Pancreatic Resection *Versus* Peritoneal Lavage in Acute Necrotizing Pancreatitis

A Prospective Randomized Trial

T. SCHRÖDER,* V. SAINIO,* L. KIVISAARI,† P. PUOLAKKAINEN,* E. KIVILAAKSO,* and M. LEMPINEN*

Twenty-one patients with acute fulminant alcoholic pancreatitis were randomly allocated to either pancreatic resection group (11 patients) or nonoperative peritoneal lavage group (10 patients). Only patients under 50 years were included in the study to minimize the role of other severe disease. These patients represented the most severe cases of acute pancreatitis at our Department, constituting only 2% of all patients with acute pancreatitis during this period. The diagnosis was based on clinical symptoms and on signs indicating severely impaired systemic organ functions. All patients underwent contrast-enhanced computed tomography (CT), which showed contrast enhancement below 30 Hounsfield units. In the operated cases, the diagnosis of necrotizing pancreatitis was verified histologically. All patients with conservative treatment had dark brown fluid at peritoneal puncture. There was a difference (nonsignificant) in mortality (3/11 and 1/10, respectively), complication rate, or in the need of reoperations between the groups. Nonoperative peritoneal lavage was followed with shorter treatment at the intensive care unit (16.2 *versus* 25.9 days, respectively,). The hospital stay also was significantly shorter in the nonoperative group (44.3 *versus* 56.1 days). The results indicate that intensive conservative treatment is justified as an initial therapy even in the most severe cases of acute pancreatitis.

From the Second Department of Surgery and the Department of Diagnostic Radiology,† Helsinki University Central Hospital, Helsinki, Finland*

A CUTE FULMINANT PANCREATITIS is the most severe form of the disease, with a life-threatening course.[1] The management of these patients is still controversial, because no medical treatment has been shown to be beneficial. The role of peritoneal lavage remains debatable,[2-7] and there are no controlled studies to compare intensive conservative and operative treatment. To perform any controlled studies between conservative and operative treatment, reliable diagnostic methods and classification of the severity of the disease are needed. There are several problems involved with multicenter studies, because of variation in cause, treatment protocol, and therapeutic methods that may lead to different results, not necessarily depending on the factors studied. Conversely the number of patients in one unit may be too small for any far-going conclusions. We have performed a single-center prospective randomized study to compare nonoperative peritoneal lavage and early pancreatic resection as the primary treatment for acute fulminant pancreatitis. Only the most severe cases of acute pancreatitis were included in the study and the diagnosis was based on an early fulminant clinical course, contrast-enhanced CT,[8,9] and histologic examination in the operated cases.

Materials and Methods

Twenty-one consecutive patients treated at the Second Department of Surgery, Helsinki University Hospital, between May 24, 1984 and September 16, 1988, were included in the study. All patients filled the entry criteria of fulminant acute pancreatitis. During the study period, a total of 948 patients with acute or acute relapsing pancreatitis were treated at the Department. Blood samples were for the estimation of the modified prognostic signs,[10] and C-reactive protein (CRP) values were taken daily.

Entry Criteria

Patients under 50 years with acute alcoholic pancreatitis were accepted. The diagnosis was based on the clinical symptoms and laboratory findings. When severe pancreatitis was suspected, a contrast-enhanced CT was performed as follows: scanning was done with a Somatom DR2 (Siemens, 8-mm slice thickness, 5 seconds scanning time) scanner. The abdomen was first scanned without intravenous contrast agent to estimate the pancreatic and

extrapancreatic changes and to localize the pancreas. Thereafter a rapid bolus of contrast agent (Conray 400, meglumine iothalamate 1 mL/kg, 400 mgI/kg) was injected intravenously, and the contrast enhancement of the pancreas was recorded by fast sequential exposure at a selected level of the pancreas. The contrast enhancement was measured at three different points in the pancreas and a curve was drawn by computer. Patients with more than four extrapancreatic scores (10) and the contrast enhancement below 30 Hounsfield units were considered candidates for the study. Before the disease was considered fulminant, the patients also had to show early signs of systemic organ failure, such as pulmonary insufficiency (PaO_2 below 60 mmHg), renal failure (urine output below 50 mL/hr, increasing urinary creatinine), shock, or peritonitis. Randomization was performed by the method of supernumerically sealed envelopes. The treatment was either nonoperative peritoneal lavage (n = 10) or subtotal pancreatic resection (n = 11).

Treatment

All patients had nasogastric suction and antibiotics (tobramycin and clindamycin). Fluid resuscitation was performed at the intensive care unit, and all patients had a urinary and central venous catheter and arterial cannula for repeated arterial gas analysis. The patients were intubated and connected to a ventilator when necessary. The gastric pH was kept above 5 with H_2-blockers and, when necessary, gastric installation of antacid was used to prevent stress ulceration.

Peritoneal lavage. In this group (n = 10), the patients were taken into the operating theater, where a peritoneal lavage catheter (Tenchhof) was inserted through a midline minilaparotomy incision under local anesthesia. Peritoneal lavage was started immediately with fluid (Peridialys III, Leiras Pharmaceuticals Inc., Turku, Finland) at a rate of 1000 mL/hr and continued for 8 to 12 days. No antibiotics or antiprotease drugs were added to the fluid. Complications of pancreatitis were treated operatively when necessary.

Pancreatic resection. The patients (n = 11) were operated on immediately after randomization. A midline incision was performed. The omentum was separated from the colon and the left colon was mobilized. Thereafter the splenogastric vessels were ligated and divided

TABLE 2. *Duration of Symptoms Before Randomization*

Duration (hr)	Resection	Lavage
<24	6	6
24–72	2	3
>72	3	1

and the spleen mobilized. The pancreatic capsule was opened on both sides of the pancreas and the pancreas was mobilized and dissected to the right side of the portal vein, where it was divided. A choledochostomy was routinely performed, and a T-tube cholangiography was done. The abdomen, and especially the pancreatic area, were drained using a total of four intra-abdominal drains. The pancreatic bed then was flushed using Peridialys III fluid, 1000 mL/hour for 8 to 12 days. When needed the complications of the disease were treated by secondary operation.

Results

The sex and age distribution of the patients is shown in Table 1. Eight patients in the resection group and nine in the lavage group had their first episode of pancreatitis, and only three (resection) and one (lavage) had relapsing episodes. Four patients in the resection group and in the six patients in the lavage group were admitted from other hospitals. The duration of symptoms before randomization is shown in Table 2.

The prognostic signs and the highest CRP value within 48 hours after admission are shown in Table 3.

CT

The duration of symptoms until the first CT examination was 63.6 and 60.0 hours, respectively. Contrast-enhanced CT was done once in eight patients in the resection group and once in seven in the lavage group. In both groups three patients had pancreatitis of intermediate severity in their first CT, but the second CT, performed 3 to 6 days later, showed progression to necrotizing pancreatitis.

Mortality and Morbidity

The duration of hospital stay was 56.1 days (range, 25 to 165) in the resection group and 44.3 days (range, 15

TABLE 1. *Age and Sex Distribution of the Patients*

Patient Group	Resection	Lavage
M	10	9
F	1	1
Age (yr)	42.1	34.4
Range	26–50	27–48

TABLE 3. *Prognostic Signs and Highest CRP Value Within 48 Hours*

Variable	Resection	Lavage
Prognostic signs	3.6 (range, 0–7)	4.3 (range, 2–8)
CRP value	210 (range, 51–274)	289 (range, 196–320)

CRP, C-reactive protein.

TABLE 4. *Mortality and Complications*

Variable	Resection	Lavage
Mortality	3/11	1/10
Respiratory insufficiency	6/11	4/10
Renal insufficiency	4/11	1/10
Sepsis	4/11	3/10
Abscess	4/11	4/10
Other major complication	5/11	7/10

to 97) in the lavage group. Treatment at the intensive care unit was 25.9 days (range, 7 to 100) in the resection group and 16.2 days (range, 5 to 52) in the lavation group. Three patients in the resection group (27%) and one in the lavage group (10%) died. The cause of death was multiorgan failure in all cases. There were no operative deaths or severe operative complications. A complicated course of the disease was seen in eight patients after resection and in five patients with peritoneal lavage. These results are summarized in Table 4. Reoperations were performed in five resected patients and in five initially nonoperated patients. The reoperations are demonstrated in Table 5.

Discussion

The results of the treatment of acute pancreatitis vary depending of the diagnosis, classification, cause, and management of the disease. Still in most series there remains a small group, 2% to 4% of all patients, who have overwhelmingly severe pancreatitis (*i.e.,* fulminant pancreatitis) and a further 5% or more who will develop local complications (*i.e.,* complicated acute pancreatitis). The present study deals only with the most severe cases. The diagnosis was based on clinical signs of multiorgan failure, contrast-enhanced CT, histology of resected specimens in operatively treated patients, and the presence of dark intraperitoneal fluid in peritoneal puncture.

The management of these patients is still a matter of debate.[11-13] In our department we have a long experience

of early pancreatic resections,[12,14] and since the onset of aggressive treatment the results have significantly improved. In a randomized study, early pancreatic resection proved to be slightly, although not significantly, better than operative peritoneal lavage in the treatment of hemorrhagic pancreatitis[13] in terms of survival. At the time of that study, some encouraging reports were given on nonoperative peritoneal lavage.[6] Based on these facts, we started a prospective, randomized trial to compare early pancreatic resection with nonoperative peritoneal lavage as the primary treatment in acute fulminant disease. Our study was already underway when Mayer et al.[7] reported their multicenter trial comparing nonoperative lavage with conservative treatment without lavage. Their study did not show any benefits of lavage. Conversely it did not have a negative influence on the results. Yet we still believe that a larger single-center study might give some new data in this respect, because we have found that tapping of the hemorrhagic peritoneal fluid often improves respiratory function, and peritoneal lavage may postpone or even dispense with the need for peritoneal or hemodialysis in renal insufficiency. In the present series, late complications were operatively treated when necessary. Five patients in the resection group and four patients in the lavage group were reoperated for necrosis or abscess in the peripancreatic region. Thus early pancreatic resection did not prevent the development of necrosis in the remaining pancreas or in the peripancreatic area. Further resection significantly prolonged the need of treatment at the intensive care unit and hospital stay. Major complications developed at an equal rate in both groups, but the mortality rate was smaller in the lavage group, 3 of 11 and 1 of 10, respectively. The cause of death was multiorgan failure in all patients. There were no operative complications. Postoperatively one patient developed a pancreatic fistula, which was operatively treated by a small pancreatic re-resection and canalization of the area. The number of patients in the present study is small because only the most severe cases of alcoholic pancreatitis with

TABLE 5. *Reoperations in Both Groups*

	Resection			Lavage	
Patient	Cause	No. of Operations	Patient	Cause	No. of Operations
1	Abscess	3	1	Chylothorax pericardiae effusion	2
2	Hematoma and necrosis	2	2	Bleeding ulcer, abscess	3
3	Exploration	1	3	Abscess, colocutaneous fistula	2
4	Abscess, tracheostomy, revision of decubitus, evacuation of hematoma, repair of Virsungian fistula and ventral hernia, neurolysis (ulnar paresis)	6	4	Abscess	3
			5	Abscess, tracheostomy, pyelostomy, closure of colocutaneous fistula, subtotal pancreatectomy	5
5	Abscess, choldochal fistula	2			
Total		14			15

the worst prognosis were included and the including criteria were very strict. We finished the study when we believed that conservative treatment was better, September 9, 1988.

The present results are in agreement with the earlier reports[15] that recommend an initial expectation and interim conservative management, with later surgical intervention when necessary for debridement of necrotic mass or treatment of other complications. We have not performed aspirations of the peripancreatic area for bacterial cultures, as suggested by Beger et al.,[16] but this probably gives further information for adequate timing of surgical intervention.

It is likely that improved results during the past years are basically due to improved initial intensive care, including respiratory support, treatment of renal insufficiency, improved treatment of sepsis, and adequate early fluid resuscitation.[17]

Acknowledgments

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