

Pancreaticoduodenectomy with en bloc vein resection for locally advanced pancreatic cancer: a case series without venous reconstruction

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Abstract: Resection with clean margin (R0 resection) is associated with better survival in patients with pancreatic cancer. Over the last decade, advancements in preoperative chemotherapy and radiation therapy in pancreatic cancer have led to expansion of indications for surgical resection. Current guidelines define pancreatic cancer with unreconstructable vascular involvement as locally advanced, or surgically unresectable. We present our experience in managing patients with locally advanced pancreatic cancer with a very unique series of patients who achieved R0 resection despite “unresectable” vascular involvement. Additionally, we review current guidelines, the ability to predict venous resection by imaging, outcomes after venous resection and reconstruction, published patency rates of venous reconstructions, and potential future implications of this novel technique.

Keywords: Locally advanced pancreatic cancer; venous resection

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Introduction

Pancreatic ductal adenocarcinoma is a formidable challenge as the fourth leading cancer cause of death in America with a 5-year survival of only 8% (1). This statistic number includes the over half of patients who are diagnosed with cancer metastasis with a 5-year survival of only 3%. However, for around 20% patients with localized pancreatic cancer, the postoperative outcome is relatively more optimistic with a 29% 5-year survival (1). Resection with clean margin (R0 resection) is associated with better survival. With recent advances in surgery, as well as adjuvant and neoadjuvant therapies, the outcome for patients with pancreatic cancer is improving. In the last decade, there have been advancements in the criteria for resectability, with a shift toward more aggressive resection to achieve

clean margin. The concept of borderline resectable disease and the benefit of resecting pancreatic cancer involving the superior mesenteric vein (SMV) or portal vein (PV) has been introduced as safe procedure since the 1990s (2-4).

Currently, pancreatic cancer with SMV and/or PV involvement more than 180 degrees are considered borderline resectable if the portal venous flow can be restored. If the vessels are not reconstructable after resection of pancreatic cancer, we consider this cancer as locally advanced. Locally advanced pancreatic cancer comprises approximately 30% of pancreatic cancer patients and has a 5-year survival rate of approximately 6% (5). Resection of the PV and/or SMV without reconstruction is scarcely discussed in the literature (6). We presented our experience of a very unique series of cases in which venous

Table 1 Resectable, borderline resectable, and unresectable definitions based on portal vein and superior mesenteric vein involvement

Guideline	Resectable	Borderline resectable	Unresectable
AHPBA (7)	No radiographic evidence of SMV and portal vein abutment, distortion, tumor thrombus, or venous encasement	Venous involvement of the SMV/portal vein demonstrating tumor abutment with or without impingement and narrowing of the lumen, encasement of the SMV/portal vein but without encasement of the nearby arteries, or short segment venous occlusion resulting from either tumor thrombus or encasement but with suitable vessel proximal and distal to the area of vessel involvement, allowing for safe resection and reconstruction	–
NCCN (8)	No tumor contact with the SMV or PV or ≤ 180 degree contact without vein contour irregularity	Solid tumor contact with the SMV or PV > 180 degrees, contact of ≤ 180 degrees with contour irregularity of the vein or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement allowing for safe and complete resection and vein reconstruction Solid tumor contact with the inferior vena cava	I. Head/uncinate process: unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus) *Contact with most proximal draining jejunal branch into SMV II. Body/Tail: unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus)
Alliance (9)	–	An interface between the primary tumor and SMV-PV measuring 180° or greater of the circumference of the vein wall, and/or Short-segment occlusion of the SMV-PV with normal vein above and below the level of obstruction that is amenable to resection and venous reconstruction	–

SMV, superior mesenteric vein; PV, portal vein.

reconstruction after resection was safely omitted. These cases emphasize the need for multi-disciplinary care and careful selection of patients with locally advanced pancreatic cancer for surgical resection at a high-volume center.

Current guidelines: borderline resectable vs. locally advanced pancreatic cancer

Consensus guidelines have been published by several organizations defining resectable, borderline resectable, and locally advanced pancreatic cancer based on its relationship with surrounding structures (*Table 1*) (7-9). The key surrounding structures are the celiac axis, superior mesenteric artery (SMA), common hepatic artery, and the SMV and/or PV.

With regard to the SMV/PV, all guidelines define borderline resectable disease with a reconstructable option after venous resection, and locally advanced disease with non-reconstructable venous occlusion. The International Study Group of Pancreatic Surgery (ISGPS) consensus statement by Bockhorn *et al.* describes a classification

system of four types of venous resections for extrahepatic mesenteric-portal venous resection (10).

- (I) Partial venous excision with venorrhaphy by suture closure;
- (II) Partial venous excision using a patch venoplasty closure;
- (III) Segmental venous resection with primary venovenous anastomosis;
- (IV) Segmental venous resection with interposed venous conduit and at least 2 anastomoses.

Notably, venous resection without reconstruction was not mentioned in these guidelines.

Ability of CT to predict need for venous resection

Determining resectability prior to surgery is dependent on high quality preoperative imaging and surgeon's experience. Multidetector computed tomography (CT) is the most commonly used modality to assess vascular involvement and distant metastasis. The accuracy of CT

to reveal resectability of pancreatic cancer was 76.9% (11). Multidetector CT protocols for pancreatic imaging typically include multiphase thin-section imaging and multi-planar reconstruction (12). MRI is likewise an excellent modality for pancreatic cancer imaging, with equivalent performance for assessment of vascular invasion (12,13).

Ishikawa *et al.* described a classification system of tumor involvement with SMV/PV based on preoperative imaging (14). Based on SMV/PV involvement on preoperative imaging, the likelihood of vascular invasion can be estimated. For example, when the tumor-vessel involvement is over 180 degrees of the vessel, the need for vascular resection can be anticipated with 84% sensitivity and 98% specificity (15). In a 2012 study by Springett *et al.*, the probability of vascular invasion was up to 40%, 80%, and 100% when the tumor has ≤ 180 degrees of contact, >180 degrees of contact, and 360 degrees of contact (16). Overall, the ability of CT to predict if vein resection is necessary in all cases is approximately 40% (17), and can be increasingly difficult after neoadjuvant therapy (18).

Overall survival and outcomes with venous resection

Mesenteric venous resection with reconstruction has been an accepted practice for pancreatic cancer with involvement of the SMV or PV since the 1990s when studies demonstrated equivalent survival of patients undergoing margin-negative venous resection compared to patients undergoing standard pancreaticoduodenectomy, as well as superiority of resection compared to nonsurgical treatment (3,4). A study comparing 75 patients with and without vein resection demonstrated no difference in survival between the two groups (19). More recent study by Roch *et al.* evaluating 90 patients with vein resection demonstrated that vein resection was not associated with worse overall survival at 1, 3, or 5 years (20). Other recent studies have also demonstrated patients with PV/SMV resection had equivalent survival outcome (21-25). Some studies have reported increased morbidity associated with venous reconstruction, providing caution to those considering this technique (26,27). A recent meta-analysis comparing venous resection with Whipple to palliative bypass and chemotherapy demonstrated no patients in the palliative group were alive at 2 years, while 40% of the resection group were alive at 3 years (28). Therefore venous resection, when R0 resection can be reasonably expected, has been accepted as the standard of care for indicated patients (29).

Patency rates

While venous resection without reconstruction is a novel concept in the literature, there are numerous studies evaluating postoperative stenosis or thrombosis of venous anastomoses. In 2015, Fujii *et al.* evaluated 197 patients who had undergone venous resection and reconstruction. Of these patients, three required immediate reoperation or anticoagulation for acute anastomotic thrombosis after surgery. Excluding these patients, the degree of patency at one year was more than 80% in 72 patients (30). Furthermore, Krepline *et al.* demonstrated that 4 of 41 venous resection patients (10%) were occluded after 12 months (31). In the shorter term, Javed *et al.* revealed that concentric narrowing was observed in 57.1% of patients, eccentric narrowing in 27.1%, complete or partial venous thrombosis in 10% at approximately 2 weeks after surgery (32). This occlusion and narrowing without significant morbidity are likely due to the development of collateral venous flow. If collateral veins are present prior to the operation, and may be preserved, a reconstruction of SMV/PV may not be necessary. Here we reported a series of 5 patients of this unique circumstance when vein reconstruction was not necessary after vein resection.

Our experience

All patients were thoroughly evaluated by our multidisciplinary team prior to the decision to go to the operating room. They underwent a classic pancreaticoduodenectomy with portal lymphadenectomy, with meticulous attention to hemostasis and preservation of collateral venous flow. A brief summary of all patients may be seen in *Table 2*.

Patient example

Patient 2 (*Table 2*) is a 52-year-old Caucasian female who was initially diagnosed with locally advanced pancreatic adenocarcinoma in April 2015. Initial CT imaging demonstrated long segment encasement of the SMV by cancer, as well as SMA abutment. She underwent 4 cycles of neoadjuvant FOLFIRINOX, as well as SBRT. Repeat CT after neoadjuvant therapy demonstrated slightly decreased size of the cancer with stable encasing and narrowing of the SMV below the PV/SV (splenic vein) confluence. Multiple collateral vessels were present on imaging (*Figure 1*).

She underwent operative exploration in October 2015. Due to the large tumor inside the head of the

Table 2 Characteristics of patients in our case series

Characteristics	Case series				
	1	2	3	4	5
Age (years)/gender	62/M	52/F	57/M	64/F	57/F
Race	Caucasian	Caucasian	Caucasian	Caucasian	Hispanic
Date of diagnosis	12/2013	4/2015	5/2016	7/2016	4/2015
Neoadjuvant chemotherapy	FOLFIRINOX, FOLFOX	FOLFIRINOX	Gemcitabine- Abraxane	FOLFIRINOX	Gemcitabine- Abraxane
Neoadjuvant radiation	SBRT	SBRT	EBRT	SBRT	EBRT
Date of surgery	9/2014	10/2015	2/2017	3/2017	3/2017
Operative time (minutes)	429	600	436	345	255
EBL	650	4,500	750	250	400
Transfusion	N	Y	N	N	N
Tumor size (cm)	2.5	2.5	3.2	3	3.5
Grade	N/A	3	N/A	3	2
Readmission	No	No	No	No	No
Complications	None	GI bleed, pancreatic fistula	None	None	None
Adjuvant therapy	Xeloda	Gemcitabine-Abraxane	N/A	N/A	5FU/irinotecan
Date of death	8/2016	6/2017	N/A	N/A	N/A
Date of recurrence	8/2015	11/2016	No	No	8/2017
Recurrence location	Local	Distant	None	None	Local
Survival from diagnosis (months)	32	26	>19	>17	>32

SBRT, stereotactic body radiation therapy; EBRT, external beam radiotherapy; EBL, estimated blood loss; N/A, not applicable; N, no; Y, yes.



Figure 1 Pre-operative CT scan demonstrating venous collaterals in Patient 2.

pancreas encasing the entire SMV, the distal pancreas was mobilized first. The SV and the PV were isolated with vessel loops. Pancreas was divided above the PV at the PV/SV confluence. The SMA was carefully dissected out on the left side of the PV. Due to the long segment of SMV encasement below the PV/SV confluence, we decided to divide the vein above the tumor and resect the Whipple specimen en bloc with SMV. After resection, a 4-cm gap was present between the proximal PV/SV confluence and the 3 branches of the SMV. We carefully preserved the collateral veins in the mesocolon. Her small bowel and colon were all viable and without congestion. To repair the narrowed PV/SV confluence after the resection, we performed a patch repair using a piece of cryopreserved femoral vein. The SMV was left in discontinuity.

Pathology returned as pT2N1M0, 2.5 cm poorly differentiated adenocarcinoma of the head of the pancreas, 3 of 17 lymph nodes positive, negative margins, and a grade

3 (poor/no response) response to therapy. The patient was treated with adjuvant Gemcitabine and Abraxane. She had distant recurrence in November 2016 and deceased in June 2017, approximately 20 months after surgery (26 months after diagnosis).

Considerations for case selection

Our series demonstrated the feasibility of the pancreaticoduodenectomy with vein resection without reconstruction for a group of patients with locally advanced pancreatic cancer. These patients overall did well following their surgeries, with 2 of 5 patients living 20–24 months after surgery (26–32 months from diagnosis) and the remaining 3 patients currently alive with ranges of 5–10 months since surgery (17–32 months from diagnosis).

It is prudent to emphasize the rigorous preoperative multidisciplinary evaluation by our experts prior to proceeding to the operating room. As previously described, while it is feasible to resect pancreatic cancer with venous involvement to achieve a R0 status, this surgical resection is not without risk (3,4,19-27). Patients in our study all had extensive venous collateralization that had developed before surgery. This collateral venous flow poses the challenge for surgical resection. Careful attention to hemostasis is imperative. Preservation of left sided collateral veins and mesenteric collateral veins is key to maintain adequate mesenteric venous drainage when the occluded SMV will be en bloc resected during pancreatotomy. At our institution, all pancreatic cancer patients undergo high-quality cross-sectional imaging with intravenous contrast appropriately timed to assess the portomesenteric axis and collateralization.

Patients with borderline or locally advanced pancreatic cancer will receive appropriate neoadjuvant treatment based on their performance status in the setting of clinical trials. Patients with local disease progression or metastasis, cavernous transformation of the porta hepatis will not be candidates for surgery.

Surgeons have to evaluate the patterns of venous collateralization before surgery. For planned pancreaticoduodenectomy, patent left-sided collateral venous flow through a PV/SV confluence or a dilated left gastric vein is necessary for possible successful resection. Alternatively, if distal pancreatotomy is planned, patent right-sided collateral venous flow through the pancreatic head, omentum and mesocolon to the liver is necessary. These patterns are critical for evaluation of any cases with

venous involvement, as previous studies have shown that the ability to predict venous resection can be challenging (17,18). Knowing all options prior to entry in the operating room empowers the surgeons with the greatest likelihood of achieving R0 resection.

Conclusions

Our current series demonstrated the feasibility of using vein resection without reconstruction during pancreatotomy for pancreatic cancer. This helped us to achieve the R0 resection and potential long-term survival. With improvements in systemic and loco-regional therapies, we will have an increased rate of surgical resection in patients with borderline resectable or locally advanced pancreatic cancer (31). It is critical to continue rigorous preoperative multidisciplinary evaluation and selecting appropriate patients for this surgical resection.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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