

Results of a Pancreatectomy with a Limited Venous Resection for Pancreatic Cancer

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Abstract

Purpose. The indications for a pancreatectomy with a partial resection of the portal or superior mesenteric vein for pancreatic cancer, when the vein is involved by the tumor, remain controversial. It can be assumed that when such involvement is not extensive, resection of the tumor and the involved venous segment, followed by venous reconstruction will extend the potential benefits of this resection to a larger number of patients. The further hypothesis of this study is that whenever involvement of the vein by the tumor does not exceed 2 cm in length, this involvement is more likely due to the location of the tumor being close to the vein rather than because of its aggressive biological behavior. Consequently, in these instances a pancreatectomy with a resection of the involved segment of portal or superior mesenteric vein for pancreatic cancer is indicated, as it will yield results that are superposable to those of a pancreatectomy for cancer without vascular involvement.

Methods. Twenty-nine patients with carcinoma of the pancreas involving the portal or superior mesenteric vein over a length of 2 cm or less underwent a macroscopically curative resection of the pancreas en bloc with the involved segment of the vein. The venous reconstruction procedures included a tangential resection/lateral suture in 15 cases, a resection/end-to-end anastomosis in 11, and a resection/patch closure in 3.

Results. Postoperative mortality was 3.4%; morbidity was 21%. Local recurrence was 14%. Cumulative (standard error) survival rate was 17% (9%) at 3 years.

Conclusion. A pancreatectomy combined with a resection of the portal or superior mesenteric vein for cancer with venous involvement not exceeding 2 cm is indi-

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cated in order to extend the potential benefits of a curative resection.

Key words Pancreatic cancer · Vascular resection · Portal vein · Superior mesenteric vein

Introduction

The only potentially curative treatment for pancreatic cancer is a surgical resection, with negative surgical margins, in patients without metastatic disease.¹⁻³ However, over 50% of the patients have distant metastases and 35% have locally advanced disease at the time a diagnosis is made.⁴ While distant spread remains an absolute contraindication for a resection, locally advanced disease may be overwhelmed by an aggressive surgical approach in selected cases. In an attempt to improve the resectability of pancreatic cancer, a regional pancreatectomy has been proposed, which means en bloc resection of the tumor together with tumor involved portal/superior mesenteric vein, arteries (aorta, celiac trunk, and superior mesenteric artery), and the surrounding lymphatic vessels, followed by the eventually required venous and arterial reconstructions.⁵ However, extended venous and arterial resections, followed by complex reconstructions, have been reported to be associated with significant morbidity^{5,6} and an unsatisfactory long-term survival.

In recent years, a significant decrease of in hospital mortality and morbidity associated with standard pancreatoduodenectomy has been observed,¹⁻³ which has led to a progressively more aggressive attempt to resection, when portal/superior mesenteric vein involvement is the sole obstacle to a complete resection of an otherwise localized tumor.¹ This possibility seems appealing, as nonresectable tumors are associated with a median survival of 9 months,⁷ whereas survival rates of 19%–

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24% at 5 years have been reported after a curative resection.^{8,9} Several reports have suggested that a resection of the pancreas and portal/superior mesenteric vein can be performed with results that are superposable to those of standard resections for pancreatic cancer, without vascular involvement.^{1,10-13} However, other series have questioned the validity of portal/superior mesenteric vein resection in this setting, thus reporting poor results in terms of survival.¹⁴⁻¹⁸ The role of portal/superior mesenteric vein resection for carcinoma of the pancreas thus remains controversial.

The above difference of the results and opinions may be explained by a different extent and length of venous involvement by the tumor in the different series, at the time of a resection. A venous resection would be justified whenever tumor adhesion to the portal/superior mesenteric vein is function of its location, rather than an indicator of biologic aggressiveness.¹² We assumed this to be the case whenever the portal/superior mesenteric vein exhibited tumor involvement not exceeding 2 cm in length on preoperative imaging, and thus elected to systematically perform a tumor and partial vein resection, whenever the need for only a minor venous reconstruction was preoperatively anticipated, in order to obtain disease-free surgical margins as far as possible. The aim of the present study was to determine whether the results of this method would validate its use in the particular setting of pancreatic cancer with portal/superior mesenteric vein involvement.

Subjects and Methods

From January 1, 2000, to December 31, 2005, 29 consecutive patients underwent an en bloc, partial portal vein or superior mesenteric vein resection for pancreatic cancer, at the Francesco Durante Department of Surgery, Rome University Hospital, and the Department of Digestive Surgery and Liver Transplantation, Regina Elena Cancer Institute, Rome, Italy. This figure represents 21% of 137 pancreatic resections for cancer performed at the same centers in the same period. The study was approved by the local ethics committee; informed consent was obtained from all patients. Twenty-one patients were male and 8 were female, with a mean age of 64 years (range 41–78 years).

Beside routine laboratory investigations, the preoperative study of the patients essentially consisted of helical, contrast-enhanced, computed tomography (CT) scanning of the chest, abdomen and pelvis: the latest 14 patients of the series were studied with a 64-slice CT scanner. Laparoscopy and angiography to assess the extension of the tumor and its vascular involvement were not performed, with the assumption that helical/ multislice CT scanning would demonstrate the extent of the neoplasm, as well as any neoplastic vascular involvement, with adequate sensitivity.

The tumor originated from the head of the pancreas in 19 patients (66%), and the body/tail in 10 (34%). The average size of the mass at preoperative scanning was 3.1 cm (range 1.7–9.9 cm). An elevated preoperative serum bilirubin level was present in 15 out of 19 patients with cancer of the pancreatic head, averaging 10 mmol/l (range 4–29 mmol/l): none of these patients underwent preoperative biliary drainage.

Overall, the imaging criteria for performing a surgical exploration and considering resection included (1) the absence of extrapancreatic metastatic disease; (2) no evidence of involvement of the celiac trunk, superior mesenteric artery, aorta and inferior vena cava, as shown by the presence of a fat plane between the tumor and these vessels; (3) a lack of invasion to the transverse mesocolon; and (4) a lack or only a minor involvement of the portal/superior mesenteric vein. A minor involvement of the portal/superior mesenteric vein was further defined as any tumor adherence or infiltration of these veins not exceeding 2 cm in length, without complete encasement of the vessel and complete luminal thrombosis. The operative criteria for a resection included (1) absence of liver and/or peritoneal metastases; (2) no extension of the tumor to the celiac trunk, hepatic artery, superior mesenteric artery, aorta, and inferior vena cava; (3) possibility of an adequate control of the portal vein, superior mesenteric vein, and splenic vein in order to perform a safe resection and venous reconstruction.

The resection was performed through a bilateral subcostal incision, including one thigh in the operative field for eventual harvesting of the greater saphenous vein, whenever the need for a venous resection was anticipated at preoperative imaging. The control of the hepatic artery proximal and distal to the gastroduodenal artery, of the origin of the splenic artery, superior mesenteric artery, portal and superior mesenteric vein proximal and distal to tumor attachment, was obtained before resection. The division of the splenic vein at its confluence with the inferior and superior mesenteric vein was performed in 10 of 17 pancreaticoduodenectomies, in order to allow for the proper control of the portal/superior mesenteric vein and facilitate venous reconstruction. The tissues around the portal vein and superior mesenteric vein were circumferentially cleared, in order to completely free up the portal vein, and the superior mesenteric vein down to the middle colic vein.10

The techniques of venous reconstruction after resection included direct suture, patch closure, and endto-end anastomosis. A direct suture was performed whenever the tumor adherence/infiltration required resection of less than one third of vein wall circumfer-

Table 1. Venous reconstruction procedures performed after a resection of the portal/superior mesenteric vein (PV/SMV) for pancreatic cancer

Lateral suture	15
End-to-end anastomosis	11
Saphenous vein patch closure	3
Total	29

ence, end-to-end anastomosis was performed in the case of circumferential vein wall involvement, whereas saphenous vein patch interposition was performed whenever vein wall involvement exceeded one third of its diameter, but did not affect the entire circumference.

According to these principles 15 patients underwent tangential resection/lateral suture, 11 resection/end-toend anastomosis, and 3 resection/patch closure (Table 1). Venous anastomoses were all completed using a 6-0 polypropylene running suture. Prior to venous clamping, 0.5 mg/kg of body weight of sodic heparin was administered intravenously, and the superior mesenteric artery was not clamped.

Of the 19 patients with a tumor of the head of the pancreas, 17 underwent a pancreaticoduodenectomy whereas 2 underwent a total pancreatectomy. Reconstruction was achieved by an end-to-end, monolayer, pancreaticojejunostomy in 14 cases, and pancreaticogastric anastomosis in 3. An end-to-side hepaticojejunostomy, and an antecolic, end-to-side gastrojejunostomy were performed in all cases. The 7 patients with cancer of the body/neck underwent a distal splenopancreatectomy, and the proximal pancreatic stump was closed with a linear TA stapler (55 Roticulator, Tyco Healthcare Group, Princeton, NJ, USA). In no case was redo pancreatic resection performed in this series.

The lymphadenectomy routinely included regional lymph nodes, i.e., pancreaticoduodenal, superior pyloric, inferior pyloric, celiac trunk, hepatic artery, superior mesenteric, and middle colic. The lymphadenectomy was not extended to para-aortic/paracaval nodes, and a perioperative frozen section examination of resected specimens was not performed. The resection margins were studied on frozen sections, requiring an extension of the pancreatic resection in 2 cases (7%). The retroperitoneal surface was inked at the site of venous resection at the time of resection, and studied on definitive sections together with the resected specimen. The pathologic stage of the disease was assessed according to the Union Internationale Contre le Cancer TNM system.^{19,20}

After venous resections, the patients were put on a regimen of low-molecular-weight heparin for 1 month and were then prescribed 100 mg/day of oral aspirin. Local and distant recurrence of the disease were assessed

with a CT-scan of the chest, abdomen, and pelvis every 6 months in the first 2 postoperative years, then on a yearly basis, or earlier if deemed necessary. Preoperative radiation therapy and chemotherapy were not routinely administered. Postoperatively they were administered according to the standard oncologic protocols.

Regarding main results, hospital mortality, operative morbidity, and disease-specific survival rate were considered. Hospital mortality was defined as any postoperative death occurring either within 30 days after operation or during the postoperative hospital stay. Postoperative morbidity included any nonfatal complication either requiring reoperation or prolonging hospital stay over 9 postoperative days. The mean postoperative length of stay was defined as the number of postoperative days spent in the hospital, with the day of surgery considered as day 1, and not considering the day of discharge. Pancreaticojejunal anastomotic leakage was defined as the drainage of amylase-rich fluid, associated with fever, leukocytosis, and sepsis, after pancreaticoduodenectomy.²¹ Pancreatic fistula was defined as drainage of amylase-rich fluid after distal splenopancreatectomy, prolonging postoperative stay beyond 9 days. Delayed gastric emptying was defined as any delay in resuming the oral food intake beyond 9 postoperative days. In the pathological analysis, the retroperitoneal margins were defined as the soft tissue margin directly adjacent to the resected specimen,²¹ whereas tumor cell infiltration of the resected portal/superior mesenteric vein was defined as the presence of neoplastic cells within the tunica adventitia and /or tunica media of the vein wall.²² Local recurrence was defined as any new neoplastic growth at the site of surgical resection, either retroperitoneal or anastomotic, symptomatic or simply detected at control CT-scan during follow-up. The patency of venous reconstruction was assessed with either Doppler ultrasound or abdominal CT-scan, during the follow-up. Late survival was defined as patients' survival after discharge from the hospital, calculated by the Kaplan–Meier method.²³ When indicated, the chi-square test was used for the statistical analysis, and P values of less than 0.05 were considered to be statistically significant.

Results

Preoperative imaging correctly predicted the extent of limited venous involvement in all the cases, and no patient exhibited an unexpected portal/superior mesenteric vein involvement exceeding a length of 2 cm. One patient died in the postoperative period of acute intraabdominal hemorrhage, thus resulting in a postoperative mortality rate of 3.4%.

Table 2. Essential operative data of 29 patients undergoing a PV/SMV vein resection for pancreatic cancer

3.4
21
330 (±40 SD)
9 (±5 SD)
700 (±160 SD)
2.2 (±0.21 SD)
16 (±5 SD)

Nonfatal complications included 2 pancreaticojejunal anastomotic leaks, 2 wound infections, 1 pancreatic fistula, and 1 gastrojejunal anastomotic bleeding, resulting in an overall postoperative morbidity rate of 21%. The mean length of operation was 330 min \pm 40 SD (range 282–540 min). The mean PV clamping time was 9 min \pm 5 SD (range 4–13 min). The mean operative blood loss was 700 ml \pm 160 SD (range 400–2200 ml), and the mean blood transfusion requirement was 2.2 units (U) \pm 0.30 SD of packed cells (range 1–5 U). The mean postoperative length of stay was 16 days \pm 5 SD (range 11–32 days) (Table 2).

At the pathological examination, 27 tumors were ductal adenocarcinomas and 2 were a squamous cell carcinoma, with a mean diameter of 3.6 cm (range 1.9-10.0 cm). Six patients had a tumor diameter of 2 cm or less. Positive retroperitoneal margins were present in 5 (17%) resected specimens. Neoplastic vein wall infiltration was identified in 22 (76%) resected veins, whereas in the remaining 24% of the cases histology was consistent with an inflammatory adhesion to the vein due to desmoplastic stromal reaction induced by the tumor. No difference in terms of the incidence of inflammatory adhesion versus neoplastic infiltration was found at pathological examination among the specimens of patients undergoing vein resection/anastomosis, patch, or lateral suture. Gastric, duodenal, jejunal, biliary, and pancreatic margins including the 2 intraoperatively reresected specimens, were always found free of neoplastic involvement. The mean number of regional lymph nodes sampled was 19 (range 11-42). Lymph nodes were found to be positive for microscopic tumor metastasis in 14 cases (48%). In 3 cases (10%) the tumor was associated with chronic pancreatitis. Overall, 5 patients (17%) were classified as stage I, 11 (38%) as stage II, and 11 (45%) as stage III disease.

The 28 patients who survived the operation were followed up for a mean period of 19 months (range 3–52 months). No patient was lost to follow-up, and none showed any evidence of thrombosis of the reconstructed veins during the follow-up period.

Sixteen late deaths occurred; one patient died of myocardial infarction 7 months after operation, while apparently free from recurrent disease; 15 patients died



Fig. 1. The cumulative survival rate after a pancreatectomy with a minor venous resection for pancreatic cancer. The *numbers above the dotted line* indicate the number of patients at risk for each time interval

of disease-related causes: liver metastases in 10 cases, peritoneal carcinosis in 3, and both in 2. Among these 15 patients, 4 also experienced recurrent disease at the site of surgery. Overall, local recurrence was 14%.

Two patients are alive with liver metastases at 15 and 38 months, respectively of the follow-up. One patient is alive and free from recurrent disease at 52 months of the follow-up.

The median survival was 19 months. Overall, cumulative (standard error) survival rates at 1, 2, and 3 years, were respectively 76% (9%), 40% (9%), and 17% (9%) (Fig. 1).

The differences in the survival related to tumor differentiation, lymph node metastasis, status of retroperitoneal margins, and tumor location (head vs body/tail) did not reach statistical significance. The median survival and 3-year survival of 108 patients operated on for pancreatic resection for cancer without vascular involvement at the same institutions, in the same time period, were respectively of 21 months and 19%. The perioperative results and survival benefits of operated patients with and without vascular involvement were retrospectively compared, and differences among the two groups did not reach statistical significance (Table 3).

Discussion

The in-hospital mortality after a pancreatectomy for adenocarcinoma of the pancreas has significantly declined in the recent years.^{24,25} Pancreatectomy has therefore become a standardized and safe treatment for adenocarcinoma of the head of the pancreas.¹⁰

A resection of the portal/superior mesenteric vein at the time of pancreatectomy for cancer remains controversial. The aggressive biological behavior of the disease

	With PV/SMV resection $(n = 29)$	Without PV/SMV resection $(n = 108)$	Р
Perioperative/distant outcome			
Operative mortality	1 (3.4%)	4 (3.7%)	NS
Operative morbidity	6 (21%)	21 (19%)	NS
Mean operative duration (min)	330	220	NS
Mean blood transfusion (U)	2.2	2.1	NS
Mean postoperative length of stay (days)	16	18	NS
Mean 3-year survival (%)	17	19	NS

 Table 3. Perioperative and distant outcome of patients undergoing a resection of pancreatic cancer with and without limited venous involvement

NS, not significant

is associated with an overall short survival even of patients undergoing potentially curative resection, therefore one may be reluctant to perform a venous resection in order to improve resectability of pancreatic cancer, with the concern of making the operative procedure more complex.¹ Other series report a poor long-term survival after pancreatic and portal vein resection for adenocarcinoma, and deem a resection inappropriate on an oncological basis whenever portal/superior mesenteric vein infiltration exists.¹⁴⁻¹⁸ Nevertheless, despite the overall dismal prognosis of pancreatic cancer, a resection remains, at the moment, the only chance of cure for this condition.

Tumors with arterial or extensive venous involvement, requiring extended resections and complex vascular reconstructions, will probably be best treated with nonresective methods. An arterial resection should therefore be strictly limited to highly selected cases, due to the difficulty of obtaining negative surgical margins, and the significant increase of perioperative morbidity and mortality.^{1,26–28}

Tumor adherence limited to the portal/superior mesenteric vein is quite common, as it affects almost 25% of the patients at the time diagnosis is made,¹⁰ therefore accepting venous adherence or limited invasion of the portal/superior mesenteric vein as a strict criterion hindering resection, would significantly limit the number of patients being offered the benefits of resection itself.¹⁰ As a consequence, it seems reasonable to assume that a venous resection should be attempted in cases bearing a high chance of obtaining negative surgical margins.^{1,26–29}

For this reason a pancreatectomy associated with a venous resection, in this series, was deliberately limited to those cases with short involvement of the portal/superior mesenteric vein at preoperative imaging, in order to achieve a potentially curative resection in as many cases as possible, thus remaining within an oncologically reasonable boundary. The relatively low incidence of positive retroperitoneal margins (17%) in the present study supports this assumption.

The results of a pancreatectomy with limited portal/ superior mesenteric vein resection in the present series favorably compare with those of other studies on portal vein resection for carcinoma of the pancreas,^{1,10-13} in terms of operative morbidity and mortality, negative tumor margins, and median survival. Furthermore, they are not worse than those reported in series of potentially curative pancreatectomy without vascular resections,^{2,3} and in our experience as well, when retrospectively compared with those of pancreatic resection for cancer without vascular involvement, the results of pancreatectomy with limited venous resection were essentially superposable. Given the retrospective nature of this study, the time length of the clinical sample, and the difficulty to obtain homogeneous, comparable groups between patients with and without vascular involvement, these encouraging results obviously need further validation with larger and hopefully prospective series.

Overall, 4 patients showed clinical or imaging evidence of recurrence of the tumor at the site of surgical resection, which seems acceptable in this particular oncologic setting. Therefore, besides improving overall survival, a resection for adenocarcinoma of the pancreas bears the significant advantage of effectively limiting the local growth of the tumor, compared to nonresective procedures. Aggressive, local spread of nonresected pancreatic tumors is well known in almost all patients to cause pain and discomfort, which are often very difficult to treat. Consequently, if in-hospital mortality and morbidity are kept low, resection remains the treatment offering not only the longest survival but also the best palliation for the patients.

Extending a resection to those cases with limited portal/superior mesenteric vein involvement will overall enable the best treatment available to be offered to a larger number of patients. In this study, the rationale for arbitrarily limiting portal/superior mesenteric vein resection to tumoral invasion not exceeding 2 cm in length was that 2 cm appeared to be the maximal extension allowing us to obtain a curative resection with a simple vascular reconstruction, and without the need for an interposition graft. It was also assumed that as far as portal vein/superior mesenteric vein adhesion or infiltration is of limited extent, it can reasonably be considered a function of tumor location, other than an indicator of biologic aggressiveness.^{10–13} The reported results seem to support this assumption.

Whenever portal/superior mesenteric veins are involved over a longer extent, the tumor can be considered to exhibit a more aggressive biological pattern for which a curative resection may be useless. Furthermore, the more complex vascular reconstructions required may yield a significantly higher rate of perioperative complications, thus overwhelming the expected benefits of a resection.

In the present series, the relatively low quantity of blood transfused, the length of surgical procedure, and mean length of hospital stay of minor vascular resections associated with a pancreatectomy, all favorably compare with those of previous reports, 1,4,10-14,18,19-21,27-29 and to those of standard resections of the pancreas for carcinoma without vascular involvement.3,8,9,24-26 The results of larger samples studies dealing with even more extended pancreatic and portal vein resections for pancreatic cancer have recently reported excellent perioperative results, such as 2.7% mortality out of 186 portal vein resections, with the aim of obtaining cancer free surgical margins and improving overall survival.³⁰ These latest findings thus support our aggressive approach towards tumors with venous involvement of limited extent.

The division of the splenic vein was required in more than half of the pancreaticoduodenectomies performed, in order to expose the splenoportal confluence for facilitating both resection and venous reconstruction. It has been feared that division of the splenic vein, when living the spleen in place, might be followed by portal thrombosis and hypertension with upper gastrointestinal bleeding;^{12,21} this complication never occurred in the present experience.

Autogenous materials for venous reconstruction include the internal jugular and the greater saphenous vein. The internal jugular vein has a diameter which is comparable to that of portal/superior mesenteric vein, and it is most suitable whenever graft interposition is required. The greater saphenous vein is an excellent patch material, and was harvested in three cases for this purpose in the present study. Prosthetic patches should be avoided in this setting in order to avoid a risk of septic complications.

Clamping of the superior mesenteric artery, before performing portal/superior mesenteric vein clamping and reconstruction, has been recommended in order to prevent bowel edema, which may render digestive sutures more difficult.²⁹ Assuming that the short portal/ superior mesenteric vein clamping time required for simple reconstructions would not cause significant bowel edema, inflow occlusion was not performed in this series, without any additional difficulty in performing pancreatic, biliary, and gastro-jejunal reconstructions.

In conclusion, the results of the present study support the assumption that an aggressive surgical attitude toward pancreatic cancer with involvement of portal/ superior mesenteric vein not exceeding 2 cm in length seems justified if not indicated. To this selected group of patients, the benefits of a potentially curative resection can be offered with a rate of operative mortality/ morbidity, surgical disease-free margins, and diseasefree survival that are equivalent to those of standard pancreatic resections for cancer.

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