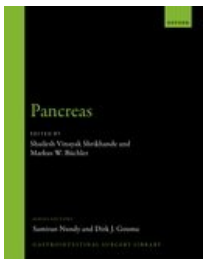

Pancreas

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CHAPTER

3 Management of Acute Necrotizing Pancreatitis C3

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Abstract

Necrotizing pancreatitis represents the most severe manifestation of acute pancreatitis, affecting 10–15% of those diagnosed with the disease. Necrotizing pancreatitis is a complex and heterogeneous disease process with a variable, but generally protracted course, often lasting 5–6 months in time. The focus of this chapter is on therapy for necrotizing pancreatitis, which has evolved substantially over the past decade. Minimally invasive treatments such as percutaneous, endoscopic, and minimally invasive surgical approaches have become first-line therapy; these techniques are often used in a combined, complementary fashion. Optimal treatment of necrotizing pancreatitis patients requires an invested clinician to help coordinate the multidisciplinary effort, and long-term follow-up is mandatory to detect late-developing complications of the disease. Improved understanding of the natural history of necrotizing pancreatitis, in conjunction with advances in critical care and expanding, appropriate application of minimally invasive therapeutic techniques, has led to improved outcomes overall in this patient population. Nevertheless, a critical deficit remains in incomplete knowledge of the fundamental underlying disease processes; current therapy is directed towards treating complications of the disease, and not the underlying disease itself.

Keywords: necrosis, necrotizing pancreatitis, step-up, endoscopic debridement, walled-off necrosis, debridement, acute pancreatitis

Subject: Surgery

Collection: Oxford Medicine Online

Introduction C3.S1

Necrotizing pancreatitis affects 15–20% of all patients suffering from acute pancreatitis. Despite an improved understanding of the disease process and advances in therapeutic strategy, this complex disease is still attended by up to 15% mortality. Necrotizing pancreatitis provides the clinical challenges of working in a multidisciplinary group, determining proper timing, and identifying appropriate approaches for intervention based on individual patient anatomy, physiology, and local expertise. This chapter provides an overview of necrotizing pancreatitis, focusing on clinical care, intervention indications, and long-term sequelae of the disease. C3.P1

Incidence, aetiology, and pathophysiology C3.S2

Necrotizing pancreatitis, with variable degrees of pancreatic and/or peripancreatic necrosis, develops in 15–20% of all patients with acute pancreatitis.[1,2,3,4] Worldwide, the incidence of acute pancreatitis is 34 per 100,000 people and, in the United States, results in about 300,000 admissions for acute pancreatitis annually.[5,6] Thus, an estimated 30,000–60,000 cases of necrotizing pancreatitis occur every year in the United States. The aetiologies inciting necrotizing pancreatitis mirror those that cause acute pancreatitis, as described in previous chapters, most commonly biliary (20–50%) and alcohol (20–40%).[7,8,9] C3.P2

The pathophysiology of acute pancreatitis development and associated risk factors have been discussed in previous chapters. In summary, regardless of the aetiology or inciting event, abnormal activation of proteolytic enzymes within the pancreatic acinar cells results in pancreatic acinar cell injury and death.[10] The activation of trypsinogen to trypsin is believed to play a predominant role in this process, a model first proposed by the Austrian pathologist Dr Hans Chiari in 1896 and supported in subsequent studies since that time.[10,11] Once released from damaged pancreatic acinar cells, trypsin activates more trypsin and additional digestive enzymes, resulting in pancreatic parenchymal autodigestion, further acinar cell injury, and injury to the vascular endothelium and surrounding interstitium.[10] Activation of the systemic inflammatory response and the coagulation cascade play a key role in acute pancreatitis and are thought to be responsible for the progression from acute pancreatitis to necrotizing pancreatitis.[12,13] C3.P3

The human immune system, and its response to antigens, requires a delicate balance of pro- and anti-inflammatory mediators acting in concert.[14] In mild acute pancreatitis, the local inflammatory response is self-limited and balanced with an appropriate anti-inflammatory response, resulting in only mild systemic inflammation and resolution of disease with supportive care alone and minimal long-term sequelae.[15,16,17,18,19,20] In contrast, severe acute pancreatitis (SAP) develops when an imbalance in the inflammatory response develops and pro-inflammatory mediators are allowed to propagate unchecked.[13,15,16,17,21] A summary of the key pro- and anti-inflammatory mediators are shown in Figure 3.1. C3.P4

Figure 3.1 Summary of key inflammatory mediators in acute pancreatitis. C3.F1

Necrotizing pancreatitis occurs when enzymatic autodigestion of the pancreatic parenchyma, vascular endothelium, and surrounding interstitium results in focal or diffuse non-viable pancreatic or peripancreatic tissue.[1] The systemic inflammatory response is intimately associated with the coagulation cascade, and compromise of the pancreatic microcirculation (arterioles, capillaries, and venules) results in ischaemic changes that lead to necrosis of the pancreas.[22,23,24] The development of pancreatic and peripancreatic necrosis further stimulates the systemic inflammatory response.[12,13,15,16,17,21] C3.P5

The impact of systemic inflammation on respiratory, renal, and cardiovascular failure in necrotizing pancreatitis deserves mention. The progression from acute pancreatitis to severe/necrotizing pancreatitis and the associated inflammatory response play a direct role in end-organ injury and multi-organ dysfunction syndrome seen in patients with necrotizing pancreatitis. Inflammatory cytokines and chemokines released from the pancreatic parenchyma are disseminated to the respiratory, renal, and cardiovascular organ systems and result in secondary localized inflammation and injury to these tissues.[25,26,27,28] Further damage to individual organ systems can occur from necrotizing pancreatitis complications and its treatment. Understanding the pathophysiology of necrotizing pancreatitis and the role of loco-regional and systemic inflammation is critical in its treatment, both in the early and late phases of the disease. C3.P6

p. 21

Definitions and diagnosis C3.S3

The 2012 revision of the Atlanta classification provides the expert international consensus definition of acute pancreatitis and all associated complications, including necrotizing pancreatitis. Organ failure in necrotizing pancreatitis is defined as a modified Marshall scoring system for organ dysfunction score of 2 or greater (Table 3.1).[1,29] Necrotizing pancreatitis is diagnosed on contrast-enhanced cross-sectional imaging as absence of pancreatic or peripancreatic enhancement, as shown in Figure 3.2.[1] Comparatively, normal pancreatic parenchyma demonstrates homogeneous enhancement with contrast administration (Figure 3.2). C3.P7

Table 3.1 Modified Marshall scoring system for organ dysfunction in acute pancreatitis (organ failure is defined as a score of 2 or greater) C3.T1

Organ system	Score				
	0	1	2	3	4
Respiratory (PaO_2/FiO_2)	>400	301–400	201–300	101–200	≤100
Renal* (creatinine)	<1.4 mg/dL	1.4–1.8 mg/dL	1.9–3.6 mg/dL	3.6–4.9 mg/dL	>4.9 mg/dL
Cardiovascular** (systolic blood pressure)	>90 mmHg	<90 mmHg Fluid-responsive	<90 mmHg Not fluid-responsive	<90 mmHg pH <7.3	<90 mmHg pH <7.2

Source: data from Banks PA, Bollen TL, Dervenis C, *et al*. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102–111; and Marshall J, Cook D, Christou N, Bernard G, Sprung C, Sibbald W. Multiple Organ Dysfunction Score: A Reliable Descriptor of a Complex Clinical Outcome. *Critical Care Medicine*. 1995;23(10):1638–1652.

* No formal correction exists for a baseline serum creatinine ≥1.4 mg/dL.

** Off inotropes.

PaO_2, partial pressure of arterial oxygen; FiO_2, fraction of inspired oxygen.

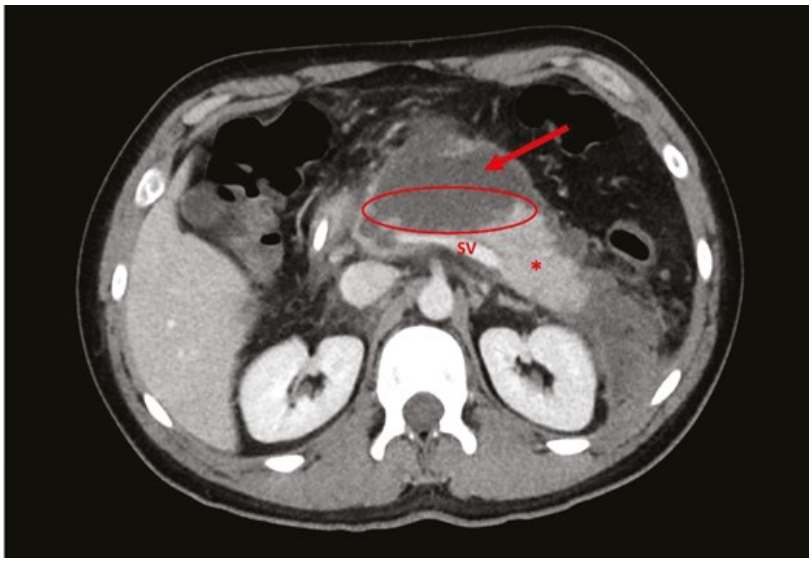


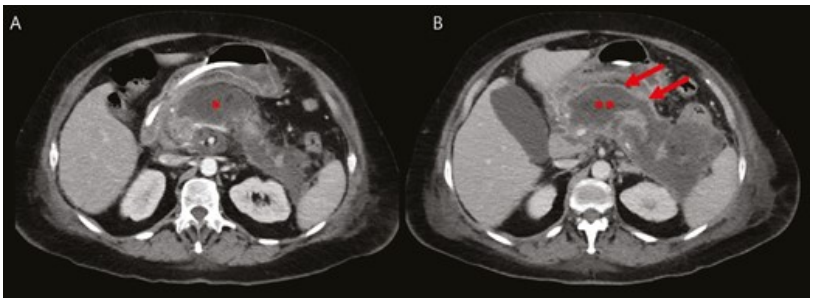
Figure 3.2 Contrast-enhanced computed tomography 2 weeks after symptom onset, demonstrating pancreatic parenchymal necrosis of the neck and body of the gland (oval), compared to normal enhancement of the tail of the pancreas (*). Note the development of peripancreatic necrosis anterior to the gland and the development of an acute necrotic collection (arrow). SV, splenic vein. C3.F2

Disease onset is defined by the timing of the onset of symptoms, and not by the presentation to hospital or the diagnosis of necrotizing pancreatitis.[1] This is a critical distinction as the onset of necrotizing pancreatitis is an important reference point for the disease course, the development of complications, and the timing of intervention. It is important to realize that the degree of pancreatic necrosis will not be appreciated on imaging the first few days after the onset of symptoms; parenchymal and peripancreatic necrosis begins to become C3.P8

apparent after 1 week.[30,31] Necrotizing pancreatitis may involve a combination of the pancreatic and peripancreatic parenchyma, isolated peripancreatic necrosis, or (uncommonly) isolated pancreatic necrosis.[32,33,34,35]

C3.P9

Local complications in necrotizing pancreatitis include acute necrotic collections (ANCs) and walled-off necrosis (WON). An ANC is a pancreatic or peripancreatic collection with liquid and/or solid necrosis within the first 4 weeks from symptom onset (Figure 3.3A).[1] After 4 weeks, the pancreatic and peripancreatic necrosis matures to WON, as time has allowed for the development of a well-defined inflammatory wall of reactive tissue (Figure 3.3B).[1] In the setting of non-necrotizing pancreatitis (interstitial oedematous pancreatitis), these terms must be differentiated from an acute peripancreatic fluid collection (<4 weeks) and a pancreatic pseudocyst (>4 weeks), respectively. It is of the utmost importance to understand the maturation phase of pancreatic and peripancreatic necrosis, as well as the volume of solid relative to liquid necrosis. The degree of solid necrosis is not determined reliably on computed tomography (CT) scan and can be better assessed with magnetic resonance imaging (MRI); however, the percentage of solid necrosis is best estimated with endoscopic or intraoperative ultrasound.[36] It is also important to understand that fluid collections in necrotizing pancreatitis are dynamic, with a tendency towards liquefaction over time.[36,37]



C3.F3

Figure 3.3 Contrast-enhanced computed tomography at 2 weeks (A) and 2 months (B) in a patient with necrotizing pancreatitis. Note the transition from an acute necrotic collection (*) to walled-off necrosis (**) characterized by the development of a well-defined inflammatory wall of reactive tissue (arrows).

C3.P10

Infected necrosis can be presumed in the setting of extraluminal gas in pancreatic and/or peripancreatic necrosis on cross-sectional imaging (Figure 3.4).[1] The diagnosis of infected necrosis is confirmed with positive bacteria and/or fungi on Gram staining and culture of aseptically obtained pancreatic necrosis specimens.[1] Routine percutaneous fine-needle aspiration (FNA) of pancreatic or peripancreatic fluid collections is only occasionally used in current practice.[38,39] The false negative rate of FNA ranges from 12% to 25% and FNA has the potential to introduce bacteria/fungus to an otherwise sterile ANC/WON.[40,41]

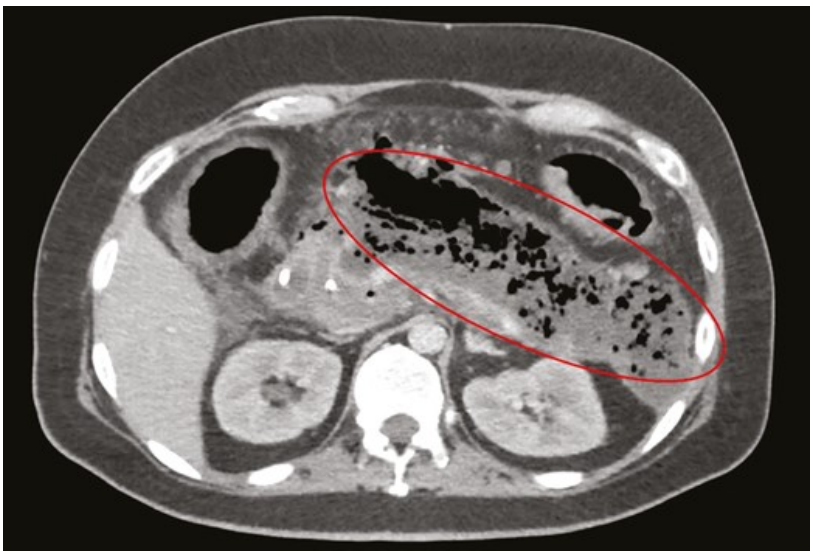


Figure 3.4 Contrast-enhanced computed tomography demonstrating an infected pancreatic necrosis with diffuse gas bubbles throughout the acute necrotic collection (oval). C3.F4

An increasingly recognized complication of necrotizing pancreatitis is the disconnected pancreatic duct C3.P11
p. 22 syndrome (DPDS). In ↳ DPDS, pancreatic parenchyma necrosis results in viable, upstream (left-sided) pancreatic tissue, in which secretions are disconnected from normal physiological pancreatic duct drainage. This syndrome is diagnosed on endoscopic (ERP) or magnetic resonance pancreatography (MRP) as extravasation of contrast or total cut-off of the main pancreatic duct (Figure 3.5).[42,43,44]

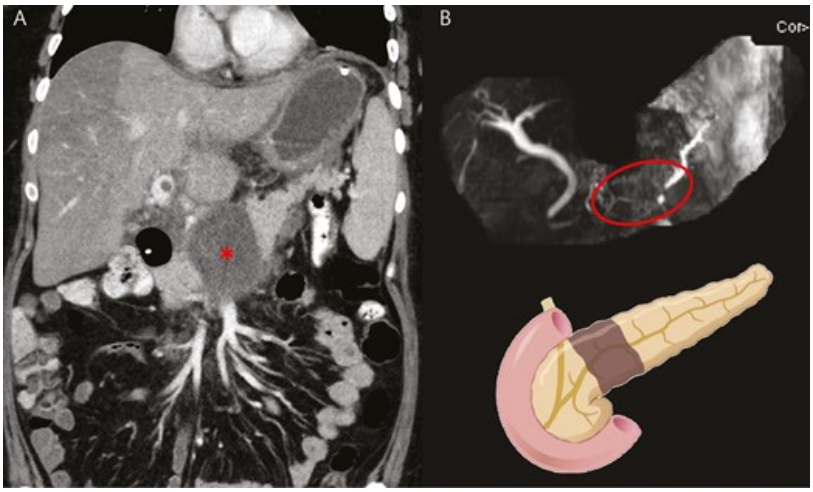


Figure 3.5 Contrast-enhanced computed tomography demonstrating necrosis involving the neck of the pancreas (A, *), resulting in cut-off of the main pancreatic duct on magnetic resonance pancreatography (B, top right, oval). C3.F5

Clinical course C3.S4

Classically, two overlapping phases are often described in acute and necrotizing pancreatitis: the early phase and the late phase. These phases are associated with the two peaks in mortality seen during the course of necrotizing pancreatitis. C3.P12

Early phase

C3.S5

C3.P13 The early phase of necrotizing pancreatitis occurs during the first 1–2 weeks after disease onset and is associated with profound activation of the systemic inflammatory response.[1] The initial symptomatology associated with necrotizing pancreatitis is typical of acute pancreatitis; however, the development of pancreatic and/or peripancreatic necrosis is often associated with clinical deterioration. A variety of clinical factors and severity scores have been shown to predict the severity of pancreatitis and have been discussed previously;[45] however, regardless of these, treatment during the early phase is strictly supportive.

C3.P14 Patients with necrotizing pancreatitis typically require aggressive fluid resuscitation due to substantial third space loss and intravascular volume depletion. Supportive care in the intensive care unit is often mandated. Respiratory, renal, and/or cardiovascular failure may be present in about 25–35% of patients.[46,47] Early enteral nutrition is advocated in all pancreatitis patients, but clinicians must consider the clinical scenario because enteral nutrition may be poorly tolerated in necrotizing pancreatitis as reactive ileus is common.[38,39,48] In patients not tolerating enteral nutrition, total parenteral nutrition is warranted as the catabolic state of necrotizing pancreatitis can rapidly produce malnutrition.[38,39] Many patients may tolerate some enteral feeding in the early course; these patients should have the remainder of their calories supplemented parenterally. Gastric ileus is common with inflammation in the lesser sac. Gastrojejunostomy feeding tubes are effective, permitting 'venting' of the stomach and downstream enteral feeding.[49]

C3.P15 Fever often develops in the early phase from the systemic inflammatory response and should not prompt prophylactic or empirical antibiotic usage as infection of the necrosis during this phase is rare. Routine 'prophylactic' antibiotic administration to prevent necrosis infection is not currently recommended.[38,39] Antibiotics should only be prescribed as treatment for documented infection or as empirical coverage during an infectious work-up in a patient with clinical deterioration.[1,38,39] During the early phase, organ failure is the predominant driving force behind mortality.

Late phase

C3.S6

C3.P16 The late phase in necrotizing pancreatitis occurs weeks to months after the onset of the disease. The overall disease duration is often 5–6 months; however, acute illness may persist up to, or beyond, 1 year.[35,50,51,52] Ongoing intensive care may be required as persistent organ failure is common and present in 35–40%.[7,46,53]

p. 23 Attention to ↳ nutrition is extremely important—critical illness and long-standing subacute inflammation can quickly result in nutritional depletion. As with the early phase, enteral nutrition is preferred to total parenteral nutrition. The route of administration (nasogastric, nasojejunal, percutaneous gastrostomy, percutaneous gastrojejunostomy) is less important and should be tailored to the individual patient.[49]

C3.P17 A number of local and systemic complications may develop during the late phase. Critical illness, systemic inflammation, and infection predispose necrotizing pancreatitis to an increased risk of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE).[54] Routine chemical VTE prophylaxis should be administered to all patients without clear contraindications and strong consideration should be given to serial four-extremity ultrasound screening to promote early DVT detection. Splanchnic vein thrombosis is also common and is the result of loco-regional inflammation and mass effect involving the portal, superior mesenteric, and/or splenic veins (Figure 3.6).[54,55] The ideal treatment strategy for pancreatitis-induced splanchnic vein thrombosis remains unknown. Left-sided, or sinistral, portal hypertension may develop and can impact the selection of intervention; spontaneous bleeding in this setting can occur but is uncommon.[56] On the other hand, bleeding from visceral artery pseudoaneurysms occurs in about 4% of necrotizing pancreatitis patients. Clinicians must be aware of this potentially life-threatening problem, which is best treated with percutaneous angioembolization (Figure 3.7).[57]

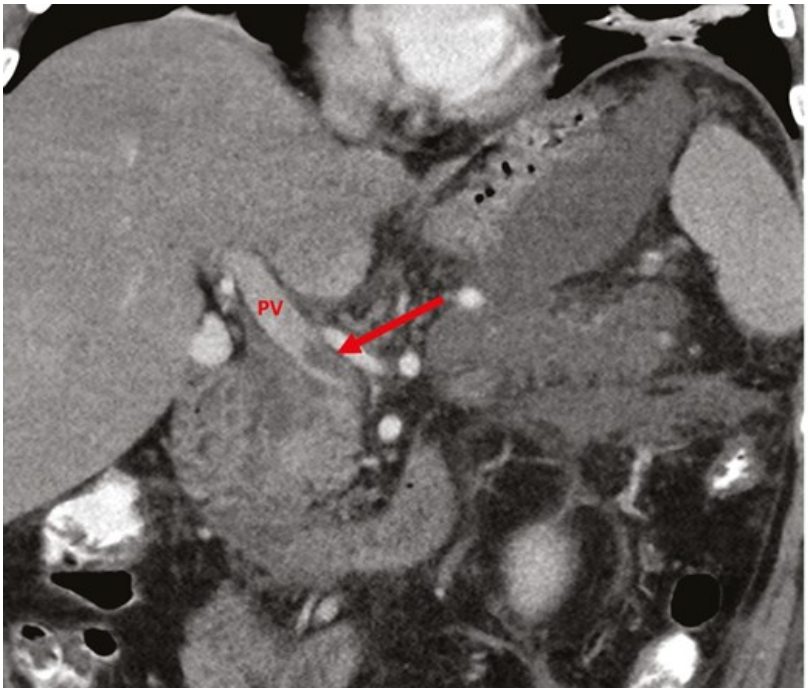


Figure 3.6 Acute non-occlusive portal vein (PV) thrombosis (arrow) from necrotizing pancreatitis. C3.F6

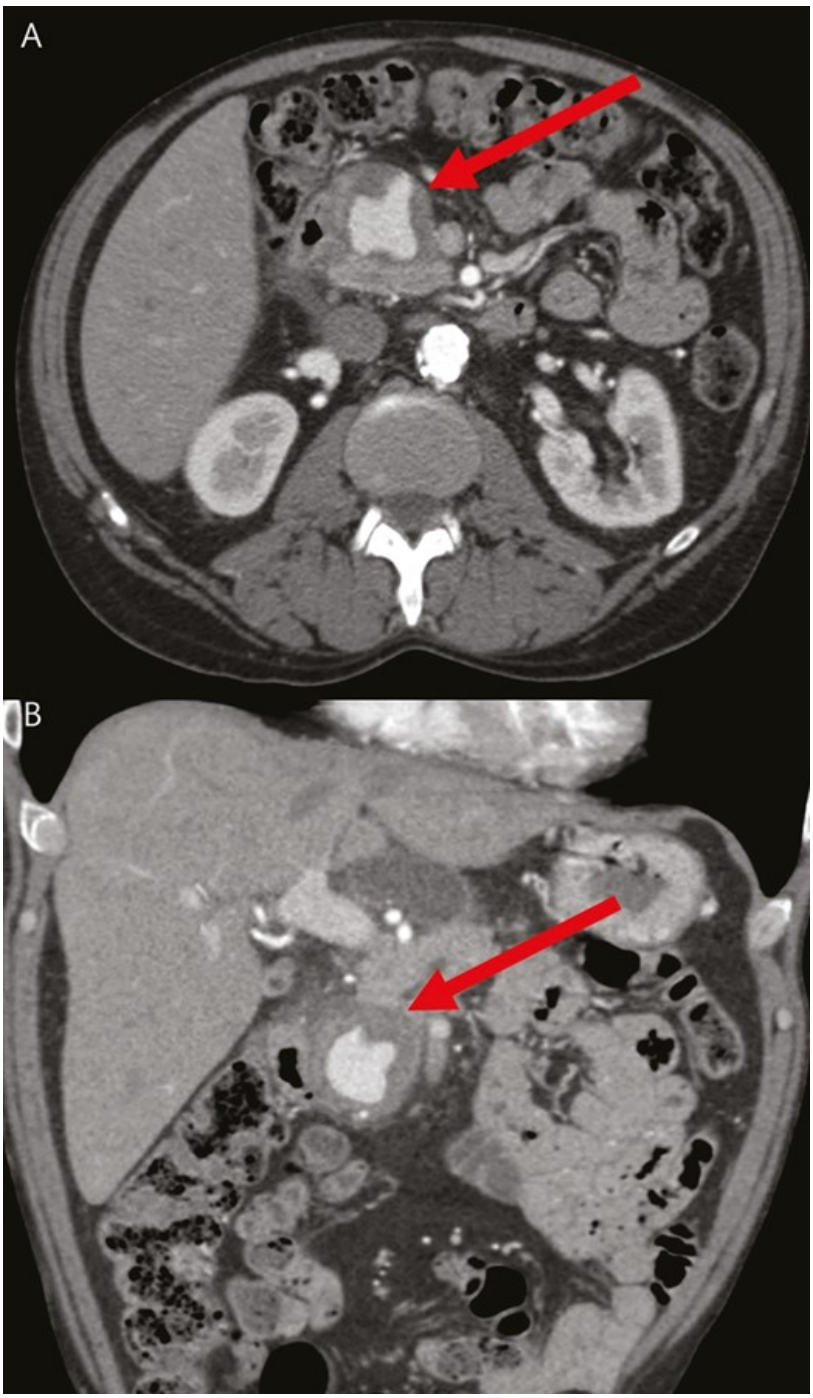


Figure 3.7 Representative axial (A) and coronal (B) computed tomography images demonstrating visceral artery pseudoaneurysm in necrotizing pancreatitis arising from a branch of the anterior pancreaticoduodenal artery (arrows). C3.F7

The impact of loco-regional inflammation extends beyond vascular complications. Gastric outlet obstruction and biliary stricture can develop from regional inflammation and/or mass effect from necrosis.[58] DPDS can result in recurrent pseudocysts, recurrent obstructive pancreatitis, and/or pancreaticocutaneous fistulae and frequently requires multiple interventions to treat (Figure 3.8).[59,60] Colonic complications, with ischaemia being the most common, are associated with considerable mortality and develop in up to 11% of necrotizing pancreatitis patients.[61,62] Spontaneous gastrointestinal fistulae may occur or develop after necrosis intervention.[51,52,61,63] C3.P18

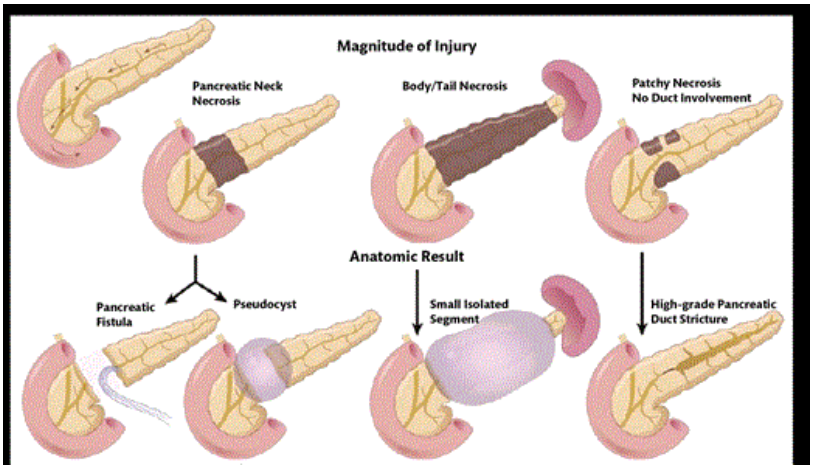


Figure 3.8 Clinical presentation of disconnected pancreatic duct syndrome in necrotizing pancreatitis. C3.F8

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Nosocomial extra-pancreatic infections are extremely common in patients with necrotizing pancreatitis.[7,46,51,64,65] In the setting of clinical concern for infection, confirmatory testing should be sought out and an appropriate duration of antibiotics should be prescribed. When infection is ruled out, empirical antibiotic therapy should be halted. Tailoring empirical antibiotic therapy based on culture is critically important, given the high incidence of antimicrobial resistance and *Clostridium difficile* infection.[64,66] Infected pancreatic necrosis develops in 20–40% of patients and is the primary indication for intervention.[7,46,53,67,68] C3.P19

When patients are suitable for discharge from inpatient treatment, several outpatient goals of care must be achieved. Nutritional optimization and physical rehabilitation should be ongoing to promote recovery and return to their baseline situation. Communication ↳ amongst the patient, the patient's outpatient care team, and the responsible pancreatologist must be readily available to monitor clinical improvement, allow for early detection of developing complications, and minimize hospital re-admission.[47] Additionally, reprieve from inpatient treatment can decrease the risk of nosocomial infection and exposure to multidrug-resistant organisms. Finally, routine short-interval follow-up should be scheduled to evaluate progress and plan for appropriate intervention, if required. C3.P20

p. 24

Intervention in necrotizing pancreatitis C3.S7

Evolution in treating necrotizing pancreatitis C3.S8

For many years, pancreatic and peripancreatic necrosis was treated by operative surgical debridement. This strategy often included multiple debridements and, in some cases, laparostomy to facilitate these planned reoperations.[69,70] Not surprisingly, historical reports of pancreatic debridement were associated with high perioperative morbidity—including enteral and pancreatic fistulae—as well as high post-operative mortality rates, often in the 25–40% range.[71,72] It is notable that mortality after pancreatic debridement has improved substantially over time, with improved understanding of the disease process and accumulated experience with operation.[73,74] The past 15 years have witnessed a remarkable change in the treatment of pancreatic necrosis. With application of contemporary 'step-up' strategies, most patients are managed successfully using minimally invasive treatment approaches, including percutaneous therapy and endoscopic-directed therapy, and often some combination of the two. C3.P21

Indications and goals of intervention C3.S9

It is important to consider general principles when approaching the necrotizing pancreatitis patient. The main goals of debridement are to control infection, evacuate fluid and solid necrotic debris, drain pancreatic fistulae (typically from the disconnected pancreas tail) either internally or externally, prevent recurrent pancreatitis (by cholecystectomy in the setting of biliary pancreatitis), and establish enteral access (Box 3.1). Importantly, it is ideal to accomplish these goals with minimal physiological disruption to uniformly frail patients. A fundamental general principle is that one single debridement technique does not fit all patients. Necrotizing pancreatitis requires a dedicated physician to lead a multidisciplinary team providing close care during this long-term illness. Selection of type and timing of intervention requires expert clinical judgement; the ideal treatment approach is individualized and depends highly on local experience. C3.P22

Box 3.1 Goals of treatment in necrotizing pancreatitis C3.B1

Goals of pancreatic debridement

- Control infection/sepsis C3.P141
- Evacuate fluid and necrotic debris C3.P142
- Provide drainage for pancreatic secretions (internally or externally) C3.P143
- Prevent recurrent pancreatitis (cholecystectomy in biliary pancreatitis) C3.P144
- Establish enteral access C3.P145
- Accomplish the above with minimal physiological disruption C3.P146

Additional important selection considerations include the patient physiology—no necrotizing pancreatitis patient is ever physiologically 'perfect' for intervention. Residual necrosis is a catabolic situation and good judgement is required to identify the appropriate window for intervention. This point speaks to the need to have at least one physician involved in a patient's care longitudinally to evaluate changes in progress. Necrosis distribution plays perhaps an equally important role in decision-making. A patient with necrosis consolidated in the lesser sac, with or without (usually with) a disconnected pancreatic tail, is ideally suited for the transgastric approach (either endoscopic or surgical) (Figure 3.9A), whereas a patient with necrosis tracking down one paracolic gutter may be approached with videoscopic-assisted retroperitoneal debridement (VARD) (Figure 3.9B). A patient with multiple retroperitoneal fields involved with necrosis may be best served with operative debridement as a first treatment step (Figure 3.9C). C3.P23

p. 25

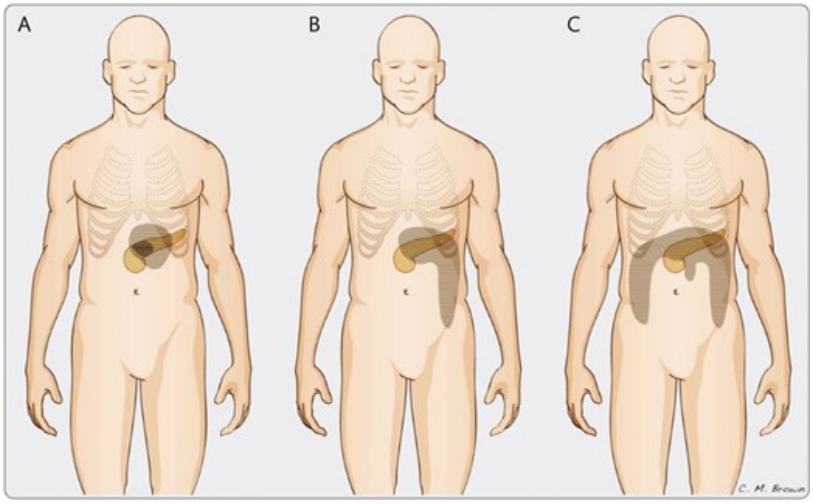

Figure 3.9 Patterns of necrosis in necrotizing pancreatitis. Necrosis confined to the lesser sac (A) may be best ideal for a transgastric approach, either endoscopic or surgical. Patients with necrosis tracking down one paracolic gutter (B) are suitable for percutaneous drainage and subsequent videoscopic-assisted retroperitoneal debridement (VARD), if needed. Multiple fields of retroperitoneal necrosis (C) may be best served with operative pancreatic debridement. C3.F9

Natural history of pancreatic necrosis C3.S10

Figure 3.10 illustrates the natural history of pancreatic and peripancreatic necrosis. In a small proportion of patients with necrotizing pancreatitis, the necrosis will resolve without any specific intervention. This is approximately 5–7% in large series.[75] A second group of patients will develop infection in the necrosis, documented either by cross-sectional imaging with gas bubbles or by sampling. A third group of patients will have persistent necrosis which, if asymptomatic, may be observed. Patients with sterile necrosis may, however, develop symptoms, including gastric outlet obstruction, abdominal pain, or 'persistent unwellness'. These patients with presumed sterile necrosis should be considered for debridement. It is notable in this latter category of presumed sterile necrosis that a significant percentage (up to 40%) will be found to have occult infection.[76] C3.P24

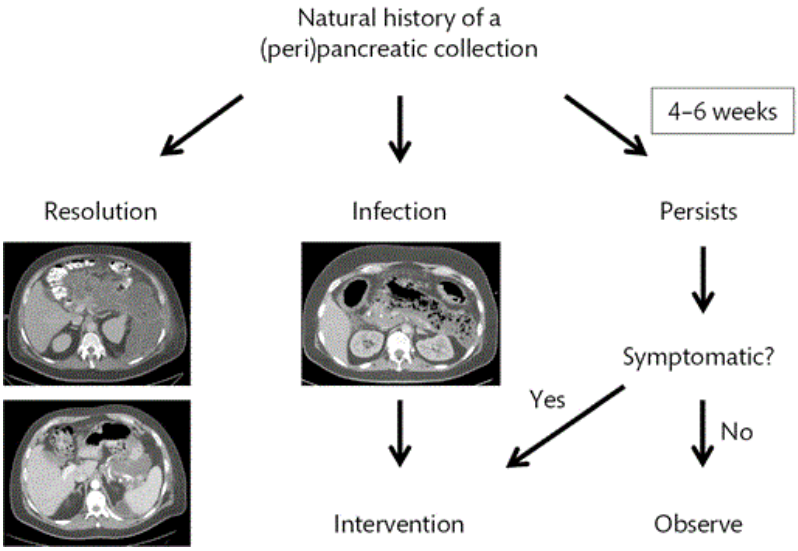

Figure 3.10 Natural history of pancreatic and peripancreatic necrosis. C3.F10

Percutaneous drainage

C3.S11

Percutaneous drainage has become the first step in the 'step-up' approach for most patients with necrotizing pancreatitis. It was initially observed in the PANTER trial that nearly a third of patients resolved their pancreatic/peripancreatic collections with percutaneous drainage alone. This finding has been validated in subsequent studies, although no study has yet identified accurate predictors of success/failure of percutaneous drainage.[35,50,63] It is important to note that once treatment begins by any approach—percutaneous, endoscopic, or otherwise—the clock is ticking and efforts should be directed towards evacuating the infected solid necrosis expeditiously. Most institutions favour a strategy of fairly short (3- to 5-day)-interval imaging, with frequent upsizing of the percutaneous drains or placement of additional drains. Clinical judgement is important once treatment has started, as the percutaneous drains by themselves will not provide definitive treatment in two-thirds of patients with pancreas necrosis (Figure 3.11). In the situation where treatment by percutaneous drainage stalls, the next step in the approach may include endoscopic 'dual therapy', sinus tract endoscopy, or operative surgical debridement.

C3.P25

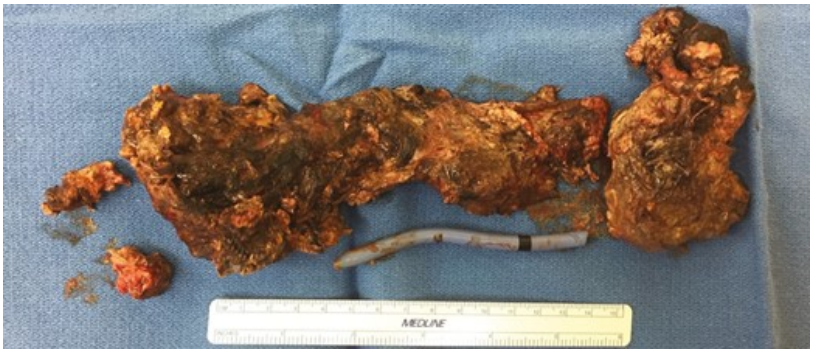

Figure 3.11 Surgical specimen of solid necrosis after operative pancreatic debridement. This patient was first treated by percutaneous drainage (blue drain on image).

C3.F11

Transgastric debridement

C3.S12

Endoscopic transgastric debridement was first described in 1996.[77] Over the next two decades, sporadic small case reports emerged in both the medical and surgical literature. More recently, enthusiasm has grown for endoscopic transgastric debridement. Patients with necrosis confined to the lesser sac are ideal candidates; as experience has accumulated, aggressive endoscopists have pushed the envelope in terms of which necrosis morphology to approach ↳ endoscopically.[78,79] Important considerations include local experience. Even in the most skilled hands, endoscopic evacuation of peripancreatic necrosis requires multiple debridement sessions under a general anaesthetic.

C3.P26

p. 26

Surgical transgastric debridement provides the ability to address pancreatic necrosis, as well as perform a cholecystectomy with cholangiography at the same setting. Several surgical groups have reported excellent results with increasingly larger series of transgastric debridement.[80] The authors' opinion is that surgical transgastric debridement should be the treatment of choice in patients with biliary pancreatitis and appropriate anatomy. Importantly, patients with disconnected pancreatic ducts may also be treated—the transgastric approach drains the disconnected tail into the stomach. These patients experience recurrent pancreatitis and fluid collections in approximately 20% of the time and should be counselled accordingly.[81,82]

C3.P27

Transabdominal minimally invasive approaches include the so-called VARD, as well as sinus tract endoscopy/necrosectomy. VARD was studied prospectively by a Dutch group in the PANTER trial.[63] A small incision permits insertion of an operating nephroscope or video endoscope to guide debridement. This approach may be performed via the left or right flank; occasionally, bilateral VARD is used to treat extensive

C3.P28

necrosis. Sinus tract necrosectomy involves a similar technical approach (i.e. use of endoscopy to guide debridement through a small incision); however, this approach is typically carried out along established drain tracts in a transperitoneal orientation.

A fundamental principle of either retroperitoneal or transperitoneal minimally invasive approach is allowing C3.P29
p. 27 an appropriate period of time for the necrosis cavity to mature. This 'window' ↳ permits adequate debridement with minimal disruption of the surrounding tissue.

Open pancreatic debridement C3.S13

Open pancreatic debridement has traditionally served as the gold standard for evacuation of infected or C3.P30
symptomatic solid necrosis. No contemporary minimally invasive approach has ever been compared to open debridement in a randomized fashion; this comparison in the current time is not feasible. Open necrosectomy provides the advantage of addressing multiple necrosis fields, biliary pathology, and potentially a small tail remnant in a single procedure. The safety of this procedure is established.[51,73,74] Safety is a particularly important consideration in the setting of superior mesenteric or splenic vein thrombosis. In this circumstance, the resultant gastric varices may lead to profound haemorrhage during transgastric approaches. Open pancreatic necrosectomy is time-tested and widely applicable to a well-trained surgeon familiar with basic surgical principles. In current times, this procedure is often time-relegated to be the last effort when other percutaneous and endoscopic approaches have failed.[51,74]

From a technical standpoint, it is important to review recent cross-sectional imaging to understand the C3.P31
distribution pattern of the residual necrosis. The authors find intraoperative ultrasound useful to localize collections. Adhesions of the small bowel to the underside of the transverse colon are quite common. A safe approach to the necrosis is obtained via the lateral paracolic gutters. Perhaps the most effective debridement tool is the 'educated finger' of the surgeon. Ring forceps also work well; however, only freely mobile necrosis should be debrided. Large-calibre closed-suction drains are placed in the necrosis bed after vigorous irrigation. Gastrojejunostomy feeding tubes facilitate post-operative management, as many patients have gastric ileus but will tolerate small bowel feeding.[49] Contemporary series of pancreatic debridement in experienced hands document excellent outcomes.[51,73] To reiterate, judgement regarding timing of operation and extent of operation is critically important. In some circumstances, 'damage control' debridement may be most useful.[74,83]

In summary, the important considerations in necrotizing pancreatitis intervention include the aetiology of the C3.P32
pancreatitis, the distribution of the necrosis (including the proportion of solid necrosis), parenchymal involvement, infection, patient physiology, and local expertise. A one-size technique does not fit all patients. A dedicated physician is required ideally to coordinate a multidisciplinary team throughout the duration of this long-term acute illness.

Outcomes, including long-term sequelae C3.S14

Modern mortality rates in all patients with necrotizing pancreatitis is about 10–15%.[7,46,53,75] In patients with C3.P33
organ failure, those with infected necrosis, and those who require intervention, mortality rates are higher, ranging from 10% to 30%.[46,50,53,63,67,73,84] The two strongest influencing factors associated with mortality are organ failure and infected necrosis.[46,53] In patients who survive an episode of acute necrotizing pancreatitis, return to function generally takes about 5–6 months. Emerging research has identified a variety of long-term disease sequelae in necrotizing pancreatitis survivors (Table 3.2).

Table 3.2 Long-term sequelae of necrotizing pancreatitis C3.T2

Long-term sequelae	Incidence (%)
Endocrine insufficiency	40–60
Exocrine insufficiency	10–40
Splanchnic vein thrombosis	50
Disconnected pancreatic duct syndrome	45
Recurrent acute pancreatitis	20
Chronic pancreatitis	10–20
Biliary stricture	16
Duodenal stricture	5

Uncommon sequelae
Tracheal stenosis
Ureteral stricture
Colonic stricture
Progressive renal failure
Pancreatic ductal adenocarcinoma
Gastrointestinal failure requiring transplant
Male impotence
Metabolic peripheral polyneuropathy
Pericardial effusion
Deafness
Blindness

Pancreatic endocrine and exocrine insufficiency after acute pancreatitis are common; the risk of pancreatic function loss is directly associated with disease severity.[19,20,85] In patients with necrotizing pancreatitis, endocrine (type 3c diabetes mellitus) and exocrine insufficiency develop in 40–60% and 10–40% of survivors, respectively.[20,85,86,87] One in five patients (20%) may experience recurrent acute pancreatitis during long-term follow-up, and chronic pancreatitis is reported to develop in 10–20%.[86,88] Pancreatic duct stricture after necrotizing pancreatitis contributes to the development of recurrent acute pancreatitis and chronic pancreatitis.[89,90] C3.P34

Several less commonly reported complications are noteworthy. Splanchnic vein thrombosis can develop in up to 50% of patients—the rate of recanalization is believed to be infrequent and often results in either left-sided or generalized portal hypertension.[54,55,91] DPDS is an increasingly recognized complication of necrotizing pancreatitis diagnosed in 45% of patients and commonly manifests itself after acute disease resolution.[35,59] Treatment of DPDS, and associated symptoms of recurrent pancreatitis and/or pseudocyst, frequently requires endoscopic and/or surgical intervention.[59,60,92,93,94] Biliary and duodenal strictures may form as a result of the local inflammatory process in necrotizing pancreatitis and frequently require intervention.[58] Gastric, duodenal, enteric, and colonic fistulae may develop during necrotizing pancreatitis or as a result of its treatment and persist after disease resolution.[61,95,96,97] Incisional hernia is more common in patients requiring laparotomy for necrotizing pancreatitis, when compared with laparotomy for other indications.[98] Rare complications from necrotizing pancreatitis or its treatment that are reported as anecdotes range from tracheal stenosis, ureteral stricture, colonic stricture, progressive renal failure, pancreatic ductal adenocarcinoma,[99] irreversible gastrointestinal failure requiring ↳ multivisceral transplant, male impotence, metabolic peripheral polyneuropathy, pericardial effusion, deafness, and blindness.

C3.P35

p. 28

An important observation relates to mental health—it is clear that most, if not all, patients with necrotizing pancreatitis are clinically depressed at some point during their disease and after its resolution. This situation has been termed ‘post-pancreatitis stress disorder’ by the pancreatologist Dr Martin Freeman and certainly deserves attention. Several studies have evaluated a variety of quality of life metrics after acute necrotizing pancreatitis resolution and the theme is long-term impairment of quality of life, regardless of treatment strategy,[85,100,101,102] although the exact impact remains difficult to quantify. These studies report that during follow-up, 40–75% of patients reported disability that prevented return to baseline, pre-necrotizing pancreatitis function.

C3.P36

After disease resolution, routine follow-up should include a focused history, physical examination, and laboratory screening for the development of these long-term sequelae in survivors of necrotizing pancreatitis.

C3.P37

Conclusion

C3.S15

The last few decades have seen a considerable evolution in our understanding of both the disease process and the technical approaches to managing pancreatic necrosis. Patients requiring interventions should uniformly be treated by the step-up approach, most often starting with percutaneous drainage and proceeding, as necessary, to endoscopic therapy or surgical therapy, or a combination of these approaches. Unanswered questions in necrotizing pancreatitis include the need to develop objective metrics to predict optimal timing for step-up, determining whether a certain patient population may benefit from operative pancreatic debridement as first-line therapy, and perhaps, most importantly, discovering and developing therapy directed towards treating the disease itself, and not simply its complications.

C3.P38

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