

Doctor of philosophy (Ph. D.) Thesis

**Modern, complex therapy of the acute
necrotizing pancreatitis**

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INTRODUCTION

The incidence of acute pancreatitis in Hungary is approximately 10-50/ 100 000/year.

On the basis of the clinical course of pancreatic inflammation, the Atlanta Classification differentiates between the mild and severe forms. The development of a fluid collection often accompanies severe pancreatic necrosis. By way of necrosis superinfection, abscess formation may occur.

The mild form of the disease usually heals with conservative therapy, however, the mortality of the severe form is significant even today, and is usually between 10-25%.

Over the past decade significant changes have taken place regarding acute necrotizing pancreatitis and the diagnosis of its complications. In addition to the generally used US (ultrasound) examination, patients with more severe APACHE 8 and a Ranson score higher than 3 undergo contrast CT. The CTSI calculated during CT signifies the severity of the disease.

Recently, a list of measurable parameters (for example, CPR, procalcitonin, TNF α , interleukins, TAP) which well-characterize the severity of the disease and its clinical course is used.

The significance of an exact and fast correct diagnosis is enormous as the therapy of acute necrotizing pancreatitis is considerably different than that of the mild form.

Those patients in whom the severe form is verified in accordance with the atlantic classification must undergo intensive therapy in a hospital setting.

The general „supportive” therapy is made up of complete fasting, the continual suction of gastric contents, pain control, and the decrease of gastric acid production. The fluid-electrolyte levels and acid-base balance of these patients who are often in shock must also be

dealt with. The treatment of ARDS (adult respiratory distress syndrome), MOF (multi-organ failure), and kidney failure are also an important part of the ICU (intensive care unit) therapy.

The aim of further specific therapy is in part to prevent surgery, or as the case may be, to delay it to a later time, and in part to ward off complications (septic necrosis, pancreatic abscess, sepsis).

In the interest of these aims, broad spectrum antibiotic prophylactic therapy against enteric bacteria (Imipenem) is commenced from the time of diagnosis (contrast CT examination).

Nasogastric feeding should be started as soon as possible in order to protect the intestinal villi.

Larger peripancreatic fluid collections should be drained percutaneously.

At the time of delayed surgery, extensive necrectomy must be performed, with exposure of the retroperitoneal space.

Rinsing of the omental bursa in the post-operative period must be employed.

These new therapeutic possibilities fundamentally changed the treatment of acute necrotizing pancreatitis.

AIMS

On the basis of the literature and previous surgical experience, at the 2nd Department of Surgery at DUHSC the answers to the following questions were pursued on the basis of analysis of the patient data treated for acute necrotizing pancreatitis:

1. To what rate does the employed antibiotic prophylaxis aid in the prevention of the development of septic necrosis?

2. How does nasojejunal nutrition prevent catabolism, and does it advantageously affect the patient's recovery?
3. Is it possible to delay surgery with the help of percutaneous peripancreatic drainage, and is surgery possibly avoidable?
4. What are the patient's views of life, and how is their quality of life?

PATIENTS AND METHODS

Between January 1, 1996 and November 30, 1996, at the 2nd Department of General Surgery of the Debrecen University Health Science Center, we treated 61 patients suffering from acute necrotizing pancreatitis who had been diagnosed either using CT examination or by taking a histological sample during surgery.

The average age of the 42 male (68,9%) and 19 female (31,1%) patients was 44,4 (range 25-87 years) years.

The cause of the pancreatic necrosis was alcohol consumption in 42 (68,9%) cases, gallstones in 13 (21,3%) cases, hyperlipidemia in 4 (6,6%) cases, blunt abdominal trauma in 4 (6,6%) cases, ERCP in 3 (4,9%) cases, and was unknown in 2 (3,3%) cases. In seven patients more than one etiological factor was demonstrated to be present.

In 6 patients ischemic heart disease, in 6 obesity, in 4 diabetes mellitus, in 4 hypertonia, in 4 alcoholic hepatopathy, in 2 alcoholic polyneuropathy and one patient each suffered from cardiomyopathy, hyperuricemia, progressive muscular dystrophy and bronchial asthma, which increased the severity of the pancreatic necrosis.

The patients' average APACHE-II and Ranson score results were 23,2 and 3,87, respectively.

All patients' therapy was begun in the ICU. The general supportive therapy consisted of EDA, suction of gastric contents, pharmacological decrease of gastric acid secretion, balancing of fluids and electrolytes, prophylactic broad spectrum antibiotic (Imipenem) therapy, use of respirator or dialysis in necessary cases, and the administration of pentoxifyllin.

In the interests of guaranteeing appropriate caloric administration and preventing septic complications, the patients' nutrition was commenced immediately with the insertion of a nasojejunal tube aided by endoscopy.

In a total of 22 cases (36,1%) percutaneous drainage was performed where larger peripancreatic fluid collections were observed. In four patients more than one collection was drained at one time.

In 69,2% of the patients with pancreatic necrosis of biliary origin, EST was performed.

Of the 61 patients, 49 (80,3%) underwent surgery once, or on more than one occasion. It was only necessary to perform immediate or „early” surgery in 9 (18,4%) cases. In the remaining 40 patients it was possible to delay surgical necrectomy to sometime after the 10th day. The indications for surgery can be observed in Table 1.

Table 1. Indications for primary surgery in 49 operated patients

Surgical indications	Patients	%
Early surgery	9/49	18,4
Acute abdomen	9/49	18,4
Delayed surgery	40/49	81,6
Infected necrosis	30/49	61,2
Non improving conservatively treated MOF	10/49	20,4

During surgery, a curved upper transverse laparotomy was performed. Necrectomy was done in the pancreatic region, and following this the retroperitoneal spaces were explored and, if

necessary, dead tissues were removed from there as well. In cases where the origin was due to gallstones, cholecystectomy was also performed. Drains were inserted into the omental bursa with the purpose of therapeutic rinsing.

During the post-operative period, the closed omental bursa was rinsed daily with 1500-3000 ml of lukewarm physiological sodium solution.

We compared our results to a patient group of 70 individuals treated earlier for ANP and who were homologous to our sample with respect to sex, age and etiology. The difference between the two groups was that in the earlier sample Imipenem prophylaxis, early nasojejunal nutrition and percutaneous peripancreatic drainage were not employed.

The quality of life of 25 patients treated for pancreatic necrosis was examined an average of 37,8 (range 12-62) months following treatment. The SF-36 questionnaire was utilized for this examination, and this was supplemented with questions related to pancreatic function.

RESULTS

Temporary abdominal distension was observed in 15 patients (24,6%) during the course of enteral nutrition, and in 5 patients the nasojejunal tube had to be re-inserted due to „slipping out”.

In 3 patients thoracocentesis was performed due to a larger amount of thoracic fluid, and in 4 patients drainage had to be performed. In all patients the collection of thoracic fluid ceased.

During treatment, the symptoms of MOF appeared in 13 patients, among which 3 recovered. Of the 5 ARDS patients, 4 were cured. In two patients, delirium tremens developed and pharmacological therapy became necessary.

Of the 49 operated patients, 19 (38,8%) had to be re-operated a total of 39 times for the indications which can be seen in Table II. With regard to the total of 61 patients, a total of 1,8 operations was performed.

To demonstrate septic necrosis in 10 patients, the procalcitonin fast test (PCT) was used. In all patients, the results measured were higher than 0,05 ng/ml. Bacterial contamination was verified in all patients.

Of the 22 patients treated with PPD, 7 (31,8%) recovered without surgery. In the remaining 15, it was possible to delay the time of surgery using PPD.

Table II. Indications of 39 re-operations

Surgical indications	Patients	%
Septic focus, abscess, peritonitis <i>Th.: necrectomy, oncotomy, drainage</i>	17/39	43,6
Non improving conservatively treated MOF <i>Th.: necrectomy, drainage</i>	6/39	15,4
Bleeding <i>Th.: ligature, tamponade</i>	8/39	20,5
Colonic necrosis <i>Th.: Hartmann's procedure</i>	4/39	10,3
Gastroi-ntestinal perforation <i>Th.: suture</i>	4/39	10,3

Of the 61 patients, 12 (20,4%) recovered without surgery. Of these patients, 5 took part solely in conservative therapy, while 7 were cured by the effects of conservative and PPD therapy combined.

Of the three patients operated due to bleeding complications, only one recovered.

Of the three patients on which the Hartmann procedure was performed due to complications of the large intestine, one died due to the serious course of their disease.

Of the 61 patients treated for pancreatic necrosis, 51, that is, 83,6% of patients recovered.

The average age of the 10 patients who died was higher (49,9 versus 44,4 years) than that of the entire group. In these patients, the average number of operations was higher (2,6 versus 1,4) than that of the total of operated patients. Among these, repeated operations were performed in three for bleeding complications. In another case a Hartmann resection was performed due to colonic necrosis. The causes of death of the 10 patients can be seen in Table III.

Table III. Causes of death of patients treated for ANP

Cause of death	Age (years)	Sex
MOF	45	male
Sepsis	41	male
ARDS	44	male
Cardiorespiratory insufficiency	72	female
MOF	33	male
Sepsis	34	male
Cardiorespiratory insufficiency	80	female
DIC, hemorrhagic shock	62	male
Sepsis	40	male
DIC, hemorrhagic shock	48	female

In 4 of those who recovered, a pseudocyst developed which did not disappear six weeks following treatment, and for this reason cystogastrostomy, or as the case may be, cystoduodenostomy had to be performed. The average days of nursing care of the total number of patients was 43,3 (14-120) days.

In the 61 patients treated for ANP, the number of immediate or early surgery, and the average number of operations (1,44 versus 1,99) was significantly lower than in the

previously treated 70 patients. The number of days of nursing care were also significantly less. Mortality was 2,5% lower (17,5% versus 19,1%) as well.

Twenty two (88%) of the questionnaires sent to measure late results were evaluated. Forty percent of our patients were treated repeatedly for mild pancreatitis. Three patients reported the development of diabetes mellitus. Weight loss was mentioned by 7 (31,8%) patients, bowel movement difficulties by 9 (40.9%), meteoric abdomen by 13 (59%), nausea by 8 (36%), and periodic vomiting by 6 (27,2%).

Fifty nine percent of the patients proclaimed to be pain-free and 59% also felt physically and spiritually balanced.

Quality of life was considered good, or as the case may be, satisfactory by 77,3% of patients. Those who had problems with digestion, those who underwent weight loss, and women had a worse quality of life.

CONCLUSIONS

- The treatment of acute necrotizing pancreatitis is an interdisciplinary task which can only be conceived with the closely combined work of general and thoracic surgeons, specialists in intensive care, radiologists, gastroenterologists, infectologists, and microbiologists.

- Prognostic systems (Ranson score, APACHE-II scoring systems) play a significant role in the early diagnosis of ANP.

- Contrast CT examination is of decisive significance in the determination of a correct diagnosis, and is capable of demonstrating the necrosis and peripancreatic fluid collections.

- Repeated US helps in the follow-up of patients.

- The supportive therapy of ANP should be started in the ICU and should be complemented with special treatment modalities.
- The procalcitonin fast test (PCT) is useful for the verification of the appearance of complications and aids in the assessment of surgical indications.
- The occurrence of surgery at a time 7-10 days after the commencement of complaints is of great importance in the treatment of ANP.
- The delaying of septic complications decreases the number of immediate or early operations.
- Early nasojejunal nutrition can be used advantageously in the treatment of ANP as this decreases the number of septic complications as well as delaying their development.
- The prophylactic use of broad spectrum antibiotic therapy prevents or delays the development of septic complications.
- Percutaneous drainage of extensive peripancreatic fluid collections can lead to complete recovery without surgery.
- The useful PPD method can prolong the time until surgery and its use decreases the number of operations necessary.
- The framework of therapeutic methods are not alternatives to each other, they can and should be used together.
- The mortality of patients treated for septic pancreatic necrosis is higher (19,2% versus 0%) than those treated for sterile necrosis.
- The application of Imipenem prophylaxis, early nasojejunal nutrition and percutaneous peripancreatic drainage together significantly decreased the number of early operations and nursing care days, and decreased the average number of operations and mortality, although this difference was not significant.

- Under the influence of the complex therapy, it was possible to decrease the mortality of ANP to 16,4%.

PUBLICATION LIST

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Total impact factor: 3,764