

# Management of Acute Pancreatitis

## Clinical Guidelines



Royal College of Surgeons in Ireland  
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# Clinical Guidelines Committee

Royal College of Surgeons in Ireland

Prof. N. O'Higgins (Chairman), Mr. P. Gillen,  
Mr. T. N. Walsh, Ms. Beatrice Doran, Ms. Paula Wilson.

## Foreword

### FOREWORD

The Clinical Guidelines Committee is pleased to present this report prepared by a Working Party on the Management of Acute Pancreatitis.

In preparing these guidelines the Working Party was asked to draw on evidence and experience derived from other international guidelines recently prepared and published from other sources. Accordingly, as is acknowledged in the Introduction, the current guidelines are in accordance with those prepared for the United Kingdom in 1998, for the World Congress of Gastroenterology in 2002 and for the International Association of Pancreatology, also in 2002.

The Working Party has ensured that the guidelines prepared for the Royal College of Surgeons in Ireland measure up to the best standards of care known and agreed by the international community of specialists while at the same time being applicable and relevant to the particular circumstances of clinical practice in Ireland. For this the Working Party deserves great credit in producing a document which is up-to-date and authoritative. It is bound to be helpful to all clinicians who treat patients with acute pancreatitis. It is a pleasure to acknowledge the members of the Working Party and to thank them for their effort.

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Niall O'Higgins,  
Chairman, Guidelines Committee.

## Working Party Members

**Professor P. Grace,**  
Limerick Regional Hospital.

**Professor M. Lee,**  
Beaumont Hospital, Dublin.

**Mr. G. McEntee,**  
Mater Hospital, Dublin.

**Mr. K. Mealy,**  
Wexford General Hospital.

**Dr. F. E. Murray,**  
Beaumont Hospital, Dublin.

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## Introduction

It is intended that these guidelines will assist clinicians in the diagnosis and management of acute pancreatitis.

### AIMS

#### The specific aims of these guidelines are:-

- (i) to assist the early diagnosis and treatment of acute pancreatitis.
- (ii) to promote risk stratification enabling a uniform standard of care throughout the country.
- (iii) to improve referral patterns for patients requiring complex monitoring, investigation or treatment.

In 1998 an expert committee in the UK set out guidelines for the management of acute pancreatitis.<sup>1</sup> The World Congress of Gastroenterology also published guidelines for the management of acute pancreatitis following its Bangkok meeting in 2002.<sup>2</sup> In addition, the International Association of Pancreatology has also prepared guidelines reflecting best practice which should allow comparative audits of the quality of patient care.<sup>3</sup> These guidelines accurately reflect expert current practice and form the basis of this report.

Despite changes in the management of acute pancreatitis in recent years, morbidity remains high and mortality is approximately 10% in many series.<sup>4</sup> No recent figures are available from Ireland. These guidelines aim to advise clinicians on the facilities required and the level of care necessary in the management of patients with pancreatitis. It is recognised, however, that the evidence base for many aspects of acute pancreatitis care is currently poor, hence, individual clinical judgement remains important.

### VALIDITY AND GRADING OF RECOMMENDATIONS

The levels of evidence have been taken from the US Agency for Health Care Policy and Research and are set out below:

#### Level Type of Evidence

- |    |   |
|----|---|
| 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 experience of respected authorities.                                 |

### Grading of Recommendations

In the text the grading of recommendation (A, B, C) depends on the evidence level supporting it.

#### Grade Evidence Levels

- |   |   |
|---|---|
| A | Requires at least one randomised controlled trial as part of the literature of overall good quality and consistency addressing the specific recommendation (evidence levels Ia, Ib).                      |
| B | Requires the availability of clinical studies without randomisation on the topic of recommendation (evidence levels 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 levels IV). |

### EPIDEMIOLOGY

The incidence of acute pancreatitis is difficult to accurately ascertain but appears to be increasing. In Ireland as in the rest of the Western World the majority of cases are due to gallstone disease and alcohol (Table 1). The most recent figures for Scotland indicates an incidence of 31.8/100,000<sup>5</sup> with similar figures for continental Europe.<sup>6,7</sup> This increased incidence may reflect increased alcohol intake, altered dietary patterns, obesity and improved diagnosis. Relapse rates remain high particularly in the alcohol-associated group, but also in those with gallstone pancreatitis and those with idiopathic pancreatitis.<sup>6</sup> Men are affected more commonly than women due to a higher alcohol

intake in this group and a greater likelihood of ductal calculi in the presence of cholelithiasis.<sup>8,9</sup>

**Recommendation: Mortality**

*Overall mortality should be lower than 10% and less than 30% in those with severe disease*

**Grade B**

## MAKING THE DIAGNOSIS

The diagnosis of acute pancreatitis is made in the appropriate clinical setting associated with a four-fold rise in serum amylase.<sup>10</sup> In some cases, the serum amylase level is equivocal and if the clinical suspicion persists this should be repeated or a 24-hour urinary collection for amylase should be made. The sensitivity of serum pancreatic amylase decreases with time from the onset of abdominal pain so the level of hyperamylasemia should be interpreted accordingly.

Measurement of serum lipase also has some merit as levels of serum lipase remain elevated for longer than serum amylase,<sup>11</sup> however measurement of serum lipase and other pancreatic enzymes such as trypsinogen, elastase-1 and phospholipase have not been shown to be superior to serum amylase estimation.

In all cases an erect chest x-ray and plain abdominal film should be taken to exclude other acute abdominal and respiratory conditions. An abdominal ultrasound should be performed to document the presence of cholelithiasis with or without ductal dilatation. This is a poor test for examination of the pancreas but may also show fluid collections in or around the pancreas and may be useful for repeated follow-up.

A CT scan is sometimes necessary for diagnostic purposes if clinical and biochemical tests and ultrasound examination are inconclusive. Occasionally laparoscopy or laparotomy may be warranted if doubt remains and other acute surgical conditions need to be excluded.

## AETIOLOGICAL ASSESSMENT

In addition to a full history and clinical examination all patients should have liver function tests performed, as early abnormal LFTs suggest a gallstone aetiology. After the acute phase, serum calcium and fasting lipid profile should be examined if the aetiology remains in doubt. Abdominal

ultrasonography should be performed to document gallstones irrespective of perceived aetiology. If negative, this should be repeated following clinical recovery when the patient may have less bowel gas which should allow a better quality scan.

Endoscopic retrograde cholangio-pancreatography (ERCP) is not warranted for an episode of self-limiting acute pancreatitis, but should be considered for those with recurrent acute pancreatitis, those with persistent elevated LFTs or jaundice or a dilated common bile duct on ultrasound.

In certain patients, if the aetiology remains in doubt magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) may have a role. MRCP and EUS should be considered in those patients who are jaundiced and initial investigation reveals no evidence of gallstones.

## SEVERITY STRATIFICATION

Stratifying patients into mild and severe pancreatitis has important implications for management and clinical resource allocation. The Glasgow scoring system (Table 2) provides the earliest set of criteria to collect and probably most reflects the patient population seen in Ireland.<sup>12</sup> Ranson (Table 3) and APACHE II (Table 4) scoring are also useful but are more complex and take longer to complete.<sup>13,14</sup> Serum C-reactive protein levels provide the best single prognostic indicator of poor outcome.<sup>15</sup> Age and obesity are also known to confer a poor prognosis.

In patients predicted to have a severe outcome i.e. greater than three risk factors using the Glasgow or Ranson set of criteria, who do not demonstrate clinical improvement within 72 hours or who demonstrate an acute deterioration, a dynamic contrast enhanced abdominal CT should be performed. CT allows confirmation of diagnosis, gives an assessment of severity (Table 5) and documents evidence of complications such as pancreatic necrosis and pseudocyst and abscess formation<sup>16</sup>. CT should take place within five to ten days of admission and facilitates radiological or surgical intervention if clinical deterioration occurs.

**Recommendation**

*The correct diagnosis and severity stratification of patients with acute pancreatitis should be made within 48 hours of admission.*

**Grade B**

## Initial Management

### MILD PANCREATITIS

Basic vital signs should be recorded and intravenous fluids should be administered. Nasogastric drainage is necessary only for persistent vomiting. A urinary catheter, antibiotics and CT scanning are not usually necessary. The majority of patients with acute pancreatitis fall into this category and will have an uneventful self-limiting illness.

### PREDICTED SEVERE PANCREATITIS

#### General Care

These patients require multidisciplinary care in a high dependency unit (HDU) or intensive care unit (ICU) setting. Initial management requires intravenous and central venous access for fluid administration and central venous pressure monitoring. A urinary catheter is required for fluid balance monitoring. A nasogastric tube may be necessary for persistent vomiting. Regular arterial blood gases help assessment of cardiopulmonary status. If cardiopulmonary compromise occurs and resuscitation proves difficult a Swan-Ganz catheter may be required. Vital signs need to be monitored hourly.

#### Recommendation:

*All cases of severe acute pancreatitis should be managed in an HDU or ICU setting with appropriate monitoring and support.*

#### Grade B

In patients with severe acute pancreatitis, dynamic contrast enhanced CT of the abdomen should be performed within five to 10 days of diagnosis. Contrast enhanced CT imaging is necessary to identify areas of non-enhancing pancreatic necrosis. The overall accuracy of dynamic contrast enhanced CT in the detection of pancreatic necrosis is 82-90%.<sup>18</sup> Dynamic CT can also identify acute pancreatic fluid collections and pancreatic abscess. These features have prognostic implications.<sup>16</sup> Balthazar et al. have proposed a CT severity index based on the amount of necrosis present and the number of acute pancreatic fluid collections present.<sup>16</sup>

### DUCTAL CALCULI AND NEED FOR ERCP

Urgent ERCP and sphincterotomy may be necessary in cases of gallstone pancreatitis which do not settle within 48 - 72 hours of admission. Randomised trials from the UK, Hong Kong and Poland indicated that complications and mortality are decreased with early ERCP and sphincterotomy in those patients suspected of having ductal calculi and acute pancreatitis.<sup>19,20,21</sup> A randomised trial from Germany, however, found a trend towards increased morbidity and mortality in those patients with acute pancreatitis randomised to early ERCP.<sup>22</sup> This latter study has been criticised due to small enrolment from many centres over a prolonged study time period<sup>2</sup>.

#### Recommendation: ERCP

*ERCP facilities and expertise should be available for patients requiring common bile duct evaluation and sphincterotomy for stone extraction or stenting, particularly for those patients with severe pancreatitis, jaundice and cholangitis.*

#### Grade A

### ANTIBIOTIC USAGE

Prophylactic antibiotic usage is commonly prescribed for patients with acute pancreatitis and a recent survey of surgeons in the UK indicated that 88% of respondents were in favour of their use.<sup>23</sup> Randomised studies have indicated a reduction in morbidity in patients with acute pancreatitis treated with prophylactic antibiotics,<sup>24-28</sup> however, a reduction in mortality has been more difficult to document.<sup>29</sup> The broad spectrum antibiotic imipenem, effective against gram-negative organisms of gastrointestinal origin and which penetrates well into pancreatic secretions, is currently the recommended antibiotic for those patients with documented pancreatic necrosis.<sup>2</sup> In Ireland, however, where gram-negative resistance is not as common some microbiologists have expressed concern regarding the use of carbapenem antibiotics and advise the use of piperacillin with tazobactam as more appropriate. Local microbiological advice should be sought and early consultation with other clinical colleagues is very valuable. This issue may need to be reviewed from time to time.

Appropriate antibiotic usage may also decrease the need for surgical intervention.<sup>29</sup> However, attention

is drawn to the fact that routine antibiotic usage may predispose to increased systemic fungal septicaemia with higher mortality.<sup>24,31-33</sup>

**Recommendation:**

*The use of prophylactic broad-spectrum antibiotics reduces infection rates but may not improve survival.*  
**Grade A**

## SURGERY FOR PANCREATIC NECROSIS: STERILE VERSUS INFECTED NECROSIS.

Current opinion indicates the need for surgical debridement in addition to antibiotic therapy for those patients with documented infected pancreatic necrosis.<sup>33,34</sup> As the mortality rate for patients with infected pancreatic necrosis is high, surgical debridement should be considered in those patients with appropriate clinical signs of sepsis with proven infected necrosis.<sup>37,38</sup> For the differentiation between sterile and infected necrosis, fine needle aspiration for bacteriology (FNAB) of pancreatic or peripancreatic necrosis appears to be safe and reliable.<sup>35,36</sup> FNAB can be guided by CT or ultrasound with low complication rates and should be used in those patients showing clinical deterioration or signs of sepsis.<sup>35,36</sup> In general, pancreatic necrosis is not suitable for percutaneous drainage, although many pancreatic and peripancreatic fluid collections can be adequately drained under CT or ultrasound guidance.<sup>37,38</sup> Local expertise should dictate the type of drainage technique used.

While conventional surgical treatment for infected necrosis has rested on laparotomy with repeated access (laparostomy), Imrie has suggested that a percutaneous route may be preferable.<sup>34</sup>

The management of patients with sterile necrosis is not as well documented in the literature, however, most patients respond to non-surgical management, although the persistence of organ dysfunction and or clinical deterioration may be an indication for operation.<sup>39-41</sup>

Specific infections of the biliary, respiratory and urinary tracts and line-related sepsis need to be treated when detected.

**Recommendation:**

*Fine needle aspiration for bacteriology should be performed to identify those patients with infected pancreatic necrosis in appropriate patients*  
**Grade B**

*Infected pancreatic necrosis in patients with signs of sepsis is an indication for radiological or surgical drainage*  
**Grade B**

*Patients with sterile pancreatic necrosis should be managed conservatively and rarely require operative intervention*  
**Grade B**

## SEVERE ACUTE PANCREATITIS – ONGOING ASSESSMENT

Patients require daily assessment, CVP and fluid balance monitoring. Nutritional support is necessary in those with acute pancreatitis. There is recent evidence that nasojejunal tube enteral feeding is superior and is feasible in the majority of patients.<sup>42-45</sup> Regular assessment of FBC, clotting and biochemical makers for sepsis, disseminated intravascular coagulopathy (DIC) and inflammatory markers is necessary. Radiological chest assessment includes regular films, ultrasound and CT scanning for the detection of fluid collections and pancreatic necrosis. Initially asymptomatic fluid collections need not be drained as many will resolve but if sepsis is suspected radiologically-guided needle aspiration and culture may be necessary.

## TIMING OF CHOLECYSTECTOMY IN PATIENTS WITH GALLSTONE PANCREATITIS

There is little evidence available to guide the clinician in this area. Cholecystectomy should be performed to prevent recurrence. It seems reasonable to aim for cholecystectomy following mild pancreatitis within two to four weeks and it can be argued that cholecystectomy should be performed during initial hospital admission.<sup>2,46,47</sup> It should be realised that with earlier surgery the likelihood of ductal calculi will be greater. However, with prolonged delay the diminished risk of ductal calculi has to be balanced against the risk of further episodes of acute pancreatitis.

Following severe pancreatitis the patient's condition and the degree of residual inflammation on CT will dictate the timing of surgery. An appropriate interval should be allowed for residual inflammation to subside and allow clinical recovery.<sup>48,49</sup> Patients who undergo necrosectomy should have cholecystectomy at that time. Some patients will be considered high risk for surgery and might be offered ERCP, sphincterotomy and ductal clearance as a safe non-operative alternative.<sup>50-54</sup> However, a recent randomised trial from the Netherlands examining outcome in patients with ductal calculi, refutes this approach.<sup>55</sup> Of 59 patients randomised to the wait-and-see policy 47% developed complications in comparison to none in the 49 patients who had undergone laparoscopic cholecystectomy following ductal clearance.<sup>55</sup>

**Recommendation:**

*Cholecystectomy should be performed to avoid recurrence of gallstone-associated acute pancreatitis*  
**Grade B**

*In mild gallstone-associated pancreatitis cholecystectomy should be performed as soon as the patient is well and ideally during the same hospital admission*  
**Grade B**

*In severe gallstone-associated pancreatitis cholecystectomy should be delayed until the initial inflammatory process has resolved*  
**Grade B**

*ERCP may be an alternative to cholecystectomy in some patients deemed not fit for elective biliary surgery following gallstone-associated pancreatitis but the high likelihood of further gallstone-related complications should be recognised if this approach is adopted.*  
**Grade B**

## INDICATIONS FOR REFERRAL TO A SPECIALISED UNIT

Indications for referral depend on the severity of attack and the resources available to treat patients locally. All patients with severe pancreatitis should be treated by a team with a specialist interest in this condition. In particular, the surgical management of patients with pancreatic necrosis is complex and should only be undertaken by those with expertise in this condition.

Required facilities provided by a specialised unit have been defined by the British Society of Gastroenterology, and include:

- (i) a multidisciplinary team consisting of specialists in the areas of surgery, endoscopy, intensive care, anaesthesia and possibly at a later stage specialists in the area of hepatobiliary surgery.
- (ii) intensive care facilities for the management of the critically ill.
- (iii) radiological facilities including ultrasound and CT and radiologists skilled in percutaneous drainage. The addition of angiography and MRI facilities are desirable but not considered essential.
- (iv) Facilities for ERCP and the ability for emergency endoscopy by an experienced endoscopist.

Patients predicted to have severe acute pancreatitis should be considered for referral to an appropriate unit if the above facilities are not available particularly in the presence of multiple fluid collections and extensive pancreatic necrosis requiring drainage or multiple organ failure requiring organ support.

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## Tables

Table 1

Common Causes	Infrequent	Rare	
Gallstones	Hyperlipidemia	Infective	Mumps
Alcohol	Hypercalcaemia		Coxsackie
Idiopathic	Drug induced steroids		AIDS
	Thiazide diuretics		Ascariasis
	Azithioprin	Autoimmune	SLE
	Trauma		Sjogren's syndrome
	Blunt abdominal		
	Post-ERCP		
	Mechanical		
	Pancreatic divisum		
	Pancreatic carcinoma		
	Periampullary diverticulum		

Table 2

Glasgow criteria used in acute pancreatitis
1. WCC >15,000 mm <sup>3</sup>
2. Blood glucose >10 mmol/L
3. Blood urea >16 mmol/L
4. LDH >600IU/L
5. AST >200IU/L
6. Plasma albumin <32g/L
7. Uncorrected plasma Ca <sup>++</sup> <2mmol/L
8. Arterial PaO <sub>2</sub> <8 kPa

Table 3

Ranson criteria used in acute pancreatitis	
Criteria present at presentation	Criteria developing within the first 48 hours
1. Age >55 years	6. Haematocrit fall >10%
2. WCC >16,000/mm <sup>3</sup>	7. Blood urea >16mmol/L
3. Blood glucose >10mmol/L	8. Serum Ca <sup>++</sup> <2mmol/L
4. LDH >350IU/L	9. Arterial PaO <sub>2</sub> <8 kPa
5. AST >250 IU/L	10. Base deficit >4 mmol/L
	11. Fluid sequestration >6L

Table 4

Criteria used for APACHE II scoring in acute pancreatitis	
<p><b>Acute physiology score</b></p> <ol style="list-style-type: none"> <li>1. Temperature</li> <li>2. Mean arterial pressure</li> <li>3. Heart rate (ventricular response)</li> <li>4. Respiratory rate (ventilated or non-ventilated)</li> <li>5. Oxygenation</li> <li>6. Arterial pH</li> <li>7. Serum sodium</li> <li>8. Serum potassium</li> </ol>	<ol style="list-style-type: none"> <li>9. Serum creatinine (Double score if ARF*)</li> <li>10. Haematocrit</li> <li>11. WCC</li> <li>12. Glasgow coma scale (score = 15 – actual GCS)</li> </ol> <p><i>The APACHE II score is given by the sum of the acute physiology score and points given for age and chronic health evaluation.</i></p> <p>*ARF: Acute renal failure.</p>

Table 5

CT finding with increased severity in acute pancreatitis
<ol style="list-style-type: none"> <li>1. Enlargement of pancreatic gland</li> <li>2. Ill-defined margins</li> <li>3. Abnormal enhancement</li> <li>4. Thickening of peripancreatic planes</li> <li>5. Blurring of fat planes</li> <li>6. Intra- and retro-peritoneal fluid collections</li> <li>7. Pleural effusions</li> <li>8. Pancreatic gas indicative of necrosis/abscess formation</li> <li>9. Pseudocyst formation</li> </ol>









**Royal College of Surgeons in Ireland**

123 St. Stephen's Green, Dublin 2, Ireland

Tel: 353-1 402 2100. Fax: 353-1 402 2460. Web: [www.rcsi.ie](http://www.rcsi.ie)