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Long-term results after pancreas resection for acute necrotizing pancreatitis

This study was designed to investigate the long-term effects of early pancreatic resection for acute necrotizing pancreatitis. During 1973–1978 40 resections were performed in our clinic. Eleven patients died initially (28 per cent). None of the four further deaths was due to pancreatitis or associated disorders. Twenty-four patients were re-examined 5–11 years after resection – one patient refused to participate. Five had not been able to return to work because of severe polyneuropathy; one more had retired because of chronic pancreatitis in the pancreatic remnant. Polyneuropathy was found in five further patients. The reason for this high incidence of polyneuropathy (42 per cent) remains unknown. Eight patients still drank excessive alcohol; three of them had had recurrent pancreatitis and dyspepsia, and insulin requiring diabetes. All but 2(92 per cent) had diabetes, 14 needing insulin – half of them at 6 months to 6 years after the resection. Moreover, 11 patients (46 per cent) suffered from dyspeptic symptoms. The results suggest that because of the high frequency of late complications, in addition to the early complications, early resection of pancreas should be critically re-evaluated as the treatment for acute necrotizing pancreatitis. If resection is used in patients with extreme pancreatic necrosis, careful and continuous postoperative follow-up will be needed.

Keywords: Pancreatitis, acute, necrosis, surgery, resection, late complications

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The basis of treatment of acute necrotizing pancreatitis is supportive intensive care with (a) adequate fluid therapy for treatment and prevention of shock, and renal and metabolic complications; (b) effective total parenteral nutrition to restore a postitive nitrogen balance and (c) artificial ventilation for treatment of lung complications[1]. However, in the most severe forms of pancreatitis these measures will be found insufficient. Two additional methods have been used to prevent the harmful systemic effects of the toxins released from a damaged pancreas: peritoneal lavage and pancreatic resection. Both are superior to conservative treatment alone in achieving immediate clinical improvement[2–4]. The only prospective and randomized study comparing pancreatic resection and peritoneal lavage favoured resection[5]. Despite a number of reports condemning pancreatic resection[1,6–8] the operation may play a role at least in extensive acute pancreatic necrosis[5,9,10]. Several reports have been published on the immediate postoperative course[10–18], but little is known of late sequelae. Moreover, the criteria used in comparing different methods of treatment are mostly based on the immediate mortality and complication rates. We have used early pancreatic resection for acute necrotizing pancreatitis since 1973, and have thus had an opportunity to study the sequelae by re-examining patients still alive over 5 years after the operation.

Patients and methods

Indications for laparotomy have been (a) peritonitis, (b) unclear diagnosis with suspicion of visceral perforation and (c) deterioration of a patient with pancreatitis despite intensive medical treatment. The pancreas has been explored by dividing the gastrocolic ligament and if the organ was dark and clearly necrotic a 'left' resection of pancreas has been performed. The resection has been extended (a) to a level of portal vein, (b) up to the middle of the head of pancreas or (c) has been near-total when only 1–2 cm sickle-shape of pancreatic remnant was left against duodenum. The biliary tract and pancreatic bed were drained[16,19].

During 1973–1978 we performed 40 pancreas resections for acute necrotizing pancreatitis. This comprises about 10 per cent of all patients treated in our hospital for acute pancreatitis[16]. The patients were operated upon between 1 and 17 days after admission to hospital (median 2 days). Eleven patients died during the immediate postoperative period mainly due to sepsis and haemorrhage (28 per cent). Of the 29 surviving patients 4 died later. One patient did not attend for examination. The remaining 24 patients were re-examined during 1984, the follow-up period thus being 5–11 years (median 8 years).

The patients were 33–65 years old (mean 48 years) at the time of re-examination. Of these 24 patients 20 had had pancreatitis of alcoholic origin, 2 of gallstones and 2 of unknown origin. The resection had been up to the level of portal vein in five patients, up to the middle of the head of pancreas in nine and near-total in ten patients.

The specimens were examined by taking at least four transverse sections at regular intervals. Routine paraffin histology was done and the extent of necrosis evaluated in each slice with the mean value being calculated. The results were assessed on a semiquantitative scale of 0–25 per cent, 26–50 per cent, 51–75 per cent and 76–100 per cent. The necrosis was evaluated in the pancreatic parenchyma excluding surrounding fat and connective tissue[19]. The amount of connective tissue in the parenchymal structures was evaluated to assess fibrosis as a possible indication of chronic pancreatitis; clear acinar changes could not be detected because of the necrotizing process. The histological findings are summarized in *Table 1*.

At re-examination the patients' general condition, working capacity and present alcohol consumption were noted. No ethanol concentrations were measured because the Finnish way of drinking is not to use alcohol daily but to use it once or twice a week and very usually very excessively. In addition the following factors were determined: change of weight since operation, abdominal discomfort, food intolerance, frequency of defaecation and the presence of fatty diarrhoea. No exocrine function tests were done. Endocrine function was studied by measuring serum C-peptide levels after a 6-minute glucagon stimulation (1 mg intravenously)[20]. Serum C-peptide is the part of proinsulin which is cleaved out in the formation of the insulin molecule. Unlike insulin, C-peptide passes in an unchanged concentration through the liver into the systemic circulation, where its level directly reflects the amount of insulin released from pancreas. Reference values after glucagon stimulation are over 0·9 nmol/l in a normal population, 0·3–0·8 nmol/l in relative insulin depletion as in adult onset diabetes and below 0·3 nmol/l manifest insulin depletion[20]. An oral glucose tolerance test was carried out on patients who did not require insulin (10 cases) by giving 75 g of glucose in 250 ml of water, the blood glucose level being measured before and 30, 60, 90 and 120 minutes after the test dose[21]. Blood haemoglobin concentration, leucocyte total and differential counts and erythrocyte sedimentation rate were measured. The levels of serum amylase, aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase were also determined.

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Table 1 *Histological findings in the resected specimens from patients with acute necrotizing pancreatitis (24 surviving patients)*

Histological parameter	Number of patients
Presence of fibrosis	7 (29%)
Extent of parenchymal necrosis	
0–25%	14 (58%)
26–50%	2 (8%)
51–75%	2 (8%)
76–100%	6 (25%)

Table 2 *Patients with dyspeptic symptoms after resection of pancreas for acute necrotizing pancreatitis*

Extent of left pancreas resection	Number of patients
Portal vein level	1/5 (20%)
Middle of pancreatic head	4/9 (44%)
Near-total	6/10 (60%)

Table 3 *Glucagon stimulated serum C-peptide level in relation to histological findings and the extent of resection in patients treated with early pancreatic resection for acute necrotizing pancreatitis*

	Serum C-peptide (nmol/l)†	
Presence of fibrosis		
Yes (7)*	0·70 ± 0·14	n.s.
No (17)	0·59 ± 0·12	
Extent of parenchymal necrosis		
0–50% (17)	0·73 ± 0·11	n.s.
51–100% (7)	0·49 ± 0·10	
Extent of left resection		
Portal vein (5)	0·35 ± 0·13	$P < 0·05$
Middle of pancreatic head (9)	0·81 ± 0·07	n.s.
Near-total (10)	0·50 ± 0·17	

* Number of cases in brackets; † mean ± s.e.m.

Results

Four of the initially surviving patients died 1–7 years after the attack of necrotizing pancreatitis. One patient committed suicide, one died of gastric cancer and two developed cardiac infarctions.

Two of the twenty-four patients re-examined had already retired before the attack of necrotizing pancreatitis. The patients were in hospital 19–124 days (mean 49 days) and thereafter on sick leave for 48–235 days (mean 105 days) total working incapability being 67–330 days (mean 154 days). Five of these could not return to work but retired due to a postoperatively developed polyneuropathy (see below). One patient retired 2 years later because of recurrent severe abdominal pains due to chronic pancreatitis in the pancreatic remnant. Two more patients retired, one on account of chronic lumbar back pain and transient radicular neuralgia but without specific findings 4 years later and the other with lumbar vertebral arthrosis and severe hypertension 7 years after pancreatitis. The extent of resection, the extent of parenchymal necrosis or the presence of pancreatic fibrosis in the specimen did not correlate with working capacity.

Eight patients (33 per cent) still continued heavy drinking. They used 250–400 g of ethanol once or twice a week. They were not, however, drunk when re-examined. Three of them had had recurrent attacks of pancreatitis. Only nine patients (38 per cent) had absolutely abstained from alcohol since their necrotizing pancreatitis.

Four patients (17 per cent) had fatty diarhoea daily. One of these was the only one to suffer significant weight-loss during the follow-up period (14 kg in 7 years). The weight of other patients had not changed by more than 5 kg. In addition, 7 patients had dyspeptic symptoms with epigastric fullness and discomfort, while 13 (54 per cent) were without any abdominal complaints. The frequency of abdominal symptoms increased with the extent of the operation (*Table 2*). The extent of pancreatic parenchymal necrosis or the presence of pancreatic fibrosis in the resected specimen were not related to the abdominal symptoms.

Twenty-two of the twenty-four patients (92 per cent) were diabetic. Fourteen of them (58 per cent) needed insulin; in seven cases this had to be started during hospitalization and in seven cases 6 months to 6 years later. Diabetes in two further patients could be controlled with daily doses of 5–10 mg glipizide orally (Mindiab®, Farmitalia Carlo Erba, Milan, Italy) and in six cases only with strict diet. Two patients were well without drugs or food restriction – even their oral glucose tolerance tests were normal, as well as serum C-peptide level after glucagon stimulation (1·09 and 1·62 nmol/l). Interestingly, these patients had undergone subtotal pancreatic resection. *Table 2* shows that no clear correlation could be found between the histology of the specimen or the extent of resection and the glucagon stimulated C-peptide level.

Ten patients (42 per cent) suffered from peripheral polyneuropathy. The symptoms were symmetrical affecting both left and right extremities. Only three patients suffered from numb and clumsy hands with slight motor weakness. One of these three patients and the other seven patients with polyneuropathy had numb lower extremities especially distally to the ankle joints, decreasing sense of touch and muscular weakness especially on dorsiflexion of ankle and toes. In five patients these symptoms so severely interfered with their lives that they had had to retire. One patient was incapable of walking without the help of crutches. These symptoms were manifested during the period of hospitalization or were found within 2 months after discharge. No clear changes (worsening or improvement) occurred in these complaints during the follow-up period. All the patients with polyneuropathy had had pancreatitis of alcoholic origin. The extent of resection, the extent of parenchymal necrosis or the presence of fibrosis in the specimen did not correlate with these neurologic symptoms.

Every patient had erythrocyte sedimentation rate, blood haemoglobin concentration and leucocyte counts within normal limits as well as serum amylases, transaminases (aspartate and alanine amino-) and alkaline phosphatase.

Discussion

During the past two decades pancreas resection has been used for treating acute necrotizing pancreatitis[22] but not without debate. Several authorities prefer conservative treatment, preferably combined with peritoneal lavage[6–8,23]. Some good results have been achieved with lavage, especially during the last few years[2,24–28], though according to the latest controlled trial lavage is unhelpful[29]. On the other hand, enthusiasm for pancreas resection has decreased and even some pioneers in this field have criticized ablative surgery[9].

When treated with resection, acute necrotizing pancreatitis has mortality rates between 13 and 64 per cent, usually just under 40 per cent[4,10–18,30–33]. The present early mortality of 28 per cent is thus comparable. No late deaths occurred due to the original disease. The reasons for the 4 deaths during the follow-up period are very common in an unselected Finnish population and cannot thus be connected with pancreatitis. The patients were incapable of work for about 5 months on average. This is a longer period than seen with elective resection (usually 1–2 months in our clinic).

The frequency and severity of polyneuropathic complaints surprised us. The symptoms and signs resembled those found in alcoholic polyneuropathy. With the lack of such epidemiological studies no comparisons could be made to the frequency of polyneuropathy in patients with similar drinking habits but without pancreatitis; no patient with pancreatitis due

to gallstones or unknown aetiology developed polyneuropathy. The onset of symptoms is found soon after pancreatic resection, which suggests a reason related to the pancreatitis itself or its treatment. During parenteral nutrition, which was given to all of these patients, a substitution of vitamin A, B, C, D, E and K, sodium, potassium, calcium and magnesium as well as chlorides and phosphates was used. Iron, iodine and chromium were not substituted during the years covered by the present material. Of these minerals, chromium deficiency may cause neurological disorders. We checked about 60 case histories of patients treated in the intensive care unit during the same years as the present patients, and none who had long-term parenteral nutrition developed neuropathies. Thus it is the disease itself or its aetiology (alcohol) that stimulates neuropathies. However, the exact mechanism still remains to be verified.

Pancreatic exocrine function or dysfunction caused fewer clinical problems than the endocrine loss. So far the complications of diabetes have not yet appeared. The slow worsening of diabetes in some cases will mean careful follow-up for years. The frequency of diabetes exceeded that in the earlier studies of resection[5,16,34]. This can be easily explained by the longer follow-up period. A lower incidence of diabetes (0–10 per cent) has been found in patients treated with peritoneal lavage[5,28]. When treated conservatively, overt diabetes has been found rarely though half of the patients have had abnormal oral glucose tolerance test[35]. When treated conservatively, both endocrine and exocrine pancreas have shown signs of recovery in a 4 year follow-up[35]. Here the trend was just the opposite.

Interestingly the extent of resection affected the exocrine but not the endocrine function of the pancreas. The histology of the specimen did not correlate with dyspeptic symptoms or the endocrine function. This is understandable because the resection was extended up to the tissue not yet necrotic[16] and it is the pancreatic remnant that remains functioning.

It was depressing to see that despite repeated advice or even orders to give up alcohol, only one-third had done so while one-third still continued to have a heavy alcohol consumption. All the 3 patients here with recurrences had dyspeptic symptoms, one had fatty diarrhoea and all needed insulin for diabetes.

It will be interesting to see whether polyneuropathies, which comprise a major problem in this series, are found in other studies. With the high frequency of late complications described here, early pancreatic resection for acute necrotizing pancreatitis can not be recommended except in the most extreme case.

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