Arterial and Venous Resection for Pancreatic Adenocarcinoma

Operative and Long-term Outcomes

Robert C. G. Martin II, MD; Charles R. Scoggins, MD; Vasili Egnatashvili, MD; Charles A. Staley, MD; Kelly M. McMasters, MD, PhD; David A. Kooby, MD

Hypothesis: Aggressive preoperative and intraoperative management may improve the resectability rates and outcomes for locally advanced pancreatic adenocarcinoma with venous involvement. The efficacy and use of venous resection and especially arterial resection in the management of pancreatic adenocarcinoma remain controversial.

Design: Retrospective review of patients entered into prospective databases.

Setting: Two tertiary referral centers.

Patients and Methods: A retrospective review of 2 prospective databases of 593 consecutive pancreatic resections for pancreatic adenocarcinoma from January 1, 1999, through May 1, 2007.

Results: Of the 593 patients, 36 (6.1%) underwent vascular resection at the time of pancreatectomy. Thirty-one of the 36 (88%) underwent venous resection alone; 3 (8%), combined arterial and venous resection; and 2 (6%), arterial resection (superior mesenteric artery resection) alone. Patients included 18 men and 18 women, with a median age of 62 (range, 42-82) years. The 90-day perioperative mortality and morbidity rates were 0% and 35%, respectively, compared with 2% and 39%, respectively, for the group undergoing nonvascular pancreatectomy (P=.34). Median survival was 18 (range, 8-42) months in the vascular resection group compared with 19 months in the nonvascular resection group. Multivariate analysis demonstrated node-positive disease, tumor location (other than head), and no adjuvant therapy as adverse prognostic variables.

Conclusions: In this combined experience, en bloc vascular resection consisting of venous resection alone, arterial resection alone, or combined vascular resection at the time of pancreatectomy for adenocarcinoma did not adversely affect postoperative mortality, morbidity, or overall survival. The need for vascular resection should not be a contraindication to surgical resection in the selected patient.

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ARTERIAL AND VENOUS RESECTION during pancreatectomy for pancreatic adenocarcinoma is still debated. In the early 1970s, Forstner1 introduced the concept of regional pancreatectomy with partial vascular resection, including type 1 (venous resection) and type 2 (arterial resection). Even with this extensive report, significant morbidity and mortality occurred, and the author questioned its true use because of the lack of control of the soon-to-be-recurrent systemic disease.

Recent reports from the mid-1990s have reevaluated the use of portal vein and superior mesenteric vein (PV-SMV) resections, clearly demonstrating equivalent morbidity and mortality compared with a standard pancreaticoduodenectomy.2-4 Nonetheless, the presence of vascular invasion on preoperative staging is still considered by many to be a contraindication for surgery, and these patients are referred to palliative chemotherapy or chemoradiotherapy.

We hypothesize that involvement at the PV–superior mesenteric confluence or the isolated hepatic artery/superior mesenteric artery (SMA) should not be a contraindication to pancreatectomy for pancreatic adenocarcinoma. The aim of this study was to evaluate the intraoperative and long-term outcomes in patients with pancreatic adenocarcinoma undergoing pancreatectomy with vascular resection.

METHODS

In a collaborative effort, we assessed 593 consecutive cases in which pancreaticoduodenec-
All patients were treated for pancreatic adenocarcinoma under the auspices of a multidisciplinary hepatopancreatobiliary disease management team that includes surgical oncologists accredited and trained by the Society of Surgical Oncology, medical oncologists, gastroenterologists, interventional radiologists, and radiation oncologists. Forty patients were considered for treatment during this period and had undergone PV-SMV and/or arterial resection and reconstruction for pancreatic adenocarcinoma.

Data examined included extensive demographics (age, sex, medical history, surgical history, history of tobacco and alcohol use, use of medications, family history, and any other possible etiologic factors), pathological features of the pancreatic lesion, venous involvement defined as PV-SMV invasion, nonneoplastic pathological findings in the pancreatic parenchyma, morbidity, mortality, and overall survival. Follow-up was obtained by the treating physician and is up-to-date from the end of the study.

Our standard diagnostic workup for a patient with pancreatic malignancy involves helical 3-phase computed tomography with 3-dimensional reconstruction or contrast-enhanced magnetic resonance imaging with pancreatic protocol. Complete obstruction or thrombosis of the PV-SMV was considered an absolute contraindication for operation. Some patients were considered for neoadjuvant chemoradiotherapy, especially if the tumor approached the SMA or the hepatic artery. This therapy included fluorouracil- or gemcitabine hydrochloride (Gemzar)—based chemotherapy with concomitant radiotherapy. In cases of PV-SMV involvement of at least 2.0 cm, preoperative chemoradiotherapy was considered, although not required. Distant metastatic disease was considered a contraindication to resection. Neoadjuvant therapy was used for locally advanced or long-segment venous involvement, with surgical therapy as the initial treatment in patients with pancreatic malignant neoplasms without this presentation.

Resection was considered for patients who did not demonstrate progression of disease or development of distant metastases during neoadjuvant chemoradiotherapy.

The resection of choice is a standard or pylorus-preserving pancreaticoduodenectomy. The reconstruction is performed through a single retrocolic jejunal limb reconstruction and antecolic gastrojejunostomy or duodenojejunostomy, with enteral feeding tubes used at the surgeon's discretion.

The type of venous resection and reconstruction is based on the quantity of venous involvement. For tumors invading the PV-SMV confluence, an end-to-end anastomosis is considered when the extent of venous resection is less than 2.0 cm in length. For longer segments, a jugular venous interposition graft is particularly well suited because it provides a good size match and low rates of infection, coupled with a low risk of complications from the vein harvest. For the end-to-end Anastomosis, adequate mobilization of the PV by taking the coronary veins and mobilizing up to the right and left PV and down to and potentially taking the first jejunal branch of the SMV allows for an adequate tension-free end-to-end anastomosis. In all cases in this series, the splenic vein was transected for added length and was not reimplemented. Tangential resections are used when venous involvement of less than 120° is encountered and the venotomy is closed primarily or with a saphenous vein patch. Alternative patch reconstructi- tion was also performed at the surgeon's discretion. Arterial sections were reconstructed with saphenous vein interposition grafts, with systemic heparin sodium used for all of the arterial resections and reconstructions. Anticoagulation was used at the surgeon's discretion and was dependent on venous clamp time. If venous clamp time was going to be longer than 20 minutes, systemic heparin was used during venous occlusion. Postoperative anticoagulation was also at the surgeon's discretion, with all patients receiving aspirin.

Frozen section of the pancreatic neck transection margin is usually performed, with additional pancreas taken if necessary, on the basis of frozen-section analysis results. Resection margins of the pancreas, distal bile duct, and retroperitoneal tissue were marked and studied in detail for the microscopic presence of tumor.

Intraoperative variables were also studied, including total blood loss, operation-related blood transfusion (transfusions during the operation and the entire hospital stay), operative time, PV clamp time, postoperative complications, hospital stay, length of hospital mortality, lymph node status, resection margins, and overall morbidity defined as occurring within 90 days of operation. Complications were identified prospectively in our databases, assigned a grade from 1 to 5 based on an established scale, and entered into the database. Examples of the grading of complications include 1 for an uncomplicated urinary tract infection; 3 for a small, contained anastomotic leak requiring no further operative therapy or drainage procedures; and 5 for death. In instances in which the grading was unclear, a score was assigned after a review of the records and a discussion between 2 of us (R.C.G.M. and D.A.K.). All in-hospital and 90-day postoperative complications were evaluated, and the most severe complication level was recorded. Infectious complications were defined by positive results of a fluid culture (eg, sputum, wound, or urine), with some criteria of a systemic inflammatory response (ie, tachycardia, fever, and hypoxia). A standard follow-up on these patients usually included a computed tomographic scan every 3 months for the first year, every 6 months for years 2 through 4, and then yearly.

The \( t \)-square, Mann-Whitney test for nominal, continuous, and ordinal variables, respectively, were used to evaluate the association of independent variables with surgical complications. Proportional hazards analysis was performed using all variables found significant by univariate analysis. Relative risks with 95% confidence intervals were calculated as measures of association. Multiple logistic regression analysis was used to determine overall outcome and differences. We considered \( P < .05 \) to be significant. Statistical analysis was performed using commercially available software (JMP; SAS Institute Inc, Cary, North Carolina).

RESULTS

In this series, 36 patients presenting for treatment of pancreatic adenocarcinoma (18 men and 18 women with a median age of 62 [range, 47-82] years) underwent PV-SMV, hepatic artery/PV, or SMA resection. All patients with pancreatic head lesions (n = 32) presented with jaundice, and the remaining 4 presented with atypical midepigastic abdominal pain. Demographic and operative data for all 36 patients are given in Table 1.

PRIOR THERAPY

Most of the patients who presented with jaundice had endoscopic stents in place for a median duration of 24 days, with 4 patients having undergone prior explor-
ARTERIAL RESECTION

All 5 arterial resections were identified on preoperative staging computed tomography, and 3 patients underwent preoperative chemoradiotherapy. Three patients had hepatic arterial involvement that was resected and primarily repaired under systemic heparinization, which continued after the specimen was removed. Margins in all 3 patients were negative for tumor, and the patients had no adverse hepatic-related complications during the perioperative period. All 3 patients had a large nodal burden, including 8, 10, and 14 positive lymph nodes, and all received adjuvant gemcitabine-based therapy. Their disease-free intervals were 10, 18, and 21 months, with overall survival of 18, 20, and 28 months, respectively.

Two patients underwent SMA resection with saphenous vein reconstruction after the entire specimen was removed. Systemic heparinization was used and reversed with systemic protamine sulfate therapy. The enteric anastomoses were performed after arterial reconstruction. Both patients had margin-negative resections: one patient had no positive lymph nodes of the 30 lymph nodes examined and the other had 6 positive lymph nodes of the 32 examined. Both had an uneventful perioperative recovery, with lengths of stay of 8 and 23 days. Both patients received adjuvant gemcitabine therapy; one patient had an overall survival of 11 months, after a disease-free interval of 10 months, and the other had an overall survival of 12 months, with no evidence of disease at the last follow-up. Neither patient had any long-term complications or reported any significant gastrointestinal tract symptoms related to diarrhea.

VENOUS RESECTION

In the remaining venous resection group, most of the PV-SMV resections were performed with a primary end-to-end anastomosis (17 patients) or a lateral venorrhaphy (16) and were closed primarily. Three patients underwent reconstruction with an end-to-end internal jugular vein or had an internal jugular vein or a polytetrafluoroethylene graft (Gortex; WL Gore & Associates, Inc, Flagstaff, Arizona) inserted to allow for reconstruction. The median operative time was 210 (range, 140-480) minutes. The median PV occlusion time was 12.5 (range, 8-44) minutes. The median estimated blood loss was 700 (range, 50-2500) mL, with concomitant median transfusion of 3 (range, 1-8) U during the patients’ entire hospital stay. Median hospital stay was 11 (range, 5-38) days.

There were no perioperative deaths in the vascular resection group during the perioperative follow-up. Fourteen patients (39%) had 18 complications, which included pulmonary complications in 3 patients, wound complications in 3, readmission for dehydration in 3, abscess in 3, pancreatic leak in 1, and other complications ranging in severity from grades 1 to 3. These rates were comparable to the mortality of 2% and morbidity of 39% for patients who underwent pancreatic resection without vascular resection ($P = .34$). Postoperative follow-up with computed tomography demonstrated no sinistral portal hypertension in the patients who underwent splenic vein ligation at the time of resection and reconstruction. Results of postoperative computed tomography demonstrated 100% patency of the PV and arterial reconstruction at 3 and 6 months.

HISTOLOGIC FINDINGS AND ADJUVANT THERAPY

A ductal adenocarcinoma was found in the pancreatic head or body in 32 patients or in the pancreatic tail in 4. The median tumor size was 3.8 (range, 2.0-8.9) cm. The ma-
Ligamentous neoplasms in the tail were large primary tumors that extended into the body, necessitating vascular resection. After resection, the resection margin was tumor free in 28 patients (78%). The SMA retroperitoneal margin was positive for tumor in 6 patients (17%) and the pancreatic duct transection margin was positive in 2 (6%). The median lymph node evaluation included 14 lymph nodes (range, 6-33), with a median positivity rate of only 1 lymph node (range, 0-14). Vascular invasion was demonstrated in 20 of the 36 patients (56%) undergoing vascular resection.

Most of the patients (22 [61%]) received adjuvant therapy in the form of adjuvant gemcitabine-based therapy or adjuvant fluorouracil and radiotherapy to the retroperitoneal margin or to the venous reconstruction.

OVERALL SURVIVAL

In an evaluation of overall survival in the entire pancreatic adenocarcinoma cohort with a median follow-up of 24 months, median survival was 18 (range, 8-42) months in the vascular resection group compared with 19 months in the nonvascular resection group (Figure). The vascular resection group had a greater incidence of node-positive disease (16 patients [44%] vs 12 [33%]) and greater nodal burden (median, 1 lymph node [range, 0-14] vs none [range, 0-5]) than the nonvascular group. Rates of margin-positive resection were similar in both groups, with 6 patients in the vascular group (17%) compared with 7 in the nonvascular group (19%). Patients who had pathologic vascular invasion (n=20) had a median survival of 16 months compared with 18 months in patients without vascular invasion (n=16) (P=.35). In an evaluation of all clinicopathologic variables, multivariate analysis demonstrated that node-positive disease (P=.02; hazard ratio, 3.4), tumor location other than in the head (P=.03; hazard ratio, 1.25), and no adjuvant therapy (P=.04; hazard ratio, 1.05) as adverse prognostic variables.

COMMENT

The purpose of this analysis was to examine outcomes of patients undergoing en bloc vascular resection at the time of pancreatoduodenectomy for adenocarcinoma. This report demonstrates acceptable perioperative morbidity and no perioperative mortality, with an equivalent overall survival in patients with PV-SMV and/or arterial involvement. Other reports have shown similar acceptable mortality and morbidity rates, with a number of studies demonstrating equivalent overall survival when compared with patients who underwent pancreatic resections without the need for vascular resection (Table 2). Based on this review, we believe that a PV-SMV resection should be anticipated on the basis of perioperative imaging techniques and that any patients suspected of having PV-SMV involvement based on preoperative imaging results should undergo resection of the PV-SMV when the involvement is confirmed. Dissection along the PV-SMV should not be used to assess gross tumor invasion because of the risk of violating the tumor as well as the risk of tearing the very friable PV-SMV intima.

The keys to the success of vascular resection in pancreatic adenocarcinoma are appropriate patient selection, beginning with high-quality cross-sectional imaging to assess solitary vessel involvement (ie, the vein alone, the artery alone, or both), length of involvement, extent of the primary tumor, and nodal disease and to ensure that patients are free of distant metastatic disease. These technical and oncologic factors should already be combined with the patient’s overall performance status, underlying comorbidities, and overall expectations for outcomes.

The techniques for PV-SMV resections are variable and include primary end-to-end anastomosis, lateral venorrhaphy with primary or patch repair, and resection and reconstruction with the internal jugular vein, the left renal vein, or a synthetic graft. Most surgeons would agree that primary resection and repair can only be performed when less than 2 cm of vein will be resected. The technique involves wide mobilization of the proximal and distal PV-SMV with ligation of the splenic vein and mobilization of the right colon to release all tension. The ischemic technique can involve concomitant occlusion of the SMA or a simple clamp-and-go technique, provided the ischemic time is less than 20 minutes. Use of a lateral venorrhaphy and a primary repair or patch is determined by the length of involvement and the mobilization of the distal venous structures. To our knowledge, there has been only 1 long-term patency study, by Smoot et al, who reviewed 64 patients undergoing pancreaticoduodenectomy with venous reconstruction. Patency was assessed at 12 months, and 11 patients (17%) had thrombosis with no difference in patency by the type of resection and reconstruction or the type of anticoagulation that was used. Thus, no data support the use of postoperative anticoagulation in venous reconstruction, but the decision is still based on the surgeon’s preference.

Based on a review of the literature and on its vast variability, the incidence of PV-SMV resection and the percentage of patients undergoing R0 resection is extensive. Japanese reports have shown an incidence of PV-SMV resections varying from as low as 58% to as high as 88% of all patients; in Western reports this percentage ranges from 3% to 41% of patients. This variability continues to demonstrate the difference in pa-
tient selection and the difference in the aggressiveness of the operation based on surgeon bias. This variance also demonstrates the true incidence of venous wall invasion after vascular resection, which has ranged in the literature from 3% to 80%.24 At present, we are unable to assess preoperatively whether a pancreatic malignant neoplasm has actually invaded the PV or the SMV or is simply densely adherent to these structures. Thus, whether to perform venous resection can usually be decided on the basis of preoperative imaging results.

The considerations for arterial resection and reconstruction are different according to anatomy, that is, the hepatic artery or the SMA. Isolated hepatic artery resection can be planned preoperatively with imaging, but can also be an intraoperative decision in the presence of a superior-based tumor that involves the gastroduodenal artery at its branching. Surgeon preparation for hepatic artery involvement is essential to achieve a margin-negative resection and can be performed in most cases with primary resection and primary repair with or without the assistance of the vascular surgeon, based on the surgeon’s experience level. Superior mesenteric involvement and planned resection of the SMA should not be based on an intraoperative evaluation and decision in the management of pancreatic adenocarcinoma. All planned SMA resections in this series were identified preoperatively and planned extensively with collaboration with a vascular surgeon and with the use of preoperative therapy to better assess the biological characteristics of the patient’s disease.

In our multivariate survival analysis, only the presence of lymph node metastasis was a predictor of overall survival. Venous vascular invasion, venous resection, and arterial invasion were not adverse predictors of outcome in this study. The limitations of this study are the 8-year duration of this analysis and the significant changes that have occurred in neoadjuvant and adjuvant therapies. Signifi-

cant advances in surgical and anesthetic therapy, radiotherapy, and chemotherapy could have affected our results. Nevertheless, we conclude from our data that a pancreatic resection should include a venous resection if the intraoperative findings demonstrate a densely adherent or invaded PV-SMV. Similarly, patients with hepatic artery or SMA involvement can undergo resection and reconstruction with appropriate outcomes after appropriately assessing the aggressiveness of the disease, extent of involvement, and patient comorbidities.

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Correspondence: Robert C. G. Martin II, MD, Department of Surgery, University of Louisville School of Medicine, 315 E Broadway, Room 313, Louisville, KY 40202 (robert.martin@louisville.edu).

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REFERENCES


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Table 2. Reported Results of Pancreatectomy With Vascular Resection From Different Centers

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Abbreviations: NA, not available; ellipses, not reported.


