

Joint Trust Management of Acute Severe Pancreatitis in Adults

A clinical guideline recommended for use

For Use in:	All clinical areas (as a reference for screening) ITU/HDU (for definitive care)
By:	All medical staff likely to manage patients with pancreatitis
For:	Patients with acute severe pancreatitis
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If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A

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Version Number	Date of Update	Change Description	Author
2.2	16/10/202	No clinical changes	Simon Fletcher

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Quick reference guideline

The following notes form a synopsis of the best evidence available and internal discussions regarding the management of pancreatitis at the Norfolk and Norwich Hospital. Please refer to the discussion document more details.

This document is for use in the management and diagnosis of acute severe pancreatitis and to guide the care of these patients on the intensive care/high dependency unit.

It is to be used by all medical staff likely to manage patients with pancreatitis.

1. **Establish diagnosis of acute pancreatitis (history, examination, serum amylase etc.)**
2. **Attempt to identify cause.** Ultrasound is usually indicated within first 24hrs
3. **Stratify disease severity using modified Glasgow Score as listed below.**

One point for each of the following:

- a. Age greater than 55 years
- b. White cell-count greater than 15×10^9 litre
- c. Glucose greater than 10mmol/litre (not diabetic)
- d. Urea greater than 16mmol/litre (when re-hydrated)
- e. PaO₂ less than 8kpa on air
- f. Corrected calcium less than 2mmol/litre
- g. Albumin less than 32g/litre
- h. LDH greater than 250units/litre

(Note transaminase levels are not included in this scoring system)

All patients with score of 3 or greater should be referred to the ITU/HDU for further assessment.

Others indicators of severity include organ dysfunction, high APACHE 2 score and other biochemical tests such as CRP. These are discussed later.

The following points refer to treatment in HDU/ITU

4. **Send base line C reactive protein and if patient not better repeat at one week.** A level of greater than 210mg/litre within four days or greater than 120mg/litre at one week is predictive of severe disease.
5. Radiological assistance. A CT scan is indicated
 - a. **To confirm a diagnosis of acute necrotising pancreatitis, if clinical diagnosis uncertain**

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- b. If patient condition deteriorates and scan may influence further management (a CT guided pancreatic aspiration may be very useful in confirming the presence of infected necrosis and guiding antibiotic management)**

As a rule the request for CT scan should be made on a consultant to consultant basis in order to best facilitate this process.

6. Prophylactic antibiotics. **Not indicated given weight of evidence**

Current evidence remains inconclusive. Since this guideline was first written there have been more trials investigating the benefits of prophylactic antibiotics in severe pancreatitis. Generally they have involved small numbers of patients and results have been contradictory, as have the conclusions of meta-analyses. At this time most authorities no longer recommend the use of prophylactic antibiotics. A possible exception is where enhanced CT scanning has demonstrated significant necrosis. Here decisions should be on an individual basis.

Antibiotics are indicated where infection is suspected or confirmed. Severe inflammation may present in an identical way to sepsis. Broad spectrum antibiotics, such as meropenem or piperacillin/tazobactam should thus be prescribed where infection is suspected. These may be discontinued or modified depending on progress, sensitivities etc.

7. Enteral nutrition. **Enteral feeding should be attempted in all patients with severe disease.**

Enteral feeding may be difficult or impossible orally or via a nasogastric tube in patients with severe disease. Placement of a nasojejunal tube should thus be considered as a priority to facilitate this after 3 or 4 days

If a patient subsequently requires a laparotomy or necrosectomy or other surgical intervention a jejunal feeding tube should be placed at this time.

8. Indications for surgery. The following are indications for consideration of surgical intervention in this patient group.
 - a. Sterile necrosis with worsening Systemic Inflammatory Response Syndrome (SIRS) /multi-organ failure**
 - b. Infected necrosis with a picture of sepsis**
 - c. Clinical picture of acute abdomen/infected collection, abscess of pseudocyst**

Please note that surgical intervention for complications of pancreatitis should be discussed with the relevant surgical team at Addenbrooke's who now provide this service

Rationale for the recommendations

There is significant evidence that if these patients are intensively managed from diagnosis, morbidity and mortality are reduced. These guidelines thus aim to identify

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high-risk patients for early referral to high dependency care. In addition a systematic approach to their care based on the best evidence available is specified here.

United Kingdom figures suggest that up to 3% of hospital admissions with acute abdominal pain will have pancreatitis. The admission data for the Norfolk & Norwich Hospital across all specialities suggests that we admit between 70 and 80 cases of pancreatitis per year and we expect to see between 15 and 20 patients with severe disease on a yearly basis.

Most common aetiological factors in the United Kingdom are gallstones followed by alcohol. There are numerous other listed causes and even after all have been addressed approximately 10% of cases do not have an obvious underlying cause. It is important to identify the causative factor as early as possible (within 48 hours) as this may have therapeutic implications.

Early use of enteral nutrition is significantly cheaper than parenteral nutrition.

Broad recommendations

See Quick reference guide

Clinical Audit Standards derived from guideline

- 1 Use of modified Glasgow Score for severe acute pancreatitis
- 2 Were all patients scored?
- 3 Were all patients with a score of 3 or more reviewed by HDU?
- 4 Were ultrasound and CT scan undertaken appropriately on all patients?
- 5 Was feeding attempted in all patients with severe disease?
- 6 Outcomes, surgical versus non-surgical management

Summary of development and consultation process undertaken before registration and dissemination

Following circulation of the provisional guidelines to all concerned, I have made a number of modifications and thus I hope the guidelines below represent a consensus. The guideline has been seen by;

- All surgeons
- All gastroenterologists
- All Intensivists (including chair of D&T committee)
- Radiology

A number of amendments were made following these consultations and general agreement has been reached.

The guideline has been reviewed and amended by Dr S Fletcher, author, in May 2010

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Distribution list/ dissemination method

Trust Intranet

References/ source documents

1. UK Guidelines for the management of acute pancreatitis. The British Society of Gastroenterology. Gut 1998 June; 42 (Supplement 2) S1-S13
2. AGA Institute Technical Review on Acute Pancreatitis. GASTROENTEROLOGY 2007;132:2022–2044
3. Acute pancreatitis at the beginning of the 21st century: The state of the art. World J Gastroenterol 2009 June 28; 15(24): 2945-2959
4. Enteral Nutrition and the Risk of Mortality and Infectious Complications in Patients With Severe Acute Pancreatitis A Meta-analysis of Randomized Trials. Arch Surg. 2008;143(11):1111-1117

These recommendations are based a review of the world wide literature published since this guideline was last updated. Three summary papers have been referenced which include the vast majority of the original research

Severity stratification

Overall mortality for acute pancreatitis in the United Kingdom is of the order of 10%. However the spectrum of disease is wide - from a mild disturbance of gastro intestinal function to fulminating disease with acute organ failure and death.

The majority of patients run a benign course and will need little more than analgesics and IV fluids in their management. Early recognition and more aggressive management of the more severe cases can significantly improve outcome.

In an attempt to identify early - within 48 hours - those in the high-risk group, a number of stratification scores have been developed. These attempt to predict which patients may develop more severe disease. Pancreatitis is an acute inflammatory process, which in its mild form causes minimal systemic disturbance and is accompanied by oedematous changes in the pancreas only.

Severe disease is defined as pancreatitis accompanied by:

1. Significant organ dysfunction
2. Necrosis
3. Infected necrosis
4. Pseudo cyst
5. Abscess

While 80% of cases will have mild disease and a very low mortality, 95% of deaths occur in the severe group. Mortality with sterile pancreatic necrosis is of the order of

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10% but may rise to 40% in infected cases. Age and co-morbidity play an important role.

Classification into severe and mild forms of the disease using clinical criteria only is accurate in 50% of the cases. Scoring systems such as Ransom, Glasgow and APACHE II are more accurate. Of these the least complicated, but also the one most frequently validated in the British population, is the **modified Glasgow Score**. This lists eight criteria to be assessed within 48 hours of admission. The worst readings are taken. They are:

1. Age > than 55 years
2. White blood count > than 15×10^9 /litre
3. Glucose > than 10mmol/litre (non diabetic)
4. Urea > 16mmol/litre (when re-hydrated)
5. $PAO_2 < 8$ kPa on air
6. Corrected calcium < 2mmol/litre
7. Albumin < 32gm/litre
8. LDH > 250units/litre (however the upper limit for the normal value at the Norfolk & Norwich Hospital is 234 units/litre!)

Note transaminase levels are not included in this scoring system.

Forty percent of patients with three or more factors will develop severe disease. Only 6% with two or less factors will. Overall this scoring is approximately 80% predictive. (Gut 84, 25, 1340-1, 1346.)

The Ranson score is generally used in the US, despite being more complicated and no more reliable.

C reactive protein levels are also predictive in this disease. A level of >210mg/litre within four days or 120mg/litre at one week is approximately 80% predictive of severe disease.

APACHE II scoring may also be helpful, especially as it includes a weighting for co-morbidity. If a score of nine is chosen it is selective, but not very sensitive, but if six is chosen despite being 95% sensitive, selectivity is in the order of 50%. APACHE II scores however, can be used for ongoing assessment and an acute deterioration often indicates the onset of sepsis.

Single or multiple organ failure is, by definition, an indicator of severity, and should thus prompt consideration of HDU review.

Management issues

Of the 10% or so of patients who die of this disease, one third dies in the first week, often with fulminating organ failure. Respiratory failure is most significant here. These patients are the ones most likely to benefit from early referral and management on a high dependency unit.

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Of the rest many will die of sepsis, most usually of pancreatic origin, but a significant number develop nosocomial pneumonia, line sepsis UTIs etc. Inevitably some die late of multi system organ failure.

Further reductions in mortality will only occur if these patients are managed aggressively with full multi speciality co-operation - surgical, gastroenterological, radiological and intensive care.

General care

Full supportive care in an appropriate environment for high risk and severely ill patients.

No benefit has been shown from the use of protease inhibitors, pancreatic enzymes secretion suppression etc.

Current evidence suggests lexipafant, a PAF antagonist, is of no benefit

Low risk patients need analgesia and fluids and probably enteral feeding when tolerated. Be aware that a few may have been misclassified.

Underlying cause

The majority of cases in the UK will have gallstones. This may not always be the precipitant, but usually is. The early use of ERCP to relieve obstruction is controversial. However, there is evidence that

1. Severe gallstone pancreatitis with jaundice/cholangitis deserves immediate ERCP
2. Severe gallstone pancreatitis with no improvement at 48 hours also deserves ERCP
3. Patients with mild disease but jaundice plus or minus bile duct distension also deserve ERCP.

The number of patients likely to require emergency ERCP at the Norfolk & Norwich Hospital on a yearly basis is very small. The number who may require ERCP hopefully on the next routine list is also likely to be in single figures. I do not think therefore that there is likely to be significant extra workload involved with this recommendation.

Radiology

Radiological expertise is integral to the management of these patients. It is recommended that all patients in the severe group should have an enhanced CT scan within 3-10 days of admission for the following reasons;

- a. It provides accurate data as to the severity of the attack (presence of necrosis, inflammation of surrounding tissues etc.)
- b. May indicate early those likely to need surgery
- c. Gives a baseline to assess the progress of the disease
- d. May be needed to identify the aetiology of the attack

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A repeat CT every two weeks gives accurate information of disease progression. A CT is also very useful in the assessment of the deteriorating patient. Often this is due to the onset of sepsis - most frequently due to infected necrosis, but also due to infected fluid collections, abscess or pseudocyst. A CT guided aspiration of suspected tissue has been shown to be extremely accurate in identifying the source of sepsis and infecting organism.

Ultrasound is of limited use in pancreatitis. Bowel gas often obscures the pancreas; inflammation is not always distinguishable from necrosis; collections and/or pseudocyst are late complications.

Prophylactic antibiotics

There is no indication for the use of antibiotics in mild cases.

The use of prophylactic antibiotics, in an attempt to prevent infection in patients with severe pancreatitis is a grey area. Trial results are inconclusive. Many are of poor methodology and contain few subjects. Neither of the recently published RCT's demonstrated a benefit. The Cochrane metaanalysis does however support their use.

Despite this all current national and international treatment guidelines do not advocate the use of prophylactic antibiotics in both mild and severe pancreatitis. A possible exception is the subgroup with CT confirmed extensive necrosis. Here decisions should be by a senior clinician on an individual basis.

Enteral nutrition

The early use of enteral nutrition in these patients is now universally advocated as ideal practice.

The extent of pancreatic damage is not modified but the instance of septic complications, measurements of disease severity (Glasgow score, APACHE II score, CRP) and the need for full intensive care support have been shown to be reduced. There may not be an overall reduction in mortality. If all attempts to feed by the enteral route fail, then TPN should be initiated. The timing here is not critical but clearly a patient should not be without nutrition for a prolonged period.

In a general intensive care population enteral feeding reduces the incidence of most nosocomial infections and possibly multi system organ failure.

To effectively feed these patients jejeunal-feeding tubes may need to be placed. Many centres now routinely place these tubes and successfully feed their critically ill patients.

Ongoing care/indications for surgery

Early detection and management of complications may be life saving. Often the patients at the worst end of the spectrum decline relentlessly and many factors, specifically to do with co-morbidity, make this inevitable.

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Objective evidence of disease progression using CRP and APACHE II scoring may however be useful when determining the need for surgical intervention.

A low-grade fever is normal in these patients.

High fever, deteriorating organ function, ARDS, rising CRP, white cell count, LFTs and worsening coagulopathy (indicative of SIRS/sepsis) all support the need for surgical intervention.

Without doubt surgical intervention in these patients is high risk.

However, there appears to be an emerging consensus as to the hard indications for active intervention. While each case should be judged on its own merit the following guidelines seem appropriate.

- a. Sterile necrosis - uncomplicated - no indication for surgery
- b. Sterile necrosis with worsening SIRS/multi organ failure - proceed to surgical debridement
- c. A picture of an acute abdomen/infected collection (with positive microbiology), abscess or pseudocyst - benefit from laparotomy and debridement +/- lavage.
- d. Infected necrosis (high mortality) - urgent laparotomy and necrosectomy