ANNALS OF SURGERY
Vol. 229, No. 3, 393–400

Reexploration for Periampullary Carcinoma

Resectability, Perioperative Results, Pathology, and Long-Term Outcome

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Objective

This single-institution experience retrospectively reviews the outcomes of patients undergoing reexploration for periampullary carcinoma at a high-volume center.

Summary Background Data

Many patients are referred to tertiary centers with periampullary carcinoma after their tumors were deemed unresectable at previous laparotomy. In carefully selected patients, tumor resection is often possible; however, the perioperative results and long-term outcome have not been well defined.

Methods

From November 1991 through December 1997, 78 patients who underwent previous exploratory laparotomy and/or palliative surgery for suspected periampullary carcinoma underwent reexploration. The operative outcome, resectability rate, pathology, and long-term survival rate were compared with 690 concurrent patients who had not undergone previous exploratory surgery.

Results

Fifty-two of the 78 patients (67%) undergoing reexploration underwent successful resection by pancreaticoduodenectomy; the remaining 26 patients (34%) were deemed to have unresectable disease. Compared with the 690 patients who had not undergone recent related surgery, the patients in the reoperative group were similar with respect to gender, race, and resectability rate but were significantly younger. The distribution of periampullary cancers by site in the reoperative group undergoing pancreaticoduodenectomy (n = 52) was 60%, 19%, 15%, and 6% for pancreatic, ampullary, distal bile duct, and duodenal tumors, respectively. These figures were similar to the 65%, 14%, 16% and 5% for resectable periampullary cancers found in the primary surgery group (n = 460). Intraoperative blood loss and transfusion requirements did not differ between the two groups. However, the mean operative time was 7.4 hours in the reoperative group, significantly longer than in the control group. On pathologic examination, reoperative patients had smaller tumors, and the percentage of patients with positive lymph nodes in the resection specimen was significantly less. The incidence of positive margins was similar between the two groups. Postoperative lengths of stay, complication rates, and perioperative mortality rates were not higher in reoperative patients. The long-term survival rate was similar between the two resected groups, with a median survival of 24 months in the reoperative group and 20 months in those without previous exploration.

Conclusions

These data demonstrate that patients undergoing reoperation for periampullary carcinoma have similar resectability, perioperative morbidity and mortality, and long-term survival rates as patients undergoing initial exploration. The results suggest that selected patients considered to have unresectable disease at previous surgery should undergo restaging and reexploration at specialized high-volume centers.

Pancreatic cancer remains the fifth leading cause of cancer death in the United States.[1] In the 1970s, the high morbidity and mortality rates and poor long-term survival after pancreaticoduodenectomy (PD) discouraged many surgeons from performing this procedure as the primary therapy for pancreatic cancer.[2,3] Over the last decade, significant improvements have been reported in the perioperative results after PD.[4–9] In addition, a number of series have reported improved long-term survival after PD for pancreatic cancer. These facts, plus the lack of effective alternative

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Accepted for publication September 25, 1998.

therapy, have led to the recognition that surgical resection offers the only hope for long-term survival in these patients.

Despite improvements in preoperative diagnostic imaging and staging, exploratory laparotomy for diagnosis and/or determination of resectability is necessary in many cases. In some patients, liver metastasis and/or peritoneal implants are obvious, and unresectability is easily confirmed.[10] In other patients, however, extensive mobilization and dissection is necessary to determine whether significant involvement of major visceral vessels would preclude resection.[11] This dissection can often be technically challenging and has the potential for significant blood loss, particularly from major venous tributaries of the mesenteric and portal venous system. Encountering such problems, the less-experienced pancreatic surgeon may inappropriately determine a patient to have unresectable disease and may subsequently perform only palliative procedures.

In recent years, a number of series have been reported addressing the role of reoperative surgery in patients with periampullary carcinoma.[12–17] Most series have demonstrated that resection can be accomplished with acceptable perioperative morbidity and mortality rates. The goal of this report is to update our experience with reoperative surgery in patients with periampullary carcinoma and to contrast these results, as well as long-term survival rates, with patients who have not undergone a recent previous surgical procedure for diagnosis, palliation, or determination of resectability.

PATIENTS AND METHODS

Between December 1991 and December 1997, 78 patients undergoing reoperation for periampullary adenocarcinoma were identified in our prospective database. Patients who had undergone a laparotomy for diagnosis and/or palliation of a periampullary carcinoma, including biliary–enteric bypass, gastrojejunostomy, cholecystectomy, or other miscellaneous procedures for periampullary or pancreatic cancer, were included in this analysis. Patients undergoing cholecystectomy for symptomatic cholelithiasis were excluded. Demographic factors, resectability rates, pathology, perioperative results, and long-term survival rates were compared to the 690 patients undergoing primary exploration for periampullary adenocarcinoma during the same period at our institution. Data were collected prospectively on all patients.

All pathologic specimens were reviewed by a single pathologist (RHH) to confirm the diagnosis of periampullary adenocarcinoma and to determine the tissue of origin of the tumor, including the pancreas, ampulla, distal bile duct, or duodenum. Procedures for benign disease, cystic neoplasms, neuroendocrine tumors, gastrointestinal stromal tumors, and tumors metastatic to the periampullary region from distant primary sites were excluded. Information regarding tumor size, site of origin, margin status, nodal status, and degree of differentiation were noted for all resected tumors.

Preoperative imaging was not standardized but was performed as per the preference of the attending surgeon. Diagnostic and staging modalities, including spiral computed tomography scanning, percutaneous transhepatic cholangiography with percutaneous biliary drainage, endoscopic retrograde cholangiopancreatography, endoscopic ultrasound, and superior mesenteric/celiac angiography, were performed as indicated. Occasionally, the studies from the referring institution were adequate and no further imaging was required. Laparoscopy has not been a component of our staging workup for periampullary carcinoma.

Surgical management for resectable periampullary cancer consisted primarily of pylorus-preserving PD, reserving hemigastrectomy for lesions involving the first or second portion of the duodenum. Partial pancreatectomy, preserving the body and tail of the pancreas, was performed except when total pancreatectomy was necessary to achieve negative surgical margins. Pancreatic–enteric reconstruction was accomplished by pancreaticojejunostomy or pancreaticogastrostomy. From 1991 to 1996, standard regional lymphadenectomy was performed. Since April 1996, our institution has been performing a prospective, randomized study comparing standard peripancreatic lymph node dissection with extended retroperitoneal lymph node dissection. Palliative procedures included biliary–enteric bypass, usually by hepatico- or choledochojejunostomy, gastrojejunostomy, cholecystectomy, and celiac axis chemical splanchnicectomy. The choice of palliative procedures was left to the judgment of the surgeon and depended on the patient's presenting symptoms and previous operative and nonoperative interventions.

The overall incidence of postoperative complications was evaluated. The need for reoperation in the immediate postoperative period was assessed. Delayed gastric emptying, pancreatic fistula, and biliary anastomotic leak were defined by previously reported criteria.[18,19] Wound infection was defined as a positive wound culture and the presence of pus necessitating opening of the wound. Intraabdominal abscess required radiographic evidence and subsequent positive cultures after percutaneous or operative drainage. Pneumonia was defined as positive sputum cultures with a corresponding infiltrate on chest radiograph, requiring antibiotics. Positive bile cultures, fever, and abnormal results on liver function tests requiring external biliary drainage and antibiotics defined cholangitis. Perioperative death was defined as death during the initial hospitalization or within 30 days of surgery.

Follow-up information was obtained through direct patient contact and review of hospital charts and surgeons' records, and by contacting the United States Social Security Administration. Survival information was available on 753 of the 768 patients.

All continuous data are presented as mean ± standard error of the mean. Differences between groups were evalu-

Table 1. RESECTABILITY RATES AND PROCEDURES PERFORMED

	Reoperative (n = 78)		Primary (n = 690)		p
	Number	Percent	Number	Percent	Value
Resected (pancreaticoduodenectomy)	52	67	460	67	NS
Palliated (not resected)	26	33	230	33	
Biliary bypass alone	2	8	25	11	NS
Gastric bypass alone	12	46	37	16	<0.0001
Biliary and gastric bypass	5	19	127	55	0.001
Other	7	27	41	18	<0.0001

ated by chi square analysis or analysis of variance where appropriate. All survival analysis was performed using the method of Kaplan and Meier.[20] The log-rank test was used to evaluate differences in survival between groups. $P \leq 0.05$ was considered significant.

RESULTS

During the 6-year period studied, 768 patients underwent operative management for periampullary adenocarcinoma. Of the 768 patients, 78 (10%) had undergone previous related surgery. By definition, the prior surgical procedure had been related to the presentation of the periampullary carcinoma and been performed for diagnosis, potential resection, or palliation of the malignant process. Only 2 of the 78 procedures were performed at our institution. Twenty-two patients (28%) underwent biliary bypass alone, which included hepaticojejunostomy, cholecystojejunostomy, and cholecystoduodenostomy; 3 patients (4%) underwent gastrojejunostomy alone; 10 patients (13%) underwent both biliary and gastric bypass; 28 patients (36%) underwent cholecystectomy alone; and 15 patients (19%) underwent miscellaneous procedures, including exploratory laparotomy with biopsy, distal pancreatectomy/splenectomy, drainage of pseudocyst, local excision of periampullary lesion, common bile duct exploration, open sphincteroplasty, and resection of extrahepatic biliary tree. The median time between initial exploration and reexploration was 12 weeks (mean 22.5 weeks; range 6 days to 3 years).

Patients undergoing reoperative procedures had a mean age of 61.6 ± 1.3 years (median 64 years) and were significantly younger than those in the primary surgery group (mean 65.5 ± 0.4 years; median 67 years; p = 0.003). Fifty-eight percent of patients (n = 45) were men, and 90% (n = 70) were white. This distribution compares to 56% men (n = 448) and 91% white (n = 630) in the control group (p = NS).

The most common signs and symptoms at the initial presentation in the reoperative group were jaundice in 73%, abdominal pain in 47%, weight loss in 32%, nausea and vomiting in 19%, and fever and chills in 5%. There was no difference in the incidence of jaundice (66%), abdominal pain (46%), nausea and vomiting (23%), or fever and chills (4%) in those undergoing primary exploration. However, a significantly greater percentage of patients had significant weight loss (46%, p = 0.02) in the primary surgery group.

Fifty-two of the 78 patients undergoing reexploration (67%) underwent successful resection by PD. This resectability rate is identical to the resectability rate in patients undergoing primary exploration (460/690, 67%). Twenty-six of the 78 patients (33%) were confirmed to have unresectable disease and underwent operative palliation, including biliary bypass alone in 8%, gastric bypass alone in 46%, double bypass in 19%, and other procedures in 27% (Table 1). This is in contrast to the 230 patients (33%) with unresectable disease in the primary surgery group, who underwent biliary bypass alone in 11% (p = NS), gastric bypass alone in 16% (p < 0.0001), double bypass in 55% (p = 0.001), and other procedures in 18% (p < 0.0001).

In patients who did not undergo resection, 69% were found to have unresectable disease because of distant metastatic disease, including liver metastases, peritoneal metastases, or distant lymph node involvement. The remaining 31% were considered to have unresectable disease secondary to major vascular involvement (*i.e.*, portal vein, superior mesenteric vein, superior mesenteric artery). This distribution of reasons for unresectability is statistically similar to the group of patients who did not undergo resection in the primary exploration group (68% distant metastatic disease, 32% major vascular involvement; p = NS).

Twelve of the 78 patients (15%) in the reoperative group received chemotherapy and/or radiation between the initial exploration and reexploration, compared with only 9 of the 690 patients (1%) in the primary surgery group (p < 0.0001).

The postoperative morbidity and mortality rates and lengths of stay for the two groups are shown in Table 2. The overall mortality rates in the reoperative group were 3.8% overall (3/78), 3.8% in patients who underwent resection (2/52), and 3.8% in patients who underwent only palliation (1/26). In the primary surgery group, these rates were 2.2% (15/690), 1.7% (8/460), and 3.0% (7/230), respectively. Thirty-three percent of the patients in the reoperative group

Table 2. OVERALL MORTALITY AND MORBIDITY RATES

		Reoperative (n = 78)	Primary (n = 690)	p Value
Mortality	Overall	3.8%	2.2%	0.38
	Resected	3.8%	1.7%	0.30
	Palliated	3.8%	3.0%	0.83
Overall complications	Resected	33%	31%	0.61
	Palliated	31%	21%	0.43
Postoperative length of stay (days)				
Resected	Mean ± SEM	12.2 ± 1.0	13.8 ± 0.6	0.45
	Median	10	10	
Palliated	Mean ± SEM	10.0 ± 1.6	12.2 ± 1.8	0.68
	Median	8	9	

had one or more complications in the immediate postoperative period, whereas 31% of the primary surgery patients had a complication (p = NS). The mean postoperative length of stay was comparable at 12.2 ± 1.0 days for the reoperative group and 13.8 ± 0.6 days for the primary surgery group (p = NS).

An in-depth analysis was performed on the subgroup of patients undergoing PD, comparing the reoperative *versus* primary groups. Patients in the reoperative group were significantly younger (62.1 ± 1.6 years *vs.* 66.2 ± 0.5 years, p = 0.009), with similar gender (56% male *vs.* 55% male) and race distributions (90% white *vs.* 92% white). Patients with resectable disease in the reoperative group were less likely to have as initial symptoms weight loss (28% *vs.* 45%, p = 0.03) or nausea and vomiting (8% *vs.* 19%, p = 0.05). In the reoperative group, jaundice was seen in 76%, abdominal pain in 39%, and fever and chills in 4%, which is similar to the incidence of jaundice (72%), abdominal pain (36%), and fever and chills (3%) observed in the primary surgery patients.

The intraoperative data comparing reoperative to primary PD are shown in Table 3. Of the 67% of patients in the reoperative group who underwent successful resection by PD, 60% underwent pylorus-preserving procedures, 88% underwent partial pancreatectomy, and 6% underwent radical retroperitoneal lymph node dissection. These results differ from those undergoing primary resection, with 76% undergoing pylorus-preserving procedures (p = 0.004), 96% partial pancreatectomy (p = 0.019), and 11% radical resections (p = 0.19). The patients in the reoperative group had a significantly longer operative time (7.4 ± 0.4 hours *vs.* 6.6 ± 0.1 hours in the primary group; p = 0.006). Despite the increased operative time, the estimated blood loss and the number of transfusions were not statistically different between the reoperative and primary surgery groups. Superior mesenteric or portal venous resection to achieve negative surgical margins was required in 2% of the reoperative group and 5% of the primary surgery group.

The pathology data are summarized in Table 4. In the reoperative group, 60% of resected tumors arose from the head of the pancreas, 19% from the ampulla of Vater, 15% from the distal bile duct, and 6% from the periampullary duodenum. In the primary surgery group, these percentages were 65%, 14%, 16%, and 5%, respectively. Patients in the reoperative group had smaller tumors (2.3 ± 0.4 cm *vs.* 2.9 ± 0.1 cm, p = 0.05) and a lower incidence of positive lymph nodes in resected specimens (48% *vs.* 70%, p = 0.001). The incidence of positive resection margins was similar, with 15% in the reoperative group and 21% in the primary surgery group (p = NS). In the reoperative group, well-differentiated tumors were seen in 4%, moderately differentiated tumors in 69%, and poorly differentiated tumors in 27% of patients. In the primary surgery group, these percentages were comparable at 5%, 63%, and 32%, respectively (p = NS).

The overall morbidity and mortality rates were identical

Table 3. INTRAOPERATIVE PARAMETERS IN PATIENTS RESECTED VIA PANCREATICODUODENECTOMY

	Reoperative (n = 52)	Primary (n = 52)	p Value
Type of resection			
Pylorus-preserving	60%	76%	0.004
Classic	40%	24%	
Extent of pancreatectomy			
Partial	88%	96%	0.02
Total	12%	4%	
Extent of lymphadenectomy			
Standard	94%	89%	0.19
Radical	6%	11%	
Operative time (hours)			
Mean + SEM	7.4 ± 0.4	6.6 ± 0.1	0.006
Median	7.3	6.6	
Estimated blood loss (cc)			
Mean ± SEM	1071 ± 109	854 ± 51	0.17
Median	950	650	
Transfusions (units PRBCs)			
Mean ± SEM	0.7 ± 0.3	0.7 ± 0.1	0.95
Median	0	0	
Vein resection	2%	5%	0.30

Table 4. PATHOLOGY IN PATIENTS UNDERGOING RESECTION BY PANCREATICODUODENECTOMY

	Reoperative (n = 52)	Primary (n = 52)	p Value
Site of origin			
Pancreas	60%	65%	0.75
Ampulla of Vater	19%	14%	
Distal bile duct	15%	16%	
Duodenum	6%	5%	
Tumor diameter (cm)			
Mean ± SEM	2.3 ± 0.4	2.9 ± 0.1	0.05
Median	2.5	2.5	
Nodal status			
Positive	48%	70%	0.001
Negative	52%	30%	
Margin status			
Positive	15%	21%	0.32
Negative	85%	79%	
Differentiation			
Well	4%	5%	0.70
Moderate	69%	63%	
Poor	27%	32%	

between the two groups (see Table 2). The specific postoperative morbidity rate is displayed in Table 5. The incidence of reoperation in the immediate postoperative period, pancreatic fistula, delayed gastric emptying, wound infection, intraabdominal abscess, pancreatitis, bile leak, cholangitis, and pneumonia was similar between the two groups. Pancreatic fistula, delayed gastric emptying, and wound infections were the most common postoperative complications in both groups.

The mean follow-up from the time of exploration at The Johns Hopkins Hospital was 14.2 ± 1.7 months for the reoperative group and 13.8 ± 0.5 months for the primary surgery group. Finally, the survival rates of patients in the two groups were compared. Patients who underwent reexploration and resection by PD (n = 52) had 1-, 2-, and 5-year survival rates of 83%, 56%, and 40%; the median survival was 23 months. In the patients with resectable disease in the primary surgery group (n = 459), the 1-, 2-, and 5-year survival rates were 74%, 46%, and 20%, respectively; the median survival was 20 months (p = 0.17; Fig. 1). In patients found to have unresectable disease at reexploration (n = 24), the 1- and 2-year survival rates were 14% and 4%, respectively; the median survival was 7 months, with the longest survival 25 months. Patients with unresectable disease at initial exploration (n = 218) had 1- and 2-year survival rates of 26% and 10% (p = 0.17; Fig. 2); the median survival was 7 months, with the longest survivor being alive at 57 months. Survival curves were also generated from the time of initial exploration, with 1-, 2-, and 5-year survival rates of 92%, 59%, and 41%, respectively (median survival 33 months; p = 0.02 *vs.* those who underwent primary surgery; Fig. 3).

Table 5. POSTOPERATIVE COURSE IN PATIENTS UNDERGOING RESECTION BY PANCREATICODUODENECTOMY

	Reoperative (n = 52)	Primary (n = 460)	p Value
Complications			
Overall	35%	35%	0.91
Reoperation	4%	4%	0.92
Pancreatic fistula	12%	8%	0.43
Delayed gastric emptying	8%	14%	0.21
Wound infection	8%	9%	0.69
Intraabdominal abscess	4%	5%	0.67
Bile leak	2%	2%	0.83
Cholangitis	2%	4%	0.47
Pneumonia	0%	1%	0.41
Postoperative length of stay			
Mean ± SEM	13.3 ± 1.3	14.5 ± 0.5	0.41
Median	11	11	

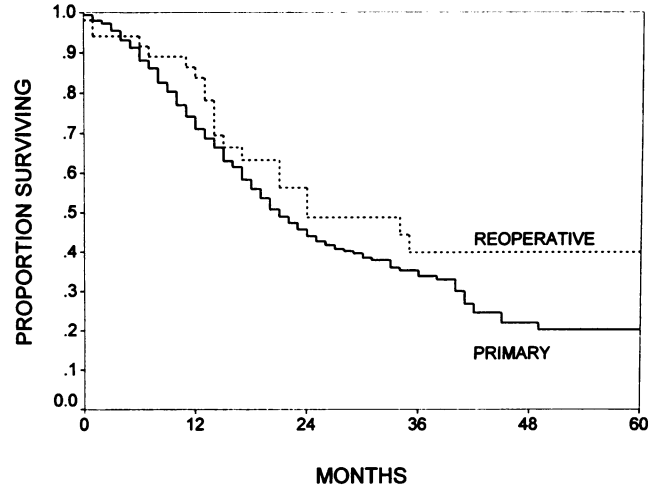

Figure 1. Kaplan-Meier survival curves in patients undergoing resection, comparing the reoperative group (n = 52, median survival 23 months, 5-year survival rate 40%) to the primary surgery group (n = 459, median survival 20 months, 5-year survival rate 20%; p = 0.17).

DISCUSSION

The early diagnosis of periampullary cancer can be difficult because of the vague and nonspecific nature of symptoms. The development of obstructive jaundice does, however, offer the potential for prompt diagnosis and referral for surgical resection with curative intent. In recent years a number of radiologic and endoscopic procedures have been developed to aid in the diagnosis and staging of this disease, including endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography, endoscopic ultrasound, spiral computed tomography, and magnetic reso-

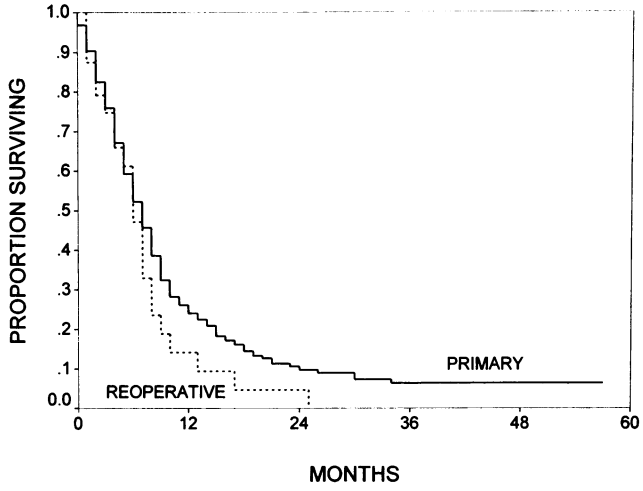

Figure 2. Kaplan-Meier survival curves in patients with unresectable disease, comparing the reoperative group (n = 24, median survival 7 months, 2-year survival rate 4%) to the primary surgery group (n = 218, median survival 7 months, 2-year survival rate 10%; p = 0.15).

nance cholangiopancreatography. However, in many patients surgical exploration remains necessary to determine the tissue diagnosis and resectability of a periampullary neoplasm.

Over the last two decades, significant improvements have been made in the perioperative results after both curative and palliative surgery[21,22] for periampullary cancer. A number of series from major centers have reported perioperative mortality rates <5% after PD,[4,8,9,23–26] and several institutions have reported series of >100 patients without a single death.[8,9,24,25] Nonetheless, the surgical management of this disease remains challenging. The complication rates remain high (30% to 40%), and a number of series have shown that although excellent perioperative results are seen in high-volume centers, the operative mortality rate remains as high as 12% to 17% in hospitals that perform a low volume of procedures for these cancers.[27,28]

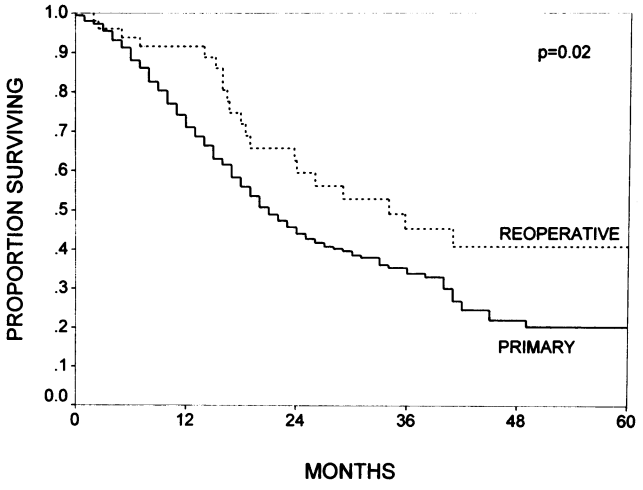

Figure 3. Kaplan-Meier survival curves in patients undergoing resection, with survival generated from the time of initial exploration, comparing patients undergoing reoperation (n = 52, median survival 33 months, 5-year survival rate 41%) with patients undergoing primary surgery (n = 459, median survival 20 months; p = 0.02).

A major challenge in the surgical management of patients with periampullary cancer is determination of resectability. Extensive dissection and mobilization of the periampullary region may be necessary to determine resectability in patients with pancreatic cancer.[11] Familiarity with the anatomy and experience in techniques of dissection are necessary to minimize complications and assess tumor resectability accurately. Surgeons unfamiliar with the anatomy and these techniques may encounter significant difficulties, primarily in recognizing major vessel involvement, which precludes resection in up to 31% of patients. Further, dissection in and around major tributaries of the portal and mesenteric venous system can be associated with a significant risk of blood loss, further discouraging the less experienced surgeon from pursuing careful dissection.

The recognition of the difficulties in the management of pancreatic cancer, as well as data suggesting improved results in the management of periampullary cancer at high-volume centers,[27,28] has led to experience at major centers in the management of patients whose disease was deemed unresectable at other institutions. This experience began as early as 1979, when Moossa et al[12] reported reexploration in 17 patients with ampullary and pancreatic cancer, with a resectability rate of 65%. In 1989, Hashimi and Sabanatham[14] reported a similar 61% resectability rate in 18 patients undergoing reoperative surgery after a palliative bypass for periampullary carcinoma. The initial report from this institution in 1991 further demonstrated the feasibility and safety of reoperative PD, with a 72% resectability rate and perioperative mortality and perioperative morbidity rates of only 2% and 38%, respectively.[15] Also, in 1994 the group at M.D. Anderson reported a single-surgeon series of 19 patients undergoing attempted PD in the reoperative setting, with a resectability rate of 74%.[16] In this study, all patients survived, and the morbidity rate was only 21%. Although this report also included 4 patients with neuroendocrine tumors, 4 of the 10 patients with adenocarcinoma who underwent resection were alive at a median follow-up of 26 months. No formal survival analysis, however, was provided in any of these series comparing the survival of patients undergoing reoperation with those undergoing resection at initial exploration at the same institution.

In this series, 10% of patients undergoing laparotomy for periampullary cancer had this procedure performed as a reoperative procedure. The resectability rates were identical between the reoperative and primary surgery groups (67%), as were the reasons for unresectability.

Comparison of the two groups of patients undergoing resection demonstrated that patients undergoing reoperation were more likely to undergo classic pancreaticoduodenal resections (as opposed to pylorus-preserving procedures and total pancreatectomy). This difference probably reflects the difficulty associated with the previously performed proce-

dures, which necessitated a more extensive procedure, because tumor size and lymph node status were more favorable in the reoperative group. The number of patients requiring superior mesenteric/portal venous resection was not different between the two groups, suggesting that the assessment of local unresectability was not always accurate at previous laparotomy.

The dissection necessary because of the previous laparotomy, the greater number of more extensive procedures, and perhaps the higher incidence of preoperative chemoradiation probably contributed to the observed increase in operative time in patients undergoing reoperative procedures (7.4 *vs.* 6.6 hours). Despite this extra time, no increase in estimated blood loss, transfusion requirements, or postoperative morbidity (overall and specific) or mortality rates was observed, demonstrating that PD is safe in the reoperative setting.

With the safety of reoperative PD being clearly demonstrated, it was then critical to compare long-term survival rates in the two groups. As expected, the survival rate in patients with unresectable disease was poor in both the reoperative and primary surgery groups, with 2-year survival rates statistically similar between the two groups. Thus, reoperation did not negatively affect survival in patients with unresectable disease, although probably it negatively influenced quality of life. In those who underwent successful resection, a trend toward improved survival was present in the reoperative group, with 1- and 5-year survival rates of 83% and 40% *versus* 74% and 20% for the primary surgery group, although this difference did not achieve significance. This trend did achieve significance when survival was calculated from the time of initial exploration.

In an analysis performed to identify factors to explain this trend for improved survival, we found that patients undergoing reoperation were younger, had a decreased incidence of weight loss and nausea and vomiting, were more likely to undergo hemigastrectomy or total pancreatectomy, and had longer operative times, but none of these factors have been shown to influence survival after resection for pancreatic or periampullary cancer.[7,9,26,29,30] Conversely, patients undergoing reoperation had a lower incidence of positive nodes on final pathologic examination, had smaller tumors, and were more likely to undergo chemotherapy/radiation, all of which have been shown to be significant positive prognostic factors for resected pancreatic and periampullary cancer.[7,9,26,29–40] Finally, there were no differences in estimated blood loss, transfusion requirements, margin status, or degree of differentiation, all of which have been identified as long-term prognostic indicators.

The trend toward improved survival in the reoperative group, therefore, is probably related to the fact that patients undergoing reoperation had less advanced tumors, even though in many cases the tumors had been deemed unresectable at a previous laparotomy. These differences may reflect a selection bias in that patients surviving long enough for reexploration are likely to represent a biologic subset of tumors with a more favorable prognosis. This is supported by the smaller tumor size, lower incidence of positive nodes, and decreased incidence of weight loss and nausea and vomiting in the reoperative group.

These data demonstrate that patients undergoing reoperation for periampullary carcinoma have similar resectability and perioperative morbidity and mortality rates as patients undergoing primary exploration. Not only is long-term survival possible in patients undergoing reoperation, but the data suggest that patients may have more favorable outcomes. These data support an aggressive approach to reexploration, especially because resection remains the only option for long-term survival in patients with periampullary carcinoma. The results suggest that selected patients considered to have unresectable disease at previous laparotomy may benefit by restaging and reexploration at specialized high-volume centers.

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