RECENT ADVANCES IN CLINICAL PRACTICE

MANAGEMENT OF ACUTE PANCREATITIS: FROM SURGERY TO INTERVENTIONAL INTENSIVE CARE

J Werner, S Feuerbach, W Uhl, M W Büchler


In recent years, treatment of severe acute pancreatitis has shifted away from early surgical treatment to aggressive intensive care. While the treatment is conservative in the early phase, surgery might be considered in the later phase of the disease. Surgical debridement is still the “gold standard” for treatment of infected pancreatic and peripancreatic necrosis. Advances in radiological imaging, new developments in interventional radiology, and other minimal access interventions have revolutionised the management of many surgical conditions over the past decades. Several interventional therapy regimens, including endoscopic retrograde cholangio-pancreatography (ERCP) and sphincterotomy, fine needle aspiration for bacteriology (FNAB), percutaneous or endoscopic drainage of peripancreatic fluid collections, pseudocysts, and late abscesses, as well as selective angiography and catheter directed embolisation of acute pancreatitis associated bleeding complications have been well established as diagnostic and therapeutic standards in the management of acute pancreatitis. Secondary to recent technical improvements in interventional therapy and minimally invasive surgery, even infected pancreatic necrosis has successfully been treated in selected patients. However, technical feasibility does not obviate sound clinical judgement. We must be cautious in the application of new technologies in the absence of well designed clinical trials. Thus minimally invasive surgery and interventional therapy for infected necrosis should be limited to clinical trials and specific indications in patients who are critically ill and otherwise unfit for conventional surgery.

INTRODUCTION

The management of acute pancreatitis has been controversial over the past decades, varying between a conservative medical approach on the one hand and an aggressive surgical approach on the other. There has been great improvement in knowledge of the natural course and pathophysiology of acute pancreatitis over the past decade.1–4 The clinical course of acute pancreatitis varies from a mild transitory form to a severe necrotising disease. Most episodes of acute pancreatitis (80%) are mild and self limiting, subsiding spontaneously within 3–5 days. Patients with mild pancreatitis respond well to medical treatment, requiring little more than intravenous fluid resuscitation and analgesia.5 In contrast, severe pancreatitis is defined as pancreatitis associated with organ failure and/or local complications such as necrosis, abscess formation, or pseudocysts. Severe pancreatitis can be observed in 15–20% of all cases.6

In general, severe pancreatitis develops in two phases. The first two weeks after onset of symptoms are characterised by the systemic inflammatory response syndrome (SIRS). Release of proinflammatory mediators is thought to contribute to the pathogenesis of SIRS associated pulmonary, cardiovascular, and renal insufficiency.6–10 In parallel, pancreatic necrosis develops within the first four days after the onset of symptoms to its full extent.11 Although SIRS in the early phase of severe pancreatitis may be found in the absence of significant pancreatic necrosis, the majority of patients with severe early organ dysfunction will have pancreatic necrosis on computed tomography (CT) scan.11–12 Late deterioration of organ dysfunction occurs most commonly in the second to third week after admission,13 and is usually the result of secondary infection of pancreatic or peripancreatic necrosis. Today, infection of pancreatic necrosis is still the major risk factor of sepsis related multiple organ failure and the main life threatening complication of severe acute pancreatitis.14–18 Infection of pancreatic necrosis can be observed in 40–70% of patients with necrotising disease.11 The risk of infection increases with the extent of intra- and extrapancreatic necrosis.15 Management of acute pancreatitis in the two phases of the disease is different. In recent years, treatment of severe acute pancreatitis has shifted away from early surgical debridement/necrosectomy to aggressive intensive medical care.6–15 While the treatment is conservative in the earlier phase of the disease, surgery must be considered in the second phase. Advances in radiological imaging, new developments in interventional radiology, and other minimal access interventions have revolutionised the management of many surgical conditions.
MANAGEMENT OF SEVERE PANCREATITIS

The most significant change in the clinical course of acute pancreatitis over the past decade has been the decrease in overall mortality to approximately 5% and for severe cases to 10–20%. Despite the reduction in overall mortality in severe pancreatitis, the percentage of early mortality from the disease differs from less than 10% to 85% between various centres and countries. This wide variation in early mortality may partially be explained by differences in health systems, socioeconomic issues, patient selection, or referral patterns to special units.

There are two primary objectives in the initial treatment of patients with acute pancreatitis. The first is to provide supportive therapy and to treat specific complications which may occur. The second is to limit both the severity of pancreatic inflammation and necrosis and the systemic inflammatory response by specifically interrupting their pathogenesis. Due to its high mortality, early surgical intervention has no role in these patients.

It is generally accepted that all patients with signs of moderate to severe acute pancreatitis should be admitted to an intensive care unit and referred to specialized centres for maximum supportive care. As complications may develop at any time, frequent reassessment and continuous monitoring is necessary. The most important supportive therapy is adequate and prompt fluid resuscitation with intravenous fluids and supplemental oxygen, with a liberal indication for assisted or controlled ventilation to guarantee optimal oxygen transport.

Infection in pancreatitis is a secondary event. Evidence indicates that bacteria from the gastrointestinal tract translocate into necrotic tissues. As the development of necrosis is currently not preventable, the rationale for the use of prophylactic antibiotics in severe pancreatitis is to prevent infection of pancreatic necrosis. Evidence for the effectiveness of prophylactic antibiotics in the reduction of septic complications and mortality of necrotising pancreatitis has been demonstrated in several randomised controlled trials. To date, inhibition of any known pathogenetic step (that is, octreotide, gabexate mesilate, lexipafant) has not effectively reduced mortality or increased long term survival in severe acute pancreatitis. Thus treatment of acute pancreatitis is still symptomatic, with no specific medication being currently available.

However, a causative therapy exists for severe gall stone pancreatitis with an impacted stone, biliary sepsis, or obstructive jaundice. Although there is no clear consensus on all indications for endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES), it is generally accepted and well established that they are indicated for acute cholangitis and/or obstructive jaundice. Under these conditions ERCP and ES ameliorate symptoms and progression of the disease when applied early. In contrast, open cholecystectomy with supraduodenal bile duct exploration and insertion of a T tube is an unacceptable emergency procedure in patients with severe gall stone associated pancreatitis. While comorbidity is a major determinant of outcome from cholecystectomy, this factor does not apply to the use of ERCP and ES.

"Surgery has little use in the early management of acute pancreatitis. Interventional endoscopy with sphincterotomy is indicated for acute cholangitis and/or obstructive jaundice in gall stone associated acute pancreatitis."

PANCREATIC INFECTION

Today, more patients survive the first phase of severe acute pancreatitis due to improvements in intensive care medicine, thus increasing the risk of later sepsis. There is no doubt that pancreatic infection is the major risk factor in necrotising pancreatitis with regard to morbidity and mortality in the second phase of the disease. The mortality rate for patients with infected pancreatic necrosis is higher than 20%, and up to 80% of fatal outcomes in acute pancreatitis are due to septic complications. In contrast, mortality for sterile necrosis is low and can usually be successfully treated by a conservative approach, although surgery might be required for late complications or persistent severe pancreatitis (table 1). Although reports have shown that some selected cases of acute pancreatitis with positive fine needle aspirates can be treated without surgery, conservative management of patients with infected necrosis and multiple organ failure is associated with mortality rates of up to 100%. There is general consensus that infected necrosis is an indication for surgical treatment or interventional drainage (table 1).

"Infected pancreatic necrosis is an indication for surgery or interventional drainage."

DIAGNOSIS OF INFECTED NECROSIS

Differentiation between sterile and infected necrosis is essential for the management of acute pancreatitis. It requires direct CT evidence of retroperitoneal gas or a positive fine needle aspiration for bacteriology (FNAB) of pancreatic or peripancreatic necrosis. The latter has been established as an accurate, safe, and reliable technique for the identification of infected necrosis. It can be guided by either CT or ultrasonography and is indicated in patients with CT proven necrosis and clinical signs of sepsis.

"Fine needle aspiration for bacteriology (FNAB) is indicated in patients with necrotising pancreatitis and..."

Table 1 Indications for surgical treatment of acute necrotising pancreatitis

| (1) Infected pancreatic necrosis |
| (2) Sterile pancreatic necrosis: |
| (a) Persistent necrotising pancreatitis |
| (b) "Fulminant acute pancreatitis" |
| (3) Complications of acute pancreatitis: |
| For example, bowel perforation, bleeding |

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surgical necrosectomy should be postponed to the third or fourth week after the onset of acute pancreatitis”

**MANAGEMENT OF INFECTED NECROSIS**

With surgical treatment, the mortality rate for patients with infected pancreatic necrosis could be decreased to approximately 20% in various specialised centres. Thus once infection develops, the therapeutic approach must be directed towards mechanical removal of infected necrotic tissue. In recent years, several alternatives to the traditional open surgical approaches have been investigated and the absolute requirement for surgical intervention in infected necrosis has been challenged.

**TIMING OF NECROSECTOMY**

Patients with severe necrotising pancreatitis can progress to a critical condition within a few hours or days after the onset of symptoms. Years ago, early surgical intervention was favoured when systemic organ complications were present. Mortality rates of up to 65% have been described with early surgery in severe pancreatitis, questioning the benefit of surgical intervention within the first days after onset of symptoms. In the only prospective randomised trial comparing early (within 72 hours of symptoms) with late (at least 12 days after onset) pancreatic resection/debridement in patients with severe pancreatitis, mortality rates were 56% and 27%, respectively. The trial was terminated because of concern about the very high mortality of early surgery. Today, there is general agreement that surgery in severe pancreatitis should be performed as late as possible. The third to fourth week after the onset of disease is agreed as providing optimal operative conditions with well demarcated necrotic tissue present, thus limiting the extent of surgery to pure debridement and to only one single intervention. This approach decreases the risk of bleeding, minimises the surgery related loss of vital tissue, and thus reduces endocrine and exocrine pancreatic insufficiency. Only in the case of proven infected necrosis or in the presence of rare complications, such as massive bleeding or bowel perforation, must early surgery be performed.

“Surgical necrosectomy should be postponed to the third or fourth week after the onset of acute pancreatitis”

**TECHNIQUES OF NECROSECTOMY**

**Standard surgical treatment**

The aim is to control the focus so that further complications are avoided by stopping the progress of infection and the release of proinflammatory mediators. A generally agreed principle of surgical management includes the organ preserving approach which involves debridement and maximisation of postoperative removal of retroperitoneal debris and exudate. Four principal methods have been advocated: (1) necrosectomy combined with open packing; (2) planned staged re-laparotomies with repeated lavage; (3) closed continuous lavage of the lesser sac and retroperitoneum; and (4) closed packing.

Necrosectomy has traditionally been undertaken by an open route. Technical details are described elsewhere. Adequate debridement can usually be achieved with a single visit to the operating theatre. While necrosectomy is performed in a more or less identical fashion, the four techniques differ in the way they provide exit channels for further slough and infected debris. In the hands of experienced surgeons, mortality rates below 15% have been described for all four techniques: (1) open packing; (2) repeated laparotomies; (3) closed packing; (4) closed continuous lavage (table 2).

The first two methods, the “open packing” and “planned staged re-laparotomies” have in common that they mandate several re-laparotomies before final closure of the abdomen. Although the incidence of recurrent intra-abdominal sepsis decreased significantly compared with single necrosectomy, postoperative morbidity remained high. There is a positive correlation between repeated surgical interventions and morbidity, including gastrointestinal fistula, stomach outlet stenosis, incisional hernia, and local bleeding. Thus these two procedures should only be considered in the rare case when early debridement is indicated. The other two techniques, necrosectomy and subsequent closed continuous lavage of the lesser sac, are avoided by stopping the progress of infection and the release of proinflammatory mediators. A generally agreed principle of surgical management includes the organ preserving approach which involves debridement and maximisation of postoperative removal of retroperitoneal debris and exudate. Four principal methods have been advocated: (1) necrosectomy combined with open packing; (2) planned staged re-laparotomies with repeated lavage; (3) closed continuous lavage of the lesser sac and retroperitoneum; and (4) closed packing.

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Techniques differ in the way they provide exit channels for further slough and infected debris. In the hands of experienced surgeons, mortality rates below 15% have been described for all four techniques: (1) open packing; (2) repeated laparotomies; (3) closed packing; (4) closed continuous lavage.

**Table 2 Outcome of different techniques for open necrosectomy**

<table>
<thead>
<tr>
<th>Technique</th>
<th>Patients (n)</th>
<th>Patients with infected necrosis (n)</th>
<th>Mortality (%)</th>
<th>Re-laparotomy (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Open packing”</td>
<td>71</td>
<td>71 (100%)</td>
<td>15%</td>
<td>1–5/pt</td>
</tr>
<tr>
<td>Bradley 1993</td>
<td>50</td>
<td>42 (84%)</td>
<td>6 (12%)</td>
<td>2–13/pt</td>
</tr>
<tr>
<td>Dranem 1998</td>
<td>28</td>
<td>28 (100%)</td>
<td>11 (39%)</td>
<td>17 (mean)/pt</td>
</tr>
<tr>
<td>Bosscha 1998</td>
<td>38</td>
<td>–</td>
<td>18 (47%)</td>
<td></td>
</tr>
<tr>
<td>Nieuwenhuis 2003</td>
<td>23</td>
<td>18 (75%)</td>
<td>4 (17%)</td>
<td>2–5/pt</td>
</tr>
<tr>
<td>“Planned re-laparotomies”</td>
<td>72</td>
<td>57 (79%)</td>
<td>18 (25%)</td>
<td>1–7/pt</td>
</tr>
<tr>
<td>Sarr 1991</td>
<td>64</td>
<td>36 (56%)</td>
<td>4 (6%)</td>
<td>11 (17%)</td>
</tr>
<tr>
<td>Tsiotos 1998</td>
<td>95</td>
<td>37 (39%)</td>
<td>8 (8%)</td>
<td>26 (27%)</td>
</tr>
<tr>
<td>“Closed packing”</td>
<td>123</td>
<td>123 (100%)</td>
<td>9 (7%)</td>
<td></td>
</tr>
<tr>
<td>Bruecher 2000</td>
<td>29</td>
<td>27 (93%)</td>
<td>7 (24%)</td>
<td>6 (22%)</td>
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<tr>
<td>Buecher 2001</td>
<td>42</td>
<td>39 (93%)</td>
<td>9 (21%)</td>
<td>7 (17%)</td>
</tr>
<tr>
<td>Nieuwenhuis 2003</td>
<td>21</td>
<td>–</td>
<td>7 (33%)</td>
<td></td>
</tr>
</tbody>
</table>
comparable and thus dependent on the preference of the surgeon. The most commonly adopted approach is that of closed lavage of the debrided cavity, first described by Beger et al in 1982 (figs 1, 2).49

The differing success reported by groups using apparently similar approaches illustrates the difficulties in comparing different or evolving techniques performed around the world. Most techniques have an average mortality of 15–25%. However, mortality in patients with established multiple organ failure is even higher.50 In the absence of randomised trials, it is impossible to determine the hidden effects of factors such as referral pattern, patient selection, comorbidity of patients, presurgical percutaneous management, and indication for surgery within the literature.

``Organ preserving necrosectomy is the surgical technique of choice for treatment of infected pancreatic and peripancreatic necrosis. Morbidity is low in techniques which provide postoperative exit channels for further slough and infected debris (continuous postoperative lavage, closed packing)''

Minimally invasive procedures for debridement of infected necrosis

The high mortality in infected pancreatic necrosis despite surgery has led to the development of several minimally invasive techniques, including radiological, endoscopic, and minimally invasive surgery, as alternative procedures. The rationale is to minimise peri- and postoperative stress in critically ill septic patients suffering from multiorgan failure. By this, the indication for intervention may be extended to patients who are otherwise unfit for surgery, although this has not been evaluated in systematic comparisons. Additionally, these techniques may be used to initially control sepsis and to delay surgery for better demarcation of necrotic tissue.

Percutaneous drainage

Interventional techniques have become increasingly important in recent years due to the now ubiquitous availability of CT scanning and ultrasonography. In 1998, Freeny et al reported for the first time a series of patients with infected acute necrotising pancreatitis who were exclusively drained by CT guided percutaneous catheter drainage.53 Earlier reports covered other infectious complications of acute pancreatitis,54 including infected pancreatic fluid collections,

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Table 3

<table>
<thead>
<tr>
<th>Technique</th>
<th>Patients (n)</th>
<th>Fistulas (pancreatic/enteric)</th>
<th>Haemorrhage</th>
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<tr>
<td>“Open packing”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradley 1993</td>
<td>71</td>
<td>46%</td>
<td>7%</td>
</tr>
<tr>
<td>Branum 1998</td>
<td>50</td>
<td>88% (72%/16%)</td>
<td>–</td>
</tr>
<tr>
<td>Bosscha 1998</td>
<td>28</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>“Planned re-laparotomies”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarr 1991</td>
<td>23</td>
<td>(26%/52%)</td>
<td>26%</td>
</tr>
<tr>
<td>Tsioos 1998</td>
<td>72</td>
<td>(19%/27%)</td>
<td>18%</td>
</tr>
<tr>
<td>“Closed packing”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fernandez-del C 1998</td>
<td>64</td>
<td>(53%/16%)</td>
<td>3%</td>
</tr>
<tr>
<td>“Closed Continuous Lavage”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farkas 1996</td>
<td>123</td>
<td>(13%/1%)</td>
<td>2%</td>
</tr>
<tr>
<td>Büchler 2001</td>
<td>42</td>
<td>19%</td>
<td>5%</td>
</tr>
</tbody>
</table>

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Figure 1  Closed lavage of the debrided cavity. The lesser sac is opened and the greater omentum divided close to the gastroepiploic vessels. Four catheters are inserted (two from each side) for postoperative continuous lavage of the lesser sac. The tip of the catheters are placed at the tail of the pancreas and behind the descending colon, as well as at the head of the gland and behind the ascending colon.

Figure 2  Closed lavage of the debrided cavity. The lesser sac is closed by suturing the greater omentum to the transverse colon for closed postoperative lavage.
pseudocysts, or abscesses, as classified by the International Symposium on Acute Pancreatitis in Atlanta.\(^7\)

Freeny and colleagues\(^53\) developed a technique of percutaneous drainage which not only drained infected necrosis passively but included necrosectomy by adding aggressive irrigation through large bore percutaneous catheters (28 F). Thirty four patients with necrotising pancreatitis and uncontrolled sepsis were treated. An average of three separate catheter sites per patient and four catheter exchanges per patient were necessary for the removal of necrotic material. Pancreatic surgery was avoided in 16 patients (47%), and sepsis was controlled in 25 patients (74%). Although nine of the latter group needed elective surgery, the surgical procedure could be avoided successfully in critically ill patients until stabilisation. Percutaneous drainage was ineffective in nine patients who needed surgery to control sepsis or bleeding (26%). The overall mortality was 12%. These four patients all were critically ill with multiorgan failure, bleeding, or shock. The recipe of success in this series was the commitment of the interventional radiologists (with often daily catheter interventions: 146 catheter exchanges, long duration of drainage of 25–152 days, no complications) and the improvement of the technique which enabled percutaneous necrosectomy. However, patients with central gland necrosis, who often present with disruption of the midsection of the main pancreatic duct resulting in a fistula, responded poorly to percutaneous drainage in the series from Seattle (cure in 4/14 (28%) and control of sepsis in 50%).

The radiological approach was taken to its limits by Gmeinwieser and colleagues.\(^55\) They combined percutaneous retroperitoneal necrosectomy, fragmentation of necrotic pancreatic and peripancreatic tissue with a snare catheter and Dormia baskets, continuous lavage of the cavity, and repeated bronchoscopic visualisation of the cavity with

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**Figure 3** (A–D) Percutaneous necrosectomy in a 50 year old male with necrotising pancreatitis based on alcohol abuse. (A) Computed tomography (CT) scan before therapy revealed an acute necrotising pancreatitis showing typical findings such as peripancreatic fluid collections and pancreatic necrosis. (B) After CT guided placement of three 16 F catheters, contrast media was applied: filling defects represent solid necrotic tissue. In addition, there was a fistula between the necrotic cavity and the stomach, as indicated by contrast media within the stomach. (C) After percutaneous removal of necrotic tissue, the cavity decreased in size and demonstrated only a few small filling defects. (D) CT scan three years after necrosectomy: normal appearance of the pancreatic head. The pancreatic body and tail cannot be delineated, resulting in an anatomical situation such as after left sided surgical pancreatectomy.
percutaneous blockade of a pancreatic duct disruption to successfully treat and avoid surgery in a young man with infected necrosis who strictly declined the surgical procedure recommended.

The same group created a technique to treat patients suffering from infected necrosis, primarily percutaneously, when signs of sepsis were present and intensive care treatment was unsuccessful. Large bore 20–28 F catheters were placed under CT and fluoroscopy guidance, routinely with a retroperitoneal approach from the left side (fig 3). Under fluoroscopy control, necrotic and solid material was fragmented and removed actively with aspiration, snares, and forceps, using peel away sheets (fig 4). Continuous lavage was performed using up to 12 litres of NaCl solution per day and additionally manual aspiration of solid material was performed on a daily basis. Fifty five of 29 patients treated by this method were successfully cured of sepsis and only three needed further elective surgery at a later time. Moreover, the intervention related complication rate was very low (table 4). Nine patients treated by this technique of percutaneous necrosectomy were re-evaluated after a median follow up period of 30 months with respect to quality of life, morphology, as well as endocrine and exocrine pancreatic function. All patients were in good general condition with respect to quality of life. Only 2/9 (22%) patients had moderate to marked changes in morphology, as observed on CT. There was mild to moderate exocrine dysfunction in 5/8 (63%) patients, and severe restriction of exocrine pancreatic function in 2/8 (25%). The oral glucose tolerance test was normal in 3/6 (50%) patients tested. One patient with diabetes in the oral glucose tolerance test had pre-existing type II diabetes requiring insulin therapy since the onset of acute pancreatitis. In 3/9 (33%) patients an oral glucose tolerance test was not performed due to known pre-existing diabetes.

Another series of catheter directed debridement of infected necrosis with a slightly different technique was published by Echenique and colleagues. The catheters used were smaller (14–16 F) but stone retrieval baskets and floppy tipped guidewires were used to break debris into smaller pieces. All 20 patients with infected necrosis were treated successfully with regard to clinical course and lesion appearance. Surgery was avoided, and no death occurred. Seven to 32 (average 17) episodes of debridement were necessary which were started on an inpatient basis and continued on an outpatient basis. Fistulas developed in 10 (50%; three to the bowel, seven to the pancreatic duct). However, all patients included in this trial were haemodynamically stable despite the presence of infected necrosis. Several other series have been published since, reporting different success rates (table 4). Again, it is almost impossible to compare these results with available data on surgical results secondary to the inhomogenity of the patient selection in the different series. Considering the publication bias for so called “negative studies”, it has to be concluded that percutaneous drainage of infected pancreatic necrosis is an option that works in the hands of some very dedicated specialists but is probably not a technique which can be recommended for routine use everywhere. Thus “can do” must be separated from “should do”. It may have a role as a temporary measure to bridge the critical early time after the onset of acute pancreatitis to a later optimal time point for definite intervention.

Endoscopic therapy

Successful endoscopic drainage of symptomatic sterile or infected pancreatic necrosis was reported by Baron et al as early as 1996. The technique applied was originally described for uncomplicated pseudocysts. Several transgastric or transduodenal drainage catheters (10 F) and a naso-pancreatic irrigation tube were endoscopically inserted into the retroperitoneum to perform necrosectomy. Lavage was continued until resolution of the collection. In this first report, 2–4 procedures were required for resolution and the mean duration of catheter placement was 19 days. Successful

Figure 4 (A–C) Necrosis of the pancreatic body and tail: After installation of a 20 F peel away sheet, a snare catheter and a Dormia basket were inserted for necrosectomy (A). After necrosectomy, the necrotic cavity was reduced without any filling defects, which would represent residual necrosis (B). Macroscopic necrotic tissue was removed using the percutaneous technique of necrosectomy (C) described by Mann and colleagues.
removal of necrosis was achieved in over 80% with no mortality. However, the majority of patients treated had no infected necrosis but residual fluid collections with debris. Almost 40% were iatrogenically infected secondarily by endoscopy. Moreover, there were serious complications in 45% of patients, including serious bleeding and gastric perforation (table 4). Additionally, it is worthy of note that up to 60% of those patients successfully drained developed further collections in the subsequent two years. Thus this series confirmed that in the presence of necrosis, drainage must be combined with some form of surgical removal of necrotic material. In 1999, Baron and Morgan described successful placement of percutaneous endoscopic jejunostomy tubes through a PEG tube and subsequently through a transgastric track into the necrotic pancreatic collections for irrigations in two cases. The theoretical advantages of this technique are that on the one hand it avoids the need for uncomfortable nasopancreatic catheters and on the other does not produce the side effects observed after percutaneous drainage, including skin irritation and external pancreatic fistulas.

Although endoscopic drainage might be applicable in some patients with necrotising pancreatitis, only a few centres have used this technique. The results in infected necrosis are only anecdotal, experience with this method is limited, and no interdisciplinary comparative data exist.

Minimally invasive procedures

Advances in laparoscopic technology and instrumentation allow the utilisation of minimally invasive techniques for management in pancreatic disease, and theoretically lessen the surgical stress in the already compromised patient.

As early as 1996, Gagner described laparoscopic debridement and necrosectomy for the treatment of necrotising pancreatitis with three different minimally invasive approaches: (1) transgastric drainage, (2) retrogastric retrocolic debridement, and (3) a full retroperitoneoscopic technique. Since then, many different techniques have been applied by several groups in the search for the easiest access to the necrotic masses in the retroperitoneum.

The laparoscopic assisted transgastric approach is similar to the endoscopic approach and somehow identical to the approach using a PEG to access the stomach. Several case reports exist which describe successful laparoscopic transgastric pancreatic necrosectomy for infected necrosis, suggesting effective debridement and internal drainage in selected patients with this minimally invasive approach. However, no larger series have been reported.

Others have approached the infected necrosis with standard laparoscopy, combining necrosectomy with splenectomy and cholecystectomy. Zhu et al published their experience of the laparoscopic approach in 10 patients. Despite the fact that they included patients with acute haemorrhagic and necrotising pancreatitis without infection which do not need surgical intervention at all, their mortality was 10%. As almost every procedure can be performed laparoscopically, this approach has not been evaluated in any larger study or in prospective randomised trials. A theoretical risk is the spread of infection into the abdominal cavity, further intraoperative difficulties in case of reoperations, and enhanced risk of erosions of the intestinal tract.

In the late 1980s, the open retroperitoneal approach with lumbotomy was used to avoid these drawbacks. This open approach allowed exploration of the pancreas and manual removal of infected necrosis. Although the mortality rates for this retroperitoneal approach compared favourably with historical controls in the same hospitals, the technique has not gained popularity because of its high complication rates. In three series, mortality varied between 20% and 33%, and local complications, mainly enteric fistulas and bleeding, were observed in 20–50%. Fagniez et al reported major morbidity, including enteric fistula (45%), haemorrhage (40%), and colonic necrosis (15%). Thus the main drawback of this open retroperitoneal approach is its narrowness and blindness about the risk of damage to visceral organs and vessels. However, the improvement in CT in recent years with its exact information about the location of necrotic tissue eases the direct retroperitoneal approach. In fact, Nakasaki et al reported successful treatment of infected necrosis by

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### Table 4: Outcome of percutaneous or endoscopic drainage

<table>
<thead>
<tr>
<th>Series</th>
<th>Patients (n)</th>
<th>Infected (%)</th>
<th>Mortality</th>
<th>Successful</th>
<th>Sepsis</th>
<th>Complications</th>
</tr>
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<tbody>
<tr>
<td>Percutaneous drainage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gmeinwieser 1999</td>
<td>29</td>
<td>100%</td>
<td>8 (27%)</td>
<td>20 (69%)</td>
<td>25 (86%)</td>
<td>Fistula 7%</td>
</tr>
<tr>
<td>Freeny 1998</td>
<td>34</td>
<td>100%</td>
<td>4 (12%)</td>
<td>16 (47%)</td>
<td>25 (74%)</td>
<td>None</td>
</tr>
<tr>
<td>Echenique 1998</td>
<td>20</td>
<td>100%</td>
<td>0</td>
<td>20 (100%)</td>
<td>–</td>
<td>Fistula 50%</td>
</tr>
<tr>
<td>Gouzi 1999</td>
<td>32</td>
<td>81%</td>
<td>5 (13%)</td>
<td>21 (65%)</td>
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<td>Fistula 52%</td>
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<td>Szentkereszty 2001</td>
<td>24</td>
<td>7</td>
<td>3 (12.5%)</td>
<td>3 (12.5%)</td>
<td>11 (45%)</td>
<td>None</td>
</tr>
<tr>
<td>Endoscopic drainage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baron 1996</td>
<td>11</td>
<td>27%</td>
<td>0</td>
<td>9 (81%)</td>
<td>–</td>
<td>Bleeding 9%</td>
</tr>
</tbody>
</table>

### Table 5: Outcome of retroperitoneal laparostomy (open surgery)

<table>
<thead>
<tr>
<th>Series</th>
<th>Patients (n)</th>
<th>Infected (%)</th>
<th>Mortality</th>
<th>Complications overall (bleeding/fistulas)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fagniez 1989</td>
<td>40</td>
<td>97%</td>
<td>33%</td>
<td>50% (45%/45%)</td>
</tr>
<tr>
<td>Villazon 1991</td>
<td>18</td>
<td>100%</td>
<td>22%</td>
<td>38% (6%/32%)</td>
</tr>
<tr>
<td>Van Vyve 1993</td>
<td>20 abscess</td>
<td>20%</td>
<td>25% (5%/20%)</td>
<td>65% (12.5%/?)</td>
</tr>
<tr>
<td>Nakasaki 1999</td>
<td>8</td>
<td>100%</td>
<td>25%</td>
<td></td>
</tr>
</tbody>
</table>
retroperitoneal laparotomy even in patients who needed reoperations after laparotomy (table 5).75

In recent years, minimally invasive techniques using the theoretical advantages of retroperitoneal access have been developed.76–79 Most groups which apply minimally invasive surgery for infected necrosis today use this retroperitoneal approach.76–81 Despite small variations in the different techniques applied, they have in common that the infected necrosis of the retroperitoneum is accessed under endoscopic visualisation with subsequent necrosectomy and lavage. The techniques involve either intraoperative dilatation of a percutaneous drain tract which was applied by ultrasound or CT guidance preoperatively, or a direct approach of the infection with a retroperitoneoscope. Depending on the localisation of the infectious tissue, access can be gained from the left or right flank, and over one or more routes. While at first the technique was used in patients after laparotomy as a reoperation, it is now even advocated as a primary approach in some patients.77, 79–80

Several reports show that the technique is applicable and that it can successfully treat some patients with infected necrosis. The results with regard to mortality and morbidity of the larger series published to date are presented in table 6. Morbidity ranges between 30% and 60%, the success rate for complete necrosectomy between 60% and 100%, and the mortality in these series between 0% and 27%. Although this seems to support the view that laparoscopic assisted necrosectomy is a safe alternative to open necrosectomy, the data have to be interpreted with caution. At first it is obvious that a careful case selection was performed in all trials and it is evident that the patients cannot be compared with those treated in series with open surgery. In the largest series published so far,80 only 24 of 45 patients were treated by minimally invasive retroperitoneal pancreatic necrosectomy. In the others, open surgery was performed for the following reasons: lack of a safe retroperitoneal guidewire access route, presence of an additional intra-abdominal complication, extensive paracolic necrotic extension, or multifocal necrotic foci. Moreover, three of the 24 attempted minimally invasive procedures could not be undertaken for technical reasons and another five required open surgery secondary to sepsis or bleeding after the initial minimally invasive approach. Thus only 35% (16 of 45) of all patients treated with necrosectomy were the right candidates for the retroperitoneoscopic technique. Although the proportion of patients undergoing minimally invasive necrosectomy increases over time with experience in the centres,77, 80 many patients will not be treated successfully with this method. An additional disadvantage is the need for repeated procedures and subsequently an increase in the length of hospital stay with the minimally invasive procedures.77–80 This contrasts with the results of the open techniques which imply a postoperative method to continuously remove residual pancreatic necrosis to achieve complete removal of the infected necrosis with a single operation in the majority of cases. During laparoscopic assisted necrosectomy there is significant potential for major injury to intra-abdominal organs or vascular structures. Indeed, all reports show quite a high incidence of serious complications, including fistula (20%–60%) and bleeding (15%), despite the preselection of patients.

Proponents of minimally invasive technologies in this clinical setting cite a desire to minimise the physiological insult in patients who are already critically ill. Although some investigators77, 80 believe that a reduction in the deterioration in organ function and the need for postoperative intensive care management can be observed in patients treated with the minimally invasive techniques, no data exist to clearly demonstrate that minimally invasive procedures are less prone to morbidity than open surgery.

In conclusion, techniques for laparoscopic necrosectomy are still evolving. Safe retroperitoneal access and necrosectomy is possible in patients with infected necrosis but not all patients, depending on size and localisation of the infectious foci, can be treated successfully. No randomised studies exist comparing one management technique with another. All studies reported involved small numbers of patients, were analysed retrospectively, and comprised selected patients with great variation in comorbidities and disease severity. Consequently, it is not possible to draw any conclusions from the literature with regard to the best interventional or surgical approach for infected necrosis. However, in the absence of well designed clinical trials, we must be cautious in the application of new technologies. Technical feasibility does not obviate the need for scientific rigor and sound clinical judgement. Thus today, outside clinical trials, minimally invasive surgery should be limited to specific indications and to those patients who are critically ill and otherwise unfit for conventional surgery.

"Minimally invasive procedures, including percutaneous drainage, endoscopic drainage, or minimally invasive surgery (that is, retroperitoneoscopy) for infected pancreatic necrosis may play a role as a temporary measure to bridge the critical early time after onset of acute pancreatitis to a later optimal time point for definite intervention. Otherwise, they should be limited to specific indications in patients who are critically ill and unfit for conventional surgery or clinical trials."

### Table 6 Outcome of minimally invasive surgery for necrosectomy

<table>
<thead>
<tr>
<th>Series</th>
<th>Patients (n)</th>
<th>Infected</th>
<th>Mortality</th>
<th>Successful</th>
<th>Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhu 200171</td>
<td>10</td>
<td>0%</td>
<td>10%</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>Retropereitoneoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gambiez 199876</td>
<td>20</td>
<td>65%</td>
<td>10%</td>
<td>75%</td>
<td>60%</td>
</tr>
<tr>
<td>Carter 200077</td>
<td>10</td>
<td>100%</td>
<td>20%</td>
<td>80%</td>
<td>28%</td>
</tr>
<tr>
<td>Horvath 200174</td>
<td>6</td>
<td>100%</td>
<td>0%</td>
<td>66%</td>
<td>33%</td>
</tr>
<tr>
<td>Castellanos 200279</td>
<td>15</td>
<td>100%</td>
<td>27%</td>
<td>–</td>
<td>40%</td>
</tr>
<tr>
<td>Connor 200380</td>
<td>24</td>
<td>58%</td>
<td>25%</td>
<td>67%</td>
<td>54%</td>
</tr>
<tr>
<td>Connor 2003 abstr80</td>
<td>36</td>
<td>76%</td>
<td>22%</td>
<td>69%</td>
<td>–</td>
</tr>
</tbody>
</table>

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MANAGEMENT OF COMPLICATIONS IN ACUTE PANCREATITIS

While surgery is still the "gold standard" for the treatment of infected necrosis, interventional intensive care is already established for the management of several complications of severe acute pancreatitis, including pancreatic fluid collections, pseudocysts, abscesses, as well as pancreatic fistulas, biliary leakages, and haemorrhage.

Pancreatic abscess

The most common complication requiring intervention after necrosectomy is a residual or recurrent infection, mostly pancreatic abscesses. These are probably a consequence of limited necrosis with subsequent liquefaction and secondary infection. In general, pancreatic abscesses develop later in the course of disease (usually after five weeks). Due to their less aggressive behaviour and circumscribed localisation, minimally invasive treatment strategies can be easily performed successfully in most of these cases. Percutaneous drainage is the treatment of choice for pancreatic abscesses and it is widely applied.

Pancreatic pseudocysts and fistula

Disruption of the pancreatic duct secondary to pancreatic necrosis leads to an accumulation of pancreatic secretion, defined as pancreatic ascites or pseudocyst, or if it is drained, as a pancreaticojejunostomy. While almost all peripheral leaks will seal in time, central defects will not resolve that easily, especially if there is no internal drainage via the pancreatic duct system into the duodenum. It is estimated that 50% of acute pseudocysts can be managed without any form of intervention, especially small (< 6 cm) and asymptomatic lesions. If leaks do not resolve, the anatomy should be diagnosed with ERCP, magnetic resonance imaging, and fistulography. Today, surgery is rarely indicated but leaks from the tail may need resection while fistulas in the head or body of the pancreas, or those which are embedded in inflammatory mass, should be internalised with an anastomosis to a Roux-en-Y jejunal loop. However, endoscopic stenting or percutaneous drainage have to be recommended in the majority of cases. If communication with the ductal system is present, internal drainage is more effective; if communication is not present percutaneous drainage is indicated. Although the interventional methods are already established for these indications, these alternatives have not been compared with surgery in clinical trials.

Haemorrhage

Life threatening haemorrhage into the gastrointestinal tract, retroperitoneum, or peritoneal cavity complicates acute pancreatitis in only 1–3% of patients. Initiation of early and definitive therapy is the cornerstone of successful management. Pseudoaneurysms occur as a result of necrotic changes in the arterial wall secondary to contact with proteolytic enzymes and other products of pancreatic suppuration. Arterial proximity to a septic or inflammatory focus appears to be the only prerequisite to their formation. Selective angiography is the diagnostic "gold standard" for localising active bleeding due to vascular necrosis. While management of vascular complications had to be managed by surgical means in the past, the angiographic approach by catheter directed embolisation can be life saving.

Haemorrhage is a rare complication of acute pancreatitis and includes bleeding pseudoaneurysms, diffuse bleeding from necrosis, and haemorrhagic pseudocysts. Several reports from recent years demonstrated that mesenteric angiography can detect the bleeding site in approximately 80% of cases and arterial embolisation can achieve definite haemostasis in 35–50%, and helps stabilise critically ill patients to permit elective surgery in another 10–20%. However, failure to correct the frequently associated infected pancreatic necrosis will lead to a high rate of recurrent haemorrhage. When emergency surgical intervention for haemorrhage is necessary, surgical ligation is sometimes impossible, and packing of the wound cavity may be necessary.

"Interventional treatment is well established as the standard treatment for complications of acute pancreatitis, including peripancreatic fluid collections, pseudocysts, and late abscesses, as well as selective angiography and catheter directed embolisation of acute pancreatitis associated bleeding complications"

PROPHYLAXIS OF RECURRENT PANCREATITIS

Recurrence of acute pancreatitis in patients with gall stones has been reported in 29–63% of cases if the patient is discharged from hospital without additional treatment. The rationale for cholecystectomy and clearance of the main bile duct in these patients is to prevent potentially avoidable recurrent attacks. Today, laparoscopic cholecystectomy is recommended during the same hospital stay for mild disease and should be delayed until sufficient resolution of the inflammatory response and clinical recovery in severe pancreatitis. In patients who are unfit to undergo surgery, elective endoscopic sphincterotomy is an established and effective alternative to cholecystectomy to lower the risk of recurrent acute pancreatitis.

"While laparoscopic cholecystectomy is the "gold standard" to avoid recurrence in patients with gall stone associated pancreatitis, ERCP and sphincterotomy are accepted alternatives in patients who are unfit for surgery"

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Conflict of interest: None declared.

REFERENCES


EDITOR’S QUIZ: GI SNAPSHOT

Answer

From question on page 418

Radiographic enteroclysis showed multiple large duodenal and jejunoileal diverticula (fig 1).

The proximal small intestine was found to have normal resorptive capacities suggested by a normal d-xylose test while intestinal bacterial overgrowth was indicated by a H₂ breath test with glucose. Extended diverticulosis of the small bowel with subsequent bacterial overgrowth was assumed to be the most likely cause of the patient’s malabsorption and weight loss. Bacterial overgrowth of the small intestine was treated with a rotating antibiotic regimen of ciprofloxacin for 10 days, metronidazole for a further 10 days, followed by tetracycline for 10 days. Simultaneously, a high calorie diet and vitamin B₁₂ supplementation was initiated. The therapy was well tolerated and the patient gained 10 kg in weight within six weeks. A follow up H₂ breath test two weeks after completing the rotating antibiotic regimen was also normal, thus indicating that bacterial overgrowth had been successfully treated. Subsequently, the patient reached his initial body weight and maintained a normal weight for more than 18 months.

Small bowel diverticulosis is rare, and in most cases an asymptomatic course of disease is observed. The maximal incidence of small intestinal diverticula is observed in the duodenum, followed by the proximal jejunum with decreasing prevalence in the distal small bowel. Assessment by enteroclysis has shown an incidence of approximately 2.0–2.3%; in autopsy series the incidence has ranged from 0.06% to 4.6%. Both duodenal and jejunoileal diverticula are thought to be acquired pulsion diverticula containing outpouchings of mucosa and submucosa. Due to the relative stasis of the intestinal contents within the diverticulum, bacterial overgrowth, malabsorption, steatorrhoea, and megaloblastic anaemia may develop. Other complications of diverticulosis of the small bowel may include abdominal pain, bleeding, diverticulitis, perforation, abscess formation, obstruction, and bile stasis.

Excluding patients with acute abdomen who need surgical intervention, the treatment of symptomatic diverticulosis should aim to correct the cause of the malabsorption by eliminating bacterial overgrowth with cyclic use of broad spectrum antibiotics. The use of antispasmodics, antacids, analgesics, and vitamin B₁₂ supplementation may result in symptomatic improvement in most patients. Resection of the involved segment of the small bowel should be considered only as a last resort and should be reserved for those patients not responding to conservative treatment.

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REFERENCES


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