

United Kingdom guidelines for the management of acute pancreatitis

Preface

These guidelines on the management of acute pancreatitis were commissioned by the British Society of Gastroenterology. They have been endorsed by the Clinical Services Committee of the British Society of Gastroenterology, the Association of Upper Gastro-Intestinal Surgeons of Great Britain and Ireland, the Pancreatic Society of Great Britain and Ireland, and the Association of Surgeons of Great Britain and Ireland.

The guidelines address the initial steps in diagnosis, investigation and treatment of acute pancreatitis, but stop short of the specific surgical management of complex cases. The nature of acute pancreatitis with its wide variation of severity and complications means that rigid guidelines may be inappropriate and difficult to apply. Thus, although these guidelines attempt to describe the highest standard of care and set audit goals, a large element of independent clinical decision making is still required. A further factor relates to the availability of local resources and expertise in the management of acute pancreatitis and this is addressed with reference to specialist units.

The list of clinicians from different specialities who are directly responsible for these guidelines together with those who were consulted at a later stage of their production is given at the beginning of this supplement. The modus operandi of the group is given within the text. These guidelines were finalised in April 1997 and will need to be revised in two years time.

Introduction and purpose of guidelines

During recent years there have been many changes in the management of patients with acute pancreatitis. These have included the general availability of computed tomography (CT) scanning, interventional radiological procedures, refinements in ITU care, and a more aggressive surgical policy in those with infected necrosis. Despite these measures, the overall mortality has remained unaltered at around 10–15% for the past two decades.^{1,2} Multicentre audits have revealed deficiencies in the management of the disease,^{3,4} with a lack of standardised protocols both within and between institutions. It is hoped that these guidelines will provide a framework for clinicians to follow when treating patients with this difficult disease.

Process of formulation of guidelines

The process of formulating any clinical guidelines requires a guideline development group, a search strategy and review of the relevant literature, synthesis of evidence (and consensus methods for topics when evidence is lacking), followed by external review.⁵

These steps were followed in the development of these guidelines on acute pancreatitis. A multidisciplinary group meeting was held (with representatives from surgery, medicine and radiology), which comprised individual presentations on aspects of acute pancreatitis, a literature review and expert re-evaluation. An initial group consensus was reached and a preliminary document produced. This was then put forward for further expert review and amended accordingly.

The guidelines were also presented for discussion in various open meetings—namely at the Pancreatic Society of Great Britain and Ireland in November 1995, the British Society of Gastroenterology in March 1996 and the Association of Upper Gastro-Intestinal Surgeons of Great Britain and Ireland in Bournemouth in April 1997.

VALIDITY AND GRADING OF RECOMMENDATIONS

The guidelines have been produced to conform to the system proposed by the North of England evidence-based guidelines development project.^{5,6}

CATEGORIES OF EVIDENCE

The strength of evidence used in the formulation of these guidelines was graded according to the following system:

- Ia evidence obtained from meta-analysis of randomised controlled trials;
- Ib evidence obtained from at least one randomised controlled trial;
- IIa evidence obtained from at least one well designed controlled study without randomisation;
- IIb evidence obtained from at least one other type of well designed quasi-experimental study;
- III evidence obtained from well designed non-experimental descriptive studies such as comparative studies, correlation studies and case studies;
- IV evidence obtained from expert committee reports or opinions or clinical experiences of respected authorities.

The evidence category is indicated after the citations in the reference section at the end of the document.

GRADING OF RECOMMENDATIONS

The strength of each recommendation depends on the category of the evidence supporting it, and is graded according to the following system:

- A requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation (evidence categories Ia, Ib);
- B requires the availability of clinical studies without randomisation on the topic of

recommendation (evidence categories IIa, IIb, III);

- C requires evidence from expert committee reports or opinions or clinical experience of respected authorities, in the absence of directly applicable clinical studies of good quality (evidence category IV).

SCHEDULED REVIEW OF GUIDELINES

The methods of diagnosis, assessment and treatment of patients with acute pancreatitis are constantly evolving, and new evidence comes to light continuously. The content and evidence base of these guidelines will therefore be reviewed in two years time.

Summary of audit goals in acute pancreatitis

These guidelines on the management of acute pancreatitis have led to the following audit goals which can be used as a measure of the standard of care. The grading of each recommendation is given and these are based on the evidence reviewed in the subsequent text.

- Mortality should be lower than 10% overall and less than 30% in severe groups (grade B).
- Correct diagnosis to be made in all patients within 48 hours of admission (grade C).
- Severity stratification should be made in all patients within 48 hours (grade B).
- Assessment of aetiology to be made in all patients with an idiopathic group of no more than 20–25% of total (grade B).
- Patients with mild gallstone pancreatitis (that is, without complications) should have definitive management of the gallstones, ideally within two weeks and no longer than four weeks (grade B).
- All cases of severe acute pancreatitis should be managed initially in an HDU or ITU setting with full systems support (grade B).
- Radiological facilities should be available to permit scanning (ultrasound, dynamic CT or magnetic resonance imaging (MRI)), percutaneous guided aspiration and drainage techniques, and more rarely angiography for the early assessment and treatment of abdominal and other complications (grade A).
- Dynamic CT scanning to be performed on all patients with severe acute pancreatitis between three and 10 days of admission subject to clinical practicalities (grade B).
- Facilities and expertise should be available for endoscopic retrograde cholangiopancreatography (ERCP) to be performed at any time for common bile duct evaluation followed by sphincterotomy and stone extraction or stenting as required, particularly but not exclusively in severe gallstone pancreatitis, jaundice or cholangitis (grade A).
- Management in, or referral to, a specialist unit is necessary in patients with extensive necrotising pancreatitis or with other complications who may require ITU care and/or interventional radiological, endoscopic or surgical procedures (grade B).

Definitions

The terminology for acute pancreatitis and its complications is often confusing and conflicting. The definitions of pancreatic inflammatory disease has been the subject of several international conferences in Marseilles 1963,⁷ Cambridge 1983,⁸ Marseilles 1984,⁹ and Atlanta 1992.¹⁰

The Atlanta meeting was directed mainly at the complications of acute pancreatitis and their definitions.¹⁰ The Atlanta classification has been used in these guidelines, and the definitions used are listed below. Ambiguous terms such as phlegmon and haemorrhagic are no longer recommended.

In addition, a further definition has been made in these guidelines of a specialist unit for the treatment of severe and complex disease.

ACUTE PANCREATITIS

Acute pancreatitis is an acute inflammatory process of the pancreas, with variable involvement of other regional tissues or remote organ systems.

SEVERE ACUTE PANCREATITIS

Severe acute pancreatitis is associated with organ failure and/or local complications such as necrosis (with infection), pseudocyst or abscess. Most often this is an expression of the development of pancreatic necrosis, although patients with oedematous pancreatitis may manifest clinical features of a severe attack.

MILD ACUTE PANCREATITIS

Mild acute pancreatitis is associated with minimal organ dysfunction and an uneventful recovery. The predominant pathological feature is interstitial oedema of the gland.

ACUTE FLUID COLLECTIONS

Acute fluid collections occur early in the course of acute pancreatitis, are located in or near the pancreas, and always lack a wall of granulation of fibrous tissue.

PANCREATIC NECROSIS AND INFECTED NECROSIS

Pancreatic necrosis is a diffuse or focal area(s) of non-viable pancreatic parenchyma, which is typically associated with peripancreatic fat necrosis. The onset of infection results in infected necrosis, which is associated with a trebling of the mortality risk.

ACUTE PSEUDOCYST

An acute pseudocyst is a collection of pancreatic juice enclosed in a wall of fibrous or granulation tissue that arises following an attack of acute pancreatitis. Formation of a pseudocyst requires four or more weeks from the onset of acute pancreatitis.

PANCREATIC ABSCESS

A pancreatic abscess is a circumscribed intra-abdominal collection of pus, usually in proximity to the pancreas, containing little or no pancreatic necrosis, which arises as a consequence of acute pancreatitis.

SPECIALIST UNIT

A specialist unit is one in which multidisciplinary expertise is available on-site. Full intensive care facilities are mandatory, together with recourse to ERCP at any stage on an emergency basis. Expert radiological input for dynamic scanning, percutaneous procedures and angiography is essential. A surgeon with pancreato-biliary expertise should supervise management.

Background**INCIDENCE AND EPIDEMIOLOGY**

Acute pancreatitis accounts for 3% of all cases of abdominal pain admitted to hospital in the UK.¹¹ The true incidence of acute pancreatitis remains contentious and accurate assessments are hampered by geographical, aetiological, and diagnostic variations. This difficulty is reflected in past reports of incidence in the UK ranging from 21 to 283 cases per million population.^{12–13} Some epidemiological evidence suggests that the true incidence is probably increasing,¹⁴ partly reflecting increased alcohol intake among the young¹⁵ but also due to gallstones in some areas.¹⁶

MORTALITY AND MORBIDITY

The precise mortality from acute pancreatitis is difficult to ascertain due to variations in diagnostic thresholds and inconsistent use of autopsy data.¹⁷ The inclusion of postmortem data will influence the mortality rate as some cases are undiagnosed in life both in the hospital³ and in the community.¹⁸ It is important to distinguish between absolute death rate and percentage case mortality.¹⁹ Despite these issues, evidence from multicentre trials of various treatments^{20–22} and from other multicentre reviews^{1–3} suggests that the death rate of clearly diagnosed cases has remained unaltered at 10–15% over the past 20 years.

CAUSES OF MORTALITY

The patterns of mortality and morbidity in acute pancreatitis have changed over time. Currently about one third of patients die in the early phase of an attack from multiple organ failure,^{2–3} which represents a reduction in early phase deaths when compared with reports from preceding decades.^{23–24} It has long been recognised that major fluid deficit occurs early in acute pancreatitis,²⁵ and it is likely that modern aggressive fluid replacement, close monitoring and ITU care have improved the outcome in such patients. Most deaths occurring after the first week of onset are due to infective complications, particularly infected necrosis.^{26–28} Other subsets of patients at high risk are the elderly with comorbid medical problems^{16–29} and certain aetiological groups—for example, postoperative acute pancreatitis.^{30–31}

The mortality of patients with necrotising pancreatitis is high and outcomes depend on a variety of factors, including the extent of necrosis, the onset of infection^{32–33} and the degree and type of surgical debridement. The overall mortality from necrotising pancreatitis is around 30–40%.³⁴ Sterile necrosis is associ-

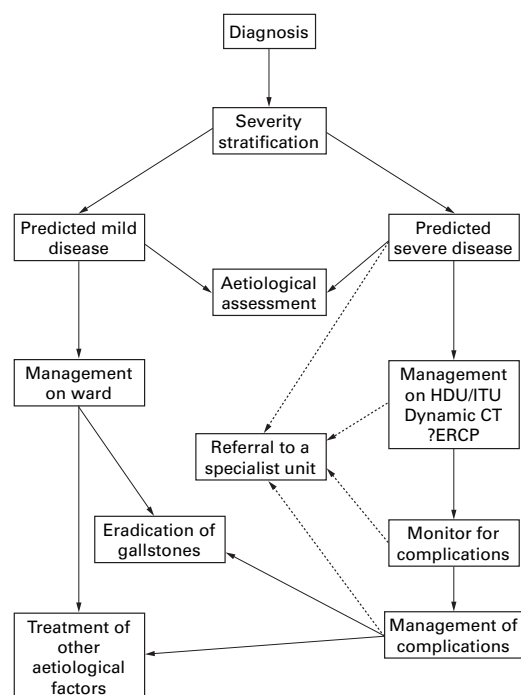


Figure 1 Summary of management steps in acute pancreatitis.

ated with a mortality of 0–11%,^{35–36} whereas that for infected necrosis averages 40%³⁷ but may exceed 70%.²⁸ Some specialist centres have reported improved outcomes following a policy of aggressive surgical debridement for infected necrosis, with mortality rates between 10 and 20%.^{38–40} There is a wide variation in mortality rates for infected necrosis reported from centres in the UK—for example, 14% mortality in Southampton⁴¹ compared with 69% in Leeds,⁴² and may reflect case severity and time of referral for patients undergoing pancreatic necrosectomy.

Recommendation: mortality

While striving constantly to reduce mortality in acute pancreatitis it is currently accepted that some patients will die. The overall mortality should be lower than 10%, and less than 30% in those diagnosed with severe disease. (Recommendation grade B.)

Outline of management of acute pancreatitis

Figure 1 outlines the management of acute pancreatitis, which can be broadly divided into three overlapping phases. The first phase includes diagnosis and assessment of severity. The second phase, running simultaneously, involves management according to disease severity with ongoing monitoring and assessment. The final phase involves the detection and management of complications (particularly in the group predicted as severe) and the evaluation and treatment of aetiological factors in all patients.

Diagnosis

The diagnosis of acute pancreatitis may be difficult to make despite the many types of investigation available. It is imperative that other life

threatening conditions are excluded (for example, mesenteric ischaemia, visceral perforation, leaking abdominal aortic aneurysm).

DIAGNOSIS—CLINICAL

A clinical history of upper abdominal pain and vomiting with features of epigastric or diffuse abdominal tenderness are the common clinical findings. Occasionally, body wall ecchymoses (Cullen's sign at the umbilicus, Grey-Turner's sign in the flanks) will be evident.⁴³ These features occur in several other acute abdominal diseases, and a diagnosis of acute pancreatitis is often unreliable if made on the clinical findings alone. Furthermore, the clinical picture may be obscured in certain circumstances, such as in the postoperative period.³⁰ On occasion, when the presentation is late, a retrospective clinical diagnosis may be made without other supporting evidence.

DIAGNOSIS—BIOCHEMICAL

In the majority of instances, given the appropriate clinical setting, the diagnosis of acute pancreatitis is made by a serum amylase activity four times above normal (or by a lipase activity greater than twice the upper limit of normal).⁴⁴ Occasionally, when the diagnosis is suspected on clinical grounds, an equivocal serum amylase will be accompanied by a diagnostic urinary amylase activity. Although less frequently available a serum lipase measurement is diagnostically accurate.⁴⁵ The advantages of measuring lipase are that its activity remains increased for longer than that of serum amylase and that there are no other sources of lipase to reach the serum⁴⁶ and thus this test has a high specificity.⁴⁷

DIAGNOSIS—RADIOLOGICAL

Plain x rays

Chest and abdominal plain x ray examinations should be performed routinely to provide a baseline picture and to exclude other pathology such as perforated viscus and intestinal obstruction.

The reported plain abdominal x ray findings in acute pancreatitis are unreliable and include a generalised or local ileus (sentinel loop), a colon cut off and a renal halo sign.⁴⁸ These appearances are non-specific and cannot be recommended for use in diagnosis. Rarely, in advanced cases, the presence of retroperitoneal gas will indicate infection.⁴⁹ Occasional helpful but non-diagnostic signs include calcified gallstones and pancreatic calcification, although this indicates chronic changes in the gland or very rarely a tumour.

Chest x ray films may show a spectrum of changes depending on the disease severity. A pleural effusion is the commonest finding, although in severe cases diffuse alveolar interstitial shadowing may suggest an acute respiratory distress syndrome (ARDS).

Ultrasound

Ultrasound examination of the abdomen may be helpful in confirming the diagnosis. A swollen pancreas may be detected, but the gland is poorly visualised in 25–50% of cases, so this

method cannot be used for definitive diagnosis.^{50–52} Ultrasound is valuable in detecting free peritoneal fluid, gallstones, dilatation of the common bile duct, and occasionally other pathology such as abdominal aortic aneurysm. Despite its unreliability in diagnostic terms ultrasound is recommended initially in all patients with suspected acute pancreatitis and may be repeated as frequently as clinical conditions dictate. An early diagnosis of gallstones is particularly important in patients thought to have severe pancreatitis as the need for an urgent ERCP would then have to be considered (see later).

Computed tomography scanning

A CT scan is occasionally indicated for diagnostic purposes if the clinical and biochemical findings are inconclusive.⁵³

DIAGNOSIS—INTERVENTIONAL/SURGICAL

Peritoneal fluid sampling

If peritoneal fluid is detected by imaging techniques in the absence of other biochemical or radiological signs of pancreatitis (for example, gland swelling), the fluid should be sampled, preferably under radiological guidance. Microscopic examination of the fluid may reveal bacterial contamination suggestive of perforation.⁵⁴ A high fluid amylase content may suggest pancreatitis, although this can occur in other acute abdominal conditions.⁵⁵ The colour of the peritoneal fluid in acute pancreatitis ranges from clear, straw coloured to "prune juice", and although this is of prognostic importance⁵⁶ aspiration of peritoneal fluid is not recommended as a routine procedure.

Surgical

Rarely, when the clinical suspicion of peritonitis is high and all other tests, including a CT scan, are inconclusive, laparotomy may be warranted.²² Occasionally, acute pancreatitis and another intra-abdominal catastrophe may coexist.⁵⁷ Laparoscopy would be a less invasive diagnostic procedure but evidence of its reliability is not available.

Recommendation: diagnosis

The correct diagnosis of acute pancreatitis should be made within 48 hours of admission. Although this may strain support and diagnostic facilities, the risk of missing an alternative life threatening intra-abdominal catastrophe demands full investigation. (Recommendation grade C.)

Severity stratification

The initial prediction of the severity of an attack of acute pancreatitis into mild and severe has important implications for management, prognostication and use of health care resources. Failure to stratify early in an attack may result in potentially avoidable deaths.^{3,4} Such stratification is initially a prediction only and becomes a fact (by definition) when systems failure or local complications supervene. No method of prediction of severity is

Table 1 Glasgow scoring system for the initial prediction of severity in acute pancreatitis

Age	>55 years
White blood cell count	>15 × 10 ⁹ /l
Glucose	>10 mmol/l
Urea	>16 mmol/l
PaO ₂	<60 mm Hg
Calcium	<2 mmol/l
Albumin	<32 g/l
Lactate dehydrogenase	>600 units/l
Aspartate/alanine aminotransferase	>100 units/l

perfect and none will predict all patients who will develop later complications. Furthermore, many who are initially classified as severe will have an uncomplicated recovery.

SEVERITY STRATIFICATION—CLINICAL

Clinical assessment alone is unreliable, and will misclassify around 50% of patients.⁵⁸ However, the Atlanta definitions state that the presence of organ failure (pulmonary, circulatory or renal insufficiency) detected clinically will indicate a severe attack.¹⁰

SEVERITY STRATIFICATION—BIOCHEMICAL AND OBJECTIVE CRITERIA

A variety of biochemical and objective criteria has been described to stratify patients into mild and severe groups. It should be noted that these criteria alone do not necessarily signify the need for subsequent surgery, as they do not accurately predict the degree of pancreatic necrosis⁵⁹ which is best assessed by contrast enhanced CT scanning.

Ranson and Glasgow scoring systems

Multifactor scoring systems^{60 61} will improve overall accuracy of prognostication to around 70–80%. The Glasgow criteria have been vali-

dated in the UK population.⁶² Three or more positive criteria based on initial admission score and subsequent repeat tests over 48 hours, constitutes severe disease (table 1).

C-reactive protein

Blood C-reactive protein (CRP) concentration has independent prognostic value. A peak level of >210 mg/l in the first four days of the attack (or >120 mg/l at the end of the first week) has a predictive performance similar to that of objective systems,⁶³ with an overall accuracy of around 80%.

In combination, CRP and Glasgow criteria may further improve prognostication.

APACHE II

The APACHE II scoring system⁶⁴ (table 2) can be used to assess the initial severity of disease and the chances of developing a subsequent complication. A score of 9 or more indicates a severe attack but excludes many with a lower score that will develop a complication. An APACHE II score of 6 or more will include nearly all complications (sensitivity 95%) but only half the patients will develop a complication (positive predictive value 50%).⁶⁵

Subsequent daily scoring by APACHE II can be used for ongoing assessment; the pattern of change indicating either recovery, disease progression or the onset of sepsis.⁶⁶

Other blood markers

A series of other inflammatory (for example, interleukin 6⁶⁷), enzymatic (for example, PMN elastase,⁶⁸ trypsinogen activation peptide⁶⁹), and non-specific markers (for example, methaemalbuminaemia⁷⁰) of the disease process have been shown to vary with clinical severity.

Table 2 APACHE II scoring system

Variable	Acute physiology score									
	High normal range					Low normal range				
	+4	+3	+2	+1	0	+1	+2	+3	+4	
Temperature (°C)	>41	39–40.9		38.5–38.9	36–38.4	34–35.9	32–33.9	30–31.9	<29.9	
Mean arterial pressure (mm Hg)	>160	130–159	110–129		70–109		50–69		<49	
Heart rate (ventricular; beats/min)	>180	140–179	110–139		70–109		55–69	40–54	<39	
Respiratory rate	>50	35–49		25–34	12–24	10–11	6–9		<5	
Oxygenation (mm Hg)										
A _{aDO₂} when F _{iO₂} >0.5	>500	350–499	200–349		<200					
P _{aO₂} when F _{iO₂} <0.5					PO ₂ >70	PO ₂ 61–70		PO ₂ 55–60	PO ₂ <55	
Arterial pH	>7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15	
Serum Na (mmol/l)	>180	160–179	155–159	150–154	130–149		120–129	11–119	<110	
Serum K (mmol/l)	>7	6–6.9		5.5–5.9	3.5–5.4	3–3.4	2.5–2.9		<2.5	
Serum creatinine (mg/100 ml)	>3.5	2–3.4	1.5–1.9		0.6–1.4		<0.6			
Double score for ARF										
Packed cell volume (%)	>60		50–59.9	46–49.9	30–45.9		20–29.9		<20	
White blood cell count (×10 ³ /mm ³)	>40		20–39.9	15–19.9	3–14.9		1–2.9		<1	
Glasgow coma scale*										

*Score = 15 – actual Glasgow coma scale.

The APACHE II score is given by the sum of the acute physiology score, the age (in years) points, and the chronic health points. Age points are assigned as follows: 0, <44; 2, 45–54; 3, 55–64; 5, 65–74; and 6, >75. Chronic health points are assigned if the patient has a history of severe organ system insufficiency or is immunocompromised, as follows: 5, non-operative or emergency postoperative patients; 2, elective postoperative patients. Organ insufficiency or an immunocompromised state must have been evident before admission to hospital and must conform to the following criteria: *liver*, biopsy confirmed cirrhosis and documented portal hypertension, episodes of past upper gastrointestinal bleeding attributed to portal hypertension, or prior episodes of hepatic failure/encephalopathy/coma; *cardiovascular*, New York Heart Association Class IV (that is, symptoms of angina or cardiac insufficiency at rest or during minimal exertion); *respiratory*, chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction—that is, unable to climb stairs or perform household duties, or documented chronic hypoxia, hypercapnia, secondary polycythaemia, severe pulmonary hypertension (>40 mm Hg), or respirator dependency; *renal*, receiving chronic dialysis; and *immunocompromised*, the patient has received treatment that suppresses resistance to infection—for example, immunosuppression, chemotherapy, radiotherapy, long term, high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection, such as leukaemia, lymphoma, AIDS. A_{aDO₂}, alveolar–arterial oxygen difference; P_{aO₂}, arterial partial pressure of oxygen; F_{iO₂}, fraction of inspired oxygen; ARF, acute renal failure.

Table 3 Contrast enhanced computed tomography (CT) grading system

Grade	CT morphology
A	Normal
B	Focal or diffuse gland enlargement; small intrapancreatic fluid collection
C	Any of the above plus peripancreatic inflammatory changes and <30% gland necrosis
D	Any of the above plus single extrapancreatic fluid collection and 30–50% gland necrosis
E	Any of the above plus extensive extrapancreatic fluid collection, pancreatic abscess and >50% gland necrosis

These factors require further evaluation and most are not currently available for routine laboratory use.

Recommendation: severity stratification

Severity stratification should be made in all patients within 48 hours. It is recommended that all patients should be assessed by the Glasgow score and CRP. The APACHE II score is equally accurate, and may be used for initial assessment; it should be used for ongoing monitoring in severe cases. (Recommendation grade B.)

SEVERITY STRATIFICATION—RADIOLOGICAL

Dynamic CT scanning

All patients predicted to have a severe attack by one or more of the objective criteria outlined earlier should undergo an intravenous contrast enhanced (dynamic) CT scan between three and 10 days after admission. The precise timing of this first CT scan will depend on clinical and logistic factors and is best performed after the initial phase of resuscitation. The combination of pre- and postenhancement appearances permits the assessment of the degree of pancreatic necrosis and surrounding peripancreatic and intra-abdominal fluid collections (table 3).⁷¹ These features add a radiological assessment of severity which is a more reliable predictor of subsequent infected necrosis or other complications requiring surgical intervention.

Recommendation: CT scanning

A dynamic CT scan should be performed in all severe cases between three and 10 days after admission. (Recommendation grade B.)

Aetiological assessment

The cause of an attack of acute pancreatitis should be sought as the aetiology will affect decision making and further therapeutic options. The incidence of “idiopathic” pancreatitis varies in different reports between 20 and 30%,⁷² and this will depend on the extent and thoroughness of the aetiological assessment⁷³ and the population under study. There is evidence that repeated investigation increases the proportion with an identified aetiology, particularly gallstones.^{74 75} The aetiological assessment should include the following features, which do need to be tailored to the clinical picture, background and age of the patient.

AETIOLOGICAL ASSESSMENT—CLINICAL

The clinical history should accurately record alcohol intake (in units per week), as well as evidence of viral exposure (prodromal illness). Comorbid medical and surgical conditions, such as HIV infection, or recent abdominal or cardiac surgery, should be noted, together with a detailed drug history.

AETIOLOGICAL ASSESSMENT—BIOCHEMICAL

Early

A gallstone aetiology is suggested by an early increase in serum aminotransferases⁷⁶ or bilirubin,⁷⁷ or both.

Late

After the acute phase, if the aetiology is not established, blood lipid and calcium concentrations should be measured. The value of early and convalescent viral studies is debatable.

AETIOLOGICAL ASSESSMENT—RADIOLOGICAL

Ultrasound

Early ultrasound scanning should be performed for gallstones and should be repeated if negative.

ERCP

In the absence of jaundice and with one mild attack of idiopathic pancreatitis an ERCP is not necessarily recommended.⁷³ In the presence of jaundice or a dilated common duct an ERCP is indicated. Furthermore, with recurrent attacks an ERCP should be performed to exclude anatomical variations (that is, pancreas divisum), the presence of ampullary or other tumours and common duct stones.⁷⁸

CT and MRI scanning in mild idiopathic acute pancreatitis

When the aetiology remains obscure a CT scan should be performed (particularly in the elderly) to exclude a tumour of the pancreas. If doubt remains about a tumour an MRI scan may add further information.

Endoscopic ultrasound, bile sampling, biliary manometry, and MRI cholangiography

Endoscopic ultrasound is emerging as another technique for detecting common bile duct stones.⁷⁹ Where available, it may be used to select which patients should undergo diagnostic or therapeutic ERCP. Bile sampling for assessment of microlithiasis⁷⁴ may be required in patients with repeated attacks of pancreatitis in whom no other cause has been found. The role of sphincter of Oddi manometry⁸⁰ and MRI cholangiography are under evaluation.

Recommendation: incidence of idiopathic pancreatitis

The aetiology of acute pancreatitis should be determined in 75–80% of cases, and no more than 20–25% should be classified as “idiopathic”. As the aetiology of acute pancreatitis varies geographically it is not possible to be dogmatic on this recommendation. (Recommendation grade B.)

Initial management of mild acute pancreatitis

Acute pancreatitis predicted to be mild by objective criteria usually runs an uneventful self-limiting course and this form of disease constitutes 80% of all attacks and less than 5% of deaths.⁸¹

GENERAL MANAGEMENT

These patients can be managed on the general ward with basic monitoring of temperature, pulse, blood pressure, and urine output. Although all patients will require a peripheral intravenous line for fluids and possibly a nasogastric tube, few will warrant an indwelling urinary catheter.

ANTIBIOTICS

Antibiotics should not be administered routinely as there is no evidence that their use in mild cases will affect outcome or reduce the incidence of septic complications.⁸² Antibiotics are warranted when specific infections occur (chest, urine, bile, or cannula related).

SPECIFIC TREATMENT

A variety of pharmacological and therapeutic treatments have been used in both mild and severe acute pancreatitis. These include aprotinin,²⁰ glucagon,²⁰ somatostatin,⁸³ fresh frozen plasma,²¹ and peritoneal lavage.²² None of these have proven value and therefore cannot be recommended.

CT SCANNING

Routine CT scanning is unnecessary unless there are clinical or other signs of deterioration.

Management of severe acute pancreatitis

Roughly 20% of patients will have an attack predicted as severe and 95% of deaths will occur in this subset.⁸¹ Management and monitoring of this group must therefore be more intensive.

GENERAL MANAGEMENT

The initial management involves full resuscitation and a multidisciplinary approach. By these means, the proportion of early deaths relating to circulatory, respiratory and renal failure can be reduced.^{2 3 23} These patients should be managed in an ITU or HDU. Such patients require as a minimum peripheral venous access, a central venous line (for fluid administration and CVP monitoring), a urinary catheter, and nasogastric tube. Strict asepsis should be observed in the placement and care of invasive monitoring equipment such as central lines, as these may serve as a source of subsequent sepsis in the presence of pancreatic necrosis.

When cardiocirculatory compromise exists, or if initial resuscitation fails to produce clinical improvement, a Swan-Ganz catheter is required for the measurement of pulmonary artery wedge pressure, cardiac output, and systemic resistance. Regular arterial blood gas analysis is essential as the onset of hypoxia and acidosis may be detected late by clinical means

alone. Nursing assessment must include as a minimum regular hourly pulse, blood pressure, CVP, respiratory rate, oxygen saturation, urine output, and temperature. These recordings may be made more frequently and must be charted accurately, along with cumulative calculations of fluid balance.

ANTIBIOTICS

Infection following severe acute pancreatitis may be due to a variety of factors related to the disease process, the treatment or the background nutritional and immunological status of the patient. There is some evidence to support the use of prophylactic antibiotics in the prevention of local and other septic complications in severe acute pancreatitis.⁸⁴⁻⁸⁶ In this respect, intravenous cefuroxime is a reasonable balance between efficacy and cost.⁸⁶ The duration of prophylactic treatment is unclear at present. Confirmed infections will require treatment in their own right.

DYNAMIC CT SCANNING

Dynamic CT scanning should be obtained within three to 10 days of admission. Non-ionic contrast should be used in all cases.

Recommendation: Severe acute pancreatitis

All cases of severe acute pancreatitis should be managed in an HDU or ITU setting with full monitoring and systems support. (Recommendation grade B.)

Gallstone pancreatitis

The management of gallstones causing an attack of acute pancreatitis will depend on the severity of the attack, and the presence or absence of jaundice or cholangitis. Some patients may have more than one possible aetiological factor—for example, gallstones and alcohol, or gallstones and a possible drug induced attack. In these cases the gallstones should be eradicated and other factors treated accordingly.

SEVERE GALLSTONE PANCREATITIS: URGENT ERCP

As an early ERCP (and sphincterotomy) may ameliorate symptoms it is important to determine rapidly whether gallstones are the cause of a severe attack. Failure of the patient's condition to improve within 48 hours despite intensive initial resuscitation is an indication for urgent ERCP and sphincterotomy in gallstone pancreatitis. Available evidence from clinical trials suggests that this intervention may reduce overall morbidity from severe attacks in this subset of patients.^{87 88} Other authors contest that only patients with biliary obstruction or biliary sepsis benefit from early ERCP and papillotomy.⁸⁹

Severe gallstone pancreatitis in the presence of increasingly deranged liver function tests and signs of cholangitis (fever, rigors, positive blood cultures) requires an immediate and therapeutic ERCP.

Recommendation: ERCP availability

Facilities and expertise should be available to perform at any time an ERCP for common bile duct evaluation followed by sphincterotomy and stone extraction or stenting as required, particularly but not exclusively in severe gallstone pancreatitis, jaundice or cholangitis.
(Recommendation grade A.)

Recommendation: gallstone eradication

Mild gallstone pancreatitis without complications should have definitive management of lithiasis (cholecystectomy and bile duct clearance if necessary), ideally within two weeks and no longer than four weeks.
(Recommendation grade B.)

An ERCP should always be performed under antibiotic cover.

CHOLECYSTECTOMY AND BILE DUCT CLEARANCE IN GALLSTONE PANCREATITIS

Ideally, patients with mild gallstone pancreatitis should have their gallstones eradicated by laparoscopic (or open) cholecystectomy within two to four weeks. Preoperative assessment of the common bile duct by liver biochemistry and ultrasound examination should be performed. The place of a routine preoperative ERCP in the absence of common bile duct (CBD) dilatation or detected CBD stones, and normal liver function tests is debatable. There are those who favour routine regular ERCP in all cases as opposed to those selected by these specific criteria.⁹⁰⁻⁹⁴ The intrinsic risks related to ERCP must be considered.⁹⁵⁻⁹⁶

Management is complicated by further variable views on the place of operative cholangiography.⁹⁷ The difficulties of laparoscopic CBD exploration and the developing technologies of this manoeuvre coupled with new methods of preoperative assessment (that is, endoscopic ultrasound) add other elements of confusion.

Management must depend on local expertise in these multioptional situations. Evidence and guidelines are therefore loose in this area but in summary it is recommended that ERCP is performed in selected circumstances with preoperative stone extraction followed by laparoscopic surgery and peroperative cholangiography if doubt exists. The management of CBD stones found at surgery will depend on the local surgical approach. Duct exploration should be performed if open surgery is undertaken. As techniques and experience develop laparoscopic duct exploration may become routine. Postoperative ERCP and stone extraction is a further option.

The timing of cholecystectomy depends on the clinical situation. In mild cases cholecystectomy should be performed as soon as the patient has recovered and preferably during the same hospital admission so as to prevent potentially avoidable recurrent pancreatitis. In severe acute pancreatitis cholecystectomy should be done at a later stage when the inflammatory process has subsided and the procedure is likely to be technically easier.⁹⁸ If local complications develop, such as pseudocyst or infected necrosis, cholecystectomy should be performed when the complications are treated surgically or have resolved.

Acute pancreatitis: ongoing assessment

All patients whether mild or severe will require ongoing reassessment on a daily or more frequent basis. The purpose is to assess recovery and to diagnose as soon as possible the development of life threatening complications. Those with severe acute pancreatitis are more likely to develop further complications and require more intensive monitoring.

Ongoing assessment consists of a review of clinical, biochemical, radiological, and bacteriological findings.

CLINICAL ASSESSMENT

In mild cases of acute pancreatitis the resolution of the abdominal signs is easily monitored. Clinical evaluation may be more difficult in an ITU environment. A prolonged ileus, abdominal distension and tenderness are adverse clinical features. An epigastric mass and vomiting suggests an acute fluid collection that may persist to form a pseudocyst. The vague and poorly defined term "failure to thrive" describes a patient who requires continued system support with features of hypermetabolism and a catabolic state which suggest the development of complications. Conversely, an unremitting low to moderate grade fever is seen commonly in necrotising acute pancreatitis and in itself does not necessarily indicate deterioration. A sudden high fever, however, may indicate the development of infection although this may arise from sources other than the pancreatic area. The onset of cardio-respiratory or renal failure are further signs of septic complications.

Although none of these clinical features alone can differentiate between sterile and infected necrosis, together they represent a picture of a patient who is failing to thrive, and will raise the index of clinical suspicion.

HAEMATOLOGICAL AND BIOCHEMICAL ASSESSMENT

Increasing leucocyte and platelet counts, deranged clotting, an increase in the APACHE II score,⁶⁶ and/or CRP concentration in blood together with biochemical features of multiple organ failure all indicate possible sepsis and the need for urgent reassessment.

RADIOLOGICAL ASSESSMENT

Plain x ray films

A chest x ray film may show pneumonic consolidation, pleural effusions and features of an ARDS.

Although not routinely recommended for ongoing assessment, a plain abdominal *x* ray may rarely reveal free gas in the retroperitoneum—a late sign, indicative of infection with gas forming organisms.

Ultrasound

Ultrasound is not usually helpful in established severe acute pancreatitis except in the evaluation and serial monitoring of fluid collections.

CT (MRI) scanning

Dynamic CT should be repeated in severe acute pancreatitis on a regular basis, usually every two weeks. This may be more frequent if there are indications of sepsis or other adverse clinical features. This investigation is important in the planning of any surgical or drainage procedures, and may occasionally avert a disaster by demonstrating a pseudo-aneurysm. MRI offers an alternative technique and avoids the cumulative radiation exposure.

Acute fluid collections

Acute fluid collections are common in patients with severe pancreatitis, occurring in 30–50% of cases.⁷¹ Those with three or more fluid collections have a greater risk of complications and death. More than one half of cases of acute fluid collections will resolve spontaneously and in an otherwise stable patient they do not require treatment. Indeed, there is a risk of introducing infection if unnecessary percutaneous procedures are performed. Indications for percutaneous aspiration include suspected infection and symptomatic collections (causing pain or mechanical obstruction).⁸¹ Asymptomatic fluid collections should not be drained.

Bacteriological assessment

If sepsis is suspected the source must be detected by microbiological examination of sputum, urine, blood, and the tips of vascular cannulae. Suspected intra-abdominal sepsis (infected acute fluid collection, infected necrosis and pancreatic abscess) will require evaluation by radiologically guided fine needle aspiration and microscopy and culture of aspirates.⁹⁹ There is some evidence that this procedure may in fact introduce infection, and so should be used cautiously and performed only by experienced radiologists.¹⁰⁰

Summary of antibiotic use in acute pancreatitis

EMPIRICAL USE

Antibiotics are not required routinely for mild acute pancreatitis.⁸² The place of antibiotics in severe acute pancreatitis is unclear. Imipenem has been recommended on the basis of studies of antibiotic penetration into pancreatic tissue.⁸⁴ Cefuroxime prescribed early in an attack has been shown to reduce the overall incidence of infections, and this has been associated with a reduction in mortality.⁸⁶

CONFIRMED INFECTION

Local infective complications

Strongly suspected or confirmed local infective complications (infected necrosis, pancreatic

abscess and infected fluid collections) will require appropriate antibiotics in addition to formal drainage by percutaneous or operative means.

Other specific infections

Where specific infection is documented—for example, biliary, respiratory, urinary or line related, then appropriate antibiotics are indicated, guided by sensitivities.

PROPHYLACTIC ANTIBIOTICS

Prophylactic antibiotics are recommended prior to invasive procedures such as ERCP and surgery. There is a place for prophylactic antibiotics early in an attack of acute pancreatitis predicted as severe; cefuroxime is currently the antibiotic recommended but the duration of treatment is unclear.

SELECTIVE GUT DECONTAMINATION

There is some evidence that selective decontamination of the gastrointestinal tract is associated with a reduction in associated infections,¹⁰¹ although it is unclear whether overall mortality is improved or whether the reduction in concomitant infections was due to the antibiotics which were also used in this study. Further evidence is required before this technique can be recommended routinely.

Summary of ERCP in acute pancreatitis

ERCP IN AETIOLOGICAL DIAGNOSIS

An ERCP may be required for the detection of gallstones, anatomical variants and tumours (see earlier).

ERCP IN SEVERE GALLSTONE PANCREATITIS AND/OR CHOLANGITIS

ERCP is indicated in severe gallstone pancreatitis with no response to treatment within 48 hours.^{87 88}

Up to 10% of patients with gallstone acute pancreatitis will develop ascending cholangitis, and this group similarly stand to benefit from ERCP, with duct drainage and clearance.¹⁰²

ERCP IN PREOPERATIVE EVALUATION OF THE COMMON BILE DUCT

Opinions vary as to the necessity of preoperative CBD assessment by ERCP in mild gallstone pancreatitis or in those with a severe attack who have not had the investigation performed earlier.^{90–94} The risks of the procedure, though small, may outweigh the benefits. These guidelines recommend preoperative ERCP if the suspicion of CBD stones is high (jaundice, deranged liver function tests, dilated CBD on ultrasound). In the absence of such features a preoperative cholangiogram should be performed during cholecystectomy rather than ERCP. When bile duct stones are detected at ERCP they should be treated by some combination of sphincterotomy, extraction and/or stent insertion.

ERCP AS THE DEFINITIVE MANAGEMENT OF GALLSTONES

In the medically unfit, endoscopic sphincterotomy may be used as the definitive

management of cholelithiasis,¹⁰³ although there is still an important role for surgery in this group.¹⁰⁴

Summary of cross-sectional imaging techniques in acute pancreatitis

CT SCANNING

Indications

The indications for CT scanning include (1) diagnostic uncertainty, (2) assessment of severe cases (within three to 10 days), (3) when clinical deterioration occurs (suggesting the development of complications), (4) guidance for interventional procedures, and (5) for the follow up and monitoring of established complications.

Technique/radiation exposure

The use of a spiral CT is preferable if this available. Precise techniques will vary according to local circumstances and machinery but generally patients will have approximately 500 ml of water soluble bowel contrast either by mouth or more usually nasogastric tube. Non-contrast alternate 10 mm slice protocols are performed from the domes of the diaphragm through the pancreas and to cover extrapancreatic inflammatory change. The pancreatic bed levels are identified from this series.

Postcontrast acquisition (using spiral or conventional techniques) is through the pancreatic bed with 5 mm collimation and a 5 mm reconstruction index. These are taken following a bolus intravenous administration of 100–120 ml of non-ionic contrast. Contrast is delivered at 3 ml per second using a power injector with image acquisition commencing approximately 40 seconds postonset of injection (this timing varying slightly according to the condition of the patient).

A dynamic CT scan involves substantial exposure to ionising radiation, which should be borne in mind as repeated scans may be necessary.

Severity assessment

Dynamic CT is currently the best method for assessing the extent of pancreatic necrosis in acute pancreatitis.¹⁰⁵ Dynamic CT should be performed in all severe cases within three to 10 days of admission. Scanning before this time may be difficult to interpret, and the delay allows greater demarcation of areas of necrosis. CT scans can be categorised as mild or severe, and hence the initial radiological appearances can be used to prognosticate (table 3).

Monitoring of complications

Follow up scans are used to detect the development of local complications. When used in conjunction with needle aspiration the early detection of infected necrosis, and hence timely intervention, is facilitated.⁹⁹ The CT evidence of disease distribution and anatomical relations is important for the planning of surgical strategy.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging is currently under evaluation in acute pancreatitis. Gadolinium

enhanced MRI can detect areas of pancreatic necrosis in a manner analogous to dynamic contrast enhanced CT scanning. The superior resolution of MRI may allow better differentiation between solid and fluid inflammatory collections than CT.^{106 107}

MRI has the added advantage of being free from ionising radiation, but the disadvantages include cost, limited availability and the practical difficulties of scanning a patient encumbered with ITU equipment.

Technique of MRI scanning

An axial T2 weighted sequence is performed through the pancreatic bed. Fat saturation may be used with the T2 weighted sequences. A second T2 weighted sequence is performed which allows coverage from lower chest to pelvis and permits a global demonstration of extrapancreatic fluid collections. Precontrast, breath-hold multislice T1 weighted rapid gradient echo sequence is performed in the axial plane. Subsequent breath-hold imaging is acquired following a bolus injection of 0.1 mmol/kg gadolinium with sequences performed at 10 and 30 seconds. A third breath-hold multislice sequence may be performed in the coronal plane after the two axial acquisitions.

Definition of a specialist unit

An argument has been made for concentrating patients with severe disease (predicted or confirmed) and/or established complications in specialist units.¹⁰⁸ Many hospitals would be able to provide such a facility which is characterised by the presence of the following:

- a multidisciplinary team of specialists in surgery, endoscopy, intensive care, anaesthesia, and full support staff. The team leader would normally be a surgeon with specific knowledge and interest in pancreaticobiliary disease;
- facilities for HDU/ITU management of critically ill patients including renal and respiratory support;
- radiological expertise permitting the use of dynamic CT, percutaneous needle aspiration and drainage procedures: the addition of MRI and angiographic facilities would be helpful but not essential;
- facilities for ERCP and all endoscopic procedures (on an emergency basis) by an experienced endoscopist.

Indications for referral to a specialist unit

EARLY PHASE REFERRAL

Indications for referral should be based on the severity of a given attack and the predicted likelihood of development of life threatening complications particularly infected necrosis. In this instance, the dynamic CT findings are pivotal, and a patient with multiple acute fluid collections and greater than 50% necrosis has an estimated risk of greater than 70% for infected necrosis.⁷¹ Such a patient should be transferred to a specialist unit elsewhere for further management if local facilities are inad-

equate. Similarly, patients with established systemic complications requiring ITU management are candidates for transfer.

LATER PHASE REFERRAL

The surgical management of the later complications, infected necrosis in particular, is beyond the remit of these guidelines. There are various surgical options available and these will depend on the clinical scenario, but all methods are attended by a high morbidity and mortality.¹⁰⁹ There is evidence that patients with infective complications are not well managed in general units³ and that late referral of patients to specialist units is associated with a higher mortality.^{42 110}

In the later phase, the development (or preferably the anticipation) of local infective complications or other complex complications such as a fistula constitute indications for referral. A patient with any other complication requiring surgery or other procedures should be transferred when local expertise is lacking.

Recommendation: referral to specialist unit

Management in, or referral to, a specialist unit is necessary in patients with extensive necrotising pancreatitis or with other complications who may require ITU care, interventional radiological, endoscopic, or surgical procedures.
(Recommendation grade B.)

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