Hepatic Resection Combined with Portal Vein or Hepatic Artery Reconstruction for Advanced Carcinoma of the Hilar Bile Duct and Gallbladder

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Abstract. Hepatectomy with vascular reconstruction for biliary malignancy remains controversial. This study aimed to clarify the indications for surgery. Patients with advanced hilar bile duct cancer (HBDC) ($n = 26$) and gallbladder cancer (GBC) involving the hepatoduodenal ligament ($n = 13$) who underwent hepatectomy were enrolled. They were divided into two groups on the basis of whether vascular reconstruction was performed (HBDC, 10 yes vs. 16 no; GBC, 5 yes vs. 8 no). Portal vein (PV) reconstruction was performed on the right branch in seven patients and on the left branch in two; hepatic artery (HA) reconstruction was done on the right branch in 11 patients and on the left branch in 1. Five patients with HBDC and one with GBC underwent both PV and HA reconstruction. Patency rates were 88.0% and 83.3% for PV and HA reconstructions, respectively. Vascular reconstruction-related morbidity occurred in one patient with fatal liver failure owing to a portal thrombus and in two patients with multiple liver abscesses caused by arterial obstruction. Microsurgery eliminated reconstruction-related morbidity. Mortality in vascular reconstruction cases was 13.3% (2/15), and in those without reconstruction it was 8.3% (2/24). Curability rates (R0 and R1+R2) were 50.0% and 56.0% for HBDC and 40.0% and 62.5% for GBC, respectively. The 3-year survivals of HBDC patients were, respectively, 33% and 42%, and the 5-year survivals were 18% and 25%, whereas for GBC the 1-year survivals were 20% and 60% and the 2-year survivals 0% and 25%. Two patients with vascular involvement who underwent PV with HA reconstruction survived more than 3 years. Hepatectomy with vascular reconstruction for selected HBDC patients offers low surgical risk and increased survival by curable resection, but it is not recommended for advanced GBC.

Hilar bile duct cancer (HBDC) and advanced gallbladder cancer (GBC) remain a challenge to surgeons. Both diseases have the propensity to invade extensively, not only along the bile duct but also into adjacent organs via the lymphatics and perineural spaces. The region of the portal vein and right hepatic artery bifurcations is often involved because these vessels run just behind the bile duct and to the left of the gallbladder neck.

With the advent of advances in surgical techniques including microsurgery, hepatic resection combined with portal vein (PV) and hepatic artery (HA) resection and reconstruction has made pos-

sible curative surgery for advanced cancer of the bile duct [1, 2]. However, this aggressive surgical approach remains controversial in regard to the balance between risk and the effect on survival. In this study we aimed to determine, from the surgical outcome, the indications for hepatectomy combined with vascular resection and reconstruction in these diseases.

Patients and Methods

The study was conducted on 39 patients in whom partial hepatectomy and extrahepatic bile duct resection were performed at the Second Department of Surgery, Yokohama City University from 1991 to 2000. Among 38 consecutive HBDC patients who underwent resection, 26 had cancer permeation to the hepatoduodenal ligament; and of 27 consecutive GBC patients who underwent resection, 13 had cancer invasion at least as deep as the subserosal layer (pT2) and permeation to the hepatoduodenal ligament. Informed consent was obtained from all patients.

The patients were classified into two groups depending on whether vascular reconstruction was performed. There were 10 HBDC and 5 GBC patients in whom vascular reconstruction was performed and 16 HBDC and 8 GBC patients in whom it was not. All the resected specimens were examined pathologically.

The background of each group is discussed using the TNM classification of malignant tumors [3] and the general rules for surgical and pathological studies on cancer of the biliary tract in Japan [4]. In the vascular reconstruction group there were significantly higher rates of PV involvement in HBDC patients and HA involvement in GBC patients (Table 1). Except for the mean age, the stage of invasion of the PV in HBDC, and the stage of invasion of the hepatic artery HA in GBC, the clinicopathologic backgrounds did not differ between the patients who did or did not undergo vascular reconstruction.

Surgical Procedure

The indications for vascular reconstruction depended on the conditions of vascular invasion shown by computed tomography (CT)

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Table 1. Background of patients.

Background	Hilar bile duct carcinoma			Gallbladder carcinoma		
	VR yes ($n = 10$) 2:3:5[a]	VR no ($n = 16$)	p	VR yes ($n = 5$) 1:3:1[a]	VR no ($n = 8$)	p
Age (years)	58 (45-67)	66 (51-75)	0.0316	71 (65-81)	63 (48-72)	0.1482
Gender (male:female)	5:5	11:5	0.2280	2:3	1:7	0.5105
pT[b]						
1	0	0	0.1904	0	0	0.2929
2	1	6		0	0	
3	9	10		2	6	
4	0	0		3	2	
pN[b]						
0	3	7	0.224	1	1	0.2622
1	1	5		2	1	
2	5	3		0	3	
3	1	0		2	1	
4	0	1		0	2	
Stage[b]						
I	0	0	0.3834	0	0	0.8351
II	1	3		0	0	
III	0	2		1	2	
IV A	9	11		0	0	
IV B	0	0		4	6	
PV[c]						
0	5 (2:2:1)	15	0.0304	4 (0:3:1)	8	0.3846
1	2 (0:1:1)	0		1 (1:0:0)	0	
2	3 (0:0:3)	1		0	0	
3	0	0		0	0	
A[c]						
0	7 (2:3:2)	15	0.2642	1 (0:1:0)	7	0.0275
1	3 (0:0:3)	1		1 (0:1:0)	1	
2	0	0		3 (1:1:1)	0	
3	0	0		0	0	
Residual tumor[c]						
0	4	9	0.0933	2	5	0.1699
1	5	2		3	1	
2	1	5		0	2	

VR: vascular reconstruction.

[a]Ratios are the number of patients who underwent reconstruction of the portal vein relative to those who underwent hepatic artery reconstruction or both portal vein and hepatic artery reconstruction.

[b]Pathologic classification of primary tumor (pT), regional lymph node (pN), stage, and residual tumor were classified according to the TNM classification of malignant tumors of the Union Internationale Contre le Cancer (UICC) [3].

[c]The degree of direct invasion to the portal system (PV) and the degree of direct invasion to the artery (A) were according to the general rules for cancer of the biliary tract of the Japanese Society of the Biliary Tract [4].

imaging, angiography, intraoperative echography, macroscopic inspection, and palpation. The PV or the HA was resected according to the invasion site, which was macroscopically diagnosed while stripping off the adventitia of vessels during skeletonization of the hepatoduodenal ligament. The cancer-free margin was confirmed by intraoperative frozen section examination of marginal tissues.

Before portal vein clamping, prostaglandin E_1 (PGE_1) (0.01 μg/kg/min) and a bolus injection of methylprednisolone (500 mg) were usually administered together systemically to minimize ischemic reperfusion injury.

Portal anastomosis for segmental resections were done in six cases under a magnifying lens using running sutures of 5-0 or 6-0 nylon and employing an intraluminal suture method for the posterior wall. Wedge resections of the portal vein were reconstructed by primary closure in three cases.

Left lobectomy and left trisegmentectomy for HBDC required portal reconstruction between the right PV or the posterior PV and the main PV in five cases. Left trisegmentectomy required an interposition graft using the external iliac vein between the posterior PV and the PV in one case. Extended right lobectomy for HBDC or right partial hepatic resection for either HBDC or GBC necessitated PV reconstruction between the left or right PV and the main PV in four cases (Table 2).

A magnifying lens was also used for arterial anastomoses in five cases prior to 1994. After 1994, a microsurgical technique was employed with the assistance of plastic surgeons using 9-0 nylon interrupted sutures after inverting the vessel by means of clamps to facilitate suturing the posterior wall.

Using an interrupted suture, end-to-end anastomosis of the left hepatic artery was performed in one cases of central bisegmentectomy for HBDC; the proper or right hepatic artery was anastomosed with the right hepatic artery (RHA) in five cases of HBDC (three left lobectomies; one left trisegmentectomy; one medial segmentectomy); and one liver bed resection was done for GBC. The RHA was anastomosed to the posterior right hepatic artery (PRHA) during one left trisegmentectomy for HBDC and one S4a+S5 resection for GBC. The gastroduodenal artery was anastomosed to the PRHA in one anterior segmentectomy for GBC, and the middle colic artery (MCA) was anastomosed to the RHA during one left hepatectomy for HBDC.

Simultaneous reconstruction of the portal vein and the hepatic artery was performed in 5 of 10 patients with HBDC and in one of 5 patients with GBC. Generally, to prevent prolonged ischemia due to simultaneous clamping of the invaded portal vein and hepatic artery, reconstruction was first performed on one of these vessels; then the other was resected and later reconstructed. Systemic hep-

Table 2. Procedures used for hepatic resection.

| | Hilar bile duct carcinoma | | Gallbladder carcinoma | |
Procedure	Present ($n = 10$) (2:3:5)[a]	Absent ($n = 16$)	Present ($n = 5$) (2:2:1)[a]	Absent ($n = 8$)
Liver bed resection	0	0	2 (1:0:1)	1
Caudate lobectomy	0	3	0	0
S4a + S5 resection	0	0	1 (0:1:0)	1
Medial segmentectomy	1 (0:1:0)	1	0	0
Anterior segmentectomy	0	1	1 (0:1:0)	0
S4a + anterior segmentectomy	0	0	0	1
S4a + S5 + posterior segmentectomy	0	0	1 (1:0:0)	0
Medial bisegmentectomy	1 (0:1:0)	0	0	0
Right lobectomy	0	3	0	0
Extended right lobectomy	1 (1:0:0)	3	0	4
Right trisegmentectomy	0	0	0	1
Left lobectomy	4 (0:1:3)	5	0	0
Left trisegmentectomy	3 (1:0:2)	0	0	0

[a]Ratios are the number of patients who underwent reconstruction of the portal vein relative to those who underwent hepatic artery or both portal vein and hepatic artery reconstruction.

S4a: dorsal portion of medial segment of the liver; S5: right anteroinferior subsegment of the liver.

Table 3. Postoperative complications.

| | Vascular reconstruction | | | | |
Parameter	PV ($n = 3$)	HA ($n = 6$)	PV+HA ($n = 6$)	Absent ($n = 24$)	Total ($n = 39$)
Morbidity	1 (33.3%)	4 (66.7%)	5 (83.3%)	17 (70.8%)	28 (71.8%)
Liver failure	1	0	1	2	4
Portal thrombosis	0	0	1	0	1
Arterial obstruction	0	1	1	0	2
Intraabdominal bleeding	0	0	0	2	2
Biliary fistula	0	1	2	3	6
Anastomotic leakage	1	3	2	4	10
Cholangitis	1	0	0	4	5
Liver abscess	0	1	1	0	2
Sepsis	0	0	1	3	4
Colitis	0	0	0	2	2
Pulmonary thrombosis	0	0	0	1	1
Pneumonia	0	1	1	3	5
Mortality (hospital death)	1 (33.3%)	0	1 (16.7%)	2 (8.3%)	4 (10.3%)

PV: portal vein; HA: hepatic artery.

arinization was not used for postoperative management. The mode of cancer recurrence after surgery was diagnosed using CT, ultrasonography, and tumor markers.

Statistical analysis was performed using the χ^2 test. Survival curves were prepared using Kaplan-Meier survival analysis, and the significance of survival was determined by the log-rank and generalized Wilcoxon tests. A value of $p < 0.05$ was considered statistically significant.

Results

Morbidity and Mortality

The morbidity rates for patients with HA reconstruction (66.7%) and those with PV + HA reconstruction (83%) were higher than that of PV cases (33%). In particular, hepaticojejunal anastomotic leakage, which was normalized through bile drainage management, occurred frequently in HA cases. However, there were no significant differences between cases in which vascular reconstruction was performed and those in which it was not (70.8%) (Table 3).

Acute fatal liver failure after surgery was encountered in one patient with thrombosis following PV reconstruction. This case occurred in 1992, early in our experience with the procedure.

Liver abscesses directly related to decreased arterial flow, were encountered in two HA reconstruction cases, both of which were performed using a magnifying lens. One patient died as a result of recurrence and a liver abscess while still in hospital after surgery. Another patient was discharged with an indwelling drainage catheter. We have had no such cases since the introduction of microsurgery in 1994. The patency rate evaluated by Doppler echography and other imaging modalities was 88.8% (8/9) in PV patients and 83.3% (10/12) in HA patients.

Mortality rates including hospital deaths due to recurrent primary disease were 13.3% (2/15) in vascular reconstruction cases and 8.3% (2/24) in those without vascular reconstruction. The mortality among PV patients was 33.3% (1/3), HA patients 0% (0/6), and PV+HA patients 16.7% (1/6).

Survival and Recurrence

Survival rates for the HBDC patients as a result of potentially curative surgery (R0 vs. R1+R2) were 50% versus 26% at the 3-year follow-up and 50% versus 10% at the 5-year follow-up ($p < 0.01$). The curability rates (R0:R1+R2) for the reconstruction and no-reconstruction groups were 50% (5:5) and 56.6% (9:7), respectively, in HBDC cases (Table 1), the survival rates of the HBDC patients were 32% and 42% after 3 years and 18% and 25% after 5
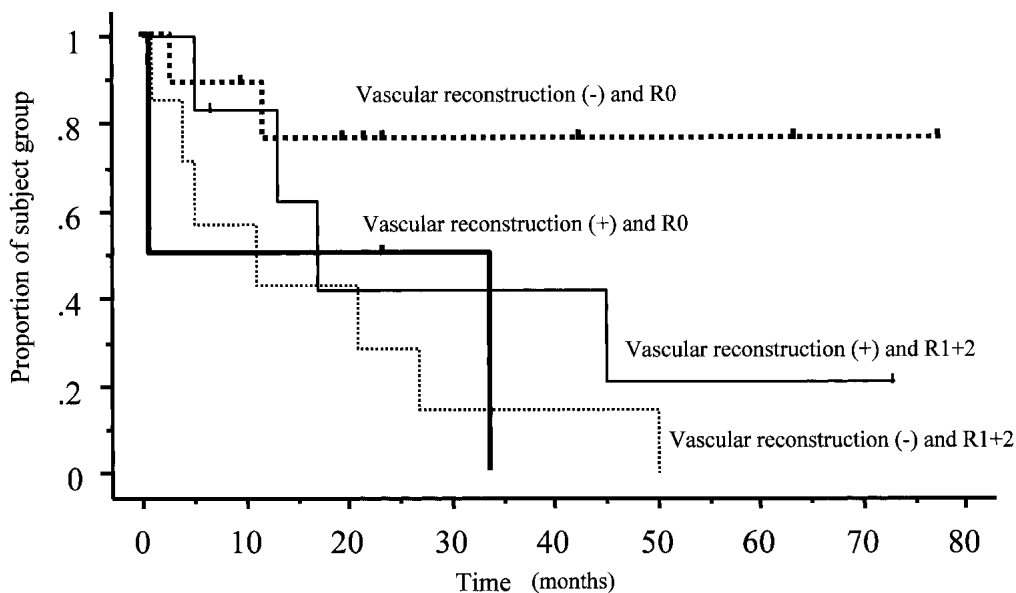
Fig. 1. Cumulative survival curves of patients with hilar bile duct carcinoma. R0: no residual tumor; R1: microscopic residual tumor; R2: macroscopic residual tumor.
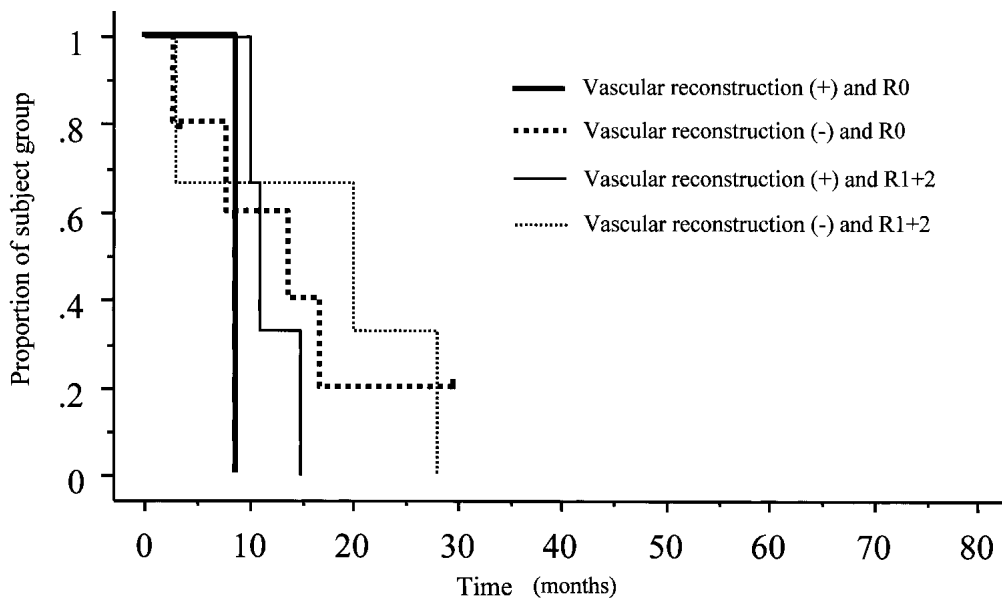
Fig. 2. Cumulative survival curves for patients with gallbladder carcinoma.

years, respectively, with the difference between them not significant (Fig. 1).

However, the 1- and 2-year survival rates resulting from potentially curative surgery for the GBC patients (R0 vs. R1+R2) were 42% versus 50% and 15% versus 18%, respectively. The curability rates (R0:R1+R2) of the reconstruction and the no-reconstruction groups among GBC cases were, respectively, 40.0% and 62.5% (Table 1); the survival rates for the GBC patients were 20% and 60% at 1 year and 0% versus 25% at 2 years, respectively (Fig. 2). Taking into consideration the fact that the vascular reconstruction group had a significantly higher rate of PV involvement in the HBDC patients, potentially curative surgery provided a survival benefit in HBDC patients but not in GBC patients.

When the disease recurred, the HBDC patients with vessel reconstruction showed a predominantly peritoneal distribution, whereas the GBC patients had a peritoneal distribution, lymph node or liver metastasis, and local recurrence (Table 4). We en-

Table 4. Site of recurrence.

Site of recurrence	Hilar bile duct carcinoma		Gallbladder carcinoma	
	Present (3/10)	Absent (8/16)	Present (5/5)	Absent (6/8)
Local	0	1	1	1
Lymph node	0	1	2	3
Peritoneum	5	6	3	1
Case number	0	1	2	2
Lung	0	2	0	1
Percutaneous transhepatic cholangio drainage tract	0	1	1	0
Pleura	1	0	0	0

Table 5. Clinicopathologic characteristics of patients who survived > 3 years.

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	58	55	61	55	72	70
Gender	Male	Male	Male	Male	Male	Male
Disease	Hilar bile duct ca.	Hilar bile duct ca.	Hilar bile duct ca.	Hilar bile duct ca.	Hilar bile duct ca.	Hilar bile duct ca.
Tumor differentiation	Moderate	Moderate	Moderate	Well	Moderate	Well
Lymph node metastasis[a]	–	+	–	–	+	–
Lymphatic vessel invasion[a]	–	+	–	–		–
Venous invasion[a]	–	–	–	+	–	
Perineural invasion[a]	+++	++	–	+	–	
Vascular involvement[a]	++	–	–	–	–	
Operation	Left lobectomy + caudate lobectomy	Left trisegmentectomy + caudate lobectomy	Medial segmentectomy + caudate lobectomy	Right lobectomy + caudate lobectomy	Anterior segmentectomy + caudate lobectomy	Extended right lobectomy + caudate lobectomy
Vascular reconstruction	PV + HA	PV + HA	–	–	–	–
Residual tumor	R1	R1	R0	R0	R2	R0
Outcome (months)	73 Dead (gastric cancer)	45 Dead	78 Alive	64 Alive	50 Dead	43 Alive

ca.: carcinoma.

[a]Lymph node metastasis, lymphatic vessel invasion, venous invasion, perineural invasion, and vascular involvement were evaluated according to the Japanese Society of Biliary Surgery (JSBS) classification [4].

countered six patients with advanced HBDC who survived more than 3 years (Table 5). Two had undergone vascular reconstruction and four had not. Two long-term survivors who underwent vascular reconstruction of both the PV and the HA had perineural invasion and vascular involvement resulting in an R1 lesion.

Discussion

As surgical techniques have developed, hepatectomy combined with vascular reconstruction has come to be performed as a potentially curative resection method for HBDC or advanced GBC. There is controversy, however, over the long-term survival benefit and the surgical risk of this approach. In this study and other reports [5–9], there were more long-term survivals of HBDC patients who underwent potentially curative resection than among patients who had had a noncurative resection.

In our study the curative resection rate of the HBDC patients who underwent vascular reconstruction was almost the same as that in patients who did not. Given the higher rate of vascular involvement in vascular reconstruction cases, it appears that vascular reconstruction contributes to increases the number of curative resections in patients with HBDC. However, fewer GBC patients with vascular reconstruction had a curative resection than those who did not undergo reconstruction, suggesting that vascular resection could be used to reduce the allocated tumor stage (e.g., from T3 to T2) in cases of HBDC but not in cases of advanced GBC.

Many reports have described hepatectomies combined with vascular resection and reconstruction for biliary malignancy [2, 4, 10–18], but few have described the survival effects or indications [1]. Neuhaus et al. [8] and Ishiyama et al. [19] reported in multivariate analyses after R0 resection that additional resection of the portal vein was the only variable with a significant influence on the survival of patients with hilar cholangiocarcinoma. Furthermore, among our cases, two patients with vascular involvement who underwent vascular reconstruction survived more than 3 years. Therefore, resection with vascular reconstruction was thought to contribute to increased local control of cancer.

In contrast, the rate of long-term survival of GBC patients with permeation as far as the hepatoduodenal ligament did not show any difference between patients with curative resection and those with noncurative resection. The reason for the absence of any difference in the long-term survival rate of GBC patients was probably that the stage was too advanced to permit a cure by local extended resection, including vascular resection and reconstruction.

Since the report of Longmire et al. [10] in 1973, several articles regarding portal vein resection and reconstruction for treatment of HBDC or GBC [11–14] have described of vascular reconstruction procedures, such as an oblique cut on the hepatic side of the portal vein to allow adjusting the caliber of the two ends [1, 14] and the intraluminal suture method with the addition of growth factor [15].

Nakao and Kondo [20] reported use of a heparinized hydrophilic catheter between the superior mesenteric vein (SMA) and the femoral or umbilical vein to avoid intestinal congestion during clamping of the portal vein. We, however, used no venous bypass under the SMA occlusion unless complete portal occlusion was anticipated to last more than 60 minutes during procedures such as combined resection of the PV and HA. In such cases an active bypass using a centrifugal pump (Biopump with Medtronic/Canada Bio-Active Surface; Medtronic Bio-Medics, Eden Prairie, MN, USA) from the superior mesenteric vein to the left portal vein, passing through the umbilical portion, could be used without heparinization.

There were some complications related to the vascular reconstruction cases, such as liver failure due to a portal thrombus at the anastomotic site [17] and a liver abscess due to obstruction of the anastomotic hepatic artery to be anastomosed. Gerhards et al. [21] reported that extended liver resections and vascular resections were found by univariate analysis to be significant predictors of increased mortality during surgical treatment for hilar cholangiocarcinoma. Recently, however, arterial reconstruction became a safe procedure with the introduction of microscopic surgery excluding reconstruction for severe atherosclerosis [17, 22]. Moreover, with the development of skill with the technique, the patency rate after PV reconstruction examined by the echocardiographic Doppler

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method rose to nearly 100%. On the basis of these reports, portal vein or hepatic artery resection and reconstruction can be recommended as a reasonable surgical approach in selected patients with HBDC in whom hepatectomy combined with vascular resection can result in curative resection. However, the long-term survival of patients with GBC who underwent vascular reconstruction was not as good as expected. Therefore treatment such as stenting together with chemoradiation is recommended in patients with GBC requiring hepatectomy combined with vascular resection to achieve curative resection.

Résumé. La reconstruction vasculaire lors de l'hépatectomie pour lésions envahissant les voies biliaires reste un sujet de débat. Cette étude a pour but de clarifier les indications chirurgicales. Les patients ayant eu une résection hépatique pour cancer du hile avancé(CH, *n* = 26) ou un cancer vésiculaire envahissant le ligament hépatoduodénal (petit épiploon) (CV, *n* = 13) ont été divisés en deux groupes selon qu'une reconstruction vasculaire a été réalisée ou non (respectivement, CH, 10 vs. 16; et CV, 5 vs. 8). Une reconstruction de la veine porte (VP) a été réalisée au niveau de la branche droite (7 patients) ou gauche (2), une reconstruction de l'artère hépatique (AH) au niveau de la branche droite (11 patients) ou gauche (1). Cinq patients atteints de CH et un atteint de CV ont eu à la fois une reconstruction de la veine porte et l'artère hépatique. Le taux de perméabilité ont été, respectivement, de 88% et de 83.3% dans les reconstructions de la VP et AH. La morbidité/mortalité en rapport avec la reconstruction vasculaire a été un cas fatal d'insuffisance hépatique secondaire à une thrombose porte et deux instances d'abcès hépatique multiples secondaire à l'occlusion artérielle. Cependant, la microchirurgie semble améliorer la morbidité en rapport avec la reconstruction vasculaire. La mortalité a été de 13.3% (2/15) lorsque la reconstruction a été pratiquée, et de 8.3% (2/24) en son absence. Les taux de cure (R0 à Rl+R2) ont été, respectivement, de 50% et de 56% en cas de CH, et de 40.0% et de 62.5% en cas de CV. La survie à trois ans chez les patients porteurs de CH a été respectivement de 33% et de 42%, et à 5 ans, de 18% et de 25%, alors que pour le CV, la survie à un an a été respectivement de 20% et 60%, et à deux ans, de 0% et 25%. Deux patients avec envahissement vasculaire qui ont eu une reconstruction à la fois de la VP et de l'AH ont survécu plus de trois ans. L'hépatectomie avec reconstruction vasculaire est possible pour des patients sélectionnés avec un risque chirurgical modéré et la résection est suivie d'une meilleure survie; cependant, on ne peut la recommander en cas de CV avancé.

Resumen. En el tratamiento del cáncer de vías biliares, la hepatectomía con reconstrucción vascular sigue estando sujeta a discusión. Este estudio pretende clarificar y puntualizar las indicaciones quirúrgicas a este respecto. Pacientes con cáncer avanzado de vías biliares (HBDC, *n* = 26) y con cánceres de vesícula biliar con invasión del ligamento hepatoduodenal (GBC, *n* = 13), sometidos a hepatectomía, fueron divididos en 2 grupos según se realizase o no, una reconstrucción vascular (HBDC: 10 vs. 16 y GBC: 5 vs. 8). Se efectuó la reconstrucción de la rama derecha de la vena porta en 7 pacientes y de la izquierda en 2; (PV). La arteria hepática (HA) se reconstruyó en 12 pacientes: la rama derecha en 11 y la izquierda en 1. En 5 enfermos con HBDC y en 1 con GBC, se restauraron tanto la vena porta (PV) como la arteria hepática (HA). La tasa de permeabilidad fue del 88% para las reconstrucciones portales (PV) y del 83.3% para las arteriales (HA). Se registraron 3 casos cuya morbilidad fue atribuible a la reconstrucción vascular; uno, de evolución fatal por fallo hepático propiciado por un trombo portal y dos, en los que se originaron abscesos múltiples de hígado tras obstrucción arterial. Sin embargo, la utilización de técnicas microquirúrgicas eliminaron la morbilidad dependiente de las reconstrucciones vasculares. La mortalidad en casos de hepatectomía con reconstrucción vascular fue del 13.3% (2/15) y sin reconstrucción del 8.3% (2/24). El porcentaje de curación (R0 hasta R1 + 2) fue del 50% y 56% para los HBDC y del 40% y 62% para los GBC. Para los H BDC la tasa de supervivencia a los 3 años fue del 33% y 42% y a los 5 años del 18% y el 25%, mientras que para los GBD la supervivencia al año fue del 20% y del 60% y a los 2 años del 0% y 25% respectivamente. Dos pacientes con invasión vascular con sendas reconstrucciones de la PV y HA sobrevivieron más de 3 años. La hepatectomía con reconstrucción vascular en pacientes seleccionados con HBDC ofrece escaso riesgo quirúrgico, incrementando la supervivencia en casos de resecciones curativas. Este proceder no se recomienda en cánceres avanzados GBC. Palabras clave: Cáncer hepatocoledocociano, hepatectomía, reconstrucción vascular, microcirugía, insuficiencia hepática aguda, abscesos hepáticos.

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