

# En Bloc Resection of the Hepatoduodenal Ligament for Advanced Biliary Malignancy

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## Abstract

**Background** En bloc resection of the hepatoduodenal ligament (HDL) for advanced biliary malignancy by hepatoligamentopancreatoduodenectomy (HLPD) or hepatoligamentectomy (HL) remains challenging, and only short-term outcomes have been reported. We showed our surgical technique of HLPD and HL, and retrospectively investigated surgical outcomes of the patients.

**Methods** Between 2003 and 2014, we performed four HLPD and three HL including major hepatectomy with concomitant caudate lobectomy. Portal vein reconstruction (PVR) was performed with a right external iliac vein graft, and hepatic artery reconstruction (HAR) was accomplished with the heterogeneous artery using the continuous suturing method.

**Results** Mean operation time and blood loss were  $575 \pm 111$  min and  $1539 \pm 950$  mL, respectively, and patency of the reconstructed vessels was confirmed postoperatively in all cases. Histologically, negative surgical margins (R0) were achieved in 57 % of patients, while the resected vascular invasion was confirmed in all patients. Overall morbidity was high at 57 %, but we have achieved no postoperative mortality. Overall median survival time of the patients was 36 months, and a patient of HL survived over 5 years.

**Conclusions** En bloc resection of the HDL based on steady vascular reconstruction can improve the surgical outcome of biliary cancer in selected patients.

**Keywords** Hepatoduodenal ligament · Biliary malignancy · En bloc resection

## Introduction

In 1986, Hanyu et al.<sup>1</sup> performed the first hepato-ligamentopancreatoduodenectomy (HLPD), consisting of right hepatectomy, pancreatoduodenectomy, and resection of the hepatoduodenal ligament (HDL) (including end-to-end por-

tal vein reconstruction [PVR] without hepatic artery reconstruction [HAR]), for advanced gallbladder carcinoma. In 1991, Mimura et al.<sup>2</sup> investigated short-term outcomes of en bloc resection of the HDL and reported in-hospital mortality in three of eight patients who underwent hepatoligamentectomy (HL) or HLPD and 18 months as the longest postprocedural survival time. To the best of our knowledge, there has been no report of long-term outcomes or precise analysis of patient outcomes after these drastic operations for advanced biliary malignancy. Although both HAR and PVR have been applied at select institutions and have been given prognostic validity, extensive resection of the HDL is not generally warranted. En bloc resection of the HDL may offer the ideal pathologic clearance of infiltrating biliary cancer cells; however, no detailed study has been conducted. Thus, to substantiate en bloc resection of the HDL, we showed our surgical technique of HLPD and HL, and also retrospectively investigated surgical outcomes of the patients.

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## Methods

### Patients

The study group comprised seven patients who were treated by en bloc resection of the HDL at our hospital between June 2003 and February 2014. Four of these patients underwent HLPD (two for gallbladder carcinoma and two for hilar cholangiocarcinoma), and three underwent HL (all for hilar cholangiocarcinoma).

Mean age of the patients was  $62.9 \pm 4.9$  years (range, 56–71 years), and the male/female ratio was 4/3. Mean body mass index (BMI) was  $22.3 \pm 5.1$  (range, 16–30.5), and patients' ECOG performance status was 0 or 1. Obstructive jaundice was observed preoperatively in six patients, and the preoperative serum total bilirubin level was controlled at  $<3$  mg/dL before surgery. According to our institutional policy, preoperative portal vein embolization (PVE) is routinely applied to candidates for extended right hepatectomy plus pancreatoduodenectomy and vascular reconstruction along with biliary reconstruction, regardless of the liver volume and function of the future remnant, and all three patients who underwent extended right hepatectomy underwent PVE 2–3 weeks before surgery by percutaneous transhepatic ipsilateral approach.<sup>3</sup>

Vascular involvement was identified as encasement of the hepatic arteries and portal vein and/or a low-density undefined mass around the vessels by multidetector row CT (MDCT), which is the most reliable means of evaluating tumor location and extension to other organs. A decision to perform en bloc resection of the HDL was based mainly on the preoperative MDCT findings, with the main indication being suspected involvement of both the hepatic artery and the portal trunk in the HDL, and if the root of the proper hepatic artery (near the common hepatic artery) was involved due to massive perineural invasion, HLPD was selected rather than HL. In two patients with gallbladder carcinoma, HLPD was performed not only because of the noted criteria but also because of extension of the biliary stricture toward the pancreatic head and/or peripancreatic lymph node swelling. Two patients with hilar cholangiocarcinoma underwent HLPD because the arterial invasion extended to the root of the proper hepatic artery and the pancreatic parenchyma. The extent of biliary tree involvement was assessed by preoperative cholangiography and/or magnetic resonance cholangiopancreatography, and for the surgery to be considered histologically curative, hepatic duct invasion of the future hepatic remnant was limited to the first-order branch.

### Surgical Techniques

After an upper midline incision with a right subcostal extension was made, absence of peritoneal dissemination and macroscopic paraaortic lymph node metastasis were confirmed via the Kocher maneuver. We then investigated the portion

surrounding the ramification of the right portal vein or the root of the umbilical vein to determine the appropriate surgical safety margin in relation to the necessary vascular reconstruction within the hepatic remnant. For HL, the caudal margin of the HDL was identified by noting the parenchymal texture of the adjacent pancreatic head, we resected the peripancreatic tissue including the peripancreatic lymph nodes, preserving the stomach and duodenum, and we divided the common bile duct at the superior border of the pancreas. The proper hepatic artery was encircled at its origin, and the portal trunk was encircled above the confluence of the splenic vein. For HLPD, the distal margin of the HDL was completely resected with the pancreatic head and duodenum, and the pancreatoduodenectomy was always performed first, preserving the plexus around the superior mesenteric artery, and the common hepatic artery was encircled at its origin. The portal vein was encircled at the same position as in HL.

The hepatic parenchyma was transected with the use of an ultrasonic surgical aspirator under hepatic vascular inflow clamping (alternating periods of 15-min clamping and 5-min declamping), and PVR was carried out after division of the hepatic ducts with the caudal portion of the liver parenchyma because PVR facilitates hepatic transection by allowing a good view of the surgical field. Before PVR, the right external iliac vein graft was picked out extraperitoneally via a second skin incision at the right upper groin. The right or left hepatic artery and proper or common hepatic artery were divided, and the portal vein was divided between the right portal branch or root of the umbilical vein and the main portal trunk. In left-sided hepatectomy, the portal vein was divided just below the ramification of the second branch, and in right-sided hepatectomy, the root of the umbilical vein was divided, and a slit was made in the stump to adjust its caliber before anastomosis to the vein graft. Under superior mesenteric artery clamping to avoid intestinal congestion, the hepatic portal vein stump nearest the liver was first reconstructed with a 6–0 polypropylene running suture under loupe magnification (Fig. 1), and the hepatic vascular clamp was moved to the center of the graft. The opposite anastomosis was begun to prevent kinking of the graft. After completion of the PVR (Fig. 2), we resumed the residual hepatic transection and removed the specimen en bloc.

HAR was performed after extirpation of the specimen. Thus, there was a short period of hepatic artery ischemia (HAI). The duration of HAI was prolonged by the hepatic transection and also PVR time, but it was acceptable in our patient series. The ends of both arteries were cut to enlarge the orifices, and side-to-side anastomosis was achieved with a 7–0 polypropylene running suture under loupe magnification (Fig. 3). In cases of HL, HAR was most often accomplished with the gastroduodenal artery, which was detached from the pancreas and rotated upward, and in cases of HLPD, HAR was generally accomplished with the right branch of middle colic artery, which was mobilized along with the middle colic



**Fig. 1** Intraoperative photograph of the portal vein reconstruction performed with an external iliac vein graft during an extended right hepatectomy. PVR is performed at the hepatic side first. An *arrow* indicates the portal trunk clamped at the confluence of splenic vein

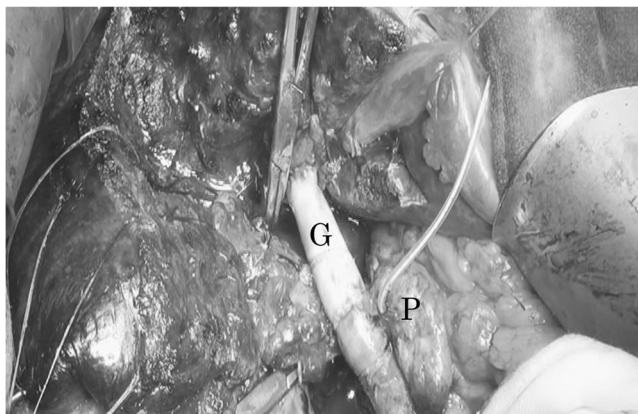
vein (Fig. 4). Systemic heparinization was not applied routinely during the perioperative period.

Finally, hepaticojejunostomy in cases of HL and modified Child's reconstruction in cases of HLPD were achieved by placing a stent across the hepaticojejunostomy and pancreatico-jejunostomy, respectively. In cases of HLPD, drains were placed in the right subphrenic place, beneath the hepaticojejunostomy, and in the cranial portion of the pancreatico-jejunostomy. Typically, these drains were removed within 1 week, but all stents were left in place for 3 weeks.

## Results

### Surgeries Performed and Surgical Details

Patients and the operative procedures are shown on Table 1. Extended right hepatectomy refers to resection of the inferior medial segment with anatomical right hepatectomy, which

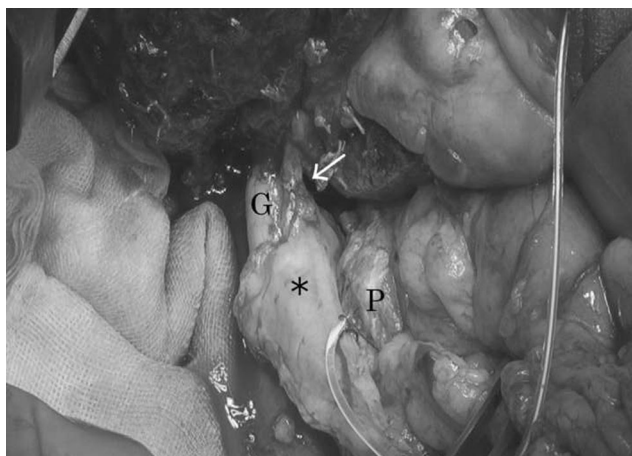


**Fig. 2** Intraoperative photograph of achievement of the portal vein reconstruction. *G* indicates the graft. *P* indicates the stump of the pancreas



**Fig. 3** Intraoperative photograph of the hepatic artery reconstruction. Both ends of the arteries were cut to ensure the adequate orifices

produces not only an appropriate margin of safety but also a good view of the root of the umbilical vein for vascular reconstruction. Mean operation time and estimated blood loss were  $575 \pm 111$  min (449–804) and  $1539 \pm 950$  mL (610–3500), respectively. Blood transfusion was required for four patients at the time of admission. The mean length of the external iliac vein graft was  $3.0 \pm 0.6$  cm (2–4); however, the graft was typically shorter for right-sided hepatectomy than for left-sided hepatectomy. Hepatic artery anastomoses involved the right hepatic artery ( $n=4$ ), left hepatic artery ( $n=1$ ), lateral branch of the left hepatic artery ( $n=1$ ), or medial branch of the left hepatic artery ( $n=1$ ). A heterogeneous artery was used as the donor artery, 3 middle colic arteries, 2 gastroduodenal arteries, 1 ileocolic artery, and 1 right gastric artery. The mean PVR and HAR times were  $22.6 \pm 4.9$  min (16–30) and  $22.1 \pm 6.9$  min (14–31), respectively. HAR was performed after extirpation of the specimen; therefore, mean HAI time for the patients was  $131 \pm 19.2$  min (106–159).



**Fig. 4** Intraoperative photograph of completion of the hepatic artery reconstruction. An *arrow* indicates the site of hepatic artery anastomosis. *Asterisk* indicates the mobilized middle colic artery with vein

**Table 1** Clinical and surgical details, per patient

Patient	Age (yr)	Sex	Disease	Procedure	Hx	OP (min)	EBL (mL)	Graft (cm)	PVR (min)	Donor artery	HAR (min)	HAI (min)
1	56	F	HCC	HLPD	LH	600	1210	3	19	MCA	16	146
2	71	F	GBC	HLPD	ERH	566	1540	3	27	MCA	31	129
3	65	M	GBC	HLPD	ERH	530	770	3	24	MCA	14	138
4	65	M	HCC	HLPD	LH	804	3500	3	16	ICA	16	106
5	58	F	HCC	HL	ERH	541	1600	2	23	RGA	28	129
6	63	M	HCC	HL	LH	449	610	3	30	GDA	22	108
7	62	M	HCC	HL	LH	537	1540	4	19	GDA	28	159

*Hx* extent of hepatectomy, *OP* operation time, *EBL* estimated blood loss, *Graft* length of the graft, *PVR* portal vein reconstruction time, *HAR* hepatic artery reconstruction time, *HAI* hepatic artery ischemia time, *HCC* hilar cholangiocarcinoma, *GBC* gallbladder carcinoma, *LH* left hepatectomy, *ERH* extended right hepatectomy, *MCA* middle colic artery, *ICA* ileocolic artery, *RGA* right gastric artery, *GDA* gastroduodenal artery

**Postoperative Course**

Intrahepatic blood flow (hepatic artery, hepatic vein, and portal vein flow) was estimated during surgery by intraoperative color Doppler ultrasound and confirmed to be adequate, and patency of the postoperative blood flow was reconfirmed by abdominal CT in all patients. Postoperative laboratory values and complications are shown on Table 2. Only patient 7 had a high postoperative serum aspartate transaminase (AST) concentration; however, postoperative MDCT showed the HAR to be patent (Fig. 5). No patient revealed sustained hyperbilirubinemia. Postoperative complications were graded according to the Clavien-Dindo classification system<sup>4</sup> and occurred in four patients (57 %): 3 intraabdominal abscess and 1 postoperative bleeding from the stump of right external iliac vein; however, there was no apparent pancreatic fistula and bile leakage corresponding to grade B pancreatic fistula (International Study Group of Pancreatic Fistula criteria<sup>5</sup>) and bile leakage (International Study Group of Liver Surgery criteria<sup>6</sup>). The postoperative mortality including 30 days and in-hospital was null.

The mean follow-up time for all patients was 34.8 months. Three patients underwent adjuvant chemotherapy, and 5-FU (including S1) or gemcitabine was administered to four patients for disease recurrence. One patient (patient 6) underwent both resection and radiotherapy for seeding tumors (three foci) 4 years after the initial surgery and survived more than 5 years, but dead by the local recurrence. Three patients remain alive, and one patient (patient 7) survives over 4 years without any sign of recurrence. Median survival time of the patients was 36 months.

**Histologic Findings**

Histologic curative resection (R0) was achieved in four of the seven patients (57 %); a positive surgical margin was found around the cut-end of bile duct in two patients (patients 3 and 5) and around the stump of common hepatic artery in one patient

(patient 1). Histologic invasion of the portal vein was seen in all cases, and invasion of the hepatic artery was seen in all but one patient (patient 3). These vascular invasions emerged as a scattering of cancer cells apart from the biliary invasion in some patients and were seemingly impossible to detect preoperatively. The main portal trunk and/or proper hepatic artery was involved (corresponding to the T4 UICC classification<sup>7</sup>) in six of the seven patients, and regional lymph node involvement was confirmed in four patients (57 %)—para-aortic lymph node metastasis was found in one patient (patient 1) and led to a histologic diagnosis of stage IVB cancer.

**Discussion**

Boerma et al.<sup>8</sup> first described block resection of the HDL ligament in autopsy cases about 30 years ago, and on the basis

**Table 2** Postoperative AST and Tbil levels and outcomes, per patient

Patient	Peak AST (IU/L)	Peak Tbil (mg/dL)	Clavien-Dindo grade	Hospital stay (days)	Outcome
1	165	1.5	0	28	DOD, 2 years
2	436	3.0	II	27	DOD, 3 years
3	315	2.0	IIIa	43	AWD, 2 years and 4 months
4	276	3.8	II	29	AWD, 8 months
5	492	4.0	0	29	DOD, 2 years and 2 months
6	279	7.1	0	24	DOD, 5 years and 10 months
7	756	2.3	IIIb	50	NED, 4 years and 4 months

*Peak* maximum postoperative value, *AST* aspartate aminotransferase, *Tbil* total bilirubin, *Hospital stay* postoperative days, *DOD* died of disease, *AWD* alive with disease, *NED* no evidence of disease



**Fig. 5** Postoperative MDCT image of the vascular reconstructions (arrows indicate the sites of hepatic artery anastomosis and portal vein anastomoses)

of a clinical review, they recommended this procedure to improve the long-term results of surgery for biliary malignancy.<sup>9</sup> In Japan, Hanyu<sup>1</sup> and Mimura<sup>2</sup> applied this radical surgery to advanced biliary malignancies, but they did not investigate long-term survival. It remains unclear whether the technical demands of en bloc HDL resection and the advanced stage of the disease will preclude the procedure from becoming a standard operation. HPD and/or concomitant portal vein resection and reconstruction for biliary malignancy have been practiced since the early 1990s, and recently, Nagino et al.<sup>10</sup> reported the prognostic value of simultaneous resection of the portal vein and hepatic artery along with hepatectomy for perihilar cholangiocarcinoma. Of course, our technique (HL or HLPD) is quite different from that of Nagino et al. because en bloc resection of the HDL requires vein graft for PVR and heterogeneous artery for HAR; direct vascular anastomoses are impossible for the newly shortened vessels. In addition, HL or HLPD yielded a cancer-free vertical margin, which is generally challenging in cases of biliary cancer, and HL/HLPD might have prevented the spillage of cancer cells from the small lymphatics and vessels around the regional lymph nodes. This challenging operation raises two questions: Is the surgical procedure safe and what is its prognostic value?

Operative safety is always a crucial issue, especially in relation to hepato-pancreato-biliary surgery. According to recent reports<sup>10–16</sup> regarding major hepatectomy with vascular resection and reconstruction (see Table 3), mortality attributed to PVR ranged from 0 to approximately 20 %. However, Miyazaki et al.<sup>11</sup> reported high HAR-associated mortality. To the contrary, Nagino et al.<sup>10</sup> described a respectably low mortality rate among patients who underwent PVR concomitant with HAR. Like Neuhaus et al.<sup>17</sup> warned of the embarrassment of HAR, HAR would be a key procedure for HL and HLPD. Sound patency of the reconstructed vessels was

mandatory for less morbidity, and we achieved it in all patients. Of course, pancreatic fistula and other major complications might yield somewhat high perioperative mortality; fortunately, we did not encounter any life-threatening side effects of surgery. We did not lose the seven consecutive patients who underwent surgery from 2003, and we believe that the technical expertise gained over time, surgeons' negotiating the learning curve, and a consistent HAR technique ensured a good postoperative course.

From the technical standpoint, PVR should be performed during hepatic transection, after division of the bile ducts along with the hepatic arteries, because a good surgical view can be obtained, and the accomplishment of PVR facilitates the residual hepatic transection. This is supported by the relatively short operation time and acceptable blood loss in our patient series. Graft selection often depends on the surgeon's preference; we preferentially used the right external iliac vein for PVR because of its caliber and its length upon harvest.<sup>18</sup> We recently addressed the functional reserve of the lower limb and quality of life after harvest of the right external iliac vein graft for grafting.<sup>19</sup> Only 3 of the 66 patients showed any morbidity related to the graft harvest, and the resulting edema increased the leg circumference by only 6 %. With the consistent HAR, the mean duration of HAI was 131 min, satisfactory postoperative hepatic artery blood flow was achieved, and no complications associated with hepatic duct anastomosis or liver function (acceptable elevation of postoperative AST values) were encountered. Therefore, we would like to stress that the artery reconstruction is not required immediately after division of the arteries. The blood supply from the diaphragm and the posterior abdomen works as collateral flow to the liver; thus, from the technical standpoint, it is important not to detach the future remnant liver from the abdominal wall. For HL, we used the gastroduodenal artery

**Table 3** Recent reports of hepatectomy with vascular resection

Authors	Year	Type(s) of vascular resection	No. of patients	Mortality
Nagino et al. <sup>11</sup>	2006	PVR	63 (a)	15.9 %
Miyazaki et al. <sup>12</sup>	2007	HAR	9 (1)	33.3 %
Nagino et al. <sup>10</sup>	2010	PVR+HAR	50 (3)	2.0 %
Bachellier et al. <sup>13</sup>	2011	PVR	55 (3)	7.2 %
Hemming et al. <sup>14</sup>	2011	PVR	42 (a)	0 %
Nuzzo et al. <sup>15</sup>	2012	PVR	42 (0)	19 %
de Jong et al. <sup>16</sup>	2012	PVR	51 (0)	17.6 %
Kaneoka et al. <sup>b</sup>	2014	PVR+HAR <sup>c</sup>	7(4)	0 %

Numbers in parentheses indicate the number of combined pancreatoduodenectomies

<sup>a</sup> Not reported

<sup>b</sup> Present study

<sup>c</sup> En bloc resection of the hepatoduodenal ligament

for reconstruction because of its proximity to the hepatic artery and because of its caliber. For HLPD, the right branch of the middle colic artery was preferentially used; however, the ileocolic artery is a good candidate when the middle colic artery is too short to mobilize for reconstruction. HAR requires a meticulous approach, and we confirmed that spatulating the artery stumps and placing continuous sutures are easily performed under loupe instead of microscope and ensure patency of the anastomoses.

The prognosis for patients undergoing en bloc resection of the HDL has been dismal, and there has been no report pointing to long-term survival. Most papers were published about 20 years before the dawn of aggressive surgical approaches for biliary cancer. As far as we know, we are the first to track the long-term results of HL and HLPD and to document a median survival time of 36 months. Two patients with hilar cholangiocarcinoma survived more than 4 years; however, gallbladder cancer showed obstructive jaundice (biliary invasion) and hepatic invasion along the Glissonian sheath, meaning that the disease process was well advanced and there was only a small chance of cure. Although we attempted the curative surgery by the technique of en bloc resection, R0 resection was actually achieved in only 57 %, suggesting that the accurate estimation of the tumor extent is quite difficult in these patients. Adjuvant chemotherapy might contribute some prognostic advantage, but this question was not explicitly assessed in our small patient group.

## Conclusion

Our radical surgical approach to far advanced biliary malignancies was performed with acceptable morbidity, despite the complexity of the procedure, which involves autologous grafting for PVR and preparing heterogeneous artery for HAR. Although the number of the patients was small, we could show their better surgical outcome. If limited to high-volume centers with experienced surgeons, this radical surgery is justified and may offer a cure to some patients who would otherwise receive only palliative care.

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