Is Combined Partial Hepatectomy With Segmental Resection of Inferior Vena Cava Justified for Malignancy?

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Hypothesis: En bloc partial hepatectomy with inferior vena cava (IVC) resection may be the only curative strategy for patients with hepatic malignancies involving the IVC.

Design: Retrospective study.

Setting: Tertiary referral center.

Patients: All consecutive patients undergoing combined partial hepatectomy with segmental IVC resection and reconstruction between 1990 and 2002. Patients with tangential excision of the IVC were excluded. Follow-up was completed by outpatient clinic visits and mail correspondence.

Main Outcome Measures: Perioperative outcomes; overall and recurrence-free survival.

Results: Nineteen patients (7 men and 12 women) underwent partial hepatectomy and segmental IVC resection and reconstruction. Median age was 59 years (range, 24-74 years). Diagnoses consisted of cholangiocarcinoma (9 patients), metastatic tumor (5 patients), sarcoma (3 patients), and hepatocellular carcinoma (2 patients). Major hepatectomies (≥3 segments) were performed in 15 patients; the caudate lobe was resected in 13. Hepatic vascular isolation was used in 13 patients. Ringed polytetrafluoroethylene grafts were used for IVC reconstruction in all but 1 patient. Transfusion was necessary in 18 patients (median requirement, 5 U). Median operative time was 6.3 hours (range, 3.7-9.0 hours), and hospitalization was 10.5 days (range, 6-41 days). Negative margins of resection were achieved in 16 patients. Complications occurred in 8 patients (42%), including 1 perioperative death (5%). There was evidence of mural thrombosis of the graft in 2 patients (both nonocclusive); warfarin sodium was used postoperatively in 14. Late graft thrombosis was evident in 2 patients. Median overall survival was 38 months (5-year survival, 21%), and recurrence-free survival was 11.5 months (5-year survival, 0%).

Conclusions: Patients with large tumors involving both the liver and the IVC are candidates for partial hepatectomy and segmental IVC resection. Resection affords the possibility of negative margins, acceptable perioperative morbidity and mortality, long-term graft patency, and prolonged survival.

Arch Surg. 2003;138:624-631

PERIHEPATIC vascular involvement by malignancy currently poses a major technical limitation to hepatic resection. In fact, invasion of the hepatic veins or inferior vena cava (IVC) has often been considered a contraindication to resection. This premise has been challenged recently, at least from the technical standpoint.1-3 Large intrahepatic or retrohepatic malignancies that invade the retrohepatic IVC or hepatic veins are problematic because resection alone without vascular reconstruction (IVC and hepatic veins) may have a prohibitive impact on systemic hemodynamics and hepatic function. Hepatic resection with reconstruction of the IVC that preserves hepatic venous and caval blood flow lessens these risks and may afford survival benefit. Standard hepatic resection techniques coupled with total vascular isolation now permit extended hepatic resection of hepatic malignancies with involvement of the IVC. Such resection can be performed either in situ4-9 or ex situ.10-12 We believe that in situ resection has broader applicability, similar versatility, and equal efficacy. We have previously addressed some issues related to resection of malignancies invading the abdominal IVC inclusive of retrohepatic involvement.1 Most reports addressing hepatic resection and vena caval reconstruction are limited to only a few cases.13-15 The purpose of our updated review is primarily to discuss our evolving technical approach to hepatic resection with segmental IVC reconstruction and assess perioperative outcomes and, secondarily, to assess long-term sur-
vival. We believe our findings support the broader use of in situ hepatic resection with IVC reconstruction for selected perihepatic or intrahepatic malignancies.

**METHODS**

**PATIENTS**

We examined the records of all consecutive patients who underwent partial hepatectomy combined with segmental resection of the IVC for malignancy between 1990 and 2002. Patients who had tangential excision of the IVC with primary lateral or patch graft venorrhaphy were excluded. Patients with non-contiguous subsegmental hepatectomies and noninfrarenal IVC resections were also excluded. Some patients in this series have been described previously in a combined series of IVC resection. This report focuses on the outcomes of the specific group of patients undergoing partial hepatectomy and IVC resection and replacement. These 19 patients account for only 0.65% of 2939 patients who had hepatic resections during the study period. Perioperative events were recorded, including mortality, morbidity, transfusion requirements, length of hospital stay, and duration of operation. Follow-up was completed by outpatient evaluation and mail correspondence. Frozen section was used routinely intraoperatively to evaluate margins of resection, and permanent histopathologic findings were recorded. Overall and recurrence-free survival were estimated by the Kaplan-Meier method.

**SURGICAL TECHNIQUE**

An example of a large tumor in the posterior aspect of the right lobe invading the retrohepatic IVC is shown in Figure 1. After exclusion of extrahepatic intra-abdominal metastases, intraoperative ultrasonography of the liver is performed to exclude occult intrahepatic metastases and to confirm resectability. Particular attention is focused on the hepatic vein of the planned hepatic remnant. The junction of the remnant hepatic vein to the IVC is assessed for patency, thrombus, and to determine whether preservation or reconstruction of the orifice will be required. After confirmation of resectability, partial mobilization of the liver and vascular isolation is undertaken. The infrarenal IVC is encircled with an umbilical tape above the level of the renal veins. Nephrectomy has also required isolation of the infrarenal IVC and the contralateral renal vein. The liver is mobilized by division of its ligamentous attachments. Large tumors may preclude complete mobilization unless the liver is mobilized by division of its ligamentous attachments. The right side of the chest is entered by thoracotomy or diaphragmatic incision. The gastrohepatic omentum is incised carefully, preserving the accessory left hepatic arteries if present. The hepatoduodenal ligament is exposed for hepatic inflow occlusion. Intraoperative ultrasonography of the liver is performed to exclude occult intrahepatic metastases and to confirm resectability. Particular attention is focused on the hepatic vein of the planned hepatic remnant. The junction of the remnant hepatic vein to the IVC is assessed for patency, thrombus, and invasion to determine whether preservation or reconstruction of the orifice will be required. After confirmation of resectability, partial mobilization of the liver and vascular isolation is undertaken. The infrarenal IVC is encircled with an umbilical tape above the level of the renal veins. Nephrectomy has also required isolation of the infrarenal IVC and the contralateral renal vein. The liver is mobilized by division of its ligamentous attachments. Large tumors may preclude complete mobilization unless the right side of the chest is entered by thoracotomy or diaphragmatic incision. The gastrohepatic omentum is incised carefully, preserving the accessory left hepatic arteries if present. The hepatoduodenal ligament is exposed for hepatic inflow occlusion. The suprahepatic IVC is exposed and encircled with a vascular tape only after control of the infrarenal IVC and hepato-duodenal ligament. Infradiaphragmatic control is attempted initially in accordance with standard liver transplant techniques. If infradiaphragmatic access is not possible because of tumor bulk, the extrapericardial suprahepatic infradiaphragmatic IVC is encircled for control. Hepatic resection is initiated by division and ligation of the appropriate lobar hepatic artery and portal vein.

Hepatic transection is initiated during a 5-minute period of hepatic inflow vascular occlusion (Figure 2). Transection is continued with an ultrasonic surgical aspirator (Cavitron; Valleylab, Boulder, Colo) without inflow occlusion to minimize the duration of warm ischemia. Inflow occlusion is used further if there is extensive parenchymal bleeding. Total vascular occlusion is deferred until the IVC requires transection to complete tumor excision. If total vascular occlusion becomes necessary, the infrahepatic IVC is clamped first, and then hepatic inflow is occluded. The suprahepatic IVC is clamped last. If hemodynamic stability cannot be maintained with volume loading after the IVC is clamped, extracorporeal venovenous bypass is performed from the infrarenal IVC to the central veins using an active centrifugal pump (BioMedicus pump; Medtronic, Inc, Minneapolis, Minn). We do not perform simultaneous clamping of the superior mesenteric artery during hepatic vascular isolation. Liver transection is completed and the IVC is resected to protect the remnant hepatic vein.

Immediately before excision of the tumor, a 5000-U heparin bolus is given intravenously. The IVC is transected below and above the tumor and removed en bloc with the tumor and involved liver. An externally supported, 20-mm ringed polytetrafal graft is used for vascular reconstruction. The proximal IVC anastomosis is always undertaken first (Figure 3). If tumor resection extends immediately to the hepatic vein oriﬁce on the IVC, all clamps are kept in place until the caval anastomosis is completed (Figure 3). The hepatic inflow clamp is released to flush the liver of accumulated ischemic byproducts. The suprahepatic clamp is relieved brieﬂy to allow back-bleeding. Importantly, the graft is ﬂushed with the patient in a Trendelenburg position and the lungs inﬂated to 30 mm Hg to avoid air embolism. If the IVC stump is 3 mm long or more, the suprahepatic IVC clamp is repositioned below the hepatic vein oriﬁce before the caval anastomosis (Figure 3, inset). Hepatic perfusion is restored, the caval anastomosis is completed, and the superior IVC clamp is then transferred to the polytetrafal graft below the anastomosis to ensure that the superior anastomosis is hemostatic. Venovenous bypass is stopped.

The polytetrafal graft is cut to an appropriate length and the lower (distal) IVC anastomosis is started (Figure 4). Graft

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**Figure 1.** Identification of the tumor in the posterior aspect of the right lobe attached to the infrahepatic inferior vena cava. Initial dissection of the inferior vena cava inferior and superior to the tumor (and the hepatic veins) and circumferential exposure of the hepatoduodenal ligament structures for clamping (see “Surgical Technique” subsection of the “Methods” section).
length is checked during maximum inspiration and expiration before it is cut. Importantly, tailoring of the graft length must account for displacement of the infrahepatic IVC by these large tumors so that the graft does not obstruct the hepatic vein once the viscera and hepatic remnant return to their normal positions at the conclusion of the operation. The graft is flushed under positive pressure ventilation and Trendelenburg position and filled with heparinized isotonic sodium chloride solution before the anastomosis is completed. Rarely, only a short segment of IVC is resected with these tumors and a primary anastomosis is possible (Figure 4, inset). The anastomoses are constructed with running 3-0 or 4-0 monofilament suture.

After hepatic hemostasis is secured and graft patency has been assessed by duplex ultrasonography, an omental wrap is placed around the graft to protect it from the viscera and minimize the risk of secondary infection (Figure 5). Suction drains, if used, should not be positioned next to the graft.

An example of a tumor before and after right hepatectomy and IVC resection and reconstruction in a patient with a leiomyosarcoma of the IVC is shown in Figure 6. The tumor clearly invades the retrohepatic IVC. The remnant left hepatic vein at the level of the superior graft–IVC anastomosis is shown in Figure 6B. Figure 6D and F confirm the perigraft fatty tissue of the omental wrap. Preoperative (Figure 6A, C, and E) and postoperative (Figure 6B, D, and F) images at comparable levels are shown.

**RESULTS**

Nineteen patients underwent partial hepatectomy with segmental resection of the IVC during the study period. Median age of patients was 59 years (range, 24–74 years).

There were 12 women and 7 men. The diagnoses included: intrahepatic cholangiocarcinoma in 9 patients, hepatic metastases from colorectal cancer in 3, IVC or retroperitoneal sarcoma in 3, hepatocellular carcinoma in 2, and other metastatic tumors in 2. These resections were the initial tumor operation in 14 patients (74%). Fifteen patients had major hepatic resection (≥3 segments). Right hepatectomy was performed in 12 patients (6 standard, 6 extended), left hepatectomy in 3 (2 standard, 1 extended), bisegmentectomy in 2, and unsegmentectomy in 2 (including 1 isolated resection of the caudate lobe). Overall, the caudate lobe was included in the specimen in 13 patients. En bloc resection required right nephrectomy in 3 patients, but no patient required renal vein reconstruction to the caval graft.

Total hepatic vascular isolation was used in 13 patients (68%). Venovenous bypass from the infrahepatic IVC to the central venous system was required in 7 patients for hemodynamic instability after IVC clamping. Mean duration of hepatic ischemia was 18 minutes. One patient required median sternotomy and cardiopulmonary bypass because tumor thrombus extended into the right atrium. No other patient had gross tumor thrombi extending intraluminally within the vena cava. An externally supported 20-mm ringed polytetrafluoroethylene graft was used in 18 patients (95%). One patient had a primary caval anastomosis. Median operative time was 6.3 hours (range, 3.7–9.0 hours). Red blood cell transfusion was required in 18 patients, with a median of 5 U (range, 0–57 U). Me-
Dian preoperative and discharge laboratory values were as follows: serum aspartate aminotransferase, 42 and 50 U/L; total bilirubin, 0.5 and 0.8 mg/dL (8.6 and 13.7 µmol/L); and alkaline phosphatase, 324 and 283 U/L, respectively. Median length of hospital stay was 10.5 days (range, 6-41 days). All perioperative survivors were dismissed from the hospital functioning independently.

Negative microscopic margins of resection were achieved in 16 patients (84%). The IVC was histologically involved by tumor in 14 patients (74%), not involved in 4, and unknown in 1. There was 1 intraoperative death from a coagulopathy. Other perioperative complications occurred in 7 patients (37%) and included myocardial infarction (2 patients) and atrial fibrillation, persistent pleural effusion, chyle leak, fluid overload requiring delayed abdominal closure, and wound infection. An additional operation was performed in the patients with chyle leak and the open abdomen.

Fifteen grafts were patent as assessed by cavography, computed tomography, magnetic resonance imaging, or duplex ultrasonography, but 2 had nonocclusive thrombi. Three patients were not studied early after operation but were clinically asymptomatic. Only 1 patient developed clinical signs of IVC occlusion (leg swelling). Two patients had late graft thrombosis noted by imaging studies at 5 and 75 months postoperatively. One of these patients also had a tibial vein thrombosis at 6 months.

Median overall survival was 38 months, and 5-year survival was 21% (Figure 7). Median recurrence-free survival was 11.5 months, with a 5-year rate of 0% (Figure 8). Patients with intrahepatic cholangiocarcinoma (n=9) had a 3-year survival of 69% (Figure 9). Local tumor recurrence was intrahepatic alone in 6 patients, perihepatic alone in 1, and combined intrahepatic and perihepatic in 2. Ten patients had no hepatic recurrence. All patients with tumor recurrence had distant disease progression.

COMMENT

The major finding of our study was that hepatic resection and IVC reconstruction can be performed safely in situ. These findings support the technical feasibility of similar approaches used by others to address both the hepatic and caval involvement of these tumors.1,2,4-9 Our long-term follow-up shows that local tumor control can be effective for these locally advanced malignancies, although most patients eventually die of distant metastases. We believe this operative approach warrants broader application for hepatic malignancies previously deemed unresectable because of retrohepatic caval invasion. Future studies that address the ischemic tolerance of the liver during resections with prolonged total vascular isolation may further expand the use of these resective techniques.

The rationale for partial hepatic and retrohepatic IVC resection has been to address the local extent of the malignancy. Most primary malignancies with direct adjacent organ invasion are classified variably by the American Joint Commission on Cancer staging system as T3
or T4 tumors, depending on the site of tumor origin. Although such T staging has not been used for the staging of primary hepatic cancers, IVC invasion by hepatic tumors is consistent conceptually with T4 tumor stage and, therefore, may be approached clinically in the same way as other T3 or T4 malignancies with en bloc resection. Current reports (Table) have confirmed the technical feasibility and safety of hepatic resection and retrohepatic caval reconstruction. However, these data are limited by the small number of patients, variable histopathologic types of tumor, and length of follow-up to determine the curative potential of such resections. Our data and others\(^3,7,9\) suggest that perihepatic control of the primary tumor can be effective. Only 50% of our patients had local disease progression. All nonperioperative deaths were associated with distant disease progression. Thus, local control of malignancy is possible by such resections. Moreover, given the expected survival associated with unresected hepatic malignancies, these data suggest some survival benefit, albeit observational. Importantly, one purpose of presenting these data was to reemphasize an operative approach to address a variety of hepatic or perihepatic malignancies with vena caval involvement. We fully recognize that our small sample size and various tumor histopathologic types preclude evidence-based conclusions on survival.

Several issues related to the technique of hepatic resection and IVC reconstruction warrant comment. We confined our study to tumors requiring segmental caval resection. All reconstructions were performed with reinforced polytetf tube grafts, with the exception of a single primary caval anastomosis. Vascular isolation of the liver and the retrocaval IVC is generally straightforward, unless limited by tumor bulk. Control of the afferent hepatic vasculature and the infrahepatic IVC should precede full mobilization of the liver. We do not isolate the hepatic artery...
tral, radial incision through the diaphragm and the caval diaphragmatic IVC can be gained easily through a central, radial incision through the diaphragm and the caval foramen.

We have performed all hepatic resections with IVC reconstructions in situ. Detailed anatomic definition of the tumor has facilitated surgical planning by the hepatic and vascular surgical team. Despite the formidable size and intrahepatic extent of these tumors, we believe that accurate and detailed anatomic extent of tumor and its vascular and biliary involvement can be defined preoperatively by the combined use of computed tomography and magnetic resonance imaging with selective dimensional angiography (computed tomographic angiography or magnetic resonance angiography). Venacavography has been used less frequently with gained experience in these procedures. Although patients undergoing these resections did require perioperative transfusion of blood products, hemorrhage was excessive in only 1 patient. That patient may have benefited from ex situ resection. Venovenous bypass from the infrahepatic IVC to central venous system was necessary for hemodynamic stability in only 7 patients.

The major limitation to in situ resection is the duration of warm hepatic ischemia. We acknowledge that the anticipated duration of ischemia is unpredictable. To minimize ischemia, we have initiated hepatic transection during a 5- to 10-minute period of hepatic vascular inflow occlusion for ischemic preconditioning.11 Hepatic transection is continued without inflow occlusion unless local factors dictate or until the suprahepatic IVC is clamped for the anastomosis of the caval graft. We have recently used perioperative allopurinol in 2 patients to potentially enhance ischemic tolerance in several patients, but we have not used other free radical scavengers.17 None of our patients developed irreversible hepatic failure, and serum enzyme markers of hepatic

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<th>Source</th>
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Source

Literature Review In Combined In Situ Partial Hepatectomy Plus IVC Segmental Resection

Abbreviations: ACC, adrenocortical cancer; CA, carcinoma; Ext, extended; HCC, hepatocellular carcinoma; IVC, inferior vena cava; PTFE, polytef; RCC, renal cell cancer; SFV, superficial femoral vein.

*See “Results” section of text for detailed information.
ischemia usually approached normal within 7 to 10 days postoperatively. The addition of other ischemic protective factors or techniques may broaden the applicability of in situ techniques in the future.

The complexity of hepatic resections requiring IVC reconstruction and the unpredictability of the hepatic ischemic time have prompted some to approach similar patients with ex situ hepatic resections and autotransplantation of the hepatic remnant. The advantages of ex situ technique include isolated hypothermic resection under the protective effects of liver perfusion and a longer time interval to perform difficult vascular reconstructions. In contrast, the disadvantages of ex situ resections include prolonged operative duration (hours), increased number of anastomoses, high perioperative mortality and liver failure rates, and a real, but small, need for salvage orthotopic liver transplantation.10:11 We believe that the similar versatility and improved safety of in situ techniques currently outweigh the theoretical advantages of complex ex situ resections. Moreover, we believe that in situ resections can be undertaken more frequently by surgical oncologists.

Patency of the hepatic veins and the IVC after resection has been good. We have not encountered late hepatic venous thrombosis evident either by imaging or clinically as a chronic Budd-Chiari syndrome. Late caval graft patency has been 91% at a median follow-up of 3 years. Both patients with late graft thromboses had discontinued anticoagulation therapy. Anticoagulation therapy was initiated in all patients with polytetrafluoroethylene grafts with systemic heparin 12 hours postoperatively and subsequently converted to oral warfarin sodium to maintain prothrombin time 2 to 3 times normal (international normalized ratio, 2.0-3.0). Most patients have been sensitive to warfarin initially because of the extent of the hepatic resection and the temporary synthetic dysfunction of the liver associated with resection and ischemia. Empirically, we have recommended that oral anticoagulation therapy be maintained for life because of the risk of thrombosis associated with venous reconstruction. Platelet inhibitors are recommended if oral anticoagulation is not possible.

Accepted for publication February 4, 2003.

This study was presented at the 110th Scientific Session of the Western Surgical Association, Vancouver, British Columbia, November 19, 2002, and is published after peer review and revision. The discussions that follow this article are based on the originally submitted manuscript and not the revised manuscript.

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REFERENCES


DISCUSSION

William C. Chapman, MD, St Louis, Mo: This is one of the largest series of combined liver and caval resections for advanced hepatic tumors. There are several aspects of this presentation that should be emphasized. First, these resections are complex and require a carefully planned strategy for successful outcome. Caval resection combined with hepatic resection predisposes the patient to significantly compromised venous return and the potential for prolonged warm ischemic injury to the liver. This is a very high-risk procedure, with previous series reporting a 10% to 33% mortality risk with such operations. So the results reported today are outstanding and the authors should be congratulated.

I do have a couple of points that I would like the authors to clarify. Based on the results in this report and the authors’ own personal preference, they champion the use of an in situ technique for liver resection. This is contrasted with the use of ex situ techniques where the liver is cold-perfused with the University of Wisconsin (UW) solution and a back-table-type resection performed with subsequent reimplantation of the liver, similar to a liver transplant procedure. The authors emphasize the advantages and disadvantages of each technique and conclude that the in situ technique is their preferred approach. I wonder if the authors might comment on a third consideration that is not discussed in their manuscript, namely, the use of an in situ resection but with complete hepatic vascular exclusion and UW cold perfusion of the liver during the resection phase. This approach utilizes venovenous bypass as proposed by the authors, but in addition the liver is perfused with
noma. Patients with cholangiocarcinoma oftentimes have a very short period of time with or without resection. That is demonstrated in the paper that the 3-year disease-free survival in patients with cholangiocarcinoma is 69%, so those patients may do well because of the nature of the disease in spite of the resection, but all of the other patients, the HCCs [hepatocellular carcinomas], the metastatic tumors, the sarcomas didn't do as well and failed by a year but were grouped with patients with cholangiocarcinomas who do better. Even though this is a technical tour de force, I can't see by the paper that you really proved that these were a positive influence on survival.

Dr Nagorney: Dr Chapman, you are very kind. There are several points you have raised that I will try to address. First of all, I wholly concur that undertaking these operations should be done by individuals who have experience in both the transplant and oncologic techniques. The purpose of our paper was to describe a technique to allow wider application of such resections for a variety of tumors. Because the descriptions of the techniques are so sparse, we felt that detailing it would be helpful. We can only leave it to each institution to decide who undertakes such operations.

Your technique of in situ perfusion of the liver as an additional option for resection of these tumors is an important one. We would reserve in situ perfusion of the liver for those cases where reconstructing the hepatic vein or the portal vein or both is required. The hepatic ischemic time of these operations is more prolonged and even more unpredictable than with our technique in selected patients who did not require portal vein reconstruction concurrently. Perfusion with UW solution and in situ resection that avoids the portal vein, hepatic artery, and bile duct anastomoses, which are required for ex situ resections, is an important one. I would prefer your technique over any ex situ resection myself.

We have not had total caval occlusion by any of our tumors. These tumors tend to grow but allow some caval perfusion. Therefore, we would reconstruct the inferior vena cava, provided blood flow continues through the inferior vena cava. If there is total occlusion of the inferior vena cava by the tumor with well-established collaterals, we would not reconstruct the IVC because it would make it a much easier operation.

Except for portal hypertension, the track record for non-autogenous graft material in the venous system has been abhorrent and unreliable. Given the small number of patients and, as Dr O'Connell has noted, limited life expectancy, we will maintain long-term anticoagulation simply because the track record of thrombosis of venous grafts is high. If the patient is intolerant of oral anticoagulation, we would use a platelet inhibitor.

And finally, the ischemic time is a real problem with this operation. Our mean total liver ischemic time was only 18 minutes because of our manipulation of the clamps during these operations. If I think it is going to be prolonged (greater than or equal to 90 minutes), we would do in situ perfusion or employ preoperative allopurinol or other agents that help improve ischemic tolerance.

Dr O'Connell, I would recognize that the survival in these patients has been limited. In our experience with liver resections, if patients have IVC involvement, whether it be by tumor thrombus or gross obstruction, I would submit that their natural history is quite brief and clearly less than 6 to 12 months. Anecdotally we have shown that there is some improvement in survival. I would certainly dispute your premise that cholangiocarcinoma has an indolent course. That is not our experience with the natural history of intrahepatic cholangiocarcinoma, which we are addressing here. There will never be a randomized controlled series with these tumors. That study is a pie-in-the-sky wish for the potpourri of tumors that we have with encountering this problem. Such studies are impractical. I believe if you can provide a technique where gross tumor is excised, some patients will benefit.