Total Pancreatectomy for Cancer

An appraisal of 65 cases

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Sixty-five patients operated with total pancreatectomy were reviewed with respect to factors influencing operative mortality and morbidity, long-term survival, and metabolic sequelae. The diagnoses were pancreatic cancer in 58 patients, periampullary cancer in three, cancer of the bile duct in two and leiomyosarcoma of the duodenum and cystadenocarcinoma of the pancreas in one patient, respectively. In nine of the 58 cases with cancer of the caput, the histological examination revealed multicentricity of the tumor. In 44%, there were signs of degeneration and fibrosis in the distal part of the gland. Hospital mortality was 23% for the entire series. After 1970 the hospital mortality was 17%, and among patients operated by senior surgeons especially trained in pancreatic surgery, the hospital mortality was 12% during the whole period. The peroperative bilirubin levels seemed to influence survival time. Among 24 patients operated before 1975 in whom the operating surgeon judged the operation as radical, a five year survival of 21% was recorded. In patients without detectable lymph node metastases, the mean survival time was 25 months. The postoperative exocrine insufficiency and diabetes were possible to control. A blood sugar level above 10 micromol/1 was found to significantly decrease the frequency of hypoglycemic attacks. Total pancreatectomy appears to be the surgical procedure preferred when radical treatment is selected.

P ANCREATIC CANCER IS INCREASING in frequency and at the moment surpasses gastric cancer in the United States where 22,000 cases are diagnosed every year. Furthermore the prognosis for patients with this type of cancer is extremely poor. Lately renewed interest in total pancreatectomy has arisen mainly due to dissatisfaction with the results of pancreaticoduodenectomy according to Whipple.[10,22] In a material of 101 patients with ductal carcinoma of the pancreas, Brooks and Culebras[4] have recently reported encouraging results in 17 cases of total pancreatectomy in comparison to 11 Whipple procedures. At the Department of Surgery, University of Lund total pancreatectomy has been the standard procedure since 1959. We felt that it was now time to review our experiences and try to evaluate factors influencing operative mortality and morbidity, long-term survival and metabolic sequelae.

Material

Total pancreatectomy for cancer has been performed in 65 patients. The diagnoses were pancreatic cancer in 58 patients, periampullary cancer in three, cancer of the bile duct in two patients, leiomyosarcoma of the duodenum and cystadenocarcinoma of the pancreas in one patient respectively. The age and sex distribution is shown in Figure 1. For comparison 76 patients operated with bypass procedures were studied.

Pancreatic cancer was classified from Stage I to IV according to Hermreck, Thomas and Friesen:[13] Stage I, local disease only; Stage II, invasion to surrounding tissue (duodenum, portal vein, mesenteric vessels); Stage III, metastases to regional lymph nodes; Stage IV, generalized carcinomas (liver metastases, peritoneal carcinomatosis).

Symptoms

The most common symptoms were jaundice, pain and loss of weight (Table 1). Trosseau's sign was observed in five cases, and in five a palpable mass was found. Twenty-two of the 58 cases (38%) with pancreatic cancer had diabetes mellitus preoperatively.

Diagnostic procedures

Exocrine insufficiency studied by the Lundh test[17] was found in 20 out of 24 investigated cases (83%). The diagnostic procedures furthermore included pancreatic
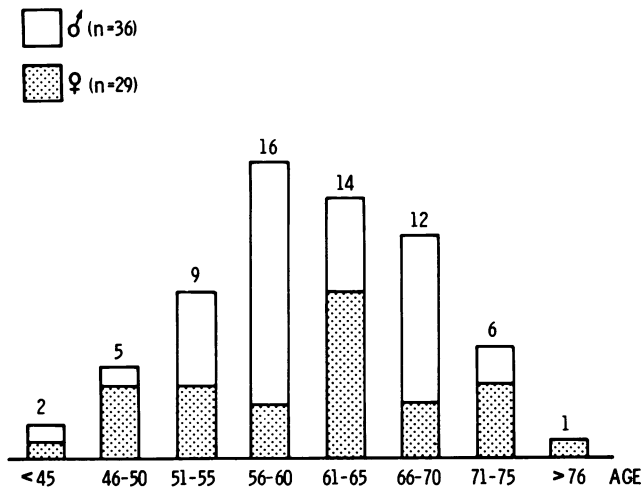
☐ ♂ (n=36)

▨ ♀ (n=29)

FIG. 1. Age and sex distribution among 65 patients pancreatectomized due to cancer.

scanning ([75]Selenium methionine) which was abnormal in 21 of 23 cases (91%) and angiography which revealed signs of pancreatic cancer in 42 of 52 cases (81%). At percutaneous transhepatic cholangiography cancer was suggested in all 26 investigated cases. ERCP was conclusive in the two cases investigated and ultrasonic examination in two of three investigated patients. During the operation fine needle aspiration and/or wedge biopsy was carried out in most cases (Table 3).

Technical remarks

Puestow incisions or left-sided transrectal incisions were used. The Rissler hook (Fig. 2) was found to significantly improve the access to the operation areas.

The great oment, pancreas, duodenum, common bile duct, gallbladder, spleen and at least 50% of the stomach were removed en bloc. A careful lymphadenectomy was always performed along the hepatoduodenal ligament, aorta, and coeliac, hepatic and superior mesenteric arteries.

The hepatico-jejunal anastomosis was done either end-to-end or end-to-side and the gastro-jejunostomy always placed antecolically. In most cases the hepatico-jejunostomy was drained postoperatively by means of a transhepatic catheter which in jaundiced patients was

TABLE 1. *Symptoms and Signs in 65 Patients Pancreatectomized Due to Cancer*

Jaundice	53
Pain	38
Loss of weight	36
Nausea	22
Diabetes	22
Palpable mass	5
Thrombus	5

TABLE 2. *Diagnostic Procedures in 65 Patients Pancreatectomized Due to Cancer*

Pancreatic function test	20/24
Scanning	21/23
Angiography	42/52
PTC (Percutaneous Transhepatic Cholangiography)	26/26
ERCP	2/2
Ultrasound	2/3
Fine needle aspiration	36/38
Wedge biopsy	16/22

generally introduced percutaneously three to five weeks before the operation, and used for preoperative drainage as well.

Pathologic Features

In one case the histological diagnosis was cystadenocarcinoma, in another leimyosarcoma and in all other cases adenocarcinoma. The localizations of the lesions are listed in Table 3. In nine of the 58 cases (16%) of cancer of the caput, tumor cells were found far from the main lesion beyond what would have been the "usual resection line" of a Whipple procedure. In 27 of the 61 cases (44%) with cancer of the head of the pancreas and periampullary region there were signs of degeneration and fibrosis in the distal part of the gland far from the tumor.

Mortality

Death within 30 days after total pancreatectomy was considered a hospital death. As shown in Figure 3 the hospital mortality for the whole material during the 17-year period was 23%. After 1970 the hospital mortality was reduced from 38% (1959–1970) to 17%. In patients operated by senior surgeons especially trained in pancreatic surgery the hospital mortality was 12% (6/48) during the whole period.

Causes of death during the first postoperative month are listed in Table 4. In 6 patients anastomosis insufficiency occurred, in four cardiopulmonary complications, in two intra-abdominal bleeding, in one an attack of hypoglycemia, in one gangrene of the transverse colon and in another hepatic failure.

Complications

Operative complications occurred in 15 patients besides those who succumbed postoperatively (Table 5). In seven cases anastomosis insufficiency was diagnosed, in seven hypoglycemia, in three gastrointestinal bleeding, in two intra-abdominal abscesses and in two septicemia. Intra-abdominal bleeding, hepatic failure and wound rupture occurred in one case each.

TABLE 3. *Location of Lesions in 65 Patients Pancreatectomized Due to Cancer*

Pancreatic caput	58
Pancreatic caput and corpus	1
Periampullary region	3
Common bile duct	2
Duodenum	1

Survival

In Figure 4 the survival rates are described in patients operated before 1975. Among 24 patients in whom the surgeon peroperatively evaluated the operation as radical a five-year-survival of 21% was recorded. The diagnosis of the patients surviving more than five years was pancreatic cancer in two, periampullary cancer in two and cancer of the bile duct in one patient. Twenty-five patients were operated upon with a palliative pancreatectomy *i.e.* the operation was not macroscopically radical. The survival rate in this group did not differ significantly from that of 76 patients with inexstirpable tumors.

In Figure 5 the survival time of patients operated with total pancreatectomy is compared with the 76 patients operated only with a by-pass operation. As expected total pancreatectomy increased the length of survival markedly. This was especially evident in Stage I–II but also–although not as marked–when Stage I, II and III were put together. In Stage III total pancreatectomy did not affect the survival time.

Factors Affecting the Survival Time

The age of the patients, duration of anesthesia, pre-operative diabetes or maximum preoperative bilirubin levels did not affect the mortality rate or length of survival. The peroperative bilirubin levels seemed, however, to correlate with the survival time. In cases with peroperative bilirubin levels below 50 μmol/l mean survival time was three times as long as in patients with levels above 50 μmol/l.

Causes of Late Mortality

As shown in Table 6, 39 patients succumbed during the follow-up period. Among these 31 had recurrency, four died from cardiovascular insufficiency, and two from gastrointestinal bleedings. It is notable that two patients died during hypoglycemic attacks two and 13 months after the operation, respectively. Eleven patients are still alive.

Metabolic sequelae

The diabetes following pancreatectomy was found to have an immediate onset, to be extremely insulin sensi-tive and to have oscillating blood glucose levels. Among our 65 patients three succumbed to hypo-glycemia. When the blood glucose levels were kept above 10 μmol/l, however, the risk for hypoglycemia decreased considerably. Furthermore, effective re-placement therapy seemed to stabilize the blood glu-cose levels. Replacement therapy was often sufficient to counteract steatorrea but we found that the efficiency of different preparations varied widely.[16]

Discussion

The most serious drawback in the management of pancreatic cancer is the lack of methods for making an early diagnosis. In the absence of these possibilities the attention has been drawn to improvement of the surgical methods. Regional pancreatectomy including resection and reconstruction of the portal vein and/or superior mesenteric artery in advanced cases has been
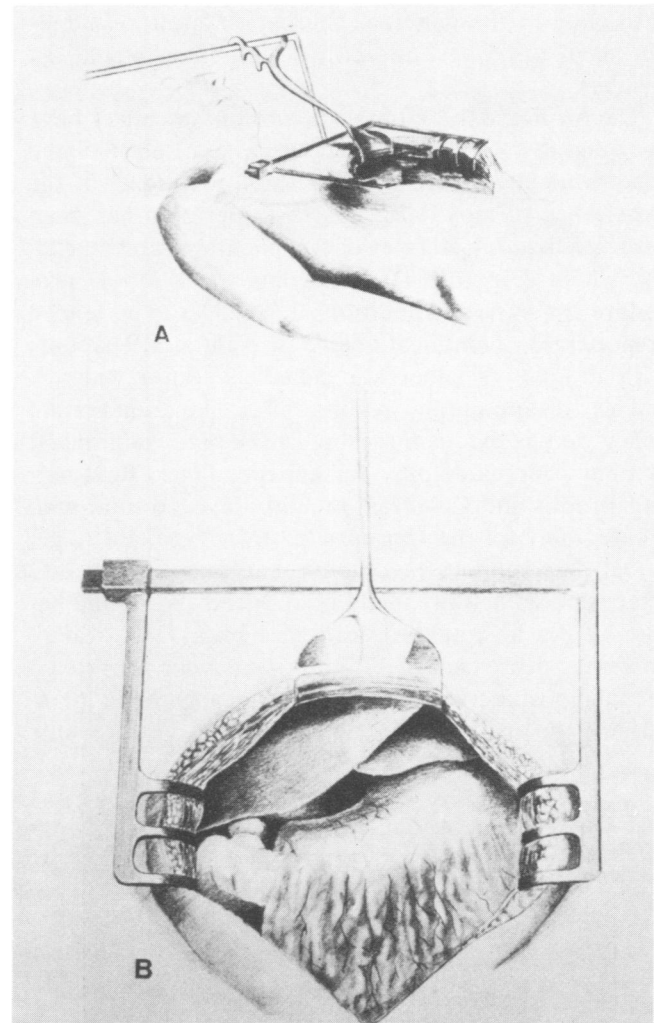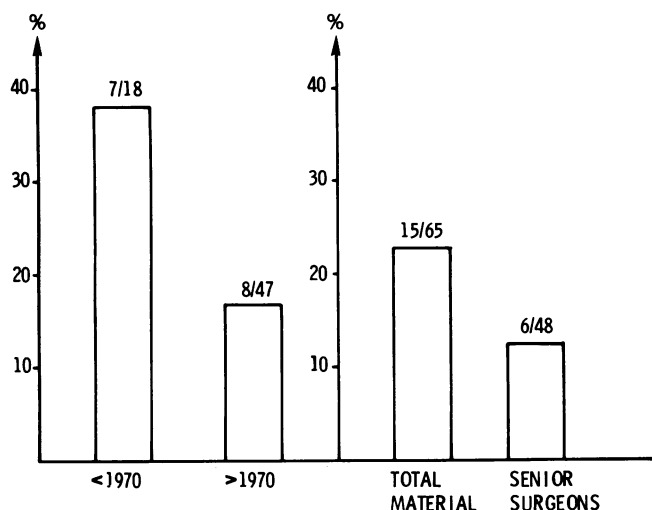

FIG. 2. The Rissler Hook.

FIG. 3. Hospital mortality.

Anastomosis insufficiency	7
Hypoglycemia	7
Gastro-intestinal bleeding	3
Abscess	2
Septicemia	2
Intra-abdominal bleeding	1
Hepatic failure	1
Wound rupture	1

suggested recently.[9,20] Although it is too early to evaluate the results of regional pancreatectomy it has been suggested that once the tumor has spread beyond the substance of the pancreas the patient's interest does not seem to be best served by such superradical aproaches.[5]

The results of the Whipple operation for cancer have been dissatisfactory. Although there have been isolated reports of low mortality after this operation,[1] in the experience of most surgeons this operation has been associated with high rates of complications and mortality.[12,19] Of 239 patients undergoing the Whipple procedure for various conditions 156 (65%) experienced postoperative complications. Only eight of 119 patients with all kinds of pancreatic cancer lived five years.[19]

This disappointing results after pancreaticoduodenectomy is the main reason for the renewed interest in total pancreatectomy for cancer. Thus, ReMine[23] and Brooks and Culebras[4] recently favored total pancreatectomy for the appropriate tumor type and stage.

Our data support the opinion that hospital mortality after pancreatectomy might be reduced. We found before 1970 a hospital mortality as high as 38% which, however, decreased to 17% after this year. Improved pre- and postoperative care, improved anesthesic methods and the organization of special intensive care units

seem to be of great value in this respect. Further we found that the experience of the operating surgeon in pancreatic surgery markedly influenced the operative mortality. This seems to justify the appraisal, operation and follow-up of patients with pancreatic cancer at special centers staffed by personnel with the greatest possible experience and interest in this disease. Thus the findings in this study are contradictary to those of Bloom and Steer[3] who recommended pancreatectomies to be performed at any hospital irrespective of the frequency of pancreatic cancer and of the surgeon's experience in pancreatic surgery.

Brooks and Culebras[4] found a mean survival time of 13 months after the Whipple procedure for pancreatic cancer (Stage I, II). Our data, like those of Brooks and Culebras, indicate encouraging survival rates following total pancreatectomy in Stage I and II and in cases where the surgeon during the operation judged the operation as macroscopically radical. In Stage III, however, the survival time was almost identical to that of patients undergoing only bypass operations. Although long-term survival after total pancreatectomy is encouraging it is obvious that the survival rates can be even further improved by proper selection of the patients for this procedure. The results of the present paper therefore support the opinion of Smith,[25] ReMine[23] and Brooks and Culebras[4] who take a midstream point of view with regard to surgery for this disease.

Postoperative diabetes and postoperative pancreatic insufficiency are often mentioned as arguments against total pancreatectomy. As regards the diabetes, three of the patients in our material succumbed during attacks of hypoglycemia. The cause of the brittle type of diabetes after pancreatectomy is not known. One explanation might be the lack of pancreatic glucagon and an-

TABLE 4. Causes of Hospital Mortality (n = 15) Among 65
Patients Pancreatectomized Due to Cancer

Anastomosis insufficiency	6
Circulatory and pulmonary insufficiency	4
Intra-abdominal bleeding	2
Insulin coma	1
Colon gangrene	1
Hepatic failure	1

TABLE 6. Causes of Late Mortality in 39 Patients Operated
with Total Pancreatectomy Due to Cancer

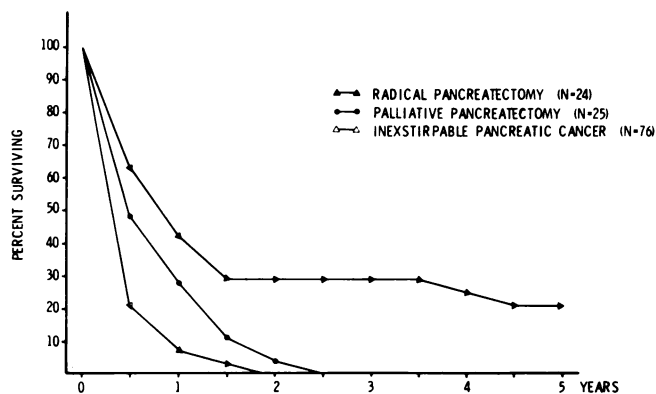|	
Recurrency	31
Cardiovascular insufficiency	4
Gastro-intestinal bleeding	2
Hypoglycemia	2

FIG. 4. Survival after radical and palliative total pancreatectomy compared with survival after by-pass procedures in cases of inextirpable cancer.

other impaired glucose resorption due to insufficient intestinal amylase levels. According to our recent experience effective replacement therapy seems to stabilize the blood glucose levels. When further relatively high blood glucose levels have been allowed in these patients the postoperative diabetes in our care during the last three years has been possible to control. Finally, it must be stated that the total pancreatectomy *per se* causes diabetes in relatively few patients as preoperative diabetes is common (38%) and as postoperative diabetes following the Whipple procedure is no rarity.

The exocrine insufficiency after total pancreatectomy is possible to control by effective replacement therapy although normalization of the fecal fat excretion is never reached.[8] We have compared different preparations and found that only a few of them caused increased intestinal enzyme levels following a test meal.[16] In the present study we found fibrosis and degeneration in the body and tail in 27 of 61 cases of cancer of the head of the pancreas or the periampullary region. As the anastomosis between the pancreatic duct and the intestine in the Whipple procedure is known to close in many cases and as, as mentioned, effective replacement preparations are available today there seems to be no reason from an exocrine point of view to save the body and tail in cases of tumors of the head of the pancreas.

Formerly at our hospital intractable pains were regarded as a reason to perform total pancreatectomy although it was obvious that radicality could not be obtained (Fig. 4). Recently long-term regional intra-arterial infusion of cytostatics (5-FU) has been proved to effectively control the pains in patients with inextirpable pancreatic cancer. Gazet[11] reported a significant relief from pain after intra-arterial 5-FU administration in 23 out of 40 patients. During the past two years we have used such treatment in 20 patients.

In ten of these patients relief from pain was reported. As palliative total pancreatectomy does not increase the survival time and as the effects of regional cytostatic therapy are encouraging we now perform total pancreatectomy only in an attempt to cure the patient. Thus total pancreatectomy is used in cases without tumor growth outside the gland. An exception to this rule is cases where the tumor is slightly attached to the portal vein as such an attachment in a proportion of the cases might be due to pancreatitis.

In the diagnosis of pancreatic cancer in jaundiced patients we highly recommended percutaneous transhepatic cholangiography (PTC), being a method with high diagnostic accuracy and relatively few complications. A further advantage with this method is that a two-step procedure can be avoided by leaving the PTC-catheter for external drainage preoperatively.[26]

Total pancreatectomy seems to be preferable to the Whipple procedure in the treatment of pancreatic cancer for several reasons: 1) the multicentricity[6,14] of the cancer; in our material cancer cells were found far from the caput lesion in nine of 58 cases. 2) Fibrosis and degenerative changes in the distal part of the gland; in 27 of 61 cases of cancer of the head of the pancreas and periampullary region in our study. 3) Elimination of one of the commonest causes of postoperative complications—the pancreatico–jejunal anastomosis. 4) Increased survival rates. 5) As preoperative diabetes is common and as the diabetes frequency following the Whipple procedure is not negligible, the total pancreatectomy *per se* causes diabetes in relatively few patients.[18] 6) The postoperative diabetes and the postoperative pancreatic insufficiency are manageable. 7) The splenectomy and the removal of the tail of the pancreas make the lymphadenectomy more optimal.
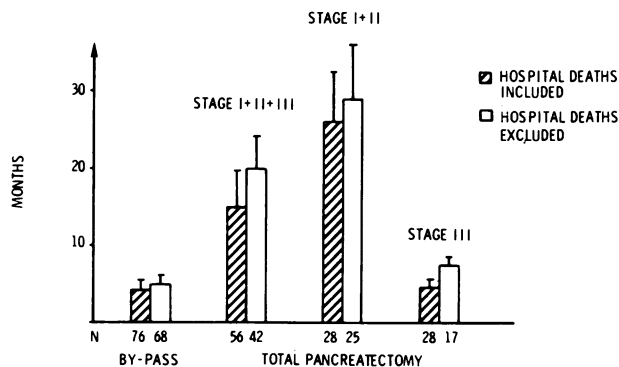

FIG. 5. Survival time after total pancreatectomy in different stages of pancreatic cancer as compared with survival time after by-pass procedures in inextirpable pancreatic cancer. Means ± S.E.M. are given.

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