Combined Resection of the Liver and Inferior Vena Cava for Hepatic Malignancy

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Objective: The objective of this paper is to review the results of combined resection of the liver and inferior vena cava for hepatic malignancy. The morbidity and mortality along with preliminary survival data are assessed in order to determine the utility of this aggressive approach to otherwise unresectable tumors.

Summary Background Data: Involvement of the inferior vena cava has traditionally been considered a contraindication to resection for advanced tumors of the liver because the surgical risks are high and the long-term prognosis is poor. Progress in liver surgery allows resection in some cases.

Methods: Twenty-two patients undergoing hepatic resection from 1997 to 2003, that also required resection and reconstruction of the inferior vena cava (IVC), were reviewed. The median age was 49 years (range 2 to 68 years). Resections were carried out for: hepatocellular carcinoma (n = 6), colorectal metastases (n = 6), cholangiocarcinoma (n = 5), gastrointestinal stromal tumor (n = 2), hepatoblastoma (n = 2), and squamous cell carcinoma in 1 patient. Liver resections performed included 13 right trisegmentectomies, 6 right lobectomies extended to include the caudate lobe, and 3 left trisegmentectomies. Complex ex vivo procedures were performed in 2 cases using venovenous bypass while the other 20 cases were performed using varying degrees of vascular isolation. In situ cold perfusion of the liver was used in 1 case. The IVC was reconstructed with ringed Gore-Tex tube graft (n = 14), primarily (n = 6), or with Gore-Tex patches (n = 2).

Results: There were 2 perioperative deaths (9%). One cirrhotic patient died of liver failure 3 weeks post operatively and 1 patient with cholangiocarcinoma died of pulmonary hemorrhage secondary to a cavitating pulmonary infection after aspiration pneumonia 6 weeks after resection. Six patients had evidence of postoperative liver failure that resolved with supportive management and 2 patients required temporary dialysis. All vascular reconstructions were patent at last follow-up. With median follow-up of 26 months, 5 patients have died of recurrent malignancy at 44, 40, 32, 26, and 24 months, while an additional patient is alive with disease at 31 months. Actuarial 1-, 3-, and 5-year survivals were 85%, 60%, and 33%, respectively.

Conclusions: IVC involvement by hepatic malignancy does not necessarily preclude resection. Liver resection with reconstruction of the inferior vena cava can be performed in selected cases. The increased risk associated with the procedure appears to be balanced by the possible benefits, particularly when the lack of alternative curative approaches is considered.

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In recent years, improved operative technique and a better understanding of the segmental anatomy of the liver have enabled surgeons to perform hepatic resections previously thought to be unresectable with a concomitant decrease in morbidity and mortality. Perioperative mortality has been reduced to less than 5% in most series and 5-year survival is reported from 30% to 50% after liver resection for primary hepatic malignancies, metastatic colorectal cancer, and other noncolorectal cancers metastatic to the liver.[1–5] In the past, patients with involvement of the inferior vena cava (IVC) by hepatic malignancy were considered poor candidates for surgical management. Untreated patients, however, have a median survival of less than 12 months[6] and chemotherapy does not really offer a curative option[7] with few 5-year survivors reported. The development of innovative surgical techniques, such as total hepatic vascular exclusion (HVE),[8] venovenous bypass,[9] and ex vivo hepatic resection,[10–12] has made a curative surgical approach to tumors involving both the liver and IVC possible. The resected IVC can be repaired primarily if the segment of IVC resected is small.[13,14] Larger resections of the IVC that cannot be repaired primarily can be reconstructed with synthetic or autogenous grafts.[15–17] This paper reports our experience with combined hepatic and IVC resection for malignant tumors.

PATIENTS

From January 1997 to December 2003, a total of 22 patients required resection of the IVS along with a portion of

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the liver for malignant disease. This number represents approximately 4% of liver resections that were performed during that time period. Eleven of these patients have been previously reported.[18] There were 15 male patients and 7 female patients. Their ages ranged from 2 to 68 years with a median of 49 years. Median follow-up after discharge from hospital was 26 months (range 1–75 months). Resections were carried out for: hepatocellular carcinoma (HCC) (n = 6), colorectal metastases (n = 6), cholangiocarcinoma (n = 5), gastrointestinal stromal tumor (GIST, n = 2), hepatoblastoma (n = 2), and squamous cell carcinoma in 1 patient. Liver resections performed included 13 right trisegmentectomies, 6 right lobectomies extended to include the caudate lobe, and 3 left trisegmentectomies. Complex ex vivo procedures were performed in 2 cases using venovenous bypass while the other 19 cases were performed using varying degrees of vascular isolation. In situ cold perfusion of the liver was used in 1 case. The IVC was reconstructed with ringed Gore-Tex tube graft (n = 14), primarily (n = 6), or with Gore-Tex patches (n = 2). Two of the patients with HCC underwent arterial chemoembolization of tumor prior to resection. One patient with HCC had cirrhosis with the remainder of cases in this series were performed in patients with noncirrhotic livers. Fifty percent of the patients with colorectal metastases had previously received adjuvant 5-fluorouracil (5-FU) + leucovorin. Two of the 6 patients with colorectal cancer (CRC) metastases also had oxaliplatin prior to liver resection, and 1 patient received 5-FU plus irinotecan chemotherapy for bulky liver disease with minimal response prior to the surgery. One of the 2 patients with GIST metastatic to the liver had undergone an attempted resection 6 months earlier by different surgeons, which was aborted due to chest wall involvement. The patient then received local radiation directed at the chest wall 2 months prior to her surgery.

All patients underwent contrast-enhanced computed tomography (CT) of abdomen (Fig. 1) and chest to assess for extrahepatic disease. Magnetic resonance imaging (MRI) was also performed in 9 of the patients and was thought to have provided additional information about the relation of the tumor to the hepatic veins and vena cava. The use of MRI decreased in the last half of the study period when good quality triphasic three-dimensional CT reconstructions became available. Patients with metastatic colorectal cancer had colonoscopy performed prior to surgery. Fifteen patients, including both patients who required ex vivo procedures, had staging laparoscopy to assess for extrahepatic disease. Patients older than 50 years were evaluated with either a stress ECG or dobutamine stress echocardiogram.

Preoperative portal vein embolization was used in only 2 of the first 11 patients but was subsequently used in 7 of the last 11 cases.[19] Remnant liver volume increased approximately 28% in patients that had preoperative portal vein embolization.

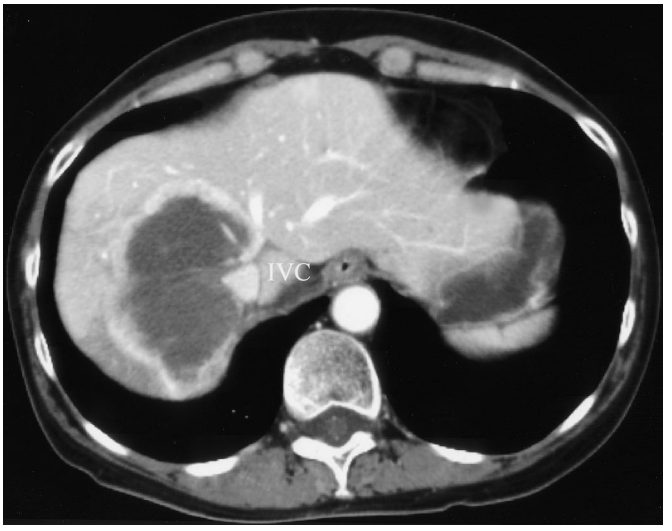

FIGURE 1. Venous phase CT demonstrating involvement of the inferior vena cava, right and middle hepatic veins by tumor.

Intraoperative ultrasound was performed in all patients to assess the number of lesions as well as to assess the relation of tumor to vascular structures. The number of lesions was 1 in 13 patients, 2 in 5 patients, 3 in 2 patients, and 4 in 2 patients (Table 1). Liver lesions involved all 3 hepatic veins in 4 cases, the right and middle hepatic veins in 12 cases, the middle and left hepatic veins in 3 cases, and the right hepatic vein only in 3 cases.

Surgical Approach to Resection

Surgery was performed through a bilateral subcostal incision with midline extension added if additional exposure was required. After mobilization of the liver, intraoperative ultrasound was performed. As much mobilization of the liver off of the vena cava was performed as possible without encroaching tumor planes prior to hepatic parenchymal transection. In 7 cases, however, the bulky nature of the tumor inhibited our ability to rotate the liver safely, and a primary anterior approach to the IVC was taken with little or no mobilization of the liver off of the IVC.[20] The hepatic parenchyma was divided using the Cavipulse Ultrasonic Surgical Aspirator (CUSA).

The approach to vena caval resection depended on the extent and location of tumor involvement. If the portion of vena cava involved with tumor was below the hepatic veins, then the parenchyma of the liver was divided exposing the retrohepatic IVC. During the earlier portion of the study period, the parenchymal transection was performed with inflow occlusion (Pringle maneuver); however, in the last few

TABLE 1. Results of 22 Patients Undergoing Combined Resection of the Liver and Inferior Vena Cava for Hepatic Malignancy

Patient No.	No. of Lesions	Procedure	Other Structures Resected	Resected Segments	IVC Repair	Tumor Type	Result
1	4	Right trisegmentectomy	90% right diaphragm, chest wall	1, 4–8	50% wall closed primarily	GIST	Persistent leg edema, DWD 32 months
2	1	Ex vivo resection/reimplantation part of segment 2 and 3	Bile duct	1, 4–8, parts of 2 and 3	1° repair short segment IVC + reconstruct LHV	HCC	AFD 72 months
3	1	Right lobe and caudate	Right kidney + diaphragm	1, 5–8	Gortex tube graft	SCC	AFD 60 months
4	2	Right trisegmentectomy		1,4–8	Gortex tube graft	HCC	DWD 26 months
5	4	Ex vivo resection/reimplant part of segment 2 and 3	Right diaphragm, bile duct	1, 4–8, parts of 2 and 3	Gortex tube graft, reimplant veins from segments 2,3	CRM	DFD 4 months
6	1	Right trisegmentectomy	Right adrenal	1, 4–8	Gortex tube graft + reconstruct LHV	Cholangio	DWD 44 months
7	2	Left trisegmentectomy		1–5, 8	1° repair short segment IVC, reimplant RHV	CRM	AFD 36 months
8	1	Right lobectomy		1, 5–8	Gortex patch	HCC	DFD 3 weeks, liver failure
9	3	Right trisegmentectomy		1, 4–8	Gortex tube graft	CRM	DWD 40 months
10	2	Right trisegmentectomy		1, 4–8	Gortex tube graft	CRM	AFD 32 months
11	1	Left trisegmentectomy	Bile duct	1–5, 8	1° repair short segment IVC	HCC	AWD 31 months
12	1	Right trisegmentectomy	Diaphragm, chest wall	1, 4–8	1° repair short segment IVC + reconstruct LHV	HB	AFD 30 months
13	1	Right trisegmentectomy	Bile duct	1, 4–8	Gortex tube graft	Cholangio	DWD 24 months
14	1	Right trisegmentectomy	Diaphragm, adrenal, bile duct	1, 4–8	Gortex tube graft	Cholangio	DFD 6 weeks, aspiration pneumonia
15	1	Right trisegmentectomy	Bile duct	1, 4–8	Gortex tube graft	Cholangio	AFD 26 months
16	2	Right lobe + caudate		1, 5–8	Gortex tube graft	CRM	AFD 22 months
17	2	Right lobe + caudate		1, 5–8	Primary repair short segment IVC	HCC	AFD 14 months
18	3	Right trisegmentectomy		1, 4–8	Gortex patch anterior wall	CRM	AFD 13 months
19	1	Right lobe, caudate + 4b		1, 4b, 5–8	Gortex tube graft	HCC	AFD 12 months
20	1	Left trisegmentectomy	Pericardium, bile duct	1–5, 8	Gortex tube graft	Cholangio	AFD 5 months
21	1	Right lobe + caudate	Diaphragm	1, 5–8	Gortex tube graft	GIST	AFD 3 month
22	1	Right trisegmentectomy		1, 4–8	Primary repair short segment IVC	HB	AFD 2 months

HCC, hepatocellular carcinoma; HB, hepatoblastoma; Cholangio, cholangiocarcinoma; CRM, colorectal metastases; GIST, gastrointestinal stromal tumor; SCC, squamous cell carcinoma; AFD, alive free of disease; AWD, alive with recurrent disease; DFD, dead free of recurrent disease; DWD, dead with recurrent tumor; LHV, left hepatic vein; RHV, right hepatic vein.

years of the study period, inflow occlusion was used less frequently. Central venous pressure was kept at or below 5 cm H_2O during parenchymal transection to minimize blood loss. Once the IVC was exposed, portal inflow occlusion was released if used, the patient volume loaded, and clamps placed above and below the area of tumor involvement (Fig. 2). The portion of liver and involved IVC was then removed, allowing improved access for reconstruction of the IVC. The placing of clamps on the IVC below the hepatic veins allowed perfusion of the liver and minimized the hepatic ischemic

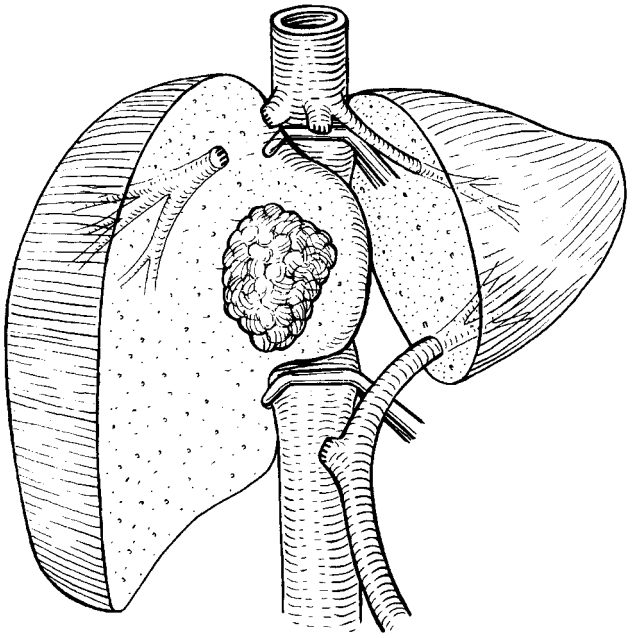

FIGURE 2. Vascular clamps are placed above and below the tumor on the IVC. The clamp above the tumor on the IVC is below the hepatic veins and allows maintenance of portal blood flow to the liver.

time. In the 1 patient with a GIST, a single clamp could be applied tangentially to the IVC (Fig. 3).

In cases in which tumor involvement did not allow placement of clamps below the hepatic veins, there were 2 different approaches. If there was only IVC and/or hepatic vein involvement, the hepatic parenchyma was divided back to the IVC and then clamps were placed sequentially on the infrahepatic IVC, the porta hepatis, and then above the hepatic veins (Fig. 4) with the liver and IVC removed en bloc. If hepatic vein repair or reconstruction was required, the remaining in situ portion of the liver was rotated up out of the patient allowing repair or reimplantation of the hepatic veins to be done under excellent visualization.

In 2 patients, there was involvement of IVC, hepatic veins, and portal structures, and it was determined that the only possibility of obtaining tumor free margins would be using ex vivo resection techniques. In these 2 patients, minimal mobilization of the liver off of the IVC was attempted in situ. The suprahepatic IVC was mobilized with the phrenic veins divided and the intrapericardial portion of the IVC lowered. In 1 case, it was necessary to open the pericardium from below to obtain adequate length for clamp placement. The portal structures were exposed with adequate length dissected for resection and reimplantation. The infrahepatic

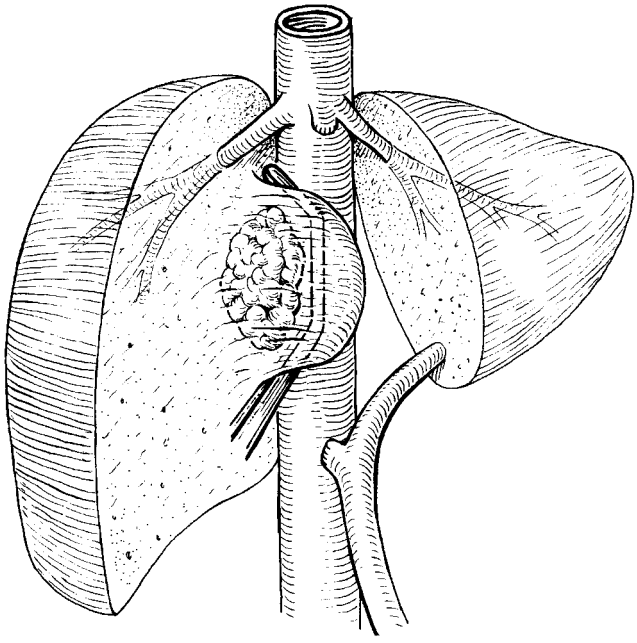

FIGURE 3. A single side biting vascular clamp is applied to the portion of the IVC involved with tumor and the IVC is repaired primarily.

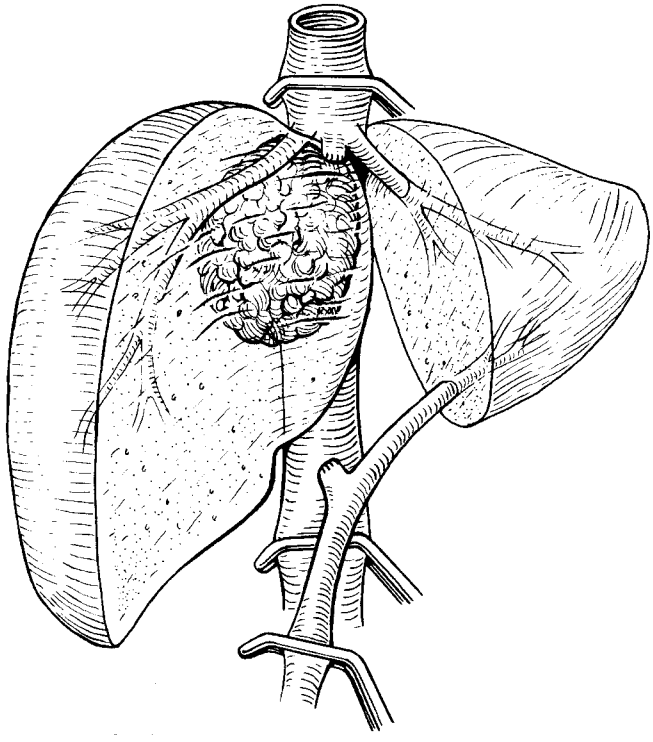

FIGURE 4. Vascular clamps are placed above and below the tumor on the IVC. The clamp above the tumor on the IVC is above the hepatic veins and therefore portal blood flow to the liver must be interrupted.

IVC was clamped and patients placed on the caval portion of venovenous bypass. The liver was removed, flushed with University of Wisconsin solution, and placed in an ice bath for back table resection. The portal outflow was then included in the venovenous bypass circuit. Liver and vascular resections as well as reconstruction of hepatic veins and IVC were subsequently performed on the back table. Mean cold ischemic time was 115 minutes with a warm ischemic time of 25 minutes.

Approach to IVC Repair/Reconstruction

The IVC was reconstructed primarily (n = 6), with ringed Gore-Tex tube graft (n = 14), or with Gore-Tex patches (n = 2). The IVC was reconstructed primarily if possible. Early in our experience, 1 patient with a GIST had 50% of the diameter of the IVC resected with primary repair resulting in a 50% narrowing of the IVC. The 5 other patients with primary repair had short segments of up to 2 cm of IVC resected and brought together end to end without the need for interposition grafts, including 1 of the ex vivo resections in which almost all of the IVC was salvaged and the left hepatic vein reconstructed on the back table. Two patients with primary repairs of the IVC required reimplantation of either the right or left hepatic vein into the vena cava as well. Two patients required 5-cm sections of the anterior wall of the IVC resected. These were repaired with thin-walled Gore-Tex patches.

The other 14 cases required from 3 to 8 cm of IVC to be resected and were reconstructed using 20-mm ringed Gore-Tex tube grafts (Fig. 5). In general, the superior anastomosis of the graft was performed first with clamps subsequently repositioned on the graft below the hepatic veins if necessary to allow release of portal inflow occlusion and reperfusion of the liver. The ex vivo resection that required a tube graft for caval replacement also required the reconstruction of the segments 2 and 3 hepatic veins using a Y graft of the portal confluence that was reversed and reimplanted into the Gore-Tex graft.[11]

Biliary reconstruction was required in the 2 ex vivo procedures, 2 left trisegmentectomies, and 3 right trisegmentectomies that required resection of the bile duct confluence to obtain a margin. In all cases, reconstruction was performed using a Roux-en-Y hepaticojejunostomy. Anastomoses were performed using interrupted 5-0 or 6-0 PDS sutures to either the left (n = 5) or right hepatic duct (n = 2). No stents were used.

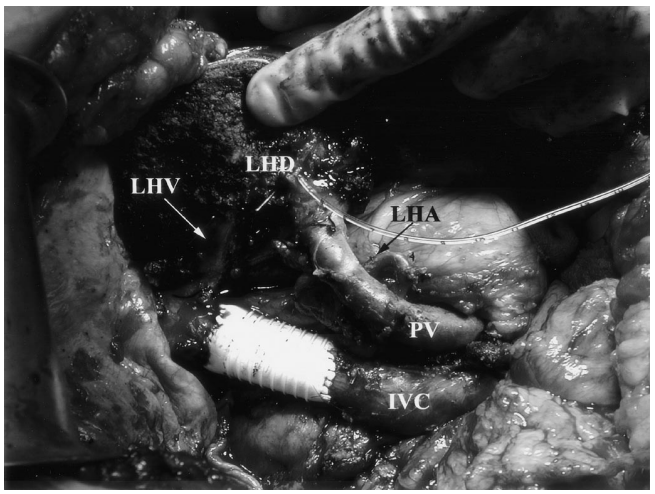

FIGURE 5. Right trisegmentectomy with reconstruction of the IVC with a Gore-Tex graft. The bile duct has been resected and the left hepatic duct (LHD) will be reconstructed with a roux-en-Y limb. IVC, inferior vena cava; LHA, left hepatic artery; LHV, left hepatic vein; PV, portal vein.

RESULTS

Results are summarized in Table 1.

There were 2 early deaths (9%): 1 from liver failure at 3 weeks in a cirrhotic patient and 1 death at 6 weeks in from pulmonary hemorrhage in a patient who had developed a severe, cavitating aspiration pneumonia. The median operative blood transfusion requirement was 2 units (range, 0–20 units) with 30% of cases requiring no transfusion. Median operative time was 4.2 hours (range, 3–8 hours). Median hospital stay was 11 days (range, 7–46 days). Resection margins were microscopically clear of tumor in 20 patients (91%); however, 4 patients had margins that were clear but less than 1 cm away from tumor. Sixteen patients showed true invasion of the tumor into the wall of the vena cava while 6 did not. Three cases of colorectal metastases and 1 case each of hepatoblastoma, cholangiocarcinoma, and HCC did not have true vascular invasion, although leaving the vessel intact would have resulted in a positive margin. Five patients developed right-sided pleural effusions that were significant enough to require drainage. Six patients had evidence of postoperative liver failure that resolved with supportive management. Liver failure was arbitrarily defined as requiring fresh frozen plasma to maintain an International Normalized Ratio (INR) < 2.0 after the first 48 hours post resection, encephalopathy, ascites requiring paracentesis or diuretics longer than 2 weeks, or a rise in bilirubin to 10 mg/dL or above that persisted longer than 10 days post resection. Two patients required temporary dialysis. Two patients developed bile leaks: 1 required percutaneous drainage and 1 required no intervention other than the drain that had been placed at the primary procedure. One of these patients had a Gore-Tex graft as vena caval replacement; however, at 26 months follow-up, there is no evidence of an infected graft. All vascular reconstructions were patent at the last follow-up. With median follow-up of 26 months, 5 patients have died of recurrent malignancy at 44, 40, 32, 26 and 24 months, while an additional patient is alive with disease at 31 months.

Actuarial 1-, 3-, and 5-year survivals were 85%, 60%, and 33%, respectively (Fig. 6). The 1 patient with a GIST that had a 50% resection of the diameter of the IVC developed moderate lower limb edema that eventually resolved 6 months post procedure. Imaging studies demonstrated a patent but narrowed IVC. All other patients had patent IVC at the last follow-up. All patients were placed on low-dose heparin perioperatively, and patients with Gore-Tex grafts were maintained long-term on a single aspirin daily.

DISCUSSION

Resection of liver tumors that involve the vena cava has become possible with lessons learned from liver transplantation. Tumors in the central or posterior segments of the liver may extend to involve the vena cava or hepatic veins that make resection using standard techniques impossible. If the tumor involvement of the IVC is small, control of the IVC can be achieved simply by placing a vascular clamp tangential to the vena cava, as was done in patient 1 in the series. Although the IVC can then be repaired primarily with a lateral venorrhaphy, this is feasible in only a small number of patients and care must be taken not to narrow the IVC excessively. In our 1 patient who had this performed, the IVC was narrowed by 50% and the patient developed persistent moderate leg edema, although the IVC remained patent. In subsequent cases, we have elected to completely transect the IVC along with resection and bring the IVC together end to end, eliminating the possibility of tangential narrowing.

Larger resections of the IVC require interruption of IVC flow. When involvement of the IVC is below the hepatic veins and there is sufficient room to place a vascular clamp above the tumor but below the hepatic veins, then liver blood flow can be maintained while resecting and reconstructing the IVC. Although we prefer to divide the liver parenchyma first with subsequent placement of clamps on the IVC, an alternative approach by Madariaga et al[15] describes replacing the IVC prior to dividing the liver parenchyma. Either approach minimizes the time that portal inflow occlusion is required. Normal livers can tolerate 60 to 90 minutes of warm ischemia[21,22]; however, it would seem prudent to minimize ischemic time if possible. In our initial report,[18] we used portal inflow occlusion during the parenchymal transection of the liver for the majority of cases. Experience gained in live donor liver transplantation has altered our practice. Currently, we perform the parenchymal transection in a similar controlled fashion as during live donor liver surgery while hepatic perfusion is maintained. While this increases the time of the procedure, it minimizes the ischemic injury to which the remnant liver is exposed. In addition, we have been applying the principle of ischemic preconditioning[23] to our liver resections in an attempt to ameliorate the effects of warm ischemia if portal inflow occlusion is required.

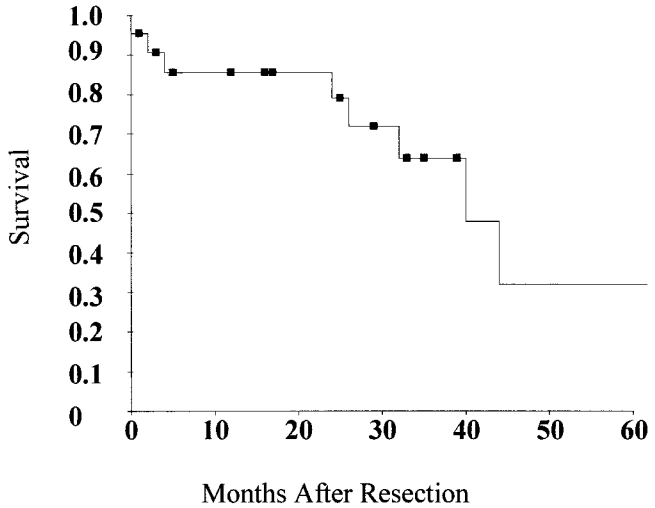

FIGURE 6. Actuarial survival of 22 patients undergoing combined resection of the liver and IVC for hepatic malignancy.

If clamps must be placed above the hepatic veins on the IVC then complete hepatic vascular exclusion (HVE) must be used.[24] HVE can result in a fair degree of hemodynamic instability and requires volume loading to maintain cardiac output.[25] Although all 11 patients who required HVE tolerated the procedure, we were prepared to use venovenous bypass if it had been required and the availability of venovenous bypass would seem essential from other reports.[13,15] In general, we mobilize as much of the liver off of the vena cava as possible prior to starting the transection of the hepatic parenchyma. However, occasionally a large bulky tumor makes the mobilization of the liver off of the vena cava difficult or even hazardous, in which case the liver parenchymal transection can be performed first, allowing exposure of the IVC without excessive rotation and traction on the liver.[20]

The need for ex vivo resection should be rare since the majority of tumors can be resected with different, less technically demanding techniques. The 2 cases that required ex vivo resection had involvement of all 3 hepatic veins, the IVC as well as portal structures. If only the hepatic veins and IVC are involved, the portal structures can be left intact (though clamped), and the vena cava divided above and below the tumor, allowing the liver to be rotated up to the surface of the operative field. This permits improved access for reconstruction of the hepatic veins or reimplantation of the hepatic veins into the vena cava. Hannoun et al have described a technique in which the liver, with portal structures intact, can be flushed via a branch of the portal vein with cold University of Wisconsin solution to extend the ischemic time tolerated by the liver.[26] When complete ex vivo resection is used and the liver is flushed with preservation solution, the transection of the liver parenchyma and the reconstruction of vascular structures take place in a bloodless field and can be done without time pressure. In both cases of ex vivo resection,

venovenous bypass was used to allow maintenance of hemodynamic stability as well as portal decompression during the prolonged anhepatic phase of the procedure. An additional reason to advocate an ex vivo approach is to improve negative margin status. In retrospect, 1 of our patients who had a positive margin when resected under HVE would likely have been resectable with a clean margin had we elected to perform the procedure on the back table. With admittedly limited experience, we think that there is a greater tendency to take wider margins and reconstruct the vasculature on the back table during ex vivo resections than in in situ resections where there is more of a tendency to preserve vascular structures at the cost of margin.

There are a variety of options for replacement of the IVC if it cannot be reconstructed primarily. Autogenous vein grafts have been used,[17,27] although if long segments of the IVC require replacement, this may not be technically feasible. Dacron has been used in the past but has been associated with relatively high thrombosis and stenosis rates.[15] Ringed 18- to 20-mm Gore-Tex is currently our graft of choice. Although the potential disadvantage of using prosthetic material is the risk of infection, neither our series nor others[13–15,28] have reported graft infection, this despite the fact that various series of liver resections report infection rates from 8% to 28%.[29] Nagorney has described the use of an omental wrap for prosthetic caval grafts when performing combined liver resection and caval reconstructions.[16] While we have not been using an omental wrap on our Gore-Tex grafts, it appears a reasonable precaution and we have recently added it as a standard step in the procedure. Long-term anticoagulation after placement of a prosthetic graft has been recommended,[16] but its value remains questionable. With little in the way of data to support its use, we have used low-dose perioperative heparin along with long-term maintenance aspirin. With this approach, all Gore-Tex tube grafts have remained patent, although follow-up is admittedly short.

Combined resection of the IVC and liver has become feasible with the application of innovative surgical techniques. It is a considerable operative challenge with high risks of mortality and morbidity. Our operative mortality was 9%. Pichlmayr et al reported 33% mortality in a series of 9 patients undergoing extensive ex vivo resection,[10] while other series of combined liver and IVC resection report mortalities of 11% to 25%.[13,15,16] Despite the high risk, for patients with tumors that are otherwise unresectable, it offers the only possibility of cure. Miyazaki et al[14] reported a 5-year survival rate of 22% after combined liver and IVC resection versus a 27% 5-year survival in patients requiring liver resection alone in an otherwise comparable group of patients with colorectal liver metastases. With the variety of different tumor types and relatively short follow-up (median, 26 months), it is difficult to comment definitively on the oncologic efficacy of this radical approach to resection. However, the overall actuarial 3- and 5-year survivals of 60% and 33%, in addition to 2 actual 5-year survivors, suggest that that we are impacting on disease progression.

CONCLUSION

It is apparent that application of combined resection of the liver and IVC expands the role of liver resection for malignancy and will benefit selected patients. The use of the techniques employed in resecting these tumors requires a specialized center where surgeons familiar with aspects of both complex hepatobiliary surgery and liver transplantation are available.

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Discussions

DR. YUMAN FONG (New York, New York): Liver resection has come a long way in the last 2 decades and lobectomies and trisegmentectomies are now commonly performed in many hospitals throughout this world. In this regard I congratulate Dr. Hemming and his colleagues for pushing the envelope further in their report indicating that combined liver and vena caval resection can be performed safely and with good mid- and long-term results.

The marked recent improvement in outcome for patients after liver resection however are due to a combination of improved patient selection and technical advances. So my questions are therefore separated into 2 categories: those related to how the authors chose the patients for surgery and those related to the technical aspects of doing the surgery.

With regard to patient selection, I note in this series all patients had fewer than 5 tumors. My first question therefore is: Were all patients with tumors completely resectable by liver and caval resection subjected to resection or were there other biological selection criteria for choosing these patients? In particular, were patients that have the greatest chance for long-term survival chosen for these extensive operations?

In my own practice, I am much more enthusiastic about subjecting someone to an extensive procedure who is responding to neoadjuvant chemotherapy. Was neoadjuvant therapy part of the overall strategy in any of the patients in the series?

I note that there were 6 patients with hepatocellular carcinoma in the series and at least one of them had cirrhosis. How many others had cirrhosis? How do the authors choose patients with cirrhosis for these extensive procedures and what are the technical differences in performing vena caval reconstruction in these cirrhotic patients?

Finally, I note with surprise that there was a single patient with squamous cell carcinoma and the fact that he is currently a long-term survivor. Was this a patient with primary squamous cell carcinoma of the gallbladder? If not, what squamous cell carcinoma metastasized to the liver in a single spot and how was this patient chosen for surgery?

As for the technical issues, I have found that bovine pericardium actually works pretty well as a patching material for vena cava. Do the authors have any experience with this?

In the manuscript the authors emphasize that they no longer use inflow occlusion during these resections in order to decrease ischemic damage to the liver. Do the authors have data supporting this as an improvement?

Finally, the authors state that 7 of the last 11 patients in the series were also subjected to a portal vein embolization before surgery. Is this because of the planned caval resection or are all patients at the University of Florida being considered for major liver resection now being subjected to portal vein embolization?

DR. JEAN-NICOLAS VAUTHEY (Houston, Texas): I rise to congratulate Dr. Hemming and his colleagues at the University of Florida for an effort to expand the option of surgical resection for a group of patients with advanced hepatobiliary malignancies with otherwise limited life expectancy. The results are excellent.

The authors used 14 ringed Gore-Text grafts without thrombosis after a median follow-up of 28 months. Five of these resections were combined with bile duct resection in a contaminated field and no graft infection was reported.

The negative margin rate is 91%, and this translates in a survival at 3 years of 63%. And there is not early drop in the survival curve, witnessing good patient selection. I have 4 questions for the authors.

The first question relates to the anticoagulation. You mention in your manuscript that you use low dose heparin postoperatively in these patients followed by aspirin. How do you manage these patients intraoperatively? Do you reverse your heparinization? Also, how do you adjust your low dose heparin? Since in the first 2 days following major liver resection there is always a rise in INR.

The second question is about hepatic vascular exclusion. I note that you have only used veno-venous bypass in 2 patients who had ex-vivo resection. That means in 11 patients you used total vascular exclusion without veno-venous by-

pass while accepting the attendant hemodynamic shifts. There is a randomized study on major hepatic resection with and without hepatic vascular exclusing showing an increase in complication and transfusions in the absence of veno-venous bypass. Do you think a comparison of total vascular exclusion with or without venous bypass is indicated and that you might have had less transfusion requirements and less infusions by using veno-venous bypass?

The third question relates to the involvement of the vena cava. Although we would agree that greater than 50% involvement of the vena cava requires resection of the vena cava, how do you decide to resect the vena cava in patients who have less than 50% involvement? You mention 3-D volumetric CT reconstruction in the evaluation of your patients. How does this compare to thin-cut CTs without 3-D reconstruction?

Finally, you had several hepatocellular carcinomas in this series. This tumor is notorious for invading the hepatic vein and the vena cava as tumor thrombose without adhesion to the hepatic vein wall or vena cava wall. Have you used the technique recently described as reduction of the tumor thrombose and resection via cavatomy without vascular resection in these patients? Did your patients have pathological involvement of the vena cava?

Dr. Robert Martin (Louisville, Kentucky): I congratulate the authors on a very impressive series. I have just 2 simple questions. What was the median and range time for clamps with both techniques? Did any of these patients have to undergo a partial aortic occlusion in order to maintain blood pressure?

Dr. J. Alex haller, Jr. (Baltimore, Maryland): I have just one additional question to extend one of the discussant's questions. This has to do with the use of veno-venous bypass. It seems to me that this would become a standardized approach to the management of all of these tumors. I realize that it requires heparinization to do that, but what is the reason for so many fantastic, innovative technical maneuvers that were used rather than adopting a straightforward standard perfusion technique for all of these patients?

Dr. Reid Adams (Charlottesville, Virginia): A very nice series demonstrating again the extension of vascular techniques along with liver resection to improve the survival for these patients. In determining your operative candidates, could you elaborate a little bit again on what Dr. Fong mentioned? That is, how do you decide who you are going to embolize? Secondly, how are you determining who you are going to resect? Are you doing volumetrics as your primary endpoint for liver remnant?

Dr. Alan W. Hemming (Gainesville, Florida): Dr. Fong, you asked regarding the criteria for patient selection, how did we choose which patients we were going to be aggressive on? We clearly don't subject every patient who has caval involvement to this operation. If you look at our median age, it was 49, although we had a few patients who we resected out to age 68. These are by and large younger patients with longer disease-free intervals, at least with colorectal metastases, and with what at least appears to us to be less aggressive or at least localized disease.

The question about whether we use neoadjuvant therapy. Over the time course of the study, from '97 to currently, we did not use neoadjuvant therapy from about 1997–2001. In the last 2 years we have begun using neoadjuvant chemotherapy. However, in this series only 3 patients had neoadjuvant therapy. We didn't particularly use a response to therapy to dictate whether or not we were going to proceed with resection. There was 1 patient who had a response that we resected, but we would have resected him if he had not responded simply because there is no other curative option available.

I think it makes me happier when I see patients respond to the neoadjuvant therapy, since big surgery does not beat the biology of the disease all the time. We need something else. So if we have additional chemotherapy that we have a hint is going to work, it makes me happier about performing an extensive procedure such as this.

How do we choose the cirrhotics to do this on? In general, I don't plan on doing very many of these in cirrhotics. I think there is only one cirrhotic in the series. And I can tell you I wasn't planning on taking his vena cava out at the time, but it became obvious during the procedure that it would be required. That patient needed a right lobectomy, so he had a fairly large future remnant liver volume. In general I wouldn't plan vascular reconstructions on a cirrhotic without a few other additional maneuvers such as portal vein embolization, assessing their volumetrics, and assessing their ICG clearance.

The squamous cell carcinoma. I was called into the operating room in the middle of that one. A kidney and part of the liver was already in the process of being removed when it became evident that the inferior vena cava needed to come out. So we took out the liver, the kidney, and the vena cava. We have no idea where it came from. It wasn't gallbladder cancer. The patient was still alive at last follow-up with no evidence of disease. Our urologists had actually preoperatively beta blocked and alpha blocked the patient thinking it was a pheochromocytoma. If you have ever tried to take a vena cava out on somebody who is alpha blocked and beta blocked, it is not easy to maintain their blood pressure with clamps on the vena cava. Bovine pericardium certainly can be used to patch vena cavas. I haven't used it particularly. There is no reason not to use it however.

Inflow occlusion. I wouldn't say that we don't use inflow occlusion, because we do. We use it if we need it. If we are having ongoing blood loss as we come through the liver, I have no problems using inflow occlusion. I think it reduces blood loss and makes the technical aspects of the operation frequently more easy. But as we gain more experience with live donor transplantation the ability to come through a liver under complete control and have no blood loss allows us to save any ischemic injury we might give the liver until we need it for vascular reconstruction therefore minimizing ischemic time.

Do we do portal vein embolization on all patients? No, we do not. We use a similar cut-off as most groups. In fact, we presented a portal vein embolization paper here at the Southern Surgical last year.

Our criteria are: If we think that the future liver remnant is going to be less than 25% of total liver volume based on preoperative 3-D CT, then we will portal vein embolize the side that is coming out so that we can get growth on the side that is staying in. Once you are talking about caval reconstruction and other vascular reconstruction, I think you are giving a bigger potential injury to the liver. In cases where we plan vascular reconstructions, if we are going to leave less than 40% of the liver behind, then we use portal vein embolization.

Dr. Vauthey asked about the anticoagulation. Low-dose heparin just means we were giving routine perioperative heparin. We weren't monitoring the PTT. We didn't either heparinize patients or reverse them intraoperatively, and they received aspirin starting on about postoperative day 3.

The question as to whether if we use veno-venous bypass would we have less blood loss than total hepatic vascular exclusion. If you have used veno-venous bypass, you know you have a certain amount of blood loss just to prime the circuit. In fact, I think many times we would actually have lost more blood in the circuit than we would have by just going ahead with total vascular exclusion. The exclusion is done at the tail end of the procedure, so we have already divided the liver. Most of the potential bleeding has already been dealt with. The liver is divided under low CVP conditions and complete vascular exclusion is only done when we are resecting the cava. So to try and compare previous series where you are doing the whole liver resection under total vascular exclusion to this is like comparing apples and oranges.

How do we decide on who needs a caval resection? That is a tough one. Because 3 dimensional CT or thin cut CT frequently show you compression or involvement of the cava but many times when you actually take the vena cava out you won't see actual invasion into the wall of the vena cava. In this series about two-thirds of patients had some evidence of involvement right through into the wall of the vessel. Two or 3 patients had invasion through right into the endothelium. About a third of patients had no real involvement with the vena cava. We would have cracked into the tumor plane had we tried to get the tumor off of the vena cava but the tumor wasn't necessarily involving the cava.

Preoperative imaging is not great for deciding exactly who has caval involvement, unless you see tumor within the lumen of the vena cava. Patients who have tumor within the lumen of the vena cava are not good candidates for this procedure. And that goes to one of the other questions about vena cava resections for HCC with tumor thrombus. By and large we don't resect vena cava. We just open the vena cava, pull the tumor thrombus out and repair the vena cava. This type of patient is not included in this series.

Dr. Martin asked about clamp times. I am not sure exactly what you mean, whether you mean on the veno-venous bypass, on the ex-vivo resections or on the total vascular exclusion cases. Total vascular exclusion cases we would clamp for between 15 to 20 minutes, really not very long. The 2 patients that were on veno-venous bypass, I think the cold ischemic time was around 110 minutes and an additional warm ischemic time of about 20 minutes. On the patients with total vascular isolation, we don't clamp the aorta. We have found we haven't needed it. You do need to volume load these patients. Let your anesthesiologist know that you are about to clamp the vena cava and that they need to volume load before you put your clamps on. There should be no need to clamp the aorta.

The last question was about veno-venous bypass and heparinization. Actually, when you are on veno-venous bypass you are not heparinized. It is a heparin-bonded circuit. The whole idea behind veno-venous bypass is to not be heparinized, so that you avoid full heparinization in standard cardiopulmonary bypass.

Dr. Adams asked about who gets embolized. I think we answered that a bit. The patients who I am going to do vascular resections on who have a volume of future liver remnant of 40% or less we try and embolize. And we do do 3-D CT volumetry beforehand. There are scattered within this series patients that we didn't plan on doing the vascular reconstructions on, and so you end up doing vascular reconstruction without pre-op embolization. So we don't always follow what sound like strict protocols.