Surgical Treatment of Necrotizing Pancreatitis

W. Uhl and M.W. Büchler

Department of Visceral and Transplantation Surgery, University of Berne, Switzerland

(Received June 28, 1996; accepted October 14, 1996)

Surgical treatment in patients with severe acute pancreatitis is still a controver-
sial subject, ranging from sole conservative to an aggressive approach. This article
gives an overview of the literature with regard to indications for surgery, tim-
ing and techniques of operative treatment concepts in severe acute pancreatitis
with special attention to the recommended necrosectomy and closed continuous
lavage of the involved retroperitoneum. Taking into account recent findings
from microbiological data we have developed a new algorithm in patients with
acute pancreatitis. All patients with proven acute necrotizing pancreatitis
receive an antibiotic therapy for 2 weeks beside the intensive care measures. So
far only one third (33 percent) had infected pancreatic necroses in the 3rd week
of the onset of the disease and were managed surgically. The delay resulted in
optimal surgical conditions for necrosectomy and a mortality rate of 9 percent.
This new concept and therapeutic approach with the early suitable antibiotic
therapy in patients with proven necrotizing pancreatitis is recommended to (1)
decrease the infection rate and (2) delay surgical intervention to the 3rd week
of the disease with optimal surgical conditions. It seems that only patients with
proven infected pancreatic necroses are candidates for surgical intervention.

INTRODUCTION

Acute pancreatitis can be classified histologically as interstitial-edematous or necro-
tizing inflammation of the pancreatic gland, and the clinical course in patients with acute
pancreatitis varies from a mild, transitory illness to a rapidly fatal disease [1, 2]. Clinical
and experimental observations have shown that in the early stage of severe acute pancrea-
titis biologically active compounds are released into ascitic fluids and systemic circulation
[3, 4]. Patients who die within the first week due to necrotizing pancreatitis suffer cardio-
vascular, pulmonary, and renal complications which determine the clinical course.
Because of improvement in intensive care therapy, and particularly with the early central
venous pressure-adjusted fluid replacement, hardly any patient with acute pancreatitis dies
within this early phase of the disease. Septic complications prevail in the later stage of
necrotizing pancreatitis, and, nowadays, local and systemic septic complications are the
most frequent cause of death in severe acute pancreatitis [5, 6, 7].

Clinical management of acute pancreatitis is based on the observation that most
patients have a mild, self-limiting disease [8]. However, there are appreciable uncertain-
ties with regard to the therapeutic schedule, since specific and effective pharmacotherapy
is not available, and the effectiveness of surgical treatment of necrotizing pancreatitis has
so far not been substantiated by controlled prospective clinical data. Undoubtedly, in
patients with acute pancreatitis and local septic complications following bacterial infec-
tion of necrotic material, surgical therapy has proved superior to the conservative treat-
ment in the past [8, 9].

*To whom all correspondence should be addressed: Professor M.W. Büchler, M.D., Department for
Visceral and Transplantation Surgery, University Hospital of Berne, CH-3010 Berne, Switzerland.
Tel.: 41-31-632-21-11; Fax: 41-31-632-97-23; E-mail: markus.buechler@insel.ch

Abbreviations: ICU, intensive care unit; CT, computed tomography.
The goals of surgical management of necrotizing pancreatitis are removal of necrotic peri- and intrapancreatic tissue, removal of pancreatogenic exudate out of the lesser sac and the peritoneal cavity with the aim of preventing systemic release of vasoactive and toxic substances. A further very important step of operative therapy is the preservation of intact vital pancreatic tissue. The need for this is based on the experience that, macro-morphologically, the necrotizing process is often represented mainly by fatty tissue necroses in and around the vital exocrine and endocrine pancreatic parenchyma [10, 11].

In the past, a variety of surgical treatment modalities (Table 1) has been propagated, including pancreatic resection [12, 13, 14], peritoneal dialysis [15, 16, 17], multiple tube drainage [18], surgical debridement and suction drainage [9, 19], necrosectomy supplemented with different postoperative treatment concepts, such as continuous local lavage of the necrotic cavities [4, 20], planned, staged relaparotomy [21] or the open packing modality [22], and nonoperative drainage using percutaneous techniques [23, 24]. However, you may have to keep in mind that the results of surgical treatment of necrotizing pancreatitis depend not only on the surgical technique used, but also on the patient group, the severity of concomitant morbidity factors, timing of surgical intervention, extent of the necrotizing process and most important by one the bacterial infection of necroses [5].

| Protocol                                | Remarks                                |
|-----------------------------------------|----------------------------------------|
| Nonoperative drainage procedures        | Not effective enough to remove pancreatic necroses |
| Pancreatic resection                    | Overtreatment                           |
| Peritoneal dialysis                     | No effect on the retroperitoneal process |
| Triple-tube drainage                    |                                        |
| Necrosectomy + closed lesser sac lavage |                                        |
| Necrosectomy + open packing             | In experienced hands good results       |
| Necrosectomy + planned, staged relaparotomy |                        |

**INDICATION FOR SURGICAL MANAGEMENT**

Undoubtedly, the development of pancreatic parenchymal and/or extrapancreatic necrosis is the critical feature determining the prognosis of acute pancreatitis. For an early assessment of the severity of acute pancreatitis, blood parameters that are simple to determine and reliable, such as C-reactive protein, PMN-elastase and serum phospholipase A₂ catalytic activity, have been shown to have high accuracy rates for the detection of pancreatic necrosis in morphologically well-defined patient populations suffering from acute pancreatitis [25, 28]. Today CT scanning [29] can therefore be restricted to cases with high levels of necrosis indicating parameters, in dealing with special questions, such as the evaluation of the intra- and extrapancreatic extent of necrosis.

There is no question that patients with proven severe acute pancreatitis should be treated in an intensive care unit, as the early phase of the disease is characterized by organ complications such as shock, lung and kidney failure caused by the release of vasoactive and toxic substances [3, 8]. A certain percentage of patients with necrotizing pancreatitis...
and organ complications can be successfully treated with intensive care measures alone and surgery can thus be avoided [30]. Intensive care treatment comprises specific forms of therapy to improve pulmonary, renal and cardiocirculatory dysfunction (Table 2).

### Table 2. ICU treatment of severe acute pancreatitis

| Parameters                                    | Treatment                                          |
|-----------------------------------------------|----------------------------------------------------|
| **Pulmonary insufficiency**                   | oxygen supply                                       |
| paO₂ < 70 mm Hg                               | mechanical ventilation                              |
| paO₂ < 60 mm Hg under oxygen                  |                                                    |
| **Renal insufficiency**                       | dopamine (low dose) + diuretics                    |
| serum creatinine > 120 μmol/l, urine volume < 30 ml/h |                                                    |
| BUN > 30 mmol/l or serum creatinine > 400 μmol/l | hemofiltration, hemodialysis                       |
| **Cardiocirculatory dysfunction/shock**       | volume replacement                                  |
| central venous pressure↓, mean arterial pressure < 70 mm Hg | dopamine (high dose)                               |
| systolic blood pressure < 90 mm Hg ≥ 10 min   | Swan-Ganz catheter                                  |
| **Metabolic disorders**                       | insulin                                             |
| hyperglycemia > 11.1 mmol/l, disseminated intravascular coagulation | fresh frozen plasma                               |
| **Sepsis**                                    | antibiotics, surgical intervention (FNP+)          |
| rectal temperature > 38.5°C, leukocytes < 4,000/>12,000/mm³, platelets < 150,000/mm³ |                                                    |
| metabolic acidosis > - 4 mmol/l               |                                                    |
| **Infected pancreatic necrosis**              | surgery (FNP+)                                      |
| fine needle aspiration                        |                                                    |
| **Biliary pancreatitis**                      | papillotomy for impacted stones                    |
| (Bilirubin↑, ASAT↑, Alk. Phosphatase↑)         |                                                    |
| endoscopic retrograde                         |                                                    |
| cholangiography (ERC/ERCP)                    |                                                    |

*FNP+ = Fine needle puncture and proof of infection by Gram stain or culture.

From a clinical point of view, surgical management is indicated in patients with necrotizing pancreatitis who develop signs of septic complications caused by the bacterial infection of necroses, primarily by gram negative germs from the intestinal flora, such as Escherichia coli, Pseudomonas, Streptococcus faecalis, etc. The overall infection rate of the necrotic material is approximately 40 - 70 percent in the first 10 days of the disease [5, 31, 32]. Patients with proven infected necroses (fine needle aspiration guided by imaging procedures) and sepsis are candidates for surgical intervention. Patients with focal or minor necroses have a moderate clinical presentation, and will therefore respond to conservative therapy [30]. Persistent organ failure, such as pulmonary and/or renal insufficiency are indications for surgical therapy, if these complications deteriorate over a period of at least 3 - 5 days of maximum intensive care treatment (Table 3). Assessment of the nonresponse of the local and systemic organ complications to conservative therapy is a very important interdisciplinary step, and forms the basis for the decision to apply surgery.
Table 3. Indications for surgery in severe acute pancreatitis (1995).

| Sepsis                              | Infected pancreatic necrosis (FNP +)* |
|-------------------------------------|---------------------------------------|
| Multiple organ failure              | Nonresponse to maximum ICU care measures |
| (Pulmonary, renal, and cardiocirculatory insufficiency) |                                       |

*FNP+: Fine needle puncture and proof of infection by Gram stain or culture

However, it seems more and more evident that the later indication for surgery in severe acute pancreatitis is necessary in a decreasing minority in the future due to improvements in intensive care therapy and appropriate antibiotic treatment. Taking into account findings from microbiological data [5, 33] and an Italian multicenter study [34] with early antibiotic treatment in proven necrotizing pancreatitis we have developed a new treatment concept (Figure 1). All patients with acute necrotizing pancreatitis are treated in the ICU and receive Imipenem (cilistatin-Na) therapy over at least 14 days. In case of clinical signs of sepsis patients underwent fine needle aspiration with Gram staining and culture. If infected pancreatic necroses are verified by this examination the indication for surgical intervention is given.

Algorithm in Acute Pancreatitis

```
   acute pancreatitis
      ↓
    CRP, LDH, Angio-CT
      ↓
     staging
      ↓
mild/edematous AP
      ↓
   severe/necrotizing AP
      ↓
    ICU
      ↓
   antibiotics
      ↓
   sepsis → FNP +
      ↓
surgery
```

Figure 1. Algorithm for clinical decision-making in acute pancreatitis (AP).

TIMING OF SURGERY

Surgical treatment of necrotizing pancreatitis is based on an exhaustive application of conservative intensive care measures. The timing of surgical intervention in severe acute pancreatitis is still a matter for discussion. The intervention can be performed “early”, that is in the acute phase, if complications arise which make an early operation absolutely necessary [35, 36] or if the diagnosis is still uncertain [37], but the intervention may also be “delayed” [38]. The rationale for the concept of delaying surgical therapy is that a certain amount of time must elapse before demarcation of the necroses occurs. However, the demarcation process cannot yet be evaluated objectively. Furthermore, there are no sufficiently objective data available on the response to conservative therapy and the efficiency of maximum intensive care treatment protocols (e.g., long-term artificial respiration or hemofiltration); however, a minimum period of intensive care therapy should be observed.
Early operative intervention in the first week of the disease is indicated only in proven early bacterial infection of the necroses or in non-responders to ICU therapy. Whenever possible surgical intervention should be delayed in our experience to obtain optimal surgical conditions for necrosectomy.

**TECHNIQUES OF SURGICAL TREATMENT**

Surgical treatment of necrotizing pancreatitis centers on the removal of the necroses and the continuous evacuation of necroses and pancreatic fluids, which may contain bacterial and biologically active material. Thus, peritoneal dialysis [16, 16, 17] alone cannot be considered to be an adequate therapy for acute pancreatitis, as has been demonstrated by Mayer et al. [17]. In this study, hospital mortality was the same in the control group and in the group treated with peritoneal dialysis (27 percent and 28 percent, respectively). The results of current clinical studies show that neither can a significant decrease in organ complications and in the mortality rate be achieved, nor is it to be expected, since the effects of peritoneal lavage are restricted to the abdominal cavity and have no influence on the persistent necrotizing process in the retroperitoneal spaces. This therapeutic approach does not provide for an evacuation of necrotic or bacterially infected tissue.

The exclusively operative implantation of several thick drainage tubes into the lesser sac, in combination with bile duct drainage (cholecystectomy plus T-drainage), gastrostomy and jejunostomy is only partly successful, as necrosectomy is lacking. The aim of this treatment form, known as triple tube drainage [18] and applied mostly in hospitals in the USA from 1970 onwards, is drainage of ascitic fluid from the lesser sac, and inhibition of the exocrine pancreatic secretion. Application of this surgical procedure has shown, however, that it does not lead to a substantial reduction in morbidity or mortality. As necroses and bacterially infected intra-and retropancreatic inflammatory necroses are not removed, it is not surprising that pancreatic abscesses develop at a frequency of up to 40 percent after application of this triple tube drainage [39].

The aim of surgical treatment of necrotizing pancreatitis with the classical resection techniques — hemipancreatectomy, partial or total pancreaticoduodenectomy — is total removal of the diseased pancreatic tissue or the whole organ [13, 14]. Partial or total pancreatico-duodenectomy also requires the removal of healthy organs (duodenum, parts of the stomach, extrapancreatic ducts) and this imposes additional stress on the severely ill patient. Furthermore, surgeons must be aware that in quite a number of cases with necrotizing pancreatitis only the external parts of the pancreas are necrotic, the pancreatic parenchyma around the pancreatic duct being intact. This type, known as superficial necrotizing pancreatitis, can easily be mistaken by the surgeon for total necrosis of the gland, leading to a wrong kind of treatment [10] if he is unaware of the overall morphology, as may be seen from a contrast-enhanced CT-scan of the pancreas. Except for the very rare cases of total pancreatic necrosis, pancreatic resection involves the risk of overtreatment and increases late morbidity and mortality mainly due to endocrine and exocrine insufficiency.

Since lavage or drainage of the retroperitoneum alone have been proved unable to bring down the high morbidity and mortality rates in necrotizing pancreatitis, other surgical principles, combined with debridement of necroses, were introduced. In the Mayo series, published by Becker et al. [40] in 1984, hospital mortality rate of patients with pancreatic abscesses was 40 percent, and the reoperation rate 31 percent. The authors were dissatisfied with these results, feeling that surgical necrosectomy with drainage alone was insufficient to achieve a significant reduction of mortality. Therefore, additional treatment protocols following surgical debridement were developed. These surgical modalities comprise the closed continuous local lavage of necrotic cavities [4, 20], multiple sump
drainage with lavage or planned frequent reoperations with or without a zipper [21] and the application of open packing with multiple redressing [22]. Multiple redressings and frequent reoperation remove the necroses and are carried out in combination with intra-operative lavage. The Boston series, reported by Warshaw [39], showed a significant decrease in hospital mortality in patients with necrotizing pancreatitis or pancreatic abscesses. The overall hospital mortality in the Boston series was 24 percent; in a later period, only 1 out of 19 patients died. In Atlanta, the open packing technique was applied exclusively [22]. Multiple redressings, however, entail many reoperations, a prolonged intensive care phase, and enormous additional stress for the patient. Multiple reoperations are also the cause of an increased occurrence of intestinal fistulae, stomach outlet stenoses, mechanical ileus, incisional hernias, and complications with severe local bleeding.

More recently, interventional techniques for the nonoperative management of necrotizing pancreatitis have been introduced. Good results were reported with large drainage tubes placed percutaneously into the necrotic areas [23, 24], using imaging procedures and avoiding surgical intervention completely. So far experience gained with this new treatment protocol has been limited, however, and this method obviously cannot guarantee total removal of infected necrotic areas. Every second patient in the series of van Sonnenberg et al. [41] had to be operated on after drainage, since the removal of necrotic tissue and the bacterially infected necroses was not complete.

BERNE PROTOCOL OF SURGICAL MANAGEMENT: NECROSECTOMY AND CLOSED CONTINUOUS LAVAGE OF THE RETROPERITONEUM

The recommended standard technique of surgical management of necrotizing pancreatitis is the careful removal of necrotic tissue (necrosectomy) and drainage/lavage of bacterially infected areas. For this postoperative therapeutic concept three comparable procedures are available today, the closed continuous lavage [4, 20], the management of planned, staged relaparotomies [21] and the open packing technique [22]. Hospital mortality in severe acute pancreatitis has been reduced to less than 15 percent with these procedures in experienced hands.

For the treatment of pancreatic necroses we perform necrosectomy supplemented by intraoperative and postoperative closed continuous local lavage of the lesser sac and of the necrotic cavities involved in the retroperitoneum. This enables a non-traumatic and continuous evacuation of devitalized necrotic tissue as well as removal of infected necrotic tissue and biologically active substances from the ongoing necrotizing process after necrosectomy. This procedure has been introduced into our clinical routine with great success.

Necrosectomy and lavage of the retroperitoneum

After opening the abdominal cavity, in most patients via an upper abdominal midline incision, the gastrocolic and duodenocolic ligaments are divided, and the pancreas is exposed. The extent of necroses in the head, body and tail of the gland can easily be assessed and measured. Debridement or necrosectomy, either digital or with the careful use of instruments, permits the exclusive removal of all demarcated devitalized tissue, preserving the vital pancreatic parenchymal tissue. After surgical debridement thorough hemostasis with transfixion stitches, using monofilament suture material is mandatory. It has become clear that it is not necessary to remove every gram of devitalized tissue, because any necrotic or necrotizing tissue is washed out by the lavage fluid later on. After surgical debridement and suturing of bleeding vessels, extensive intraoperative lavage is performed, using equal or more than 6 liters of normal saline solution, in order to clear the surface of the pancreatic and peripancreatic tissues. For postoperative closed continuous
local lavage (the necrotizing process is of course still going on) two or more double-lumen Salem sump tubes (20-24 Ch) and single-lumen silicone rubber tubes (28 - 32 Ch) are inserted, so that at least a regionally restricted lavage is effected. The gastrocolic and duodenocolic ligaments are sutured again to create a closed retroperitoneal lesser sac compartment for the postoperative continuous lavage. In the first seven postoperative days, the amount of lavage fluid is 35-40 liters with rapid reduction during the following days, depending on the clinical course and appearance of the outflowing fluid (in regular intervals measurement of pancreatic enzymes and bacteriological examinations). For the lavage a slightly hyper-osmotic fluid is used, mostly the normal continuous ambulatory peritoneal dialysis solution. The drainage tubes are removed successively within 2-3 weeks.

From November 1993 to September 1995 a total of 64 patients with acute pancreatitis were admitted to our University Hospital of Berne. Due to indicators of necrosis (CRP > 120 mg/l) 32 patients suffered from acute necrotizing pancreatitis proven by contrast-enhanced CT. All patients with proven necrotizing pancreatitis received Imipenem (cilastatin-Na) therapy over at least 14 days in a dosage of 3 x 0.5 g/day. In case of clinical signs of sepsis patients underwent fine needle-aspiration with Gram staining and culture. All patients with acute necrotizing pancreatitis were treated in the ICU with maximum conservative therapy measures. In 11/32 patients (34 percent) infected pancreatic necrosis were found by fine needle aspiration analysis (E. coli, Enterococcus, Staphylococcus aureus, Klebsiella and Candida) after a mean of 21 ± 3.3 days after the onset of the disease leading to a delayed surgical intervention in these patients. The surgical group (n = 11) was treated with necrosectomy and closed retroperitoneal lavage over a mean of 23 ± 7.8 days. One patient developed an abscess which was successfully managed by an interventional approach. No other reinterventions were necessary. The mean total length of hospital stay in sterile and infected acute necrotizing pancreatitis were 25 ± 8.9 and 65 ± 13.5 days, respectively. Mortality rates were 9 percent (1/11) and 0 percent (0/21) in infected and sterile acute necrotizing pancreatitis, respectively.

REFERENCES

1. Warshaw, A.L. A guide to pancreatitis. Compr. Ther. 6:49-55, 1980.
2. Uhl, W., Büchler, M., Bege,r H.G.: A clinicopathological classification of acute pancreatitis; In (eds): Beger, H.G., Büchler, M. W., and Malfertheiner, P. Standards in Pancreatic Surgery. Berling Springer, 1993, pp. 34-43.
3. Beger, H.G., Bittner, R., Büchler, M., Hess, M., and Schmitz, J.E. Hemodynamic data pattern in patients with acute pancreatitis. Gastroenterol. 90:74-79 1986.
4. Beger, H.G., Krautzberger, W., Bittner, R., Block, S., and Büchler, M. Results of surgical treatment of necrotizing pancreatitis. World J. Surg. 9:972-979, 1984.
5. Beger, H.G., Krautzberger, W., Bittner, R., Büchler, M., and Block, S. Bacterial contamination of pancreatic necrosis. A prospective clinical study. Gastroenterol. 91:433-438, 1986.
6. Allardyce, D.B. Incidence of necrotizing pancreatitis and factors related to mortality. Am. J. Surg. 154:295-299, 1987.
7. Buggy, B.P. and Nostrant, T.T. Lethal pancreatitis. Am. J. Gastroenterol. 78:81-814, 1983.
8. Beger, H.G. and Büchler, M. Decision-making in surgical treatment of acute pancreatitis: Operative or conservative management of necrotizing pancreatitis? Theor. Surg. 1:61-68, 1986.
9. Warshaw, A. L. and Jin, G. Improved survival in 45 patients with pancreatic abscess. Ann. Surg. 202:408-417, 1985.
10. Leger, L., Chiche, B., Ghouti, A., and Lovel, A. Pancreatitis aigues, nécrose capsulaire superficielle et atteinte parenchymateuse. J. Chir. (Paris) 115:65-70, 1978.
11. Becker, V. Pathological anatomy and pathogenesis of acute pancreatitis. World J. Surg. 5:303-313, 1981.
12. Edelmann, G. and Boutelier, Ph. Le Traitement des pancréatites aigues nécrosantes par l'ablation chirurgicale précoce des portions nécrosées. Chirurgie 100:155-167, 1974.
13. Alexandre, J.H. and Guerrerir, M.T. Role of total pancreatectomy in the treatment of necrotizing pancreatitis. World J. Surg. 5:369-377, 1981.
14. Hollender, L.F., Meyer, C., Marrie, A., da Costa, S.E., and Castellanos, J.G. Role of surgery in the management of acute pancreatitis. World J. Surg. 5:361-368, 1981.
15. Wall, A.J. Peritoneal dialysis in the treatment of severe acute pancreatitis. Med. J. Aust. 2: 281-287, 1965.
16. Lasson, A., Balldin, G., Genell, S., and Ohlsson, K. Peritoneal lavage in severe acute pancreatitis. Acta. Chir. Scand. 150:479-484, 1984.
17. Mayer, A.D., McMahon, M.J., Corfield, A.P., Cooper, M.J., and Williamson, R.C.N. Controlled clinical trial of peritoneal lavage for the treatment of severe acute pancreatitis. N. Engl. J. Med. 312:399-404, 1985.
18. McCarthy, M.C. and Dickermann, R.M. Surgical management of severe acute pancreatitis. Arch. Surg. 117:476-480, 1982.
19. Watermann, N.G., Walsky, R.S., and Kasdan, M.L. The treatment of acute hemorrhagic pancreatitis by sump drainage. Surg. Gynecol. Obstet. 126:963-974, 1968.
20. Beger, H.G., Büchler, M., Bittner, R., Block, S., Nevalainen, T., and Roscher, R. Necrosectomy and postoperative local lavage in necrotizing pancreatitis. Br. J. Surg. 75:207-221, 1988.
21. Sarr, M.H., Nagorney, D.M., Much, P., et al: Acute necrotizing pancreatitis: Management by planned, staged pancreatic necrosectomy/debridement and delayed primary wound closure over drains. Br. J. Surg. 78:576-581, 1991.
22. Bradley, E.L. III. Management of infected pancreatic necrosis by open drainage. Ann. Surg. 206:542-550, 1987.
23. Gerzof, S.G., Robbins, A.J., Johnson, W.C., Birkett, D. H., and Nabseth, D.C. Percutaneous catheter drainage of abdominal abscess: A five-year experience. N. Engl. J. Med. 305:653-657, 1981.
24. Mueller, P.R., Ferrucci, J.T., Halasz, N.A., and Simeone, J.F. Temporizing effect of percutaneous drainage of complicated abscess in critically ill patients. Am. J. Roentgenol. 142:821-826, 1984.
25. Büchler, M., Malfertheiner, P., Uhl, W., and Beger, H.G. Sensitivity of antiproteases, complement factors and C-reactive protein in detecting pancreatic necrosis. Results of a prospective clinical study. Int. J. Pancreatol. 1:227-235, 1986.
26. Büchler, M., Malfertheiner, P., Schädlich, H., Nevalainen, T.J., Friess, H., and Beger, H.G. Role of phospholipase A, in human acute pancreatitis Gastroenterol. 97:1521-1526, 1989.
27. Uhl, W., Büchler, M., Malfertheiner, P., Martini, M., and Beger, H.G. PMN-elastase in comparison with CRP, antiproteases, and LDH as indicators of necrosis in human acute pancreatitis. Pancreas 6:253259, 1991.
28. Büchler, M. Objectivation of the severity of acute pancreatitis. Hepatogastroenterology 38:101-108, 1991.
29. Block, S., Maier, W., Clausen, C., Bittner, R., Büchler, M., Malfertheiner, P., and Beger, H.G. Identification of pancreas necrosis in severe acute pancreatitis. Gut 27:1035-1042, 1986.
30. Büchler, M., Malfertheiner, P., Uhl, W., and Beger, H.G. Conservative treatment of necrotizing pancreatitis in patients with minor pancreatic necrosis. Pancreas 3:592, 1988.
31. Gerzof, S.G., Banks, P.A., and Robbins, A.H. Role of guided percutaneous aspiration in early diagnosis of pancreatic sepsis. Dig. Dis. Sci. 29:950, 1984.
32. Bassi, C., Falconi, M., Girelli, R., Nifosi, F., Elio, A., Martini, N., and Pederzoli, P. Microbiological findings in severe pancreatitis. Surg. Res. Commun. 5:1-4, 1989.
33. Büchler, M., Malfertheine, P., Friess, H., Isenmann, R., Vanek, E., Grimm, H., Schlegel, P., Friess, T., and Beger, H. Human pancreatic tissue concentration of bactericidal antibiotics. Gastroenterol. 103:1902-1908, 1992.
34. Pederzoli, P., Bassi, C., Vesentini, S., and Campedelli, A. A randomized clinical trial of antibiotic prophylaxis of septic complications in acute necrotizing pancreatitis with imipenem. Surg. Gynecol. Obstet. 176:480-483, 1993.
35. Kivilaakso, E., Fräki, O., Nikki, P., and Lempinen, M. Resection of the pancreas for acute fulminant pancreatitis. Surg. Gynecol. Obstet. 52:493-498, 1981.
36. Poston, G.J. and Williamson, R.C.N. Surgical management of acute pancreatitis. Br. J. Surg. 77:5-12, 1990.
37. Ranson, J.H.C., Rifkind, K.M., Roses, D.F., Fink, S.D., Eng, K., and Spencer, F.C. Prognostic signs and the role of operative management in acute pancreatitis. Surg. Gynecol. Obstet. 139:69-81, 1974.
38. Larvin, M., Chlamers, A.G., Robinson, P.J., and Mc Mahon, M.J. Debridement and closed cavity irrigation for the treatment of pancreatic necrosis. Br. J. Surg. 76:465-471, 1989.
39. Warshaw, A.L. Inflammatory masses following acute pancreatitis. Surg. Clin. North Am. 54:620-637, 1974.
40. Becker, J.M., Pamberton, J.H., Di Magno, E.P., and Jestrup, D.M. Prognostic factors in pancreatic abscess. Surgery 96:455-460, 1984.

41. Van Sonnenberg, E., Wing, V.W., and Casola, G. Temporizing effect of percutaneous drainage of complicated abscesses in critically ill patients. Am. J. Radiol. 142:821-826, 1984.