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Treatment of pancreatic necrosis – the Multimodal Glasgow Algorithm

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1. Introduction

The 2013 APA/IAP consensus document (44) outlined the principles of early targeted organ support, nutritional (enteral) optimisation, avoidance of antibiotic prophylaxis / ERCP (in the absence of jaundice), and delayed minimally invasive intervention embedded within a "step-up" framework where possible. An in-depth discussion of the evidence supporting these principles is beyond the scope of this chapter and will be dealt with elsewhere. This chapter will focus on the indications and rationale for intervention, and the options available within a multi-modal management algorithm.

2. Revised Atlanta Classification of Acute Pancreatitis

The original Atlanta classification (7) of acute pancreatitis characterised clinical behavior as mild or severe acute pancreatitis and intervention for necrosis was often focused on early removal of sterile or infected necrosis usually by open necrosectomy. This simplistic dichotomization proved inadequate in clinical practice until the revised Atlanta Criteria (4) recognized the importance of early systemic organ dysfunction and multiple organ failure in determining disease severity and outcome. The management of local complications is heavily influenced by the degree of systemic disturbance, and this is reflected in an additional category of "moderately severe" pancreatitis. In addition to disease severity, mortality is strongly associated with age, comorbidity and the presence of infection, which has been recognized in an addendum adding a category of "critical" recognizing those patients with sepsis and organ failure are associated with the highest mortality (27).

Table 1: Grades of severity for acute pancreatitis (4)
(based on the clinical parameters of the presence or absence of organ failure and / or complications)

Mild acute pancreatitis

- No organ failure
- No local or systemic complications

Moderately severe acute pancreatitis

- Organ failure that resolves within 48 h (transient organ failure) and/or
- Local or systemic complications without persistent organ failure

Severe acute pancreatitis

- Persistent organ failure (>48 h)

Furthermore, this classification further categorises local complications on the basis of time from presentation (< or > 4 weeks) and on the presence of necrosis, leading to definitions aimed at permitting comparison of case series **(Table 2)**. The "early" phase is characterized by the initial host response to the pancreatitis, the severity being determined by the magnitude or organ disturbance /failure, and a "late" phase typified by the persistence of organ dysfunction and the management of local or systemic complications. The vast majority of acute fluid collections without necrosis will resolve within 4 weeks and a persistent fluid collection with minimal or no necrotic component ("pseudocyst") is very rare. Collections may be sterile or infected. The majority of clinically significant peri-pancreatic complications are therefore related to either acute necrotic collections (<4 weeks) or walled-off pancreatic necrosis (>4 weeks). This temporal separation is somewhat arbitrary, as the clinical management and surgical approach is determined by multifactorial individual patient factors. However, this does serve to provide a timeline beyond which, if appropriate, intervention should be delayed. **(Figure 1).**

Table 2: Local complications in acute pancreatitis (2012 Revised Atlanta Classification)

Time scale	Necrosis absent	Necrosis present
< 4 weeks	**Acute peripancreatic fluid collection** (peripancreatic fluid associated with interstitial oedematous pancreatitis with no associated peripancreatic necrosis)	**Acute necrotic collection** (a collection containing variable amounts of both fluid and necrosis; the necrosis can involve the pancreatic parenchyma or the extrapancreatic tissues)
> 4 weeks	**Pancreatic pseudocyst** (an encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis)	**Walled-off necrosis** (a mature, encapsulated collection of pancreatic or extrapancreatic necrosis that has developed a well-defined inflammatory wall)
Infection	Each collection type may be sterile or infected	

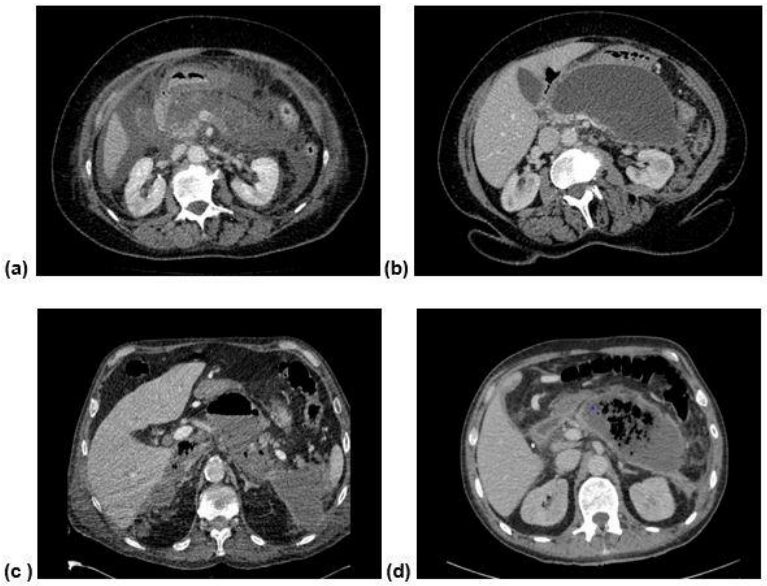


Figure 1. Contrast enhanced CT in a 69 yr old woman with severe acute gallstone pancreatitis at (a) 5 days showing an acute necrotic collection (ANC) and (b) Walled off Necrosis (WON) at 7 weeks subsequently managed by laparoscopic cystgastrotomy and cholecystectomy (c) fluid level in an acute necrotic collection suggestive of spontaneous fistulation (clinically well) and (d) loculated gas within an Infected Acute necrotic collection suggestive of bacterial contamination (clinical sepsis).

3. Indications for Intervention for Pancreatic Necrosis – the Bi-Phasic Model

Two distinct phases of mortality are seen in acute pancreatitis: Early death (arbitrarily defined as within two weeks of onset) is usually a consequence of progressive multiple organ failure (23). Late mortality is usually a consequence of local pancreatic complications related to pancreatic or peri-pancreatic necrosis. Whereas intervention during the early phase of illness is usually counterproductive, timely and appropriate intervention for specific local complications (1) can be life-saving. Although the incidence of acute pancreatitis has been increasing, the overall case mortality has been falling for several decades. Mortality in the sub-group with severe acute pancreatitis is also falling, attributed to improvements in intensive care management, minimally-invasive approaches to management, advances in vascular intervention, nutritional support and the development of specialist centres. The IAP/APA consensus document provides a broad framework on which to structure management of what are invariably complex and individual management algorithms. The main impact of these improvements has been to support patients better and for longer through the early phase of illness, allowing interventions for local complications to be carried out later and by less invasive methods.

Surgical intervention for necrosis in the first 2 weeks carries a high risk of morbidity and mortality and is therefore to be avoided (24), in the absence of specific complications such as bleeding or mesenteric ischaemia. Whilst intervention may eventually be required for a persistent walled off necrotic collection, intervention for an acute necrotic collection before it has matured sufficiently to become encapsulated is usually only indicated in the presence of secondary infection as evidenced by a secondary clinical and biochemical deterioration, coupled with CT evidence of infection such as small pockets of gas (9). Gas within a collection is not in itself an indication for intervention as spontaneous enteric discharge of a collection may be associated with clinical improvement, in which situation there is often a gas/fluid level, and therefore any imaging result needs to be interpreted in the overall clinical context.

Once a decision is made that intervention is required, these poorly demarcated pancreatic (and peri-pancreatic) collections can be managed by a variety of approaches. Freeny and his colleagues (15) in the 1990's, showed that aggressive percutaneous sepsis control would promote recovery in the absence of formal necrosectomy, although a number required subsequent surgical intervention. A number of minimally invasive approaches have since been described, including percutaneous necrosectomy (MIRP) (10), Video-Assisted Retroperitoneal Debridement(VARD) (21), endoscopic cystgastrostomy (42), and laparoscopic cystgastrostomy (17). Laparoscopic direct necrosectomy was described in the 1990's but has failed to gain popularity due to technical difficulty (16), and so far there are only 2 recent retrospective studies describing laparoscopic necrosectomy alone with a total of 29 highly selected patients and no follow-up was available for either study (26, 45).

There is evidence that minimal access techniques may pose less of a challenge to the patient's systemic inflammatory response and in our own experience, patients have reduced requirements for the post-operative intensive care management (12). The choice of approach in worldwide clinical practice is often influenced by local resource limitations and familiarity with a particular technique, but most now have foundation within a "step-up framework".

4. Management Techniques for Sepsis Associated with Acute Necrotic Collections

Initial "Step-Up" Drainage

Whereas a number of differing minimally invasive techniques had been described in cohort series showing benefit over historical controls, the PANTER trial (40) from the Dutch Pancreatitis Study Group, provided good quality randomised data regarding the management of infected pancreatic necrosis. Patients requiring surgical intervention for pancreatic necrosis were randomised to either primary open necrosectomy or a 'step-up' approach based on percutaneous drainage as the initial intervention, with progression to retroperitoneal debridement (VARD) with lavage if no improvement was observed. The composite endpoint of death or major complication demonstrated a significant benefit with the "step-up" approach. Indeed 35% were successfully managed with percutaneous drainage alone and did not require any subsequent debridement. There is now a consensus advocating a principle of early organ support, nutritional optimisation, followed ideally by delayed and selective minimally invasive intervention if required.

The choice between initial percutaneous or endoscopic drainage is based on the position of the collection relative to the stomach, colon, liver, spleen and kidney. Furthermore, the ability to perform EUS guided puncture within an ITU setting, without the need for patient transfer to the radiology department for CT guided drainage, may influence the management decision where a patient is in extremis, and unstable to transfer. In general, our practice has been to approach lateral collections and those extending behind the colon from the left or right flank by a percutaneous approach, preferring endoscopic drainage for medial retrogastric collections where a percutaneous route may be compromised by overlying bowel, spleen or liver. Improved delivery devices (35) to enable rapid deployment of self-expanding metal stents SEMS may represent a significant advance by allowing adequate and rapid initial drainage, whilst minimizing the risk of haemorrhage due to lateral compression of the drain tract by the SEMS. The route of percutaneous drainage should ideally take into account the probability of subsequent "step-up" escalation, siting the drain as lateral and inferior as possible, avoiding the costal margin, but the initial priority must be sepsis control. If the route of initial drainage is suboptimal, alternative secondary access can be obtained, sometimes resulting in a combination of percutaneous and endoscopic techniques.

The choice of one approach over another is determined by the clinical condition of the patient, local experience and expertise, anatomical position / content of the collection, and the time from presentation / maturation of the wall of the collection. There is an acceptance that due to the complexity of presentation, no single technique will be suitable for all patients, and the aim should be to provide a multimodal multi-disciplinary approach. Our current management algorithm has emerged from a process of continuous evolution based on increased experience of the "step-up" concepts, the approach in the last decade being for solid predominant or infected necrotic collections to be managed percutaneously by MIRP or VARD, and for late, well-organized and predominantly fluid collections to be managed by endoscopic or laparoscopic transgastric drainage, but these concepts are now being assessed in randomized trials (2, 39).

Secondary "Step-Up" Management Following Primary Drainage (Figure 2)

Enhanced Catheter Drainage (+/- Lavage)

The "step-up" concept is based on the

stabilisation of patients in organ failure and sepsis, as a bridge to surgery or as definitive treatment in a proportion of patients. Some authors have promoted secondary “upsizing” or insertion of multiple drains if immediate sepsis resolution is delayed, rather than proceeding to one of the necrosectomy techniques described below. Freeny et al first described a series of 34 patients with infected acute necrotizing pancreatitis primarily treated with image guided percutaneous drain (PCD) as an alternative to primary surgical necrosectomy (15) focusing on the placement of multiple large-bore catheters and vigorous irrigation, and was successful in avoiding the need for surgical necrosectomy in 47% of the patients. Lee and his colleagues routinely undertook stepwise dilation to 20FG along with twice weekly lavage (22), with resolution in 83% but two prospective studies have suggested a more realistic primary success rate of PCD of 33% to 35% (20, 40). Early PCD placement before 3 weeks is associated with a prolonged course and more frequent drain exchanges (30, 31), underscoring the importance of maturation of walled off necrosis before intervention. Persistent external fistulas occur in up to one third of patients.

The Dutch Pancreatitis Study Group have compared the success of further upsizing of PCD vs VARD as the initial enhanced step-up procedure if immediate resolution does not occur and have shown more that 50% of patients will settle without formal necrosectomy in the dilatation alone group. Drawbacks include limited ability to remove necrotic debris, prolonged hospitalisation and the need for multiple procedures. The use of grasping forceps (3) to extract the debris after sequential tract dilatation has been described in a small series as has the use of assist devices such as stone retrieval baskets (11), but these techniques are seldom performed in clinical practice. A dedicated team of surgeons/ radiologists willing to perform meticulous catheter care, with frequent upsizing of drainage catheters and frequent imaging to localize the loculated undrained areas is critical for successful percutaneous management of necrotizing pancreatitis (15).

Percutaneous Necrosectomy / VARD

Both MIRP and VARD retroperitoneal techniques are modifications of the open lateral approach initially described in the 1980’s by Fagniez (13) which utilised a loin / subcostal and retrocolic approach to allow debridement of pancreatic and peripancreatic necrosis. This open approach was associated with major morbidity (enteric fistula 45%, haemorrhage 40%, and colonic necrosis 15%), and failed to gain popularity.

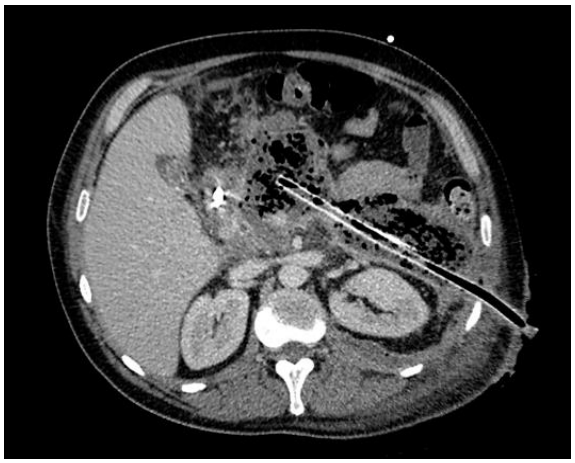
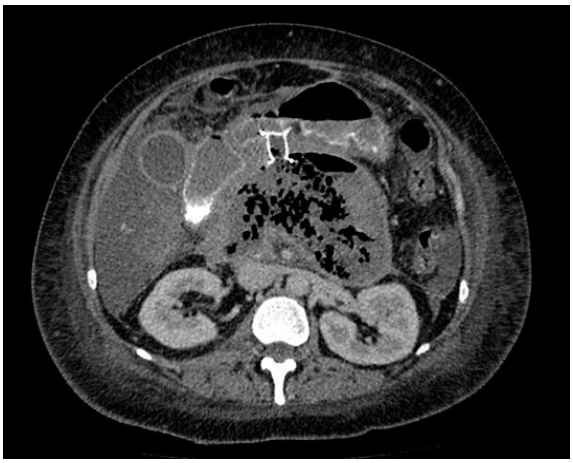
(a)  (b) 

Figure 2. Initial “step-up’ drainage using (a) MIRP percutaneous lavage drain and (b) EUS guided transgastric cystgastrostomy with SEMS.

For both minimally invasive techniques, a left-sided small diameter percutaneous drain is ideally placed into the acute necrotic collection between the spleen, kidney and colon. Right-sided, or trans-peritoneal drainage are also possible. In those who fail to respond adequately to simple drainage this access drain is then used as a guide to gain enhanced drainage of the collection.

Minimally Invasive Pancreatic Necrosectomy

For percutaneous necrosectomy, the catheter is exchanged for a radiological guidewire then a low compliance balloon dilator is inserted into the collection and dilated to 34 FG. Access to the cavity is then maintained by an Amplatz sheath through which is passed an operating nephroscope, which allows debridement under direct vision. The nephroscope has an operating channel that permits standard (5 mm) laparoscopic graspers as well as an irrigation/suction channel. The directed, high flow lavage promotes rapid evacuation of pus and liquefied necrotic material, revealing black or grey devascularised pancreatic tissue and peri-pancreatic fat which, if loose, is extracted in a piecemeal fashion until, after several procedures, a cavity lined by viable tissue or granulating pancreas is created. At the end of each procedure an 8FG catheter sutured to a 24 FG drain is passed into the cavity to allow continuous post-operative lavage of warmed fluid initially at 250 ml an hour. Subsequent conversion of the lavage system to simple drainage may be all that is required prior to recovery or the procedure may be repeated until sepsis control is achieved and interval CT confirms resolution.

Video-Assisted Retroperitoneal Debridement (VARD)

A Video-Assisted Retroperitoneal Debridement (VARD) procedure is performed with the patient placed in a supine position with the left side 30–40° elevated. A subcostal incision of 5 cm is placed in the left flank at the mid-axillary line, close to the exit point of the percutaneous drain. Using the *in situ* percutaneous drain as a guide, the retroperitoneal collection is entered. The cavity is cleared of purulent material using a standard suction device. Visible necrosis is carefully removed with the use of long grasping forceps, and deeper access under direct vision is facilitated using a 0° laparoscope, and further debridement performed with laparoscopic forceps. As with a percutaneous necrosectomy, complete necrosectomy is not the aim of this procedure and only loosely adherent pieces of necrosis are removed, minimizing the risk of haemorrhage. Two large bore single lumen drains are positioned in the cavity and the fascia closed to facilitate a closed continuous postoperative lavage system.

Endoscopic Necrosectomy

Endoscopic cystgastrostomy was initially reported for the management of a mature pancreatic abscess with minimal necrosis (5), but the technique has evolved in the last 10 years to become an established Natural Orifice (NOTES) procedure, with endoscopic transmural exploration and debridement of the retroperitoneum. Single-step drainage under EUS guidance may be carried out by either a trans-gastric or less commonly a trans-duodenal route and is preferred to "blind" drainage as EUS allows for identification of the collection where there is no obvious bulge seen within the stomach and helps identify a safe route for puncture, free from intervening vessels (18, 41). The presence of significant walled off necrosis (WON) is no longer considered a contraindication, but concerns do remain regarding the adequacy of endoscopic drainage, particularly in solid predominant or larger collections. The principles are similar to those discussed above, with initial simple drainage of a collection under pressure, followed by subsequent “step up” tract dilatation and potential necrosectomy.

The procedure involves puncture of the collection with either a 19G needle or cystotome, with dilatation of the track followed by placement of two or more plastic pigtail stents. Increasingly, metallic stents may be used which facilitate subsequent endoscopic access to the cyst cavity for debridement of necrosis. Where there is evidence of infection or systemic sepsis it is our practice to use a naso-cystic catheter, which can be used for continuous lavage of the cavity. Factors associated with a failure of resolution are large size and retro-colic extension of the collections and in these cases, other approaches or combinations of approaches should be considered (31, 37). Other options include the multiple gateway technique (41), where two or three transmural stents are placed under EUS guidance, one of which is used for nasocystic cavity lavage and the others to facilitate drainage of necrotic debris.

Where there is extensive necrosis, delayed endoscopic necrosectomy may be required (34). It is our practice to defer this for a week following the initial drainage procedure to allow the fluid component to drain and any associated sepsis to improve. A recent systematic review (38) of 14 studies including 455 patients found an overall success rate of 81% and mortality of 6%, but these studies are in highly selected patients and all but one was retrospective. One small randomized trial (2) has compared endoscopic with surgical drainage and found a reduction in significant complications with the endoscopic approach.

Endoscopic necrosectomy is however a challenging procedure and not without risk. Major complications including fatal air embolism, bleeding and perforation occurred in 26% of patients in the multi-centre GEPARD (33) study. The use of CO2 insufflation is therefore now recommended. A persistent problem is the lack of availability of suitable endoscopic devices to facilitate necrosectomy and although endoscopic access to the cyst cavity is now facilitated by metallic stents, piecemeal necrosectomy using standard graspers, baskets and snares is a time consuming and painstaking process (39). One possible modification is the use of intra-cavity hydrogen peroxide to facilitate necrosectomy although further experience is required before this can be recommended for routine practice (36).

Despite these limitations, initial experience has been promising (33), and an early randomised pilot study exploring the outcome of endoscopic transmural drainage vs. minimally invasive intervention (VARD) (the PENGUIN trial (2)) suggested at least equivalence, if not benefit, from endoscopic drainage. This study has been criticised due to very small numbers and an excessive mortality (40%), compared to historical results, within the VARD arm. The results of the on-going TENSION trial (39) are awaited with interest.

Open Surgical Necrosectomy

Open necrosectomy is still employed but increasingly has been replaced by the procedures described above. Three general variations of open necrosectomy are currently practiced, and remain widespread whilst experience of minimally invasive approaches increases. These can also be used within a step up framework with preoperative percutaneous drainage, allowing control of sepsis prior to intervention. Although the procedures are broadly similar in terms of the necrosectomy, they differ in terms of how they prevent recurrence of an infected collection within the debridement cavity: 1) open necrosectomy with open or closed packing, 2) open necrosectomy with continuous closed postoperative lavage, and 3) programmed open necrosectomy.

In all approaches, the abdomen is entered though a midline or preferably a bilateral

subcostal incision, as this minimizes contamination of the lower abdomen and allows bilateral paracolic access. The pancreas is exposed by dividing the gastrocolic omentum or gastrohepatic omentum to access the pancreas through the lesser sac. Open transgastric debridement has recently been proposed to minimise post-operative peritoneal contamination (32).

Open Necrosectomy with Open Packing

Bradley described this technique in 1987 (8), sepsis control being achieved by leaving the abdomen open following debridement, packing the cavity as a laparostomy (8). Planned re-intervention with sequential pack changes allows resolution with healing by secondary intention. Drains may be placed in addition to the packing. Open packing techniques have been reported to have higher incidences of fistulae, bleeding, and incisional hernias as well as a slightly higher mortality rate (19).

Open Necrosectomy with Closed Packing

Following necrosectomy to achieve sepsis control (28), primary closure of the abdomen over gauze-stuffed Penrose drains is performed with the intention to fill the cavity and provide some compression (14). Additional silicone drains (Jackson-Pratt) may be placed in the pancreatic bed and lesser sac for fluid drainage. The drains are removed sequentially, starting 5 to 7 days postoperatively, allowing a gradual involution of the cavity.

Open Necrosectomy with Continuous Closed Postoperative Lavage

After debridement, where possible a closed peripancreatic compartment is reconstituted by suturing the gastrocolic and duodenocolic ligaments over large bore drains allowing flank to flank continuous lavage (6). Postoperative continuous lavage is instituted at 1 to 10 L per day and continued until the effluent is clear and the patient shows improvement in clinical and laboratory parameters (43). No evidence is available to suggest the best irrigation fluid, the optimal number or caliber of drains, or the duration of irrigation.

Programmed Open Necrosectomy

In response to the bleeding and fistulation that can arise following aggressive necrosectomy, this approach attempts to initially perform a more conservative debridement, with the intention of performing repeat procedures every 48 hours until debridement is no longer required. This mimics the “minimal hit” concept associated with the step up approaches. The pancreatic bed is drained or packed, and the abdomen is closed by suturing mesh or a zipper to the fascial edges of the wound (29). The addition of intra-abdominal vacuum dressings may encourage granulation of the pancreatic bed, and it has been suggested they may reduce the number of operations and mortality, but there is little data to support this and they have been associated with enteric fistulation (25).

5. Management *for* late WON

Indications for intervention for WON are: (1) Infection, (2) Nutritional failure, (3) Persistent abdominal pain. The decision on when to intervene and the choice of intervention are made within a multidisciplinary environment with consideration of all available options. Spontaneous resolution of even large acute walled off necrotic collections are not infrequent and often continued non-intervention is the best approach, particularly where continued maturation of a collection may be anticipated and where the clinical picture is improving. In any individual case, the choice of intervention may be guided by factors including the clinical picture, the position of the collection in relation to the stomach and duodenum and available expertise.

Laparoscopic Cystgastrostomy

For many years, the conventional approach to the management of late WON was open pancreatic cystgastrostomy, with

necrosectomy. This procedure can now be safely and effectively carried out using a laparoscopic approach and this represents the main alternative to endoscopic cystgastrostomy. Our current technique for laparoscopic cystgastrostomy is as follows: An open sub-umbilical cut down is employed. Further 12 mm and 5mm ports are inserted on the patient's left and right side with the specific port site placement being determined by the anatomical position of the retro-gastric collection. Adhesions are divided to expose the anterior gastric wall. An anterior gastrotomy (5-10 cm long) is then performed using the harmonic scalpel (Ethicon Endo-Surgery, Inc, Cincinnati, Ohio, USA). The superior leaf of the opened stomach is lifted toward the anterior abdominal wall to maximise access and delineate the area of adherence between the cyst and the posterior aspect of the stomach. This is achieved by passing a straight needle 2/0 suture through the abdominal wall, the anterior stomach wall and back out of the abdomen. A key advance has been the use of a "Step" dilatation port system (Covidien plc. Dublin, Ireland) to achieve initial cyst puncture, allow tract dilatation and maintain access until insertion of the initial staple device. Following aspiration of the collection contents to relative dryness, the port is withdrawn leaving the suction instrument within the collection to maintain access, and a stapled cystgastrostomy is performed using 4-5 firings of the angulating Universal Endo GIA stapler (Covidien plc, Dublin Ireland). Necrotic debris within the cavity is removed and placed in the fundus of the stomach. Once adequate debridement and haemostasis have been assured, the anterior gastrotomy is closed using a running 3/0 monofilament suture (BiosynTM , Covidien plc, Dublin Ireland), with the integrity of the closure then tested by insufflating the stomach through an oro-gastric tube, while the anastomosis is held under lavage fluid. Post-operative fluid and diet is allowed as tolerated. In this complex cohort of patients, suitability for hospital discharge is often multi-factorial, but may be within 36 h of surgery when dietary intake is adequate. Where gallstones are present, a simultaneous laparoscopic cholecystectomy is performed. Our initial results have been presented elsewhere and we are currently undertaking a randomized trial of EUS-guided endoscopic vs laparoscopic cystgastrostomy for WON (17).

Endoscopic Ultrasound Guided Cystgastrostomy / Necrosectomy

The technique of EUS guided drainage is as described above, the principle difference being the indication of failure to thrive rather than sepsis control. Many reports in the literature describe EUS-guided drainage of "pseudocysts" but is now recognised that true pancreatic pseudocysts are rare following acute pancreatitis as some degree of necrosis is usually present where collections persist. The revised Atlanta criteria defines these collections as WON, but there is still a spectrum of clinical presentations. WON may have varying degrees of fluid content and infection may be present, with or without systemic disturbance or organ failure. EUS-guided drainage of these collections is now an established technique in specialist units and several different modifications to the technique have been described. The frequent requirement for repeated endoscopic procedures, particularly in the presence of significant necrosis, have led to a former preference to select fluid predominant WON collections for this approach, but this assumption is being currently challenged in a randomized trial in our unit.

Management of Complications

Early Procedure Related Complications: SIRS / Bacteraemia Requiring Critical Care Support

For patients with established organ failure, drainage has an unpredictable effect on patients and the clinical picture may improve or

may worsen, at least temporarily. Evidence now supports a "step up" approach in the presence of organ failure and so initial management in these patients should be either percutaneous or endoscopic drainage, with more definitive intervention deferred until organ failure stabilises or improves.

Following any intervention, however minimal, it is not unusual for patients to show signs of significant SIRS or post procedure bacteraemia, and this may necessitate critical care admission for organ support. Our experience has been that minimally invasive approaches are less likely to cause the development of new organ failure, and this has been born out in randomized trials (40). More significant deterioration is common following open necrosectomy and this is therefore no longer the preferred approach.

Acute or Delayed Haemorrhage

Peri-procedural haemorrhage following initial drainage may be due to bleeding from submucosal or perigastric vessels during endoscopic or percutaneous drainage, and is usually self-limiting. Bleeding from the cavity itself is more likely during necrosectomy, particularly if carried out too early or too aggressively. Venous bleeding is more common in this situation and may occur during the procedure or in the post-operative period. It will usually resolve with correction of any coagulopathy but tamponade may be required, either by simply clamping the percutaneous drain, insertion of a modified Sengstaken-Blakemore tube (having amputated the gastric balloon), or gauze packing if there is sufficient cutaneous access following a VARD procedure.

Secondary haemorrhage is occasionally sudden and massive, but there is usually a prelude with a self-terminating “herald bleed”, presenting clinically with haemorrhage into a retroperitoneal drain or by a gastrointestinal bleed following transluminal drainage. Secondary haemorrhage is usually of arterial origin and is often a consequence of persistent local sepsis. This is now the major cause of death in patients with infected pancreatic collections and rapid intervention may be life-saving. Initial controlled volume support of the circulation and a simultaneous emergency CT angiogram is followed by angiography and embolization if appropriate. Upper gastrointestinal endoscopy in this setting is usually non-diagnostic and should therefore not delay radiological assessment which allows definitive management. The increased intra-cavity pressure associated with haemorrhage into an infected cavity, may result in escalating organ dysfunction through bacteraemia and sepsis. Timely consideration of further intervention to improve surgical drainage is important once bleeding has been arrested.

Enteric Fistulation

Spontaneous discharge of a pancreatic collection into the gastrointestinal tract is common and may occur in the presence or absence of infection. This should be suspected when a collection contains gas, particularly where a gas/fluid level is present, in a patient who is not systemically unwell. Indeed, discharge of a collection into the stomach or duodenum can be associated with an improvement in a patient's condition. In our experience, foregut fistulation will usually resolve without the need for intervention (other than adequate drainage of a collection by percutaneous or endoscopic means) but fistulation into the colon is often associated with clinical deterioration and persistent sepsis. Some form of defunctioning procedure is usually required and in occasional cases, formal colonic resection with exteriorisation may be required.

6. Late complications

Pancreatic Fistulation

Persistent pancreatic fistula is a common sequel of percutaneous necrosectomy or VARDS. Disruption of the pancreatic duct is common in the presence of extensive necrosis, and although resolution is the norm, persistent fistulae can be a challenging management problem. If a pancreatic fistula persists once resolution of sepsis and any significant collection has been confirmed by CT, pancreatic duct stent insertion at ERCP is the management of choice. Failure of resolution thereafter is often associated with more extensive parenchymal loss, or a disconnected pancreatic tail with loss of continuity of the main pancreatic duct. Prolonged catheter drainage will lead to maturation of the fistula tract and planned interval drain removal may result in spontaneous resolution or development of a late pseudocyst, which can often be resolved by transmural endoscopic cystgastrostomy. The avoidance of pancreatic fistula is one of the main advantages of endoscopic (or laparoscopic) drainage of pancreatic collections.

Disconnected Pancreatic Tail

Following extensive necrosis or complete necrosis of a section of the neck or body of the pancreas, complete separation of the main pancreatic duct in the pancreatic tail may occur leading to a persistent fistula and "disconnected duct syndrome". This may lead to persistence of a pancreatic fistula or a late "pseudocyst" following initial successful management of a pancreatic collection. Ductal occlusion at the pancreatic neck precludes trans-papillary access but if this has not occurred, intra-cystic trans-papillary stenting or a stent bridging the defect into the tail, may result in resolution. If trans-papillary access is not possible, the preferred option is transmural EUS guided drainage with placement of long-term pigtail stents although in some patients, distal pancreatectomy may be required. This however is a challenging procedure, particularly, as is commonly the case, where there have been previous interventions.

7. Conclusion

Clinical complexity and diversity precludes algorithm driven management in severe acute pancreatitis. Three phases of management exist (1) organ support (2) sepsis control and (3) failure to thrive; based on an understanding of the evolution of necrosis/collections and the dynamic nature of the physiological response in acute pancreatitis the rationale and interventional approach chosen will differ depending on the specific issues that need to be addressed. Maintaining nutritional competence throughout is essential. Individual patient management within a step-up framework remains key, utilizing a multimodal approach focused on delayed minimally invasive intervention where possible.

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