Arterial resection at the time of pancreatectomy for cancer

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Background. *Tumor-induced arterial abutment/encasement has been traditionally a contraindication to surgery in patients with localized pancreatic cancer (PC). One recent meta-analysis reported greater mortality rates in this setting. We report herein a series of planned arterial resections in carefully selected patients who responded favorably to combined modality therapy for localized PC.*

Methods. *We reviewed all patients with PC and arterial encasement treated between May 2011 and September 2013; all patients received an extensive course of neoadjuvant therapy before surgery.*

Results. *Of 15 patients taken to surgery, 2 had peritoneal disease at laparoscopy, and therefore, laparotomy was not performed. Pancreatectomy (pancreaticoduodenectomy, 3; distal, 8; central pancreatectomy, 1; total, 1) was performed in the remaining 13, 10 of whom required arterial resection. The most common operation was an Appleby procedure. Of 10 patients who underwent combined pancreatectomy and arterial resection, their median age was 62 years (range, 33–75), median operative time was 7.5 hours, and median blood loss was 725 mL. Complications occurred in 3 of 15 patients with no perioperative mortality. Median duration of hospital stay was 9 days (range, 5–19). An R0 resection was achieved in 11 (85%) of 13 patients. At a median follow-up of 21 months, 8 of these 13 resected patients (62%) are alive without disease.*

Conclusion. *Planned arterial resection at the time of pancreatectomy can be performed with acceptable morbidity and mortality; patient selection and induction therapy are likely critically important variables that seem to impact patient outcome. Those patients with stable or responding disease after induction therapy represent the subset of patients with potentially favorable tumor biology in whom extended resections may enhance survival duration. (Surgery 2014;155:919-26.)*

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ARTERIAL RESECTION for pancreatic cancer (PC) has remained an area of controversy since Fortner first introduced the concept as part of regional pancreatectomy in the 1970s.[1] After initial enthusiasm, the poor long-term survival and increased morbidity in the 1980s and early 1990s led to a withdrawal of support for arterial resection at the time of pancreatectomy. More recent reports, however, have demonstrated acceptable morbidity and mortality associated with certain types of vascular resection (primarily vein resection) at the time of pancreatectomy with long-term survival equivalent to that for patients who did not require such extended resections.[2,3] Clearly, a complete, gross resection of the tumor is necessary (albeit not sufficient) to achieve long-term survival. Physicians have struggled with how to identify those patients likely to benefit from such extensive and high-risk operations directed at the primary tumor in the context of a disease that is metastatic at diagnosis in most patients. Currently, venous resection and reconstruction have become somewhat routine when the pancreatic tumor cannot be separated from the adjacent superior mesenteric (SMV) or portal vein (PV).[4,5] Increasingly complex venous procedures, such as mesocaval shunting, distal splenorenal shunting, and interposition grafting, are now being reported after intensive induction/neoadjuvant therapy.[5] With the advent of more effective systemic therapies, attention is being refocused on the potential benefit of removing the primary tumor, even in the setting of complex arterial abutment or encasement, when it is the only site of measurable disease after a period of induction therapy.

In contrast with venous resection, arterial resection at the time of pancreatectomy remains an

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infrequent event, and only small case series have been published.[6] These reports, however, have rarely described the planned intent of the operation; by this we are referring to whether the arterial resections were a planned event associated with appropriate preoperative preparation, or were the result of intraoperative findings or perhaps occasionally owing to an inadvertent arteriotomy-surgical misadventure. Increased mortality following arterial resection reported in a recent meta-analysis may, therefore, be biased by including patients who, because of intraoperative complications, underwent an unintended arterial resection/reconstruction.[7] In contrast, we report a series of patients with preoperatively defined arterial encasement amenable to complete operative resection who were carefully selected for operation after what we believe to be a favorable response to induction therapy.

PATIENTS AND METHODS

Tumor-induced encasement of the celiac axis (CA) or common hepatic artery (CHA) was defined as a tumor-vessel interface of >180°. In addition to arterial encasement defining borderline resectable/locally advanced disease (stage of disease depending on the artery involved), all patients in this report had biopsy confirmation of adenocarcinoma without evidence of distant metastatic disease on cross-sectional imaging with computed tomography and often also magnetic resonance imaging and positron emission tomography. Treatment sequencing involved several steps. First, a minimum of 2 months of neoadjuvant chemotherapy followed by complete restaging to include clinical assessment, repeat imaging, and reassessment of relevant tumor markers (carbohydrate antigen 19-9, carcinoembryonic antigen). Patients eventually considered for surgery were those who (at restaging) had no evidence of disease progression on imaging, maintained an Eastern Cooperative Oncology Group performance status of ≤2, and had a stable, or preferably a decline, in tumor marker profile. After systemic therapy, chemoradiation was given over 6 weeks and after a 4- to 5-week recovery, restaging was performed again before considering potentially curative operative resection of the primary tumor and adjacent vascular structures. Patients who went on to operation were those who tolerated induction therapy with acceptable toxicity (performance status often improved), had stable or responding disease on repeat cross-sectional imaging, and experienced a stable or decrease in tumor marker profile.

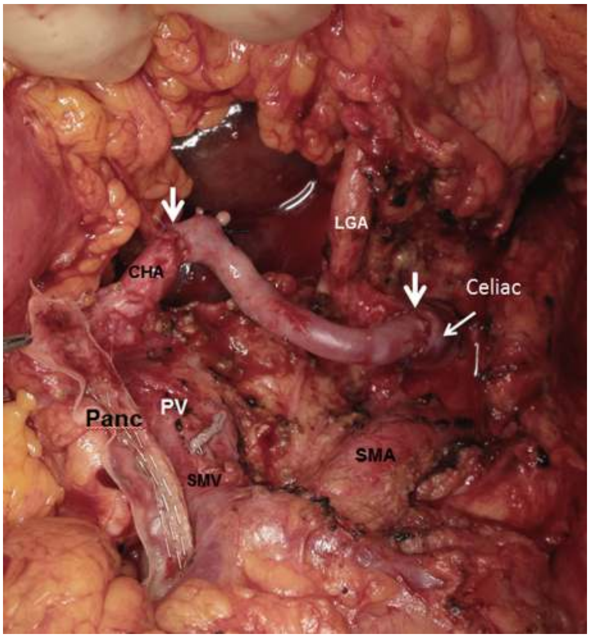

Fig 1. Modified Appleby procedure to include a 'supercharged' celiac axis reconstruction. Following distal pancreatectomy and celiac axis resection, the stump of the celiac axis was anastomosed to the stump of the common hepatic artery using a reversed saphenous vein graft to augment flow through the pancreaticoduodenal arcade. *Short wide arrows* mark the anastomoses. *CHA*, Common hepatic artery; *LGA*, left gastric artery; *Panc*, stapled end of pancreas; *PV*, portal vein; *SMA*, superior mesenteric artery; *SMV*, superior mesenteric vein.

Pancreatic resections were performed as described previously.[8] When resecting the CA, arterial reconstruction was performed using a reversed saphenous vein graft (RSVG) from the CA stump to the CHA just proximal to the origin of the gastroduodenal artery (GDA); the distal few millimeters of CHA were used for the anastomosis to allow for revascularization of the GDA and the proper hepatic artery [PHA]; Fig 1. Revascularization of the distal-most CHA was performed based on (1) the authors' bias that it would maximize hepatic and gastric perfusion especially if the left gastric artery was also taken with the CA; (2) such increased perfusion restores normal arterial flow, which may prevent complications such as hepatic abscess or delayed gastric emptying (admittedly, there are no data we know of to support the concern that some degree of ischemic gastropathy could affect gastric emptying); and (3) most important, revascularization of the distal CHA is usually straightforward and adds very little time to the operation if the stump of the CA is available. Resection of the CHA alone was followed by either direct end-to-end anastomosis or by

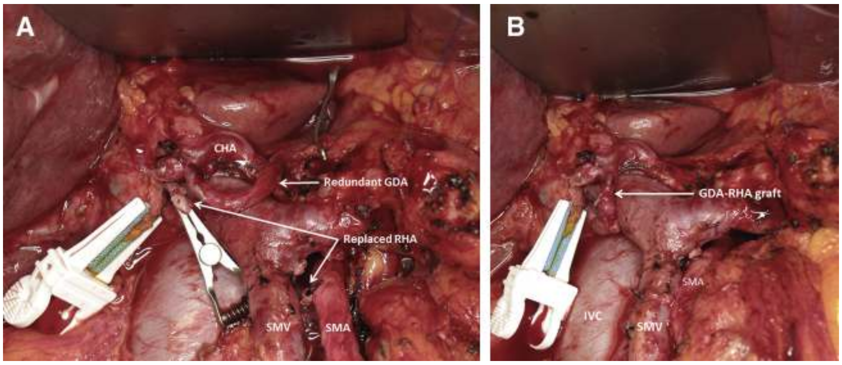

Fig 2. *A*, After pancreaticoduodenectomy and resection of a replaced right hepatic artery (RHA), a long length of the gastroduodenal artery was available (distant from tumor) to anastomose to the distal end of the replaced RHA (seen here ligated at its origin from the SMA). *B*, The gastroduodenal-RHA anastomosis is complete. *CHA*, Common hepatic artery; *GDA*, gastroduodenal artery; *IVC*, inferior vena cava; *SMA*, superior mesenteric artery; *SMV*, superior mesenteric vein.

incorporating a RSVG. Resection of a replaced right hepatic artery (RHA) arising from the superior mesenteric artery (SMA) was reconstructed (in this report) with the GDA which was preserved and anastomosed to the distal end of the resected RHA (Fig 2). Pathologic evaluation of the surgical specimen was completed as per the *AJCC Cancer Staging Manual*; an R1 resection was defined as microscopic evidence of tumor at the inked SMA and/or CA margin or tumor present in the en face sections of the hepatic duct or pancreatic transection margins.[9] Postoperative reconstruction (pancreaticoduodenectomy, total pancreatectomy) and routine patient management has been published previously.[10]

RESULTS

Between May 2011 and September 2013, 15 patients were taken to the operating room for pancreatectomy with planned arterial resection after extensive programs of induction therapy. Successful resection of the primary tumor was accomplished in 13 patients, 10 of whom required arterial resection; 7 of 10 had locally advanced disease, and 3 had borderline resectable PC.[11] To place these numbers in perspective, during this same time period we treated a total of 37 patients with locally advanced PC; 30 (81%) were not deemed candidates for operation owing to the absence of a favorable response to induction therapy, the anatomy of the tumor precluding a safe operation, or owing to the performance status/medical comorbidities of the patient. Herein, we sought to more critically review the 15 patients who underwent operation for arterial encasement.

Nonoperative therapies for the 15 patients who underwent surgery are outlined in Table I. One patient did not undergo preoperative chemoradiation (received only preoperative chemotherapy); all others underwent chemotherapy followed by chemoradiation. The most common treatment sequencing was FOLFIRINOX followed by gemcitabine- or capecitabine-based chemoradiation (5,040 cGy) which was given to 11 patients.

Diagnostic laparoscopy was performed in all patients after anesthesia induction. Despite restaging immediately before operation, 2 patients were found to have radiographically occult peritoneal metastases at the time of laparoscopy and did not proceed to laparotomy. Three additional patients underwent pancreatectomy (pancreaticoduodenectomy in 1, distal subtotal pancreatectomy in 2) without need for arterial resection. In these latter 3 cases, the intraoperative impression of the surgeon was that the artery in question could be separated from the tumor without jeopardizing a potentially curative oncologic resection. This impression was supported by frozen section pathologic examination of tissue taken at the time of arterial microdissection, which was interpreted as benign and confirmed on final permanent pathology.

Arterial resection. Arterial resection at the time of pancreatectomy was required in 10 patients including 6 women and 4 men with a median age of 62 years (range, 33–75). Distal pancreatectomy with CA resection (Appleby procedure) was performed in 6 patients; 1 underwent a central (middle segment) pancreatectomy with CA resection, 2 underwent pancreaticoduodenectomy that required hepatic artery resection, and 1 patient

Table I. Chemotherapy and chemoradiotherapy before surgery: Postoperative adjuvant therapy was uncommon

Patients (n = *15*)	*Chemotherapy*	*Cycles*	*Chemoradiotherapy*	*Adjuvant therapy*
1	FOLFIRINOX	12	Gem-XRT	Gem/NAB
2	FOLFIRINOX/FOLFIRI	4/4*	Gem-XRT	None
3	FOLFIRINOX	4	Gem-XRT	None
4	Gem	12	Gem-XRT	None
5	Gem-NAB	9	None	None
6	FOLFIRINOX	4	Gem-XRT	Pending
7	FOLFIRINOX	6 + 2*	Gem-XRT	None
8	FOLFIRINOX	4	Cape-XRT	None
9	FOLFIRINOX	12	Gem-XRT	None
10	FOLFIRINOX	6	Chemo-XRT	None
11	Gem/Ox	12	Gem/NAB; XRT	None
12	FOLFIRINOX	8	Cape-XRT	None
13	FOLFOX	5	Cape-XRT	Gem
14†	FOLFIRINOX	4	5FU-XRT	N/A
15†	FOLFIRINOX	4	Gem-XRT	N/A

*This 4/4, treatment changed owing to oxaliplatin toxicity; 6 + 2, patient given chemo, then chemoXRT followed by 2 further cycles preoperatively.
†Laparotomy not performed as extrapancreatic disease was documented at the time of laparoscopy.
Cape, Capecitabine; *5FU*, 5-fluorouracil; *Gem*, gemcitabine; *N/A*, not applicable; *NAB*, nab-paclitaxel; *Ox*, oxaliplatin; *XRT*, external beam radiotherapy.

Table II. Operations performed to include arterial resection

Patient	*Operation performed*	*Vessels resected*	*Reconstruction*
1	Appleby	CA, CHA, SMV-PV	IJV interposition (for SMV-PV)
2	Appleby	CA, CHA, LGA	RSVG interposition
3	Appleby	CA, CHA, LGA	None
4	Appleby	CA, CHA, LGA	RSVG interposition
5	Appleby	CA, CHA, LGA	RSVG interposition
6	Appleby	CA, CHA, LGA	None
7	Central panc	CA, CHA	RSVG interposition
8	Whipple	CHA,PHA, SMV-PV	RSVG interposition (CHA-RHA); IJV interposition (for SMV-PV)
9	Whipple	RHA	GDA-RHA primary anastomosis
10	Total panc	CHA; SMV-PV	CHA-PHA primary anastomosis; SMV-PV primary anastomosis

CA, Celiac axis; *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *IJV*, internal jugular vein; *LGA*, left gastric artery; *panc*, pancreatectomy; *PHA*, proper hepatic artery; *PV*, portal vein; *RHA*, right hepatic artery; *RSVG*, reversed saphenous vein graft; *SMV*, superior mesenteric vein.
Patients 1–7 were staged as having locally advanced pancreatic cancer at the time of diagnosis; patients 8–10 staged as having borderline resectable disease.

underwent total pancreatectomy that also required hepatic artery resection (Table II).

Of the 7 patients who required CA resection, we chose to revascularize ("supercharge") the distal CHA in 4 using a RSVG from the stump of the CA; the left gastric artery was resected in 3 of these 4 patients (CA divided proximal to the origin of the left gastric). In the remaining 3 patients who required CA resection, we performed a traditional Appleby procedure: In 1 patient (no. 1, Table II) the left gastric artery was preserved and the RHA arose from the SMA; in 1 patient (no. 3, Table II), the CA origin was not suitable for an anastomosis owing to a friable aorta at that level, and this patient underwent a traditional Appleby with resection of the left gastric artery; and finally, in 1 patient (no. 6, Table II), there was a replaced RHA from the SMA and after CA resection, we had a strong arterial pulse in both the right gastric artery (arising from the PHA) and the right gastroepiploic artery (arising from the GDA). In this latter case, the only benefit to revascularizing the distal CHA would be enhanced gastric perfusion beyond that achieved with retrograde flow in the GDA and therefore this was not performed. In summary, of the 7 patients who underwent CA resection, only 1 patient underwent a traditional Appleby with left gastric artery resection in the absence of a replaced RHA (no. 3, Table II); all other patients had either revascularization of the distal CHA ("supercharged Appleby") or reversed flow in the GDA to supply predominantly the

Table III. Operative characteristics and follow-up

Clinical course	*Median (range)*
Operative time (min)	417 (298–574)
Estimated blood loss (mL)	800 (300–2,500)
Postoperative complications (*n*)	
Reoperation	1
Clostridium difficile infection	1
Urinary tract infection	1
Mortality (30- and 90-day; in-hospital)	0
Duration of hospital stay (d)	9 (5–9)
Follow-up (mo)	
NED (*n* = 7)*	21 (12–30)
AWD (*n* = 6)	27.5 (17–38)
DOD (*n* = 1)	9
Immediate postoperatively (*n*)	1

*Excludes recently operated patient.
AWD, Alive with disease; *DOD*, dead of disease; *NED*, no evidence of disease.

stomach (accessory right hepatic from the SMA to supply the liver). Although our experience is modest, after CA and CHA resection, pulsatile flow in the right gastric and right gastroepiploic arteries will likely only be present if there is a replaced hepatic artery from the SMA (or less likely, a preserved LGA with a replaced left hepatic artery); otherwise, retrograde flow in the GDA needs to supply both the liver and stomach, usually resulting in decreased gastric perfusion. This clinical observation is what caused us to revascularize the distal CHA in the patients described.

Three patients underwent CHA resection and reconstruction at the time of either a pancreaticoduodenectomy (n = 2) or total pancreatectomy (n = 1). Concomitant venous resection (2 internal jugular vein interposition grafts, 1 primary anastomosis) was required in 3 of the 10 patients who underwent arterial resection.

Surgical and pathologic results. Median operative time for the 10 patients was 7.5 hours with a median blood loss of 725 mL. Postoperative complications occurred in 3 of 10 patients who underwent combined pancreatic/arterial resection as listed in Table III. A single patient required reoperation the day after resection for hemorrhage from a small branch of the right gastric artery consistent with a retractor-related injury and remote from the arterial resection and anastomotic site. There were no pancreatic fistulae. We placed tube jejunostomies in all patients for postoperative enteral feeding and therefore, do not have accurate data on gastric emptying. Oral intake was advanced at home as tolerated by the individual patient. No patient required prolonged (>1 week) nasogastric tube placement or had persistent nausea or vomiting. Median alanine aminotransferase (as a marker of hepatic ischemia from insufficient arterial inflow) on postoperative day 1 was 36 U/L (range, 15–132). Only 2 patients had a further increase in alanine aminotransferase. No patient displayed evidence of ischemic gastropathy and no patient developed postoperative gastrointestinal bleeding.

Owing to the known association of autonomic denervation of the mid-gut with rapid gastrointestinal transit, we carefully monitored bowel function. Two patients required anti-diarrheal medication at discharge. The first was discharged with tincture of opium (10 mg/mL, 0.5 mL tid) and 2.5 mg diphenoxylate/0.025 atropine (Lomotil) 1 tab 4 times daily, after complete skeletonization of the SMA as well as resection and reconstruction of a replaced RHA. The second patient who required antidiarrheal treatment underwent distal pancreatectomy and resection of the CA (preserving the origin of the left gastric artery) as well as resection of the SMV-PV confluence reconstructed with an internal jugular vein graft. This patient was discharged with loperamide on an as-needed basis.

Pathologic characteristics of the resected tumors are detailed in Table IV. Of note, only 2 patients were found to have metastases in regional lymph nodes. Despite arterial encasement on preoperative imaging, only 1 patient actually had vascular invasion of the tunica adventitia of the resected arterial wall. Most tumors were well or moderately differentiated. There were 11 R0 resections and 2 R1 resections.

Short-term follow-up. Excluding the most recent patient (no. 6, Table II) operated on in September 2013, median follow-up for all patients was 21 months (range, 9–38). At the time of last follow-up, of the 13 patients who underwent successful pancreatectomy, 8 remain alive without disease at a median of 21 months (range, 12–30) from the time of diagnosis, 1 patient was just recently treated and has inadequate follow-up, and 5 have developed recurrent disease (distant, not local) at a median of 33 months (range, 20–38) from diagnosis; all 5 remain alive with disease at the time of manuscript submission. One of the 2 patients found to have peritoneal disease at laparoscopy died of disease 9 months from the date of diagnosis; the other remains alive with disease.

DISCUSSION

The distinction between borderline resectable and locally advanced PC is determined by the

Table IV. Pathologic characteristics of the 13 resected patients

Parameter	n *(range)*
Median tumor size (cm)*	2.5 (0–5.5)
Lymph nodes	
Median number examined	24 (11–39)
Median number positive	0 (0–4)
N0	11
N1	2
Margin status (no of patients)	
R0	11
R1	2
R2	0
Perineural invasion (no of patients)	
Present	11
Not identified	2
Lymphovascular invasion (no of patients)	
Present	0
Not identified	11
Indeterminate	2
Vascular invasion (no of patients)	
Present†	1
Not identified	12
Differentiation (no of patients)	
Well	6
Moderate	5
Poor	1
Indeterminate	1

*Tumor size could not be assessed in 1 patient owing to treatment effect.
†Actual tumor invasion into adjacent perimuscular artery was identified in 1 patient.

degree of tumor-artery interface; abutment is the term used to define a tumor-artery interface of ≤180° and encasement defines an interface of >180°. Borderline resectable PC is defined as tumor abutment of the SMA or CA, a definition based on the clinical observation that induction therapy may sterilize at least the periphery of the tumor, thereby facilitating a complete resection. As the tumor-artery interface increases from abutment to encasement, a complete gross resection of all disease becomes less likely; a reasonable assumption based on clinical observation/experience. The borderline resectable category also includes tumor abutment/encasement of a short segment of the hepatic artery usually at the origin of the GDA, or an occluded SMV-PV amenable to reconstruction. In contrast, locally advanced PC includes those patients whose tumors (1) encase (>180°) the CA or SMA; (2) encase the hepatic artery with no technical option for resection/ reconstruction usually owing to distal arterial encasement extending to the hepatic hilum; or (3) occlude the SMV-PV with no technical option for venous resection and reconstruction (no visible proximal or distal target for interposition grafting).[12] In general, these patients are rarely considered for operative intervention. The distinction between borderline resectable and locally advanced PC allows clinicians to set realistic treatment goals/expectations. For example, close to 50% of patients with borderline resectable PC, as defined by venous abutment/encasement or limited arterial abutment, are suitable candidates for surgery after induction therapy.[12,13] The 3 patients with borderline resectable PC who required arterial resection in this report were accurately defined anatomically but clearly of a more complex nature than one commonly associates with this stage of disease. In contrast, resection of the primary tumor is uncommon in patients with locally advanced disease; for example, 7 of 37 highly selected patients in this report (19%), less than half of the resectability rate seen with borderline resectable disease. Accurate staging is also necessary to enroll patients in clinical trials and develop optimal, off-protocol treatment sequencing. As demonstrated in this report, there are occasional patients classified properly as having locally advanced disease who may be considered for such extended operative procedures after a favorable response to induction therapy; as induction/systemic therapy becomes more effective, such patients may become more common.

Most important, all current national consensus guidelines favor induction therapy (chemotherapy/chemoradiation) for patients with borderline resectable disease and initial systemic therapy for those with locally advanced PC. We and others maintain that such patients should not be taken directly to the operating room.[14,15] The patients considered herein for major vascular resection all received systemic therapy before being considered for surgery. Treatment included ≥2 months of systemic therapy (>2 months if the tumor was clearly responding to therapy on detailed imaging), followed by chemoradiation with restaging again before operation. At the time of post-treatment restaging, patients considered for such extensive operations had consistent criteria of treatment response: Performance status ≤2 and improved; carbohydrate antigen 19-9 stable or decreased; in addition, no evidence of metastatic disease on cross-sectional imaging. The selection process afforded neoadjuvant sequencing allows one to apply operative resection and its associated morbidity only to those most likely to benefit. Unfortunately, at present, this still represents a minority of patients with locally advanced PC. Those patients taken to the operating room all underwent same-anesthetic diagnostic laparoscopy, and the abdomen was not opened if metastatic disease was proven by frozen section biopsy. Operations performed included either pancreaticoduodenectomy with resection of the CHA or replaced RHA, or distal pancreatectomy with CA/CHA resection; only 1 patient underwent total pancreatectomy. As reported herein, arterial reconstruction with interposition grafting from the CA origin to the distal CHA (modified or "supercharged" Appleby) was preferred. When resecting the CA to include the left gastric artery (CA divided proximal to the left gastric artery origin), in the absence of interposition grafting, the SMA is immediately asked to supply the liver and stomach via retrograde flow from the GDA. Gastric perfusion is then via the right gastric artery (most often arising from the PHA or the right or left hepatic artery [distal to the GDA]) and the right gastroepiploic artery (arising from the GDA) often in the setting of some element of venous congestion if the left gastric vein was also resected; it is critically important that the right gastroepiploic vein is preserved and not inadvertently injured during the operation. Based on our anecdotal observation that there may not be a palpable pulse in the right gastric and gastroepiploic arteries when the CA is divided at its origin proximal to the take-off of the left gastric artery, we have revascularized the CHA with a RSVG from the CA stump. This is usually not difficult and restores normal forward flow in the PHA and GDA, enhancing arterial perfusion of the liver and stomach. In fact, we had only 1 patient in this report who underwent a traditional Appleby with resection of the CA proximal to the left gastric artery in the absence of a replaced RHA (no. 3, Table II). In this patient, the aorta was not suitable for a proximal anastomosis possibly owing in part to the dose and schedule of his chemoradiation. This patient was relatively young and otherwise healthy (nonsmoker) and was found to have a palpable pulse in both the PHA and the right gastroepiploic artery after resection of the CA/left gastric artery. The other patient who underwent resection of the CA proximal to the left gastric artery origin and did not receive a "supercharge" RSVG to the CHA (no. 6, Table II) had a replaced RHA arising from the SMA and also was found to have a palpable pulse in both the PHA and the right gastroepiploic artery after resection of the CA. In this situation, reversed flow in the GDA (to supply the stomach) is less prone to a steel phenomenon from the liver, because the liver is perfused by a dominant RHA, which was not altered by the operation performed.

Importantly, patients were not considered for operation if (1) their SMV-PV was occluded and there was no technical option for resection/reconstruction (absence of suitable distal or proximal venous target); (2) CA resection was required and tumor encasement of the CHA extended laterally to the GDA thus eliminating an intact GDA-right gastroepiploic artery circulation necessary to preserve gastric perfusion; or (3) they had encasement of the SMA—this latter finding on computed tomography imaging was obviously subject to some element of clinical judgment when determining what was abutment versus encasement. All patients were treated in a high-volume, multidisciplinary, PC treatment center with their clinical status, imaging, and laboratory studies reviewed at all restaging time points in a multidisciplinary conference where consensus was reached regarding treatment sequencing to include surgery.[16]

Despite the complexity of requiring major arterial resection/reconstruction, including 3 patients with concomitant SMV-PV resection, there was no operative mortality. The morbidity noted in this series is less than previously reported which likely reflects careful preoperative review of the patient's imaging and a well thought-out preoperative plan for vascular resection/reconstruction.[8] Arterial resection/reconstruction done in the setting of an intraoperative misadventure is unlikely to achieve the same results. This distinction between a planned extended operative procedure and the same high-risk procedure performed emergently, often without proximal and distal control of a bleeding vessel (with tumor still intact), is what makes review of the retrospective literature on vascular resection at the time of pancreatectomy inaccurate.

As noted by our group and others, after an extensive period of neoadjuvant chemotherapy and chemoradiation, nearly all (11 of 13) patients were pathologically node negative (median lymph node count, 24), and all underwent a complete gross resection of the tumor (11 of 13 R0; 2 of 13 R1).[17,18] We believe these results reflect the response to preoperative therapy and the sterilization of at least the periphery of the tumor afforded by radiation therapy. We defined a positive margin as tumor present at the inked SMA or CA margin of resection, or tumor present in the en face sections of the hepatic duct or pancreatic duct transection margins. A definition of margin positivity that uses a defined distance (eg, within 2 mm) from the inked margin would likely produce a different rate of R0/R1 resections. As preoperative imaging demonstrated tumor abutment, we conclude that a negative margin at the site of arterial abutment (assuming removal of all perineural tissue adjacent to the vessel) was secondary to the effects of induction therapy. Interestingly, 11 of the 13 patients had well or moderately differentiated tumors; it is likely that the extended period of neoadjuvant therapy allowed for selection of those patients with favorable tumor biology. It should also be noted that even though all patients had computed tomography evidence of arterial abutment/encasement, only 1 patient in the entire group had histologic invasion of an arterial wall on final pathology. These tumors have a particular ability to spread along the perineural plexus that surrounds these major visceral arteries often without invasion of the tunica adventitia. This biology of the tumor raises the possibility that with improved neoadjuvant therapy, more patients may actually be eligible for operative resection than current imaging techniques may suggest.

An obvious limitation of this study is the small sample size (and short duration of median follow-up), which at present reflects the highly selected nature of this patient population. However, as we gain greater experience with novel treatment sequencing to include more effective systemic therapies, a greater number of patients may be referred for operative consultation having evidenced response to induction therapy with the primary tumor representing the only site of measurable disease. The principles outlined herein may be of use to multidisciplinary teams when considering patients for such extended local therapies to include operative resection of the primary tumor and adjacent vasculature.

In conclusion, extended pancreatic resection after an extensive course of neoadjuvant therapy can be performed safely using standard principles of vascular and oncologic operations. Such patients would otherwise be treated nonoperatively, either with a treatment break or consideration of maintenance chemotherapy. To the extent that pancreatectomy remains necessary (albeit not sufficient) to achieve long-term survival and possible cure, such extended pancreatectomies may represent the optimal treatment alternative for otherwise good risk patients who can tolerate multiple treatments in series to include operation after aggressive induction therapy.

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