

The role of surgery in the management of acute pancreatitis

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B Gloor, W Uhl, CA Muller, MW Buchler. The role of surgery in the management of acute pancreatitis. *Can J Gastroenterol* 2000;14(Suppl D):136D-140D. The clinical course of an episode of acute pancreatitis varies from a mild, transitory form to a severe necrotizing form characterized by multisystem organ failure and mortality in 20% to 40% of cases. Mild pancreatitis does not need specialized treatment, and surgery is necessary only to treat underlying mechanical factors such as gallstones or tumours at the papilla of Vater. On the other hand, patients with severe necrotizing pancreatitis need to be identified as early as possible after the onset of symptoms to start intensive care treatment. In this subgroup of patients, approximately 15% to 20% of all patients with acute pancreatitis, stratification according to infection status is crucial. Patients with infected necrosis must undergo surgical intervention, which consists of an organ-preserving necrosectomy followed by postoperative lavage and/or drainage to evacuate necrotic debris, which appears during the further course of the condition. Primary intensive care treatment, including antibiotic treatment, delays the need for surgery in most patients until the third or fourth week after the onset of symptoms. At that time, necrosectomy is technically easier to perform and the bleeding risk is reduced, compared with necrosectomy earlier in the disease course. In patients with sterile necrosis, the available data strongly support a conservative approach (ie, intensive care unit treatment). Surgery is rarely necessary in these patients.

Key Words: *Acute pancreatitis; Infected necrosis; Necrosectomy; Sterile necrosis; Surgery*

Rôle de la chirurgie dans le traitement de la pancréatite aiguë

RÉSUMÉ : L'évolution clinique d'un épisode de pancréatite aiguë varie d'une forme transitoire bénigne à une forme nécrosante grave, caractérisée par une insuffisance plurisystémique, qui se révèle fatale dans 20 à 40 % des cas. La pancréatite bénigne ne requiert aucun traitement spécialisé et la chirurgie ne s'impose que pour traiter les facteurs mécaniques sous-jacents, comme les calculs biliaires ou les tumeurs de la papille de Vater. Par contre, il faut identifier le plus rapidement possible les patients atteints d'une pancréatite nécrosante grave, et ce, dès le déclenchement des symptômes, afin d'instaurer un traitement intensif. Dans ce sous-groupe de patients, représentant environ 15 à 20 % de tous les sujets souffrant de pancréatite aiguë, la stratification selon le stade de l'infection est cruciale. Les patients qui présentent une nécrose infectée doivent subir une intervention chirurgicale qui consiste à enlever la partie nécrosée en préservant l'organe, suivie d'un lavage post-opératoire et (ou) d'un drainage afin d'évacuer tous les débris nécrotiques apparus au cours de la maladie. Chez la plupart des patients, les principaux traitements intensifs, dont l'antibiothérapie, retardent le recours à la chirurgie, jusqu'à la troisième ou la quatrième semaine suivant le déclenchement des symptômes. À ce moment, il est plus facile de procéder au débridement et le risque hémorragique diminue comparativement à une résection des tissus nécrosés effectuée plus tôt au cours de la maladie. Selon les données disponibles, chez les patients qui présentent une nécrose stérile, une approche conservatrice est préférable (traitement à l'unité des soins intensifs). La chirurgie est rarement nécessaire chez ces patients. Une étude portant sur ce type d'approche, chez 74 patients souffrant de pancréatite nécrosante, a estimé la mortalité globale à 8 % (six patients sur 74).

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Acute pancreatitis (AP) is primarily a noninfectious inflammation of the pancreas. Many different etiological factors are known, with gallstones and alcohol overindulgence as the leading causes in the Western world. Patients with AP present with a wide spectrum of clinical signs, ranging from almost imperceptible symptoms to severe disease that results in multisystem organ failure (MSOF) and death. Still, the exact early pathophysiology is largely unknown. Fortunately, in 80% to 85% of AP patients, pancreatic injury consists of an interstitial edema, and AP is mild and subsides spontaneously within one to two weeks. These patients can be managed on a regular ward with supportive care including intravenous fluid replacement, analgesics and restriction of oral intake (1). In the remainder of AP patients, however, the disease may progress to severe necrotizing pancreatitis, a potentially fatal disease characterized by systemic inflammatory response syndrome leading to MSOF (2). Over the past decade, knowledge about AP and its management has increased considerably. Several recently published studies investigating the role of various inflammatory cytokines indicate that the progression to systemic disease evolves according to a predictable scheme (3,4). Improvements to our therapeutic strategies, in both the intensive care unit (ICU) and the operating room, have also contributed to a reduction in morbidity and mortality in patients with severe AP.

This review outlines the indication and the timing of surgery with regard to the etiology, the course and severity of the attack, and the occurrence of local complications in patients with AP.

THE ROLE OF ETIOLOGY IN TREATMENT CONCEPTS

It has been supposed that the differences in clinical course, therapeutic management and outcome of AP are due to underlying etiological factors. It was reported that AP may be more severe when induced by endoscopic retrograde cholangiopancreatography (ERCP). This finding is explained by the fact that in those patients with necrotizing pancreatitis, infection of the necrotic tissue is more likely if the pancreatic duct has been manipulated beforehand. Indeed, patients in the post-ERCP group had a higher rate of infected necrosis as compared with patients with another etiology of acute pancreatitis (5). In another trial, 190 patients with AP were studied prospectively, analyzing the severity of the disease, serum enzymes, indicators of necrosis, systemic complications and mortality with regard to etiology. It was clearly shown that once pathogenetic mechanisms have initiated AP, the course and outcome of the disease are not influenced by the underlying etiological factor (6).

Etiology indicates surgical intervention only in those cases caused by mechanical factors. For example, in patients with an obstructing tumour at the papilla of Vater that is responsible for the AP, endoscopic sphincterotomy and/or temporary, short term plastic stenting may prevent further deterioration, and resection is required once the attack has resolved. Similarly, in pancreas divisum, a papillotomy of the minor papilla may resolve the problem.

GALLSTONE PANCREATITIS

In Western countries, approximately 40% of all cases of AP are associated with gallstones in the gallbladder and the common bile duct. There is strong circumstantial evidence that stones in the distal common duct cause pancreatitis when they temporarily obstruct the pancreatic duct orifice at the ampulla of Vater. Despite many efforts, however, it is still uncertain how these stones actually cause the pancreatic inflammation (7).

Once the diagnosis of gallstone pancreatitis is established, treatment may take one of two directions that are influenced by the clinical course. In almost all patients with mild to moderate disease, treatment consists of the routine medical management of the pancreatitis, which includes withholding oral intake, providing pain relief with analgesics, and restoring fluid and electrolyte losses intravenously. In most cases, the patient responds to this treatment regimen, and vital signs and serum enzyme abnormalities return to normal within one week of hospitalization. At that point, laparoscopic cholecystectomy should be performed and bile duct clearance must be documented. This may be achieved either by an ERCP examination preoperatively or by a laparoscopic common duct exploration during cholecystectomy. If there is doubt whether any stones remained behind in the bile duct at the time of operation, it is mandatory to perform an immediate postoperative endoscopic cholangiography with sphincterotomy and stone extraction (8,9). Performing cholecystectomy during the same hospital stay as the initial surgery has been shown to be safe and well tolerated in these circumstances. It avoids the high probability of recurrent gallstone pancreatitis that accompanied the older practice of 'interval cholecystectomy' (10). Also, the removal of the gallbladder during the same admission reduces the economic cost to society in terms of loss of work time and repeated hospitalization (8).

In patients whose condition deteriorates despite treatment, in those with cholangitis or cholestasis, and in those with severe pancreatitis on admission, one must consider the possibility that a gallstone is impacted at the ampulla of Vater. These patients should be managed in intensive care, with optimal cardiovascular and ventilatory support, and given broad spectrum, intravenous antibiotics. As early as possible, especially in those with concomitant cholangitis, the patient's condition should be stabilized and they should undergo an endoscopic cholangiography, usually combined with a sphincterotomy, to allow the bile duct to be cleared of stones (11-13). No stents should be inserted because of the inherent risk of infection. The patient should be returned to the ICU, and medical management of the patient should be continued, with the expectation of improvement. Similarly, when endoscopic examination reveals no evidence of duct obstruction, medical management should continue. Surgery during the first few days in patients with severe AP, from any cause, is almost never indicated (1,14,15). Theoretically, there is only one exception: an impacted gallstone at the ampulla of Vater that cannot be removed by endoscopy. However, the authors have never been confronted with such a situation.

TABLE 1
Goals of surgical interventions in severe necrotizing acute pancreatitis

Treatment aim	Remarks
Removal of pancreatogenic exudates (peritoneal cavity and lesser sac)	Prevents systemic uptake of vasoactive and toxic substances (mediators of systemic inflammatory response syndrome)
Removal of necrotic tissue (pancreatic necrosis and fatty tissue necrosis)	Is not achieved by nonoperative drainage procedures or by peritoneal dialysis alone
Preservation of intact vital pancreatic tissue	Is easier if surgery is delayed until demarcation of necrosis has occurred (more than two weeks)
Evacuation of further necrotic tissue in the ongoing necrotizing process	Additional operative treatments are mandatory (either lavage or repeated laparotomies)

TABLE 2
Key factors in decision-making for the treatment of acute pancreatitis

Categorization procedure	Tools	Remarks
Stratification according to disease severity	Serum C-reactive protein, contrast enhanced computed tomography, magnetic resonance imaging*	Patient with necrotizing pancreatitis need early intensive care unit treatment including antibiotic treatment
Discrimination between sterile, infected pancreatic and/or peripancreatic necrosis	Computed tomography or ultrasonographically guided fine-needle aspiration, Gram staining and microbiological culture	Infected necrosis should be treated surgically [†]

*Technique is evolving and is not yet widely available or standardized; [†]May also be treated by a drainage procedure, provided the necrotic tissue is well demarcated and can be removed completely

TREATMENT OPTIONS IN PATIENTS WITH ACUTE NECROTIZING PANCREATITIS

Effective treatment of necrotizing pancreatitis requires the removal of necrotic tissue and continuous evacuation of necrotic debris and pancreatic fluids, which may contain bacterial and biologically active mediators. The goals of surgical intervention in severe AP are listed in Table 1. Nonoperative drainage procedures or peritoneal lavage without extensive rinsing of the retroperitoneum usually may not be sufficient to clear the necrotic tissue. Pancreatic resection, on the other hand, completely removes necrotic tissue but always includes the resection of healthy tissue and is thus usually unnecessary overtreatment. High mortality rates and a poor long term prognosis, due to endocrine and exocrine insufficiency in those patients who survive (16-19), preclude routinely applying pancreatic resection to patients with necrotizing pancreatitis.

Several centres in the United States and Germany have reported superior results of organ-preserving procedures compared with series in which pancreatic resection was applied (20-25). Begor et al (24) performed necrosectomy with continuous postoperative local lavage in a prospective study involving 95 patients with necrotizing pancreatitis. Surgery was performed at a median of seven days after the onset of symptoms, and hospital mortality was 8.4% (24). Another institutional study by Bradley (20) reported the results of 71 patients with infected necrosis managed by open drainage with scheduled abdominal re-explorations. Overall mortality in this series was 15%; Bradley currently favours open drainage with contingent secondary closure and high-volume lavage. Another recent series of 64 patients with ne-

crotizing pancreatitis performed debridement, followed by closed packing of the abdominal cavity with stuffed drains, and drainage by closed suction. Patients underwent surgery a median of 31 days after diagnosis, and overall mortality was 6.2% (21). Another study treated patients with necrotizing pancreatitis by performing planned repeated operative necrosectomies and interval abdominal wound closure using zippers. Seventy-two patients were treated with a hospital mortality of 25% (22).

WHICH PATIENTS WITH NECROTIZING PANCREATITIS NEED SURGERY?

The decision to operate on a patient with AP is often difficult and requires mature clinical judgement. Important questions to be answered are whether the patient suffers from mild or (evolving) severe disease, and, if severe disease is present, whether the necrotic tissue is infected (Table 2). Surgery for AP is only appropriate in patients with severe necrotizing disease (1). If the necrotic pancreatic and/or peripancreatic tissue is found to be infected, surgery is accepted worldwide as the treatment of choice. If infected necrotic tissue is not immediately and completely removed, sepsis and septic MSOF almost inevitably occur, leading to a mortality rate of almost 100% (26,27).

In contrast, in patients with sterile necrosis, there is considerable controversy about the indication for and the timing of surgery. Theoretically, necrosectomy eliminates the risk of the necrosis becoming infected. Furthermore, removal of necrotic tissue is thought to prevent or reduce the risk of the systemic spread of inflammatory mediators and toxic substances, allowing for the interruption of the sys-

temic inflammatory process. Unfortunately, in patients with sterile necrosis, early surgical therapy cannot achieve all of these goals. Inflammatory mediators are released at a very early stage of the disease. Cytokine production during severe AP begins shortly after pain onset and peaks within 36 to 48 h (3). Surgery clearly is not the tool to interfere with the stimulation of the various cascade systems contributing to systemic inflammatory response syndrome. The improvement of intensive care management can take a great deal of the credit for the advancement in the overall outcome in patients with severe AP (28). To keep the morbidity of surgical therapy low, surgery should be delayed until three to four weeks after onset of the disease to allow the necrotic tissue to demarcate from vital tissue (1). This approach decreases the risk of bleeding and minimizes the surgery-related loss of vital tissue, which can lead to surgery-induced endocrine and exocrine pancreatic insufficiency (29). Aultman et al (30) recently reviewed their results in seven patients suffering from acute necrotizing pancreatitis. Between 1980 and 1989, multiple operations for debridement and necrosectomy were performed; the mortality rate was 86% (six of seven patients). They then adopted an initial nonoperative approach in 19 patients and the mortality rate dropped to 10.5% (two of 19). Similarly, Paajanen et al (31) analyzed the outcome after different treatments in patients with severe AP. When the operative strategy was early formal resection (n=13), the mortality rate was 54%. With early laparotomy and abdominal lavage (n=15), the mortality rate was 40%, and when the treatment protocol changed to late necrosectomy (n=17), the mortality rate decreased to 24%. A recent report provides mortality rates for patients with sterile necrosis treated either conservatively or surgically in the same institution. Branum et al (32) analyzed their results in 50 patients operated on for necrotizing pancreatitis. This study treated eight patients with sterile necrosis surgically; three (42%) died, leading the authors to the policy that they would be "trying not to operate on [patients with] sterile necrosis". Mier et al (33) prospectively compared early (within 48 to 72 h after onset of pain) and late (at least 12 days after onset of pain) necrosectomy in 36 patients with severe necrotizing pancreatitis, and found late surgical intervention superior to early necrosectomy. Rattner et al (34) stated that early surgical debridement is beneficial even in patients with sterile necrosis. However, the study did not include a control group of patients with sterile necrosis who did not undergo surgery. Thus, their data do not support debridement in all cases of necrotizing pancreatitis. An important drawback of surgery is the risk of secondary infection of previously sterile necrosis. Several authors have reported a considerable infection rate after surgery for sterile necrosis (Table 3) (35-38).

Nevertheless, some patients with sterile necrosis do not improve, despite ICU treatment; some authors advocate surgery in such patients. In a large retrospective series of 172 patients with sterile necrosis, 107 (62%) were managed surgically whereas the remainder were treated conservatively. The surgical group was characterized by higher Ranson and APACHE II scores and C-reactive protein serum

TABLE 3
Postoperative infections of the residual pancreatic tissue and mortality in patients with preoperative sterile necrosis

Author (reference)	Number of patients in study	Number of patients who developed pancreatic infections	Mortality (%)
Smadja and Bismuth (35)	38	14 (37%)	9 (24%)
Widdison et al (36)	130	37 (28%)	22 (17%)
Uomo et al (37)	23	6 (26%)	5 (22%)
Rau et al (38)	18	8 (44%)	6 (33%)

levels on admission. Mortality rates were not statistically different between the two groups, with 13.1% for patients treated surgically and 6.2% for those treated nonsurgically. It was concluded that persistent or increased organ complications, despite intensive care management, indicate surgery for patients with sterile necrosis (39). However, there is no established uniform definition of when a patient should be considered a 'nonresponder' to maximum ICU treatment. Thus, clinicians may see the necessity for surgical intervention at different time points.

In the event of rapidly progressing MSOF in patients with sterile necrosis despite ICU treatment, surgical measures, such as conservative treatment, may not be the solution. These cases are called 'fulminant AP' and, fortunately, are rarely seen; they represent less than 2% of all patients with severe AP (40,41). In a recent report from a tertiary referral centre, three of four patients who died early (ie, within 10 days of the onset of necrotizing pancreatitis) died because of multiorgan failure without apparent bacteremia or sepsis (22). Given the poor outcome after both conservative and surgical therapy in patients deteriorating under maximum ICU treatment, the authors do not know whether and when to operate. Hardly any data are available in the literature for cases of fulminant AP. Again, clear definitions of 'nonresponse' to intensive care therapy are necessary and should be used consistently. In a recent prospective unicentre trial (1), it was shown that patients with sterile pancreatic necrosis could be managed conservatively, yielding a mortality rate of 1.8% (one of 56), whereas patients with infected necrosis undergoing surgery died in 19% of cases (five of 27) (1).

SUMMARY

Stratification of patients according to disease severity early in the disease process allows for the early establishment of ICU treatment, including adequate antibiotic treatment in those suffering from necrotizing pancreatitis. In patients with infected necrosis, surgery is the most effective approach to remove necrotic tissue. An organ-preserving technique is the preferred treatment. There is almost no indication for surgery in patients with sterile necrosis. For the subgroup of patients with sterile necrosis that does not respond to maximum ICU treatment, it is difficult to give evidence-based, medical recommendations. However, there is support for a conservative approach to treating these patients.

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