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Comparison of Conventional Surgical Resection, Radioactive Implantation, and Bypass Procedures for Exocrine Carcinoma of the Pancreas 1975–1980

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To examine the efficacy of a variety of procedures for treatment of biopsy proven exocrine adenocarcinoma of the pancreas, a retrospective review of 231 patients surgically treated at a single institution from January 1975 through December 1980 was performed. Thirty-nine patients underwent resection for cure, of which 19 were conventional resection, 33 I^{125} implantation, 76 biliary or GI bypass, and 83 biopsy alone, a resectability rate of 16.9%. There was one pancreatic fistula in the implant group. Median survival following implant was 8 months (0%, 30-day mortality) and, for conventional resection (n = 19), 17 months with an inhospital mortality of 16%. Median survival excluding inhospital mortality was 17 months for the conventional resection group. For bypass, median survival was 4 months (p = 0.0001 *vs.* conventional resection) with an inhospital mortality of 14%. Of patients discharged from hospital, 5 of 16 (31%) survived 2 years in the conventional resection group, while 4 of 132 (3%) survived 2 years in the nonresected groups. Only one patient (5% of resected) has survived 4 years in the conventional resection group, although eight others are alive and at risk in this group. Resectability rate for patients referred with adenocarcinoma of the pancreas remains low. The only long-term survivors are in those patients undergoing resection. Local implantation with I^{125} requires prospective evaluation because of an apparent influence on palliation without significant morbidity.

CARCINOMA OF THE PANCREAS is a disease which has persistently eluded cure, regardless of approach. This retrospective review of surgically treated exocrine pancreatic carcinoma at Memorial Hospital from 1975–1980 was undertaken to review the results of a variety of treatments for carcinoma of the pancreas in a single institution over a limited time period. This report includes standard therapy, *i.e.*, surgical resection, biliary and gastric bypass procedures and an alternative: I^{125} implantation. The latter form of therapy has been suggested to improve palliation,[9,16,17] and was performed in 33 patients of 231 reported here. Regional pancreatectomy, an extended resection for cure which has been previously reported,[7] is undergoing re-evaluation (J. Fortner et al., in preparation).

Materials and Methods

The charts of all patients coded for surgical treatment of carcinoma of the pancreas from January 1975 through December 1980 were reviewed. Only patients with a confirmed exocrine carcinoma arising in the pancreas were included. Exclusions consisted of those patients with endocrine tumors, sarcomas, and concomitant malignancies which did not allow definition of the pancreatic lesion as primary or secondary. Three patients with fully malignant cystadenocarcinoma are included. Patients in whom the tumor was felt to be originating from the periampullary region were excluded.

Two hundred and seventy-six charts of patients with pancreatic cancer were available and 45 patients were

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TABLE 1. *Sites of Other Malignancies*

Type	Number
Breast	6
Colon	4
Larynx	2
Endometrium	2
Tonsil	2
Tongue	2
Kidney, Bladder, Alveolar ridge, Thyroid, Lung, Prostate, Salivary (1 each)	7

excluded by the above criteria, leaving 231 patients as the basis of this report. An additional three were subsequently excluded as they had extra-abdominal procedures.

Results

Two hundred and twenty-eight patients had abdominal exploration for exocrine pancreatic cancer in the 6-year period 1975–1980. Median follow-up was 5 months. The diagnosis of adenocarcinoma was biopsy proven in 97% of the patients by material obtained at Memorial Hospital or review of outside slides. Of the seven patients without a histologic diagnosis, one had a positive biopsy at an outside hospital not reviewed at Memorial. Diagnosis in the remainder was made on clinical grounds at laparotomy and none of these patients were long-term survivors.

Twenty-one patients with pancreatic carcinoma had 25 prior malignancies, including four patients whose carcinoma of the pancreas was their third malignancy. Carcinoma of the breast was the most common lesion followed by carcinoma of the colon and a variety of other malignancies. No patient had evidence of active disease at the time of diagnosis of pancreatic carcinoma (Table 1).

Ninety-three patients were female, 135 male. The mean age for the entire group was 60 years with a range of 27–85 years. Mean and median ages for each operative group are listed in Table 2.

The resectability rate in this series was 16.9%. One hundred and two of the 228 (45%) patients had a laparotomy prior to presentation at Memorial Hospital. In only 60 patients (26%) was a histologic diagnosis established prior to operation at Memorial whether by operative, percutaneous, or endoscopic biopsy. Survival in all

TABLE 2. *Patient Age (Years)*

Procedure	*n*	Mean	Median	Range
Biopsy	80	57	59	39–85
Bypass	76	63	65	40–84
Implant	33	61	63	43–75
Resection	39	56	58	27–73
Regional	20	54	53	27–68
Other	19	60	61	32–73
All patients	228	60	60	27–85

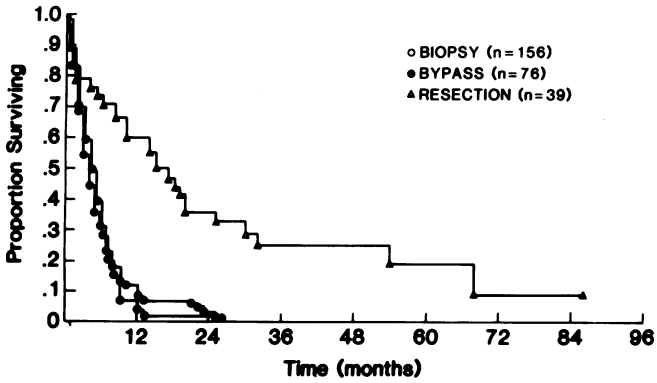

FIG. 1. Comparison of surgical resection, biopsy, and bypass procedures for exocrine carcinoma of the pancreas. Life table analysis by log rank test demonstrates that survival following resection is significant at p = 0.001 *vs.* both bypass and biopsy. Survival following bypass and biopsy is not different.

groups is shown in Figure 1. Median survival for all patients undergoing pancreatic resection was 18 months, with a 30-day operative mortality of 18% (Table 3). Excluding patients with cystadenocarcinoma median survival of patients resected for cure was 15 months. Excluding operative mortality, median survival for all resected patients was 20 months.

Twenty patients who underwent regional pancreatectomy during this period are included in an analysis currently being prepared (Fortner et al., in publication). This group produced the only 5-year survivors, one patient dead of disease at 68 months and one free of disease at 86 months.

Patients having resections other than regional pancreatectomy underwent a variety of procedures listed in Table 4. The median survival for patients undergoing standard pancreatic resection was 17 months. When the three patients with cystadenocarcinoma are excluded, the median survival was 14 months. For this 5-year period, there is no statistically significant difference in survival between the regional pancreatectomy and the other pancreatic resection groups, although numbers are small. When operative mortalities are excluded from survival

TABLE 3. *Procedure, In-hospital and Long-term Survival*

Procedure	No. Patients	Mortality 30 day	Mortality In Hospital	Median Survival Months
Biopsy	80	15%	16%	4
Biopsy alone	48	19%	20%	3
Biopsy, previous bypass	32	9%	9%	6
Bypass	76	12%	14%	4
Implant	33	0%	3%	8
All resection for cure	39	18%	23%	18
Conventional resection*	16	19%	19%	14
Resection	19	16%	16%	17

* Excludes cystadenocarcinoma.

calculations, median survival for conventional resection is 17 months with a 30-day and inhospital mortality rate of 16% and an incidence of major complications of 16%. One patient exsanguinated in the operating room during an attempted pancreaticoduodenectomy. Only two patients in this group required reoperation for complications in the post-op period. The longest survivor is dead of disease at 54 months post-op. Two patients are alive and free of disease at 40 and 45 months follow-up, both with cystadenocarcinomas. Of the 11 patients in both resection for cure surgical groups who survived greater than 24 months, six had positive lymph nodes. Both cystadenocarcinomas were in the node negative groups.

There was one inhospital death in the 33 patients undergoing interstitial implantation with I^{125} and seven (21%) major post-op complications in this group. There was only one pancreatic fistula occuring in a patient who had multiple pancreatic biopsies to establish the diagnosis of carcinoma. Half of the other six major complications occurred in patients having concomitant bypass procedures and cannot be directly attributed to the implant. Twenty-two of the 33 implanted patients (66.7%) had a biliary or G.I. bypass done, half at the time of implantation and half prior to presentation at our institution. Median survival for this group was 8 months with the longest survivor alive and no evidence of disease at 33 months. There is no significant difference in survival between the resection and implant groups. It should be noted that nine of these patients had liver metastases at the time of implantation. The remainder of the group underwent implantation because of fixation of the tumor to major vascular structures, presence of positive lymph nodes, or the patient's age or medical condition was felt to preclude resection. The suggestion that post-operative pain was palliated by this procedure cannot be documented.

Seventy-six patients underwent biliary or G.I. bypass with a median survival of 4 months. Operative mortality was 12% at 30 days, 14% inhospital. Only 25% of this group had undergone prior exploration.

There were 80 patients who had biopsy or laparotomy only, with a 30-day mortality of 15%. In calculating survival, this group was divided into the 32 patients who had undergone biliary or G.I. bypass prior to admission and those who had not. Median survival for patients previously undergoing bypass was 6 months while median

TABLE 4. *Type of Procedure in the Surgical Resection Group*

Types of Resection	No. Patients
Regional pancreatectomy	20
Pancreaticoduodenectomy	10 (includes 4 patients with portal vein resection)
Total pancreatectomy	4 (includes 1 patient with portal vein resection)
Distal pancreatectomy	5

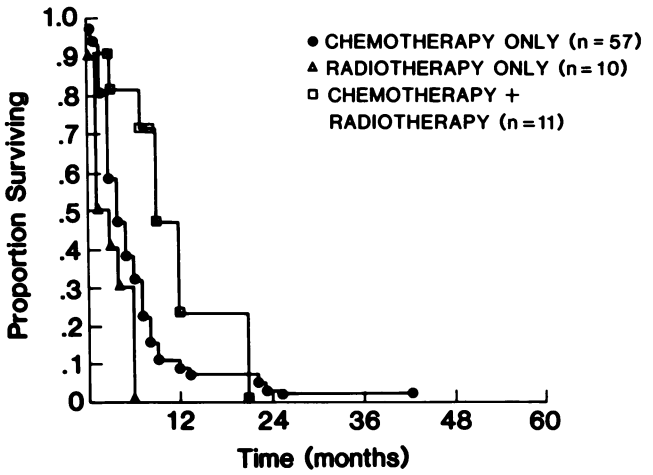

FIG. 2. Comparison of adjuvant therapies for exocrine carcinoma of the pancreas. Life table analysis by log rank test demonstrates that survival following treatment with chemotherapy and radiotherapy combined is significant at p = 0.004 *vs.* treatment with chemotherapy alone or radiotherapy alone in biopsy and bypass patients.

survival for those having a biopsy was 3 months. Median survival was 4 months for the entire biopsy group.

Further therapy in the form of chemotherapy and external radiation significantly increased survival for the biopsy and bypass patients. A survival advantage was demonstrated for patients receiving both chemo and RT (n = 11) (p = 0.004) (Fig. 2). Combination treatment was compared to chemotherapy alone or radiation therapy alone which, in turn, had no statistically significant survival benefit over no treatment when all patients not

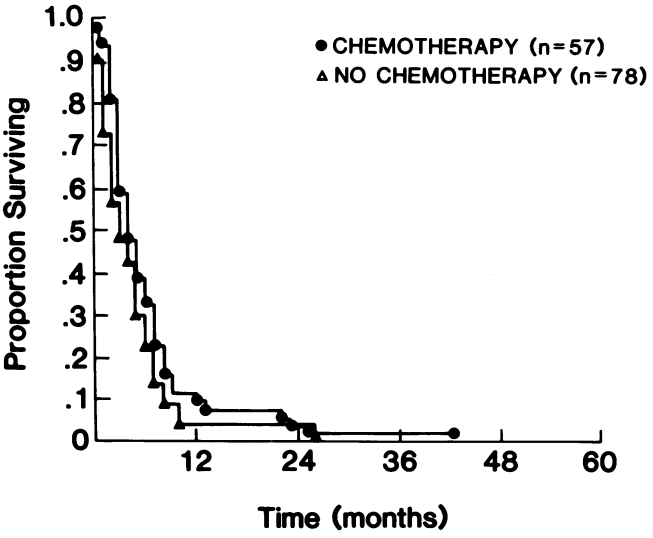

FIG. 3. Comparison of chemotherapy *vs.* no chemotherapy for exocrine carcinoma of the pancreas. Life table analysis by log rank rest demonstrates that survival following treatment with chemotherapy is no different than survival in patients receiving no chemotherapy in the biopsy and bypass group.

TABLE 5. *Results of Pancreatic Resection for Cure of Exocrine Cancer*

Author	Year	Years of Treatment	No. Patients	No./Year	Operative Mortality	Mean Survival Months
Herter	1982	39	82	2	19%	9
Fortner	1981	9	36	4	15%	N.S.
Longmire	1980	21	50	2	N.S.	16*
Edis	1980	25	162	6	16%	10 (med)
Brooks J.	1975	10	16	1	13	23
Knight	1978	10	16	1	14%	16
Portland Coop	1967	10	27	2	22%	22
Mossa	1979	7	52	7	8%	23
Tepper	1976	10	31	3	16%	11
Nakase	1975	25	430	17	22%	12 head 10 b + t 5 total
Shapiro	1975	Selected	24	—	8%	11
Wilson	1974	16	13	1	23%	10
Feduska	1971	11	16	1	44%	7
Crile	1970	Selected	28	—	N.S.	6
Bowden	1958	26	51	2	31	9
All patients			1034	4†	18†	12†
Present study	1982	6	39	7	18%	18

* = median.
b + t = body and tail.
N.S. = not stated.
† = average.

resected for cure were compared as to the benefit of chemotherapy (Fig. 3).

Discussion

The outlook in carcinoma of the pancreas continues to be grim.[2,5,8,11-13] The increased availability of sophisticated diagnostic equipment does not seem to have resulted in earlier detection of pancreatic carcinoma. Resectability rate in this series was 16.9% compared to a resectability rate of 26.8% in 190 patients with carcinoma of the head of the pancreas seen at our hospital from 1932–1958.[3]

TABLE 6. *Bypass Procedures*

Author	Year	No. Pts.	Mortality	Survival (mean) Months
Herter	1982	152	17%	6
Longemire	1980	103	—	6
Van Heerden	1980	151	6%	6*
Brooks, D.	1980	51	24%	7 6*
Brooks, J.	1975	35	15%	5.8
Knight	1978	155	22%	7
Portland Coop	1967	248	18%	5.4
Moosa	1979	31	6%	6
Nakase	1975	1791	21%	5 -head 3 -b + t 3 -total
Shapiro	1975	24	4%	8
Wilson	1974	80	14%	6
Feduska	1971	60	33%	6
Crile	1970	28	—	8
Bowden	1958	114	57%	5
All Patients		3023	18%†	6†
Present series	1982	76	12%	4

* = median.
b = body.
t = tail.
† = average.

Advances in perioperative care and an aggressive surgical approach do not seem to have produced appreciable gains in survival. Median survival for the entire resected group excluding cystadenocarcinoma is 15 months, little different from that reported by other authors (Table 5). Edis, reviewing the Mayo Clinic experience, found a median survival of 10 months after pancreatic resection excluding inhospital deaths.[5] Longmire reported a 16.2-month mean survival after pancreaticoduodenectomy in a group which included periampullary carcinomas.[11] Herter had similar results in 82 patients undergoing resection with a mean survival of 14 months after pancreaticoduodenectomy and 9 months after total pancreatectomy.[8] The longest mean survival in a large group of patients is that reported by Moosa.[12] For 52 patients resected between 1970 and 1977, mean survival was 23 months. The minimal number of patients resected with curative intent is highlighted in Table 5.

In addition to limited survival, the operative mortality associated with pancreatic resection has been high (Table 5). Nakase, in a review of 430 operative cases in Japan, cites a 22% operative mortality,[13] a figure similar to that in the Mayo Clinic[5] and Columbia series.[8] The 30-day operative mortality in this series was 18% in spite of the limited period of time reviewed.

More extensive procedures in the form of regional pancreatectomy did show an apparent increase in median

survival, but not to a statistically significant degree. It should be emphasized that, in our present experience, the need to resect part of the portal vein was not a limiting factor in what we consider conventional resection. The use of regional pancreatectomy in 36 patients for a variety of neoplastic and non-neoplastic diseases has been reported.[7] The 30-day mortality in that series was 15%.

The benefit in survival seen (median = 9 months) from a postoperative combination of chemotherapy and radiation (n = 11), may have been due to many factors, including good performance status and patient selection. The suggestion may warrant further investigation.

The chemotherapy alone (n = 57) and external beam irradiation alone (n = 10) did not influence survival significantly is consistent with prior reports, but again subject to gross selection bias.

Bypass procedures and biopsy alone were associated with median survivals of 4 and 3 months and operative mortalities of 12% and 15%, reflecting both the advanced disease present in many of these patients and the inadequacy of these procedures as palliation. The group of patients undergoing bypass elsewhere, then biopsy at Memorial, with a median survival of 6 months is a selected group of patients not representative of the biopsy patients as a whole. Proponents of bypass as definitive therapy rather than resection report a median survival of 8 months in selected patients (Table 6).[4]

The technique of interstitial implantation resulted in survival not significantly different from that of resection in this series, in spite of the inclusion of patients with metastatic disease in the implant group. Whittington et al. report a median survival of 1 year in a group of 11 patients treated with I^{125} implant plus PHD (precision high dose) external beam therapy.[19] Shipley and co-authors reported a projected mean survival of 11 months for 12 patients without metastatic disease implanted at the Massachusetts General Hospital.[16] Mortality and morbidity associated with implantation in all reports has been low.[9,16,17] Whether long-term survival in selected patients comparable to that obtained by resection could be achieved by implantation is not evaluable in this retrospective review. The relative freedom from morbidity suggests that a prospective study may be of value.

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