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Superior Mesenteric-Portal Vein Resection in Patients With Pancreatic Adenocarcinoma Is Safe and May Increase Survival

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Extension of pancreatic adenocarcinoma into adjacent vasculature often necessitates resection of the portal vein (PV) and or superior mesenteric vein (SMV) during pancreaticoduodenectomy (PD). Our study describes the surgical technique and results of PV/SMV resection in pancreatic adenocarcinoma patients. Between January 2008 and October 2013, 252 patients underwent PD for pancreatic malignancy. A total of 42 PV/SMV resections were performed (28 men, 14 women). Patients were categorized into 2 groups according to the degree of invasion into the portal vein wall: Group A (n = 16), extended compression of the portal vein wall by the surrounding carcinoma without true invasion, and Group B (n = 26), true invasion including intramural and transmural invasion. Morbidity of the 42 patients was 35%; there was no operative mortality, and overall 1-, 3-, and 5-year survival rates were 60%, 21%, and 12%, respectively. No differences in tumor size, margin positivity, nodal positivity, or survival rates were observed between groups. Resection of the PV/SMV is safe and does not increase morbidity or mortality. Tumor involvement of the PV/SMV is not associated with histopathologic signs that are predictive of a poor prognosis. The "artery first" approach should be considered as a means to facilitate safe venous resection and reconstruction.

Key words: Pancreatic adenocarcinoma – Pancreaticoduodenectomy – Superior mesenteric portal vein resection

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Pancreaticoduodenectomy (PD) is regarded as the standard curative procedure for carcinoma in the head of the pancreas, and the associated mortality has dramatically decreased to below 5%; however, only 10% to 20% of all patients are candidates for PD.[1–3] Close proximity of the pancreatic head to major venous structures often results in abutment or encasement of the superior mesenterico-portal venous (SMPV) system by the tumor. In this situation, cure can be achieved only by complete extirpation of the tumor in conjunction with en bloc resection of the SMPV structures.[4,5] Several recent series have reported comparable postoperative morbidity and mortality outcomes from patients undergoing PD with or without venous resection (VR).[6–8] There is growing agreement[9] that venous involvement is not necessarily a sign of locally advanced disease but rather a result of the anatomic location of the tumor in relation to the vessels. Furthermore, recent studies have shown that long-term survival after portal vein/superior mesenteric vein (PV/SMV) resection does not differ from survival in patients who undergo PD alone, provided clear resection margins are achieved.[6,7]

Because VR can be achieved safely and with greater awareness of the prognostic significance of the status of the posteromedial resection margin, nonresectability is now determined by involvement of the superior mesenteric artery (SMA). This change, along with the need for early determination of resectability before an irreversible step is made, has promoted the development of an "artery-first" approach.[10,11] The "artery-first" technique may also add to the safety of venous resection.[12,13] Early dissection of the SMA results in tumor attachment only to the involved veins, so clamping the portomesenteric confluence may be easier and shorter.

The aim of the present study was to describe the surgical technique and results of PV/SMV resection in patients with pancreatic adenocarcinoma at our institution between 2008 and 2013. We also evaluated tumor invasion of the PV/SMV and surgical margins microscopically.

Methods

Between January 2008 and October 2013, 252 patients underwent PD for pancreatic malignancy. A total of 42 (16.7%) patients underwent resection of the portal vein, the mesentericoportal confluence, the superior mesenteric vein, or a combination of these resections. Of these, there were 28 men and 14 women, aged 34 to 73 years (mean: 55.8 years).

All patients were assessed by history, physical examination, biochemistry, and serum carbohydrate antigen 19.9 (CA19.9) levels. Imaging studies included either a contrast-enhanced CT or a magnetic resonance scan. Endoscopic ultrasonography with fine needle aspiration biopsy was used in selected patients as directed by the multidisciplinary team. Patients were excluded from resection if there was extrapancreatic metastasis, tumor encasement, or abutment of more than 180° of the SMA or the celiac axis, or if there was an occluded MPV system.

All operations were performed with a standard technique. Extended dissection of regional lymph nodes was not routinely performed. VR was performed when the pancreatic mass could not be mobilized from the SMPV confluence; we strongly discourage a trial dissection along the portal vein to assess tumor invasion because of the risk of opening the tumor. Since 2009, we have advocated an "artery-first" technique in which the SMA is first dissected to rule out tumor invasion (Fig. 1). The SMA was dissected along the plane of its adventitia to the junction of the third and fourth parts of the duodenum with a right-angled dissector. At a point 1 to 2 cm from the origin of the SMA, a anomalous or accessory hepatic artery can be identified. If present, this vessel was looped and safeguarded. If the tumor invaded the SMA, resection was abandoned at this stage and palliative measures were taken. This allows the posterior resection margin to be freed from the SMA and ensures that the entire dissection can be performed before the PV/SMV is divided. This technique also facilitates a "no-touch" approach to prevent dissemination of tumor cells into the portal circulation.

The venous reconstruction was performed primarily with an end-to-end anastomosis; interposition of a vascular graft was rarely needed. Because of presumed tumor adherence, the splenic vein should be ligated when the level of the splenic vein was invaded. We tried to preserve the coronary vein (left gastric vein) if it was a main branch of the portal vein, because this ensures venous drainage of the stomach.

The histology on all resection specimens confirmed pancreatic ductal adenocarcinoma. The patients were categorized into 2 groups according to the degree of invasion of the portal vein wall: Group A (n = 16), extended compression of the portal vein wall by the surrounding carcinoma without true invasion, and group B (n = 26), true invasion including intramural and transmural invasion. The degree of invasion into the portal vein wall

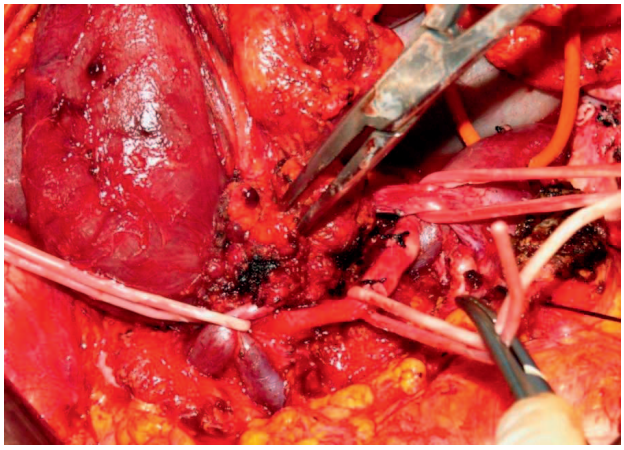

Fig. 1 "Artery-first" technique: the SMA is first dissected to rule out tumor invasion.

was classified histologically into 3 types: type I, tunica adventitia invasion; type II, tunica media invasion; and type III, transmural invasion involving the intima.

Follow-up was conducted by letters, telephones, hospital charts, and patient interviews. The survival rate was calculated using the Kaplan–Meier method and was compared using the log-rank test. Other comparisons were performed using the unpaired student's *t* test or the chi-square test. A *P* value less than 0.05 was considered statistically significant.

Results

Overall, 252 patients underwent PD from 2008 to 2013, of these, 42 had PV/SMV resection. A total of 10 vessels were reconstructed with Gore-Tex artificial blood vessels, the remaining 32 vessels could be constructed with a primary end-to-end anastomosis. Intraoperative data and postoperative complications are listed in Table 1.

Table 1 Intraoperative data and postoperative complications

	N	%
Intraoperative		
Operation time, min (range)	245 (185–365)	
Blood loss, mL (range)	650 (200–1800)	
Blood transfusion volumes	450 (0–1000)	
Clamp time, min (range)	12 (8–25)	
Postoperative complications		
Perioperative mortality	0	0
Surgical complications	10	23.8
Nonsurgical complications	5	11.9
Pancreatic leakage	3	7.1
Intra-abdominal bleeding	1	2.4
Intra-abdominal abscess	2	4.8
Delayed gastric emptying	1	2.4
Mild cholangitis	2	4.8
Disruption of abdominal wound	1	2.4

The PV/SMV was examined microscopically for cancer invasion in the 26 patients composing Group B, while external compression without true invasion was observed in the 16 patients of Group A.

There was no difference in mean age, gender ratio, tumor location, or adjuvant chemotherapy between groups. Pathologic findings are listed in Table 2; there was no difference in tumor size, margin positivity, nodal positivity. Group B was histologically classified into 3 types: type I (15 patients), tunica adventitia invasion; type II (10 patients), tunica media invasion; and type III (1 patient), transmural invasion involving the intima, with liver metastasis identified 3 months after the operation.

The overall 1-, 3-, and 5-year survival rates were 60%, 21%, and 12%, respectively. Cumulative 1-, 3-, and 5-year survival rates for patients with true invasion and without true invasion were 63%, 25%, and 13% and 58%, 19%, and 12%, respectively (Fig. 2). There was no significant difference in survival time. The mean survival of patients with microscopically positive margins was only 5.5 months compared with 23 months in patients with microscopically negative margins.

Discussion

En bloc resection of PV/SMV increases the resectability and curability of pancreatic adenocarcinoma.

Table 2 Patient demographics and pathologic findings

	Group A (n = 16)	Group B (n = 26)	*P* value
Age, mean ± SD (y)	54.5 (34-71)	56.9 (39-73)	0.16
Sex (male:female)	10:6	17:9	0.23
Tumor size (cm)	4.5 ± 2.1	4.9 ± 2.5	0.17
SMPV length (cm)	3.5 ± 2.0	3.0 ± 1.6	0.25
Site of tumor			
Head	10	18	
Neck	5	6	
Body	1	2	0.09
Chemotherapy			
Yes	10	18	
No	6	8	0.20
Resection rate			
R0	15	24	
R1	1	2	0.19
Lymph node metastasis			
Yes	12	20	
No	4	6	0.15

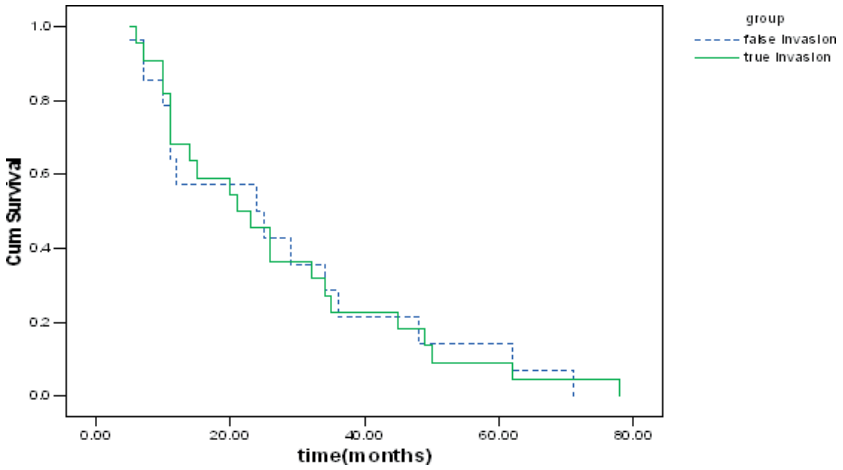

Fig. 2 Cumulative survival rates of patients with true invasion (Group B) and without true invasion (Group A).

However, a meta-analysis from 2006 concluded that patients who underwent PV/SMV resection had poor survival. This was explained by aggressive tumor biology, because a high proportion of N1 patients (67.4%) were observed.[13] In contrast, recent studies have leaned more toward the view that venous involvement is an expression of tumor size and anatomic localization rather than a sign of aggressive tumor biology.[9,14] With decreasing morbidity and mortality rates, en bloc PD with venous resection has been shown to confer a survival benefit.[7,15]

In our study, the morbidity and mortality were 35% and 0%, respectively, which did not differ from data previously reported in studies evaluating the safety of PV/SMV resection.[7,15] Compared with standard PD, there was no difference in perioperative morbidity and mortality despite a longer operation time and higher operative blood loss and transfusion requirements in patients who underwent PV/SMV resection. It is unlikely that large local or regional pancreatectomy in poorly selected patients with advanced disease was associated with the increased patient death and morbidity previously reported. We performed PV/SMV resection in carefully selected patients who had no evidence of tumor extension to the SMA or celiac axis.

The rationale for en bloc VR in patients with pancreatic adenocarcinoma is to achieve negative histologic margins. Microscopically negative (R0) resection can be difficult to achieve in these patients given the close proximity of the tumor to the SMA neural plexuses. For a given tumor size and stage, cases with limited PV/SMV wall invasion or abutment undergoing PV/SMV resection should have a similar survival to those undergoing standard PD, provided a R0 resection can be achieved.[7] This is partly confirmed by our study. Although 80.9% of our patients had local lymph node metastases (N1), the overall 1-, 3-, and 5-year actuarial survival rates were 60%, 21%, and 12%, respectively, but in the patients with positive margins (3/42 patients), the mean survival time was only 5.5 months.

When the perioperative evaluation of vein involvement was compared with the final histologic examination, 26 of our patients (62%) had invasion of the vascular wall, whereas 16 (38%) did not have histologic evidence of tumor invasion. It is widely accepted that the perioperative distinction between inflammatory adhesions and true tumor infiltration is difficult even if a frozen section had been previously performed.[5,16] We strongly discourage trial dissection along the portal vein or shaving the tumor off of the portal vein during resection; with separate resection and reconstruction of the involved portion of the portal vein, transecting the tumor may result in a higher rate of tumor recurrence. The consequences of PV/SMV resection in patients without venous invasion were investigated in a recent French study of 34 consecutive patients who underwent routine PV/SMV resection. The study showed that patients with pancreatic carcinoma and no venous involvement who had PD with PV/SMV resection had a significantly longer overall survival than patients in a matched control group who had PD without venous resection.[17]

In our series, a comparison of the survival rates according to whether or not histologic portal vein invasion was present did not reveal a significant difference, indicating that PV/SMV invasion may

not be a key factor in patient survival. Venous involvement is not associated with histopathologic signs that are predictive of a poor prognosis; it is rather an expression of tumor size and anatomic localization than of aggressive tumor biology.[14] If a tumor invades into the tunica intima; however, the prognosis is very poor,[18] as no patients with invasion of the tunica intima have survived more than 6 months. It is likely that transmural invasion signifies an advanced state with the possibility of occult systemic seeding of the neoplastic cells. In our study, only 1 patient had transmural invasion into the tunica intima, and this patient died of multiple liver metastases 2 months postoperatively. Imaging modalities that enable the determination of transmural vascular invasion, such as endoscopic, laparoscopic, or intravascular ultrasonography should be used to prevent noncurative, nonpalliative pancreatectomy.[19]

In the present study, the median survival was 23.0 months, which is far better than expected compared with the 13-month median survival reported in Siriwardana and Siriwardena's 2006 meta-analysis. This favorable survival may be owed in part to the high proportion of clear resection margins obtained in our study (92.8% R0); the novel artery-first technique we employed may have resulted in better clearance of the tumor and positive lymph nodes. Pancreatic adenocarcinoma that abuts the SMPV system usually lies close to the SMA and the associated perivascular neural plexuses. The proximity of the latter 2 structures implies that a higher R1 resection rate is likely to occur at the SMA margin during PV/SMV resection, particularly in patients with larger tumors. Some reports have found that the R1 resection rate was significantly higher in patients undergoing PD + VR compared with a PD − VR group.[7,20] Artery-first techniques aim to achieve a R0 posterior margin and allow for early recognition of arterial invasion before a point of no return is reached. This technique provides for en bloc resection of the head of the pancreas along with retroperitoneal tissue, including lymph nodes and the extrapancreatic nerve plexus, as well as venous resection. The technique facilitates early identification and control of an anomalous or accessory hepatic artery arising from the SMA. Early division of the SMA margin allows pancreatic mobilization towards the left, with dissection of splenic vessels and ligation of collaterals. This allows transection of the pancreas at any level. The "artery-first" technique may also add to the safety of venous resection. Early dissection of the SMA results in tumor attachment only to the involved veins, so clamping of the portomesenteric confluence may be easier and shorter. This technique also facilitated a "no-touch" approach to prevent the dissemination of tumor cells into the portal circulation.

In conclusion, our data demonstrate that it is possible to perform pancreatectomy combined with PV/SMV resection without increasing patient morbidity and mortality. Tumor involvement at the PV/SMV is not associated with histopathologic signs predictive of a poor prognosis, and venous involvement appears to be an expression of tumor size and anatomic localization rather than of aggressive tumor biology. As complete tumor resection appears to be the basis for long-term survival in patients with pancreatic adenocarcinoma, PV/SMV resection should only be performed when a margin-negative resection is expected to be achieved. Median survival was far better than expected, particularly as a considerable number of patients' lymph node metastases were included. The "artery first" approach should be considered as a means to facilitate safe venous resection and reconstruction whenever a tumor is thought to involve PV/SMV.

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