 0.048), duration of liver ischemia (*P* = 0.005) and preoperative liver function being Child-Pugh B (*P* = 0.025) (Table 5).

The median follow-up time was 20 mo (range, 2-48 mo). No patient was lost during follow-up. A total of 8 patients (3 in type I2H2, 2 in type I2H1, 2 in type I1H2, and 1 in type I1H1) died from tumor recurrence within 6 mo after the operations. Overall 1- and 3-year actuarial survival rates for HCC were 60% and 45% and for ICC were 55% and 38%. Twenty-five patients developed recurrence. Local recurrence in the liver occurred in 16 patients, in brain in 3, and in lung in 4, and abdominal cavity metastasis was detected in 2. Disease-free 1- and 3-year survival rates for patients with HCC were 18% and 8% respectively, and for patients with ICC were 16% and 9%. All AE patients were alive without recurrence and metastasis at the last follow-up.

DISCUSSION

In the present study, 54 patients who underwent liver resection combined with IVC and/or HVR were included. ICC, HCC, AE and colorectal metastasis were the main causes leading to IVC encroachment. Undoubtedly, when liver diseases have involved the hepatocaval confluence, resection and reconstruction of the vascular structures remain technically difficult. A variety of vascular exclusion techniques, IVC reconstruction strategies, and other innovative surgical methods have brought hope for patients in this late stage^[21,22].

Due to the high postoperative morbidity and

Table 2 Intra- and postoperative results

Variables	I1H1 (n = 9)	I2H1 (n = 23)	I1H2 (n = 5)	I2H2 (n = 12)	I3H1 (n = 5)	
					IVC resection and replacement (n = 2)	Only IVC resection (n = 3)
RL:REL:RT:LLE:LT	3:2:2:1:1	4:6:8:2:3	0:1:2:2:0	2:4:3:2:1	1:0:1:0:0	1:2:0:0:0
Tumor size (cm)	7.2 (2.9-14.3)	8.7 (7.1-15.4)	9.2 (3.9-9.9)	9.6 (7.2-16.1)	9.4 (6.6-12.2)	8.3 (7.1-10.2)
Operative blood loss (mL)	460 (310-950)	740 (450-1250)	570 (450-1050)	1020 (550-1700) ^a	680 (550-810)	450 (350-560)
Need for blood transfusion	1	8	0	7	1	0
Transfusion volume (mL)	400	550 (200-950)	0	600 (300-850) ^c	400	0
Operation duration (min)	290 (210-420)	592 (480-800)	520 (250-860)	750 (310-1150) ^a	580 (490-670)	320 (240-440)
No. of patients using TVE	2	23	3	12	2	0
No. of patients using PM	5	17	2	8	2	2
Duration of TVE (min)	50 (40,60)	62 (46-90)	48 (35-68)	73 (37-89) ^a	49 (39-57)	0
Duration of PM (min)	25 (10-35)	36 (15-45)	22.5(20-25)	38 (10-50)	30 (15-15)	30 (15-15)
Reconstruction detail	IVCR: direct suture in 4, with a patch in 5; HVR: no	IVCR: replacement; HVR: no	IVCR: with a patch in 5; HVR: reimplant to ePTFE in 1, to residual IVC in 4	IVCR: replacement; HVR: with a patch in 3, reimplant to ePTFE in 5, to residual IVC in 4	IVCR: replacement; HVR: no	IVCR: no; HVR: no
Surgical technique						
Anti-situm	0	0	0	2	1	0
<i>Ex vivo</i>	0	0	0	6	0	0
<i>In situ</i> perfusion	0	2	1	5	0	0
Postoperative liver function						
Serum maximum AST (IU/L)	460 (220-870)	557 (240-1240)	490 (230-590)	630 (330-1350)	520 (370,670)	665 (265-768)
Serum maximum ALT (IU/L)	565 (345-1350)	695 (230-1510)	520 (280-1020)	710 (340-1405)	610 (410-810)	685 (210-830)
Serum maximum PT (s)	14.1 (12.2-16.3)	15.4 (13.3-16.9)	14.8 (12.8-15.9)	15.4 (13.4-17.5)	16.4 (15.5-17.3)	15.5 (13.7-16.7)
Serum maximum TB (mmol/L)	33.4 (28.5-44.7)	36.8 (29.4-56.9)	33.7 (31.2-47.7)	45.0 (34.1-55.6)	35.0 (27.0-43.0)	33.1 (28.0-56.1)
Hospital stay (d)	11 (7-17)	15 (9-24)	12 (8-22)	19 (13-28)	14 (11-17)	16 (13-19)

Data are shown as median (range) or *n*. ^a*P* < 0.05 *vs* each other type; ^c*P* < 0.05 *vs* each other type except for I2H1. RL: Right lobectomy; REL: Right extended lobectomy; RT: Right tri-segmentectomy; LLE: Left extended lobectomy; LT: Left tri-segmentectomy; TVE: Total vessel exclusion; PM: Pringle maneuver; IVCR: Inferior vena cava reconstruction; HVR: Hepatic vein reconstruction; ALT: Alanine transaminase; AST: Aspartate transaminase; PT: Prothrombin time; TB: Total bilirubin.

Table 3 Postoperative complications

Variable	I1H1 (n = 9)	I2H1 (n = 23)	I1H2 (n = 5)	I2H2 (n = 12)	I3H1 (n = 5)	
					IVC resection and replacement (n = 2)	Only IVC resection (n = 3)
Total number	1	8	2	8 ^a	2	1
Biliary leak	1	1		1		
Liver failure		2		2		
Ascites	1	4	1	2	1	1
Jaundice				1		
Hemorrhage requiring reoperation			1			
Thrombosis of reconstructed vessels						
Hepatic vein				1		
Inferior vena cava		1				
Intraabdominal abscess				1		
Reconstructed vessel infection		2		2	1	
Wound infection						
Respiratory complication		1		1		
Clavien-Dindo classification						
Grade I - II	1	7	2	6	1	1
Grade III - V	1	4	0	5	1	0
90-d mortality	0	4	0	5 ^a	0	0

Data are shown as *n*. ^a*P* < 0.05 *vs* I1H1; Liver failure: peak bilirubin concentration > 7 mg/dL, peak international normalized ratio > 2.0, refractory ascites, encephalopathy. Ascites: > 500 mL/d lasting longer than 3 d. IVC: Inferior vena cava.

mortality rates, though technically feasible, it remains controversial as to whether or not we should perform radical resection with vascular reconstruction for lesions invading IVC and other major vessels.

However, prognosis of malignant tumor involved IVC is unfavorable when performing hepatectomy without IVC reconstruction^[10]. R0 resection combined with IVC reconstruction may have a better short- and long-

Table 4 Univariate analysis of factors predictive of death

	All patients (<i>n</i> = 54)	Operative death		<i>P</i> value
		Yes (<i>n</i> = 9)	No (<i>n</i> = 45)	
Age (yr)	49.7 (39-72)	53 (45-72)	49 (39-67)	0.249
Sex ratio (M:F)	34:20	6:3	28:17	0.801
Preoperative chemotherapy	4	1	3	1.000
Preoperative PVE	9	2	7	1.000
Tumor type				
Colorectal metastases	8	2	6	0.864
Hepatocellular carcinoma	11	2	9	1.000
Cholangiocarcinoma	26	4	22	1.000
Alveolar echinococcosis	9	1	8	1.000
Preoperative TB > 34 μmol/L	6	1	5	1.000
ICG-R15 over 10%	9	3	6	0.327
Child-Pugh B	6	4	2	0.004
No. of segments resected	4.7 (3-6)	5.1 (4-6)	4.6 (4-6)	0.189
Classifications				0.157
I1H1	9	0	9	0.328
I2H1	23	4	19	1.000
I1H2	5	0	5	0.576
I2H2	12	5	7	0.028
I3H1	5	0	5	0.576
IVC replacement				
Yes (I2 + 2 cases in I3)	37	9	28	0.044
No (I1 + 3 cases in I3)	17	0	17	
Hepatic vein reconstruction				
Yes (H2)	17	4	13	0.600
No (H1)	37	5	32	
Duration of ischemia (min)	68.7 (0-112)	87.7 (62-112)	64.9 (0-106)	< 0.001
Operative blood loss (mL)	721.5 (310-1250)	769.0 (550-1250)	712.3 (310-780)	0.389
Blood transfused amount (mL)	174.1 (0-950)	219.4 (0-950)	165.8 (0-850)	0.501
Duration of operation (min)	554.8 (210-1150)	709.6 (310-1150)	523.7 (210-860)	< 0.001
R0 resection	49	7	42	0.401
Tumor size	8.7 (2.9-16.1)	9.5 (8.8-16.1)	8.6 (2.9-15.4)	0.062

Data are shown as median (range) or *n*. PVE: Portal vein embolization; TB: Total bilirubin; ICG-R15: Indocyanine green retention rate at 15 min; IVC: Inferior vena cava.

Table 5 Multivariate binary logistic regression analysis of factors predictive of death

	OR (95%CI)	<i>P</i> value
IVC replacement	37.56 (1.46-945.32)	0.048
Duration of ischemia	1.65 (1.02-2.58)	0.005
Child B or C	1.82 (1.14-2.89)	0.025

IVC: Inferior vena cava.

term prognosis than cases which only underwent hepatectomy or conservative treatment, but further prospective studies are needed to investigate it.

In Table 6, we summarized the morbidity and mortality rates of the patients who underwent liver resection and IVC reconstruction in previous reports. In the present study, total postoperative morbidity rate was 40.7% (22 patients) and the operative mortality rate was 16.7% (9 patients; Table 3). Artificial vascular graft was the most commonly used material due to the shortage of xenogenous vessels and a larger surgery injury when utilizing autogenous vein^[23]. Though graft infection was a life-threatening complication of artificial tube graft, many studies including ours showed that graft infection rate after artificial graft replacement was

< 10%^[15,24,25]. For type I2H2, postoperative mortality rate was higher than the other types, which may be related to the longer operation time, longer ischemic time, more blood loss and higher postoperative morbidity rate. Consequently, for patients in type I2H2, it was still controversial about whether we should perform such an extensive operation.

Most of the previous studies demonstrated that it was difficult to assess IVC involvement preoperatively relying on imaging technique^[15,24,25]. Though intraoperative ultrasonography and cavography were performed to help confirm the IVC invasion, the true IVC invasion rate confirmed by pathological examinations after surgery was only 60% in our study (data not shown). For malignant infiltrative-growth diseases, including ICC and AE (characterized by tumor-like growth), R0 resection was a primary goal of treatment. IVC resection was necessary when it was infiltrated or embraced by the lesions which cannot be divided totally. For HCC and colorectal liver metastases (the tumor usually compress rather than encroaches the vessels), sometimes we could not achieve R0 resection when the IVC was surrounded by the tumor; thus, IVC replacement was performed in some of these patients. Multi-organ infiltration was

Table 6 Literature review of the reported series of hepatectomies combined with inferior vena cava resection

Ref.	Hospital mortality	Hospital morbidity	No. alive/total (follow-up time)
DuBay <i>et al</i> ^[13]	11.1% (1 of gastrointestinal bleeding and multiple organ failure)	22.2%	6/9 (2-33 mo)
Malde <i>et al</i> ^[15]	11.4% (4 of multiple organ failure)	40.0%	16/35 (1-140 mo)
Azoulay <i>et al</i> ^[31]	4.5% (1 of sepsis and multiple organ failure)	64.0%	11/22 (7-84 mo)
Madariaga <i>et al</i> ^[21]	11.0% (1 of liver failure)	22.2%	6/9 (3-156 mo)
Giordano <i>et al</i> ^[25]	4.0% (1 of liver failure)	39.1%	16/23 (1-33 mo)
Hemming <i>et al</i> ^[24]	8.3% (liver failure and multiple organ failure)	43.0%	46/60 (median 31 mo)
Yamamoto ^[29]	28.6% (1 of sepsis, 1 of liver failure)	28.6%	2/7 (2-72 mo)
Lodge <i>et al</i> ^[10]	25% (1 of sepsis and multiple organ failure, 1 of respiratory and renal failure)	87.5%	7/8 (0.5-30 mo)

not a surgical contraindication for AE. Given the lack of alternative curative approaches, a radical operation with complete removal of the parasitic lesions was the best beneficial way to achieve radical treatment^[26-28]. However, IVC resection combined with reconstruction in AE patients was still controversial considering the severe complications related to the IVC replacement.

Moreover, multivariate analysis in the present study showed that IVC replacement was a prognostic factor predictive of operative death ($P = 0.048$); thus, indications of IVC replacement should be controlled strictly. In our experience, we have established the IH classification according to the range of tumor invasion. According to the extent of caval involvement, the IVC was reconstructed using a tube graft (I2), direct suture or with patches (I1). For I3 (IVC was totally occluded), if there were no symptoms and life-threatening complications associated with caval obstruction and portal hypertension (Figure 2), the IVC was removed without replacement (empirically, when renal vein pressure was < 40 mmHg, the kidney function was not affected). Once the collateral circulation could not compensate the IVC stricture or occlusion, IVC replacement was necessary. In our study, 3 patients with AE were given IVC resection without reconstruction and had good short- and long-term survival. As for H1, we protected the hepatic vein of the residual liver during the operation and HVR was unnecessary. If 3 hepatic veins were involved (H2), hepatic vein plasty (with autogenous vein graft or ePTFE patches) or reimplantation (to the tube graft or residual IVC) was carried out to recover hepatic outflow. However, the criteria of IVC reconstruction in different centers are not identical due to the small sample size and patient heterogeneity (Table 7).

Vascular exclusion methods, including intermittent Pringle maneuver, TVE and CIBH, are all widely utilized in different centers^[24,25,29-31]. In our study, multivariate analysis showed that duration of liver ischemia was a factor predictive of operative death ($P = 0.005$). When the duration of anticipated TVE was longer than 60 min, hypothermic hepatic perfusion (University of Wisconsin solution, chilled to 4°C) was applied to acquire an extended period of time (the longest was 102 min in our study) and protect the remnant liver. Kim *et al*^[32] used a new technique of extracorporeal

hepatic venous bypass to avoid hypothermic perfusion successfully. They sutured a part of cryopreserved iliac vein to the hepatic vein stump of the remnant liver and a cannula for hepatic venous bypass was placed in it to drain the blood to the internal jugular vein. When we carried out *ex vivo* and anti-situm, consistent with some of the previous reports^[10,21,29], we used VVB if hemodynamic intolerance and splanchnic congestion occurred. Our criterion was: a decrease in mean arterial pressure $> 30\%$ and/or a decrease in cardiac index $> 50\%$. However, Zhang *et al*^[33] have performed *ex vivo* liver resection and liver autotransplantation without VVB in order to shorten anhepatic time. After removing en bloc liver and IVC, they replaced the IVC transiently with a tube graft before reconstructing the IVC with autogenous veins. In one of our patients, we also utilized synthetic caval graft to replace the resected part of IVC combined with transient portacaval shunt reconstruction. A vena cava vessel made by autogenous veins was applied to replace the IVC eventually. This technique is feasible and it could take place of VVB in selected patients.

If the lesions involved 3 hepatic veins at the hepatic vein confluence (H2), then *ex vivo*, *in situ* perfusion and anti-situm technique were applied. In these cases, hepatic vein reconstruction of the remnant liver should be done^[17]. *In situ* perfusion and anti-situm technique were preferable for protection of the portal structures. However, if the portal triads were also involved, *ex vivo* technique had to be used. We have performed *ex vivo* liver resection followed by autotransplantation on several patients with advanced AE. The IVC were replaced using autogenous vein graft or artificial graft. We propose that AE may be a specific indication for *ex vivo* technique, with better prognosis than in malignant cancers.

In conclusion, liver resection combined with IVC and/or HVR is technically feasible with acceptable short-term survival. However, IVC replacement should be prudent as it was a risk factor related to postoperative death. In addition, preoperative liver function should be given special attention and intraoperative liver ischemia time should be shortened to reduce postoperative mortality. The proposed IH classification, which divided the patients into 5 groups according to the range of vascular invasion, may be meaningful in selecting procedures

Table 7 Surgical technique of reported series of hepatectomies combined with inferior vena cava reconstruction

Ref.	Year	No. of cases	Indication	IVC repair type			Hepatic vein reconstruction	VVB	Perfusion	Technique	IVC reconstruction criteria
				Tube	Patch	Suture					
DuBay <i>et al</i> ^[13]	2009	9	IVC leiomyosarcoma = 4; ICC = 2; PCC = 1; Metastases = 1; Malignant schwannoma = 1	7	0	0	Into the native IVC = 1; Into the graft = 5; Primary repair = 1	Not described	9	<i>In situ</i> perfusion	Not described
Malde <i>et al</i> ^[15]	2011	35	metastasis = 21; HCC = 6; ICC = 3; Other conditions = 5	11	2	22	Not described	Not described	12	<i>In situ</i> perfusion = 13; Anti situm = 3; <i>Ex vivo</i> = 6	< 2 cm: direct suture; > 2 cm: with patches; > 50% of the circumference and longitudinally infiltration: replacement
Azoulay <i>et al</i> ^[31]	2006	22	Metastasis = 9; ICC = 8; HCC = 2; Other cancers = 3	10	4	8	Into the native IVC = 4; Into the graft = 2	12	9	<i>In situ</i> perfusion = 9; Anti situm and <i>ex vivo</i> = 0; TVE only = 12; Others = 1	< 30% circumference: longitudinally suture; 30%-50% circumference: transversely suture; > 50% circumference: replacement
Madariaga <i>et al</i> ^[21]	2000	9	Metastasis = 1 IVC leiomyosarcoma = 3; ICC = 3; other cancers = 2	8	0	1	Into the graft = 1; Primary repair = 1	1	0	<i>In situ</i> perfusion, Anti situm and <i>ex vivo</i> = 0; TVE only = 3	Not described
Giordano <i>et al</i> ^[25]	2011	23	Metastases = 13; ICC = 3; HCC = 4; Others = 3	7	0	16	Into the graft = 1	4	4	<i>In situ</i> perfusion = 4; Anti situm = 0; <i>Ex vivo</i> = 0	< 30% of the circumference: suture; > 50% of the circumference: replacement
Hemming <i>et al</i> ^[24]	2012	60	ICC = 26; HCC = 16; Metastases = 13; Others = 5	38	14	8	Into the graft = 4	6 (<i>ex vivo</i>)	8	<i>In situ</i> perfusion = 8; <i>Ex vivo</i> = 6; Anti situm = 0	< 3 cm longitudinally: end-to-end anastomosis; > 5 cm sections of the anterolateral wall: with patches; 3-8 cm longitudinally: replacement
Yamamoto ^[29]	2012	7	ICC = 2; HCC = 5	4	1	2	Into the graft = 4	0	7	Anti-situm = 7	> 50% of the circumference: replacement
Lodge <i>et al</i> ^[10]	1999	8	Metastasis = 8	3	4	1	Into the native IVC = 1; Into the graft = 3	6 (4 <i>ex vivo</i> and 2 TVE)	Not described	<i>Ex vivo</i> = 4; TVE only = 4; Anti situm = 0	< 60° circumferentially and < 2 cm longitudinally: clamp tangentially

PCC: Perihilar cholangiocarcinoma; IVC: Inferior vena cava; HCC: Hepatocellular carcinoma; ICC: Cholangiocarcinoma.

for patients with hepatocaval confluence infiltration. However, due to the small sample size and patient heterogeneity in the present study, this classification still needs to be investigated in more studies. For example, IVC replacement and HVR must be applied in type I2H2 patients to achieve R0 resection. Nevertheless, such an aggressive treatment is controversial for colorectal liver metastasis and HCC because alternative treatment approaches with lower morbidity and mortality could be

applied. Consequently, the proposed IH classification describes anatomic issues but may not have identical significance in guiding surgical approach and indicating postoperative prognosis in different liver diseases.

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COMMENTS

Background

Though technically challenging, hepatectomy combined with major vascular resection and reconstruction has been performed in many centers because it was the only way to achieve R0 resection. However, the surgical indications and protocols were different and controversial in different centers.

Research frontiers

The authors investigated the short-term outcomes and risk factors predictive of postoperative death for patients with lesions adjacent to the hepatocaval confluence.

Innovations and breakthroughs

The authors established the "IH classification" dividing the patients into 5 groups according to the range of vascular invasion, which was meaningful in selecting procedures for patients with hepatocaval confluence infiltration.

Applications

In this study, the authors present their surgical guideline and outcomes about the combined liver and inferior vena cava (IVC) resection in 54 patients with different kinds of liver lesions invading the hepatocaval confluence. The IH classification was established based on our experience, which can be a reference for other surgeons.

Peer-review

This is an interesting paper reviewing the center's experience with a very challenging group of patients with liver malignancies and IVC or hepatic vein involvement.

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