



Surgery

UNIVERSITY OF TORONTO

Management of Acute Pancreatitis

A Clinical Practice Guideline developed by the
University of Toronto's Best Practice in Surgery

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Section 1. General Information

Aim

The aim of this guideline is to make recommendations on the management of acute pancreatitis with regards to diagnosis, severity assessment, and management of mild, severe, and complicated pancreatitis.

Outcomes of interest

Complications, including both infections and non-infectious, mortality, length of hospital stay, and re-admissions associated with acute pancreatitis.

Target population

Patients with a new presentation of suspected acute pancreatitis

Intended users

General surgeons, internists, intensivists, emergency physicians, interventional radiologists, and therapeutic endoscopists.

Rationale

Acute pancreatitis can range from a mild, self-limiting disease that requires no more than supportive measures to severe disease with life-threatening complications. The most common causes of acute pancreatitis are gallstones and binge alcohol consumption¹. There has been an increase in the incidence of acute pancreatitis reported worldwide. Despite improvements in access to care, imaging, and interventional techniques, acute pancreatitis continues to be associated with significant morbidity and mortality.

A systematic review of clinical practice guidelines in acute pancreatitis management revealed 14 guidelines published between 2004 and 2008 alone². Although these guidelines have significant overlap in their recommendations for the diagnosis and management of acute pancreatitis, small areas of disagreement regarding recommendations for timing and type of nutrition and management of gallstone pancreatitis remain. More concerning have been recent studies auditing clinical management of acute pancreatitis which have reported significant areas of non-compliance with evidence-based recommendations³⁻⁹. This presents an additional challenge in terms of creating understandable and implementable recommendations for the diagnosis, management, and follow-up of patients with acute pancreatitis, and emphasizes the need for regular audits of clinical practice within a given hospital to ensure compliance.

The purpose of the document is to provide evidence-based recommendations for the management of acute pancreatitis in the University of Toronto Division of General Surgery as part of the Best Practice in General Surgery initiative.

Overview of process

A scoping review was performed to elucidate the clinical practice guideline literature in acute pancreatitis management. An electronic search of Medline was conducted using the Medical Subject Headings "pancreatitis" and "clinical practice guideline" from 2002 - 2013. A 2010 systematic review of acute pancreatitis clinical practice guidelines which includes all the most recent guidelines was identified². An electronic search of Medline was performed for January 2010 to January 2014 to update the systematic review. The following Medical Subject Headings were used: "pancreatitis", "acute necrotizing pancreatitis", "alcoholic pancreatitis", and "practice guidelines." The results were limited to articles published in the English language. Relevant guidelines were selected and associated references reviewed. UpToDate articles on acute pancreatitis diagnosis and management were also reviewed for their references¹⁰ (current as of January, 2014).

Recommendations based on evidence as well as consensus were identified in the literature, and for each recommendation the primary supporting evidence was reviewed by a panel of experts. This panel then made recommendations based on best current evidence which they tailored to the U of T hospital system.

Definitions of Key Terms (based on the 2012 Atlanta Classification of Acute Pancreatitis¹¹)

Diagnosis of acute pancreatitis (2 of the following)

- Abdominal pain (acute onset of a persistent, severe, epigastric pain often radiating to the back)
- Serum lipase activity (or amylase) at least three times greater than the upper limit of normal
- Characteristic findings of acute pancreatitis on CT or MRI

Mild acute pancreatitis

- No organ failure, local or systemic complications

Moderately severe acute pancreatitis

- Organ failure that resolves within 48 hours and/or
- Local or systemic complications without persistent organ failure

Severe acute pancreatitis

- Persistent organ failure >48 hours

Interstitial edematous pancreatitis

- Acute inflammation of the pancreatic parenchyma and peri-pancreatic tissues, but without recognizable tissue necrosis

Necrotizing pancreatitis

- Inflammation associated with pancreatic parenchymal necrosis and/or peri-pancreatic necrosis

Organ failure and systemic complications of acute pancreatitis

- Respiratory: $\text{PaO}_2/\text{FiO}_2 \leq 300$
- Cardiovascular: systolic BP <90 mm Hg (off inotropic support), not fluid responsive or pH <7.3
- Renal: serum creatinine increase of $\geq 50\%$ over baseline within 7 days, absolute increase in serum of creatinine $\geq 26.5 \mu\text{mol/L}$ in 48 hours, or urine output of <0.5cc/kg/hr for more than 6 hours

Local complications of acute pancreatitis

- Acute Peri-pancreatic Fluid Collections (APFCs)
- Pancreatic Pseudocysts
- Acute Necrotic Collections (ANCs)
- Walled-Off Pancreatic Necrosis (WOPN)

Section 2. Guideline recommendations

1. Diagnosis of acute pancreatitis

- 1.1 Serum lipase should be performed in all patients with a suspected diagnosis of acute pancreatitis. A 3-fold elevation of serum lipase from the upper limit of normal is required to make the diagnosis of acute pancreatitis.
- 1.2 Ultrasonography should be performed in all patients at baseline to evaluate the biliary tract and in particular to determine if the patient has gall stones and/or a stone in the common bile duct.
- 1.3 Magnetic resonance cholangiopancreatography(MRCP) is recommended only in patients in whom there is elevation of liver enzymes and in whom the common bile duct is either not visualized adequately or is found to be normal on ultrasound.
- 1.4 Computed tomography (CT) should be performed selectively when 1) a patient presents with significant abdominal pain and a broad differential diagnosis which includes acute pancreatitis, or 2) in patients with suspected local complications of acute pancreatitis (e.g. peritonitis, signs of shock, suggestive ultrasound findings). CT for assessment of local complications is most useful after 48-72 hours after the onset of symptoms rather than at the time of admission. Unless contraindicated (e.g. renal dysfunction), intravenous contrast should be given in order to assess for pancreatic necrosis once patients are adequately fluid resuscitated and normovolemia restored.

2. Assessment of severity

- 2.1 A serum C reactive protein (CRP) level of 14 286 nmol/L (150 mg/dL) or greater at baseline or in the first 72 hours is suggestive of severe acute pancreatitis, and is predictive of a worse clinical course. Thus, CRP should be performed at admission and daily for the first 72 hours after admission.
- 2.2 Acute Physiologic Assessment and Chronic Health Evaluation APACHE II Scores should be calculated on admission and daily for the first 72 hours after admission. An APACHE II Score of 8 or higher at baseline or in the first 72 hours is suggestive of severe acute pancreatitis, and is predictive of a worse clinical course.
- 2.3 Severe acute pancreatitis should be diagnosed if a patient exhibits signs of persistent organ failure for more than 48 hours despite adequate intravenous fluid resuscitation.

3. Supportive care

- 3.1 Supportive care, including resuscitation with isotonic intravenous fluids (e.g. Ringer's Lactate solution), pain control, and mobilization should be the mainstay of treatment of patients with mild acute pancreatitis
- 3.2 Careful consideration of transfer to a monitored unit should be made in patients with 1) Severe acute pancreatitis based on APACHE II Score greater than 8, CRP greater than 14 286 nmol/L (150 mg/L), or organ dysfunction for more than 48 hours despite adequate resuscitation; 2) Evidence of present or evolving organ dysfunction defined as follows:
 - Respiratory ($\text{PaO}_2/\text{FiO}_2 \leq 300$, or respiratory rate > 20 breaths per minute)
 - Cardiovascular (hypotension despite aggressive fluid resuscitation [systolic BP < 90 mm Hg off of inotropic support or drop of sBP > 40], need for vasopressors [not fluid responsive], or pH < 7.3)
 - Renal (≥ 1.5 fold increase in serum creatinine over 7 days, increase of $\geq 26.5 \mu\text{mol}$ in serum creatinine over 48 hours, urine output $< 0.5 \text{ml/kg/h}$ for ≥ 6 hours and/or Need for aggressive,

ongoing fluid resuscitation defined as evidence of severe haemoconcentration (Hb > 160, HCT > 0.500)

Patients with one or more of the above criteria and a body mass index (BMI) above 30 (or BMI > 25 in Asian populations) should be monitored carefully, with a lower threshold for transfer to a monitored unit given the worse course of disease in the obese patient population.

4. Nutrition

- 4.1 Patients who present with mild acute pancreatitis should receive a regular diet on admission. If patients are unable to tolerate an oral diet owing to abdominal pain, nausea, vomiting, or ileus, they may be allowed to self-advance their diet from withholding oral food and fluids (NPO) to a regular diet as tolerated.
- 4.2 In patients with severe acute pancreatitis, enteral nutrition should be commenced as soon as possible following admission (within 48 hours). A nasojejunal tube is not superior to feeding by nasogastric feeding tube; thus, commencement of feeds should not be delayed for the purpose of placing a nasojejunal feeding tube. Enteral feeding is recommended over parenteral nutrition.

5. Prophylactic antibiotics

- 5.1 Prophylactic antibiotics are not recommended in patients with mild or severe acute pancreatitis

6. Diagnosis and Management of Local Complications of Acute Pancreatitis

- 6.1 Repeat CT should be considered with new (or unresolving) evidence of infection (eg: leukocytosis, fever) without a known source, new inability to tolerate oral/enteral feeds, change in haemodynamic status, or evidence of bleeding.
- 6.2 Patients who have extensive necrotizing acute pancreatitis, who show no clinical signs of improvement following appropriate initial management, or in whom other complications develop should be managed in consultation with, or at institutions with therapeutic endoscopy, interventional radiology, surgical and intensive care expertise in dealing with severe acute pancreatitis.
- 6.3 Patients with acute peripancreatic fluid collections with no radiological or clinical suspicion of sepsis should be observed, and image-guided fine needle aspiration (FNA) should be avoided due to the risk of introducing infection into a sterile collection.
- 6.4 When there is radiological or clinical suspicion of infected necrosis in patients with acute necrotic collections (ANCs) or walled-off pancreatic necrosis (WOPN), image-guided FNA with culture should be performed to distinguish infected from sterile necrosis.
- 6.5 Sterile necrosis based on negative FNA and/or stable clinical picture should be managed non-operatively, and antibiotics are not indicated. The exception is unstable patients in whom sepsis is suspected but no source has been identified: treatment with broad spectrum antibiotics on speculation may be indicated while an appropriate work up (bacterial and fungal cultures, CT) is carried out.
- 6.6 Antibiotics should be prescribed only in patients with infected necrosis confirmed by FNA or if there is gas within a collection visualized on CT scan. Antimicrobial therapy should be tailored to FNA culture speciation and sensitivities; however, empiric treatment with antibiotics active against the most common pathogens in infected pancreatic necrosis (*Escherichia coli*, *Bacteroides species*, *Enterobacter species*, *Klebsiella species* and *Streptococcus faecalis*, as well as other gram positive organisms such as *Staphylococcus epidermidis* and *Staphylococcus aureus*) may be considered until final culture results are available.
- 6.7 In patients with FNA-confirmed infections of ANCs or WOPN, a step-up approach of antibiotics and image-guided drainage, followed by surgical intervention if necessary, is indicated. Surgical

consultation should occur early; however, surgical intervention should be delayed until later in the course of disease whenever possible. Minimally invasive image-guided or endoscopic drainage is recommended as first line therapy, and multiple drains may be necessary. Surgery should be considered for cases in whom less invasive approaches fail, but should be delayed long enough to allow demarcation of necrotic pancreatic tissue.

- 6.8 Pancreatic pseudocysts which are asymptomatic should be managed non-operatively. Intervention is indicated in pseudocysts that are symptomatic, infected, or increasing in size on serial imaging, and should be performed in a high volume centre.

7. Management of patients with acute gallstone pancreatitis

- 7.1 Endoscopic retrograde cholangiopancreatography (ERCP) should be performed early (within 24-48 hours) in patients with acute gallstone pancreatitis associated with bile duct obstruction or cholangitis. In unstable patients with severe acute gallstone pancreatitis and associated bile duct obstruction or cholangitis, placement of a percutaneous transhepatic gallbladder drainage tube should be considered if ERCP is not safely feasible.
- 7.2 Cholecystectomy should be performed during the index admission in patients who have mild acute pancreatitis and should be delayed until clinical resolution in patients who have severe acute pancreatitis.
- 7.3 If cholecystectomy is contraindicated in patients because of medical comorbidities, ERCP and sphincterotomy should be considered prior to discharge in patients with acute gall stone pancreatitis.

Section 3. Guideline recommendations and supporting evidence

1. Diagnosis of Acute Pancreatitis

- 1.1 Serum lipase should be performed in all patients with a suspected diagnosis of acute pancreatitis. A 3-fold elevation of serum lipase from the upper limit of normal is required to make the diagnosis of acute pancreatitis.**

Serum lipase has a slightly higher sensitivity for detection of acute pancreatitis, and elevations occur earlier and last longer as compared with elevations in serum amylase^{12 13}. One study demonstrated that at day 0-1 from onset of symptoms, serum lipase has a sensitivity approaching 100% and for serum amylase it was 95%¹³. For days 2-3 at a sensitivity set to 85%, the specificity of lipase was 82% compared with 68% for amylase. Serum lipase is therefore especially useful in patients who present late to hospital. Serum lipase is also more sensitive as compared with serum amylase in patients with pancreatitis secondary to alcohol¹². Furthermore, simultaneous determination of serum lipase and amylase only marginally improved the diagnosis of acute pancreatitis in patients with acute abdominal pain¹³.

- 1.2 Ultrasonography should be performed in all patients at baseline to evaluate the biliary tract and in particular to determine if the patient has gall stones and/or a stone in the common bile duct.**

Biliary stones and alcohol are the causes of acute pancreatitis in 70%-80% of cases¹⁴. It is important to distinguish between these etiologies due to differences in management. Right upper quadrant ultrasound is the primary imaging modality for suspected gallbladder pancreatitis due to low cost, availability, and lack of radiation exposure¹⁵. Ultrasound has a sensitivity and specificity >95% in the detection of gallstones, although the sensitivity may be slightly lower in the context of ileus with bowel distension, commonly associated with acute pancreatitis¹⁶⁻¹⁹. Ultrasound can also identify gallbladder wall thickening and edema, gallbladder sludge, peri-cholecystic fluid, and a sonographic Murphy's sign, consistent with acute cholecystitis. When these signs are present, the positive predictive value of ultrasound in the diagnosis of acute cholecystitis is >90% and additional studies are rarely needed²⁰.

- 1.3 Magnetic resonance cholangiopancreatography(MRCP) is recommended only in patients in whom there is elevation of liver enzymes and in whom the common bile duct is either not visualized adequately or is found to be normal on ultrasound.**

MRCP is useful in identifying CBD stones and delineating pancreatic and biliary tract anatomy. A systematic review that included a total of 67 studies found that the overall sensitivity and specificity of MRCP to diagnose biliary obstruction were 95% and 97%, respectively. Sensitivity was slightly lower for detection of biliary stones, at 92%²¹. However, the cost of MRCP should limit its use in the diagnosis of gallstones or acute cholecystitis especially with the availability and utility of ultrasound for the same purpose.²²

- 1.4 Computed tomography (CT) should be performed selectively when 1) a patient presents with significant abdominal pain and a broad differential diagnosis which includes acute pancreatitis, or 2) in patients with suspected local complications of acute pancreatitis (e.g. peritonitis, signs of shock, suggestive ultrasound findings). CT for assessment of local complications is most useful after 48-72 hours after the onset of symptoms rather than at the time of admission. Unless**

contraindicated (e.g. renal dysfunction), intravenous contrast should be given in order to assess for pancreatic necrosis once patients are adequately fluid resuscitated and normovolemia restored.

In severe disease, a CT scan is useful to distinguish between interstitial acute pancreatitis and necrotizing acute pancreatitis and to rule out local complications²³. However, in acute pancreatitis these distinctions typically occur more than three to four days from onset of symptoms, which makes CT scan of limited use on admission unless there is a broad differential diagnosis which must be narrowed^{23 24}. CT scan evidence of necrosis has been shown to correlate with the risk of other local and systemic complications²⁵⁻²⁷. Complications that can be recognized on abdominal CT scan include pancreatic fluid collections, gastrointestinal and biliary complications (such as obstructions), solid organ involvement (such as splenic infarct), vascular complications (such as pseudoaneurysms, splenic vein thrombosis) and pancreatic ascites²⁸⁻³⁰.

2. Assessment of Severity

2.1 A serum C reactive protein (CRP) level of 14 286 nmol/L (150 mg/dL) or greater at baseline or in the first 72 hours is suggestive of severe acute pancreatitis, and is predictive of a worse clinical course. Thus, CRP should be performed at admission and daily for the first 72 hours after admission.

Summary of Evidence

Levels of CRP above 150 mg/dL at 48 hours from admission discriminate severe from mild disease. At 48 hours, CRP levels above 150 mg/dL have a sensitivity, specificity, positive predictive value, and negative predictive value of 80%, 76%, 67%, and 86%, respectively, for severe acute pancreatitis³¹. Plasma levels greater than 180 mg/L within the first 72 hours of disease onset have been correlated with the presence of necrosis with the sensitivity and specificity both >80%. However, its peak is generally 36-72 h after admission, so the test is not helpful in assessing severity on admission^{32 33}. CRP rises steadily in relation to the severity of pancreatitis, is inexpensive to measure, and testing is readily available³⁴⁻³⁶.

2.2 Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II Scores should be calculated on admission and daily for the first 72 hours after admission. An APACHE II Score of 8 or higher at baseline or in the first 72 hours is suggestive of severe acute pancreatitis, and is predictive of a worse clinical course.

A variety of reports have correlated a higher APACHE-II at admission and during the first 72 hours with a higher mortality (<4% with an APACHE-II <8 and 11–18% with an APACHE-II ≥8)³⁷⁻⁴³. The advantage of the APACHE-II score is the availability of this information within the first 24 hours and daily thereafter. In general, an APACHE-II score that increases during the first 48 hours is strongly predictive of the development of severe pancreatitis, whereas an APACHE-II score that decreases within the first 48 hours strongly predicts mild pancreatitis. There are some limitations in the ability of the APACHE-II score to stratify patients for disease severity. For example, studies have shown that it has limited ability in distinguishing between interstitial and necrotizing pancreatitis, which confers different prognoses^{27 42 44}. At 24 hours, the score also has limited utility. In one recent report, APACHE-II scores generated within the first 24 h had a positive predictive value of only 43% and negative predictive value of 86% for severe acute pancreatitis⁴⁵. Even with its limitations, a report of 49 patients found that generic measures of disease severity like the APACHE-II score were superior to disease specific scoring systems in predicting mortality⁴⁶. For instance, the Ranson score was found to be a poor predictor of severity in a meta-analysis of 110 studies⁴⁷. The APACHE-II score has also been shown to be superior to several CT scoring systems for assessing severity of acute pancreatitis⁴⁸.

2.3 Severe acute pancreatitis should be diagnosed if a patient exhibits signs of persistent organ failure for more than 48 hours despite adequate intravenous fluid resuscitation.

The organ failure based criteria for the prediction of severity in acute pancreatitis are taken, in part, from the modified Multiple Organ Dysfunction Score⁴⁹ presented by Banks et al. in their revision of the Atlanta Classification⁵⁰. A diagnosis of severe acute pancreatitis should also be made if a patient exhibits signs of persistent organ failure for > 48 hours, despite adequate intravenous fluid resuscitation.

In a study of 174 patients who developed early organ failure due to pancreatitis (within the first week), Johnson and Abu-Hilal (2004) examined the mortality and morbidity associated with transient organ failure (resolving in < 48 hours) and persistent organ failure (lasting > 48 hours). In the transient organ failure group (n = 71), there was a 1% mortality rate and 29% of these patients went on to develop local complications of pancreatitis, while in the persistent organ failure group (n = 103) there was a 35% mortality rate, with 77% of patients developing a local complication⁵¹. In a study of 759 patients with acute pancreatitis, patients with SIRS lasting for > 48 hours were demonstrated to have a significantly higher rate of multi-organ dysfunction (as determined by the mean Marshall Score) and death compared with those with transient SIRS lasting < 48 hours (4 vs. 3 and 25.4% vs 8%, respectively, p < 0.001 in both cases)⁵².

In a recent meta-analysis of 12 clinical studies examining the impact of obesity on severity of acute pancreatitis, Chen et al. (2012) demonstrated significantly increased risk of severe acute pancreatitis (RR=2.20, 95% CI 1.82–2.66, p < 0.05), local complications (RR=2.68, 95% CI 2.09–3.43, p < 0.05), systemic complications (RR=2.14, 95% CI 1.42–3.21, P < 0.05) and in-hospital mortality (RR=2.59, 95% CI 1.66–4.03, P < 0.05) when compared with non-obese patients⁵³. Due to these increased risks, special consideration should be given to patients with suspected severe acute pancreatitis and BMI > 30 (or BMI > 25 in Asian populations).

3. Supportive Care

3.1 Supportive care, including resuscitation with isotonic intravenous fluids (e.g. Ringer's Lactate solution), pain control, and mobilization should be the mainstay of treatment of patients with mild acute pancreatitis

Animal studies have shown aggressive fluid replacement supports pancreatic microcirculation and prevents necrosis⁵⁴. There have been no high quality trials to test the effectiveness of aggressive fluid resuscitation in acute pancreatitis, and approach to fluid resuscitation in acute pancreatitis remains an under investigated topic⁵⁵. However, poor outcomes have been shown in human studies reporting more deaths and necrosis in patients with haemoconcentration. In one observational study, all patients who received inadequate fluid replacement as measured by rise in hematocrit at 24 hours developed necrotizing pancreatitis⁵⁶. Further, a recent study compared the use of normal saline versus Ringer's Lactate in goal-directed and standard fluid resuscitation in acute pancreatitis. In this RCT (n = 40), Wu et al. (2011) found that after 24 hours of resuscitation there was an 84% reduction in the incidence of SIRS in patients resuscitated with Ringer's Lactate (p = 0.035), as well as a significant reduction in CRP from 104 mg/dL to 54 mg/dL when Ringer's Lactate was selected over normal saline (p = 0.02)⁵⁷.

Pain control is an important part of the supportive management of patients with acute pancreatitis. Therefore, in the absence of any patient-specific contraindications, a multimodal analgesic regimen is recommended, including narcotics, non-steroidal anti-inflammatories, and acetaminophen^{58 59}.

There are no studies assessing the impact of different models of critical care delivery and outcomes in patients with severe acute pancreatitis. However, a systematic review of 26 observational studies showed that critically ill patients cared for by an intensivist or using an intensivist consultant model in a closed

ICU had a shorter duration of ICU stay and lower mortality than similar patients cared for in units without such staffing patterns⁶⁰.

3.2 Careful consideration of transfer to a monitored unit should be made in patients with 1) Severe acute pancreatitis based on APACHE II Score greater than 8, CRP greater than 14 286 nmol/L (150 mg/L), or organ dysfunction for more than 48 hours despite adequate resuscitation; 2) Evidence of present or evolving organ dysfunction defined as follows:

- **Respiratory (PaO₂/FiO₂ ≤ 300, or respiratory rate > 20 breaths per minute**
- **Cardiovascular (hypotension despite aggressive fluid resuscitation [systolic BP <90 mm Hg off of inotropic support or drop of sBP > 40], need for vasopressors [not fluid responsive], or pH <7.3**
- **Renal (≥1.5 fold increase in serum creatinine over 7 days, increase of ≥26.5µmol in serum creatinine over 48 hours, urine output <0.5ml/kg/h for ≥6 hours and/orNeed for aggressive, ongoing fluid resuscitation defined as evidence of severe haemoconcentration (Hb > 160, HCT > 0.500)**

Patients with one or more of the above criteria and a body mass index (BMI) above 30 (or BMI > 25 in Asian populations) should be monitored carefully, with a lower threshold for transfer to a monitored unit given the worse course of disease in the obese patient population.

There are no studies assessing the impact of different models of critical care delivery and outcomes in patients with severe acute pancreatitis. However, a systematic review of 26 observational studies showed that critically ill patients cared for by an intensivist or using an intensivist consultant model in a closed ICU had a shorter duration of ICU stay and lower mortality than similar patients cared for in units without such staffing patterns⁶⁰.

4. Nutrition

4.1 Patients who present with mild acute pancreatitis should receive a regular diet on admission. If patients are unable to tolerate an oral diet owing to abdominal pain, nausea, vomiting, or ileus, they may be allowed to self-advance their diet from withholding oral food and fluids (NPO) to a regular diet as tolerated.

4.2 In patients with severe acute pancreatitis, enteral nutrition should be commenced as soon as possible following admission (within 48 hours). A nasojejunal tube is not superior to feeding by nasogastric feeding tube; thus, commencement of feeds should not be delayed for the purpose of placing a nasojejunal feeding tube. Enteral feeding is recommended over parenteral nutrition.

The underlying pathogenesis of acute pancreatitis is the premature activation of proteolytic enzymes resulting in the autodigestion of the pancreas. In the past, it was accepted practice that bowel rest would limit the inflammation associated with this process⁶¹. Recently, however, a series of RCTs have convincingly shown that early oral/enteral feeding in acute pancreatitis is not associated with adverse effects, and may be associated with significant decreases in pain, opioid usage, and food intolerance⁶²⁻⁶⁴. Furthermore, Eckerwall et al. (2007) demonstrated that oral feeding on admission for mild pancreatitis was associated with a significant decrease in length of stay from 6 to 4 days ($p < 0.05$) when compared to patients maintained NPO⁶⁵. The major benefits from early feeding appear to be effective only if commenced within the first 48 hours following admission⁶⁶, and the current recommendation based on a 2010 meta-analysis of 32 RCTs is to commence oral feeding at the time of admission if tolerated, or otherwise within the first 24 hours^{66 67}. Finally, a low fat diet was shown to be preferable to clear fluids on

admission for mild acute pancreatitis due to a higher caloric intake with no associated adverse effects^{63 64}. There is no evidence to suggest that a low fat diet is preferable to a regular diet.

A 2010 Cochrane meta-analysis of eight RCTs with 348 patients comparing enteral nutrition (EN) to total parenteral nutrition (TPN) for acute pancreatitis showed reduced mortality (RR 0.50, 95% CI 0.28 to 0.91), multi-organ failure (RR 0.55, 95% CI 0.37 to 0.81), systemic infection (RR 0.39, 95% CI 0.23 to 0.65), operative interventions (RR 0.44, 95% CI 0.29 to 0.67), local septic complications (RR 0.74, 95% CI 0.40 to 1.35), and other local complications (RR 0.70, 95% CI 0.43 to 1.13)⁶³. Mean length of hospital stay was reduced by 2.37 days in EN versus TPN groups (95% CI -7.18 to 2.44). Furthermore, a subgroup analysis of EN versus TPN in patients with severe acute pancreatitis showed a RR for death of 0.18 (95% CI 0.06 to 0.58) and a RR for multi-organ failure of 0.46 (95% CI 0.16 to 1.29). Several meta-analyses have shown similar results, with significant reductions in infectious complications, mortality, and multi-organ dysfunction when enteral nutrition is commenced within the first 48 hours following admission^{62, 64, 65}.

A meta-analysis of 4 prospective studies of patients with predicted severe acute pancreatitis (n=92) demonstrated no change in intolerance of feeding (RR=1.09; 95% CI 0.46 – 2.59, p=0.84) or in mortality (RR=0.77; 95% CI 0.37 – 1.62, p=0.5) when given enteral feeds by nasogastric feeding tube versus nasojejunal feeding tube⁶⁶. In a more recent meta-analysis of 3 RCTs (n=157), Chang et al. found no significant differences in the incidence of mortality (RR=0.69, 95% CI: 0.37 to 1.29, p=0.25); tracheal aspiration (RR=0.46, 95% CI: 0.14 to 1.53, p=0.20); diarrhea (RR=1.43, 95% CI: 0.59 to 3.45, p=0.43); exacerbation of pain (RR=0.94, 95% CI: 0.32 to 2.70, p=0.90); and meeting energy balance (RR=1.00, 95% CI: 0.92 to 1.09, p=0.97) between patients fed through nasogastric and nasojejunal feeding tubes⁶⁷. While no high quality RCTs exist on this topic, to date, there has been no evidence to suggest that enteral feeds should be delayed for the purposes of acquiring a nasojejunal feeding tube, especially in light of morbidity and mortality benefits of commencing enteral feeds with in the first 48 hours.

Although semi-elemental, immune-enhanced, and probiotic containing enteral feeds showed initial promise in the management of severe acute pancreatitis, meta-analyses still indicate that there is insufficient evidence to recommend the use of any of these nutritional formulations at this time^{62, 68, 69}. Given its promise in the context of other critically ill and septic patients⁷⁰⁻⁷², the use of probiotics in the management of acute pancreatitis may yet prove effective as research continues.

5. Prophylactic antibiotics

5.1 Prophylactic antibiotics are not recommended in patients with mild or severe acute pancreatitis

A 2010 meta-analysis of seven RCTs with 404 patients comparing prophylactic antibiotics versus placebo in CT proven necrotising pancreatitis concluded that there was no statistically significant effect on reduction of mortality with therapy (8.4% versus 14.4% in controls, P = 0.07), and infected pancreatic necrosis rates: (19.7% versus 24.4% in controls, P = 0.47). Non-pancreatic infection rates (23.7% versus 36% respectively, P = 0.08); and overall infections (37.5% versus 51.9%, P = 0.12), respectively, were also not significantly reduced with antibiotics. Need for operative treatment and fungal infections were not significantly different⁶⁸.

Similar results were found in a 2008 meta-analysis of seven RCTs with 467 cases of CT proven necrotizing pancreatitis comparing prophylactic antibiotics with placebo or no treatment. The rate of infected pancreatic necrosis was not significantly different (antibiotic group 17.8%, compared with 22.9% in controls, RR 0.81 (95% CI 0.54 to 1.22). There was a non-statistically significant decrease in mortality in the antibiotic group versus controls (9.3% vs. 15.2%), RR 0.70 (95% CI 0.42 to 1.17). Subsequent subgroup analysis confirmed antibiotics were not statistically significantly superior to controls in reducing the rate of infected necrosis or mortality⁶⁹.

A 2012 meta-analysis of 11 RCTs looking at the effectiveness of prophylactic antibiotic coverage calculated the NNT to be 1,429⁷⁰, and yet another meta-analysis of 14 RCTs (n = 841) showed no statistically significant reduction in mortality (RR 0.74 [95% CI 0.50-1.07]), incidence of infected pancreatic necrosis (RR 0.78 [95% CI 0.60-1.02]), incidence of non-pancreatic infections (RR 0.70 [95% CI 0.46-1.06]), or in surgical interventions (RR 0.93 [95% CI 0.72-1.20])⁷¹.

In light of the lack of demonstrated benefit of prophylactic antibiotics in the treatment of AP, the adverse effects of this practice must be carefully considered. In a prospective, randomized trial (n = 92), Maravi-Poma *et al.* demonstrated a three-fold increase in the incidence of local and systemic fungal infection with *Candida albicans* (from 7% to 22%) in patients with prolonged treatment with prophylactic antibiotics⁷², a finding consistent with other similar studies⁷³⁻⁷⁵. In addition, overuse of antibiotics is associated with the increased risk of antibiotic-associated diarrhea and *Clostridium difficile* colitis⁷⁶, and the selection of resistant organisms⁷⁷, all of which suggest that the adverse effects of prophylactic antibiotic coverage outweighs any benefit offered by the practice.

6. Diagnosis and Management of Local Complications of Acute Pancreatitis

- 6.1 Repeat CT scan should be considered with new (or unresolving) evidence of infection (eg: leukocytosis, fever) without a known source, new inability to tolerate oral/enteral feeds, change in haemodynamic status, or evidence of bleeding.**
- 6.2 Patients who have extensive necrotizing acute pancreatitis, who show no clinical signs of improvement following appropriate initial management, or in whom other complications develop should be managed in consultation with, or at institutions with therapeutic endoscopy, interventional radiology, surgical and intensive care expertise in dealing with severe acute pancreatitis.**

Two recent review articles on acute pancreatitis have summarized the importance of managing patients with complications of AP at high volume centres in which all services are well versed in the multidisciplinary step up approach to severe and/or complicated AP^{78 79}.

- 6.3 Patients with acute peripancreatic fluid collections with no radiological or clinical suspicion of sepsis should be observed, and image-guided fine needle aspiration (FNA) should be avoided due to the risk of introducing infection into a sterile collection.**

FNA has been established as an accurate, safe and reliable technique for identification of infected acute peri-pancreatic fluid collections (APFCs), pancreatic pseudocysts, acute necrotic collections (ANCs), and walled-off pancreatic necrosis(WOPNs)^{25 80-82}. However, FNA of pancreatic pseudocysts, APFCs, ANCs, and WOPNs should not be performed in the absence of a clinically or radiologically suspected infection due to the small, but documented, risk of introducing an FNA-associated infection into a previously sterile collection^{83 84}.

- 6.4 When there is radiological or clinical suspicion of infected necrosis in patients with acute necrotic collections (ANCs) or walled-off pancreatic necrosis (WOPN), image-guided FNA with culture should be performed to distinguish infected from sterile necrosis.**

Elevations in white blood count and temperature may occur in sterile necrosis and be similar to those seen in patients with infected necrosis⁴², therefore, it is difficult to distinguish between these conditions clinically. FNA has been established as an accurate, safe and reliable technique for identification of

infected necrosis^{25 80-82}. A 1995 retrospective observational study⁸¹ assessed the value of CT guided FNA in 104 patients with acute pancreatitis suspected of having pancreatic infection on the basis of systemic toxicity and CT evidence of severe pancreatitis. Cultures were positive in 58 aspirates of which all but two were confirmed surgically (two died without confirmation). Of the 53 patients with sterile pancreatitis, all but two aspirates judged to be sterile by FNA were validated on the basis of negative cultures obtained surgically, or by clinical resolution of pancreatitis without need of surgery (two died without confirmation). There were no complications. These findings are consistent with other studies^{25 80 82}.

6.5 Sterile necrosis based on negative FNA and/or stable clinical picture should be managed non-operatively, and antibiotics are not indicated. The exception is unstable patients in whom sepsis is suspected but no source has been identified: treatment with broad spectrum antibiotics on speculation may be indicated while an appropriate work up (bacterial and fungal cultures, CT) is carried out.

Elevations in white blood count and temperature may occur in sterile necrosis and be similar to those seen in patients with infected necrosis⁴². Therefore, it is difficult to distinguish between these conditions clinically, and if infected necrosis is suspected, a FNA is indicated rule out infection (see 5.3). Most patients with sterile necrosis respond to conservative medical management^{25 85}. For these patients, there have been several retrospective reports suggesting that a delay in surgical necrosectomy and at times a total avoidance of surgery results in less morbidity and mortality than early surgical debridement⁸⁶⁻⁹². Secondly, when sterile necrosis is debrided surgically, a common sequela is the development of infected necrosis and the need for additional surgery^{87 92-94}. In at least one report, patients so treated had a very high mortality⁹². Finally, in one randomized prospective trial that compared early to late surgery in a small number of patients with sterile necrosis, there was a trend to greater mortality among those operated on within the first three days following admission⁸⁶.

6.6 Antibiotics should be prescribed only in patients with infected necrosis confirmed by FNA or if there is gas within a collection visualized on CT scan. Antimicrobial therapy should be tailored to FNA culture speciation and sensitivities; however, empiric treatment with antibiotics active against the most common pathogens in infected pancreatic necrosis (*Escherichia coli*, *Bacteroides species*, *Enterobacter species*, *Klebsiella species* and *Streptococcus faecalis*, as well as other gram positive organisms such as *Staphylococcus epidermidis* and *Staphylococcus aureus*) may be considered until final culture results are available.

Antibiotics should only be prescribed in patients with infected necrosis confirmed by FNA or if there is gas within a collection visualized on CT scan. Antimicrobial therapy should be tailored to FNA culture speciation and sensitivities, however, empiric treatment with antibiotics active against the most common pathogens in infected pancreatic necrosis may be considered until final culture results are available (*Escherichia coli*, *Bacteroides species*, *Enterobacter species*, *Klebsiella species* and *Streptococcus faecalis*, as well as other gram positive organisms such as *Staphylococcus epidermidis* and *Staphylococcus aureus*^{95 96}).

Although insufficient evidence exists to make definitive recommendations regarding empiric anti-microbial therapy choices in infected pancreatic necrosis, a number of studies have looked at the pancreatic penetration of various antibiotics. Imipenem and ertapenem have both been shown to penetrate pancreatic tissue and pancreatic fluid at levels exceeding the MIC90 for the most commonly seen bacteria, after as little as a single IV dose^{97 98}. Similar findings were documented for moxifloxacin, with concentrations greater than the MIC90 after a dose of 400mg, either orally or by IV⁹⁹. An *In Vitro* study of the most commonly isolated bacteria from pancreatic necrosis – *E.coli*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Bacteroides fragilis* – compared the effectiveness of imipenem, ertapenem, and moxifloxacin against these pathogens. While all three demonstrated good coverage in this *In Vitro*

pancreatitis model, moxifloxacin demonstrated superior activity against *Enterococci*, and demonstrated slightly better anaerobic coverage¹⁰⁰.

The most common bacteria cultured from pancreatitis-associated collections are enteric microorganisms, such as *Escherichia coli*, *Bacteroides species*, *Enterobacter species*, *Klebsiella species* and *Streptococcus faecalis*, as well as other gram positive organisms such as *Staphylococcus epidermidis* and *Staphylococcus aureus*^{95 96}. When treating complications of AP empirically with antibiotics while results of a septic work up are pending, care must be taken to provide anti-microbial coverage for these common pathogens.

6.7 In patients with FNA-confirmed infections of ANCs or WOPN, a step-up approach of antibiotics and image-guided drainage, followed by surgical intervention if necessary, is indicated. Surgical consultation should occur early; however, surgical intervention should be delayed until later in the course of disease whenever possible. Minimally invasive image-guided or endoscopic drainage is recommended as first line therapy, and multiple drains may be necessary. Surgery should be considered for cases in whom less invasive approaches fail, but should be delayed long enough to allow demarcation of necrotic pancreatic tissue.

The mortality rate of patients with infected pancreatic necrosis is higher than 30%, and up to 80% of fatal outcomes in acute pancreatitis are due to septic complications resulting from pancreatic infection^{24 101 102}. The conservative management of infected pancreatic necrosis associated with multiple organ failure has a mortality rate of up to 100%¹⁰³. Surgical treatment of patients with infected pancreatic necrosis is associated with mortality rates that are as low as 10-30% in some specialized centers^{25 85 104}. However, the benefit of a step-up approach to surgery was shown in a 2010 RCT of 88 patients. The trial randomized patients with confirmed or suspected infected necrosis to open necrosectomy or a step up approach of percutaneous drainage followed, if necessary, by minimally invasive retroperitoneal necrosectomy. New-onset multiple-organ failure occurred less often in patients assigned to the step-up approach than in those assigned to open necrosectomy (12% vs. 40%, $p = 0.002$). The rate of death did not differ significantly between groups (19% vs. 16%, $p = 0.70$). Patients assigned to the step-up approach had a lower rate of incisional hernias (7% vs. 24%, $p = 0.03$) and new-onset diabetes (16% vs. 38%, $P = 0.02$)¹⁰⁵.

A small RCT by Mier et al. (1997) compared the mortality in 41 patients with fulminant pancreatitis undergoing either early (48-72 hours following admission) or late necrosectomy (at least 12 days post admission)⁸⁶. The mortality odds ratio for the early surgery cohort when compared to those undergoing late necrosectomy was 3.94, and the study was stopped due to this finding despite the fact that the small sample size resulted in a lack of statistical significance. Wittau et al. (2010) showed a similar and statistically significant reduction in mortality from 41% to 18% ($p = 0.026$) when necrosectomy was performed early in the course of illness (less than 2-3 weeks) compared to a delayed approach to surgical intervention (waiting 29 days or longer)¹⁰⁶. Accepted indications for necrosectomy still include persistent evidence of organ dysfunction and sepsis, or patients requiring ongoing ICU treatment for more than one month following admission for SAP.

Walled-off pancreatic necrosis (WOPN) is the result of the organization of ANCs or APFCs over time by a wall of granulation or fibrotic tissue without epithelial lining^{50 107}. In the context of a FNA-proven infected WOPN, surgical intervention, if indicated, should be delayed until after the third or fourth week to allow demarcation of the viable pancreatic tissue and peri-pancreatic necrosis¹⁰⁸. If intervention is required before the fourth week, percutaneous drainage serves as a bridge to more definitive procedure¹⁰⁷. Multiple treatment modalities have been described, including endoscopic drainage, percutaneous retroperitoneal and surgical approaches. Minimally invasive approaches (laparoscopic, percutaneous retroperitoneal and endoscopic) are equally effective as open surgical approach¹⁰⁹⁻¹¹¹.

6.8 Pancreatic pseudocysts which are asymptomatic should be managed non-operatively. Intervention is indicated in pseudocysts that are symptomatic, infected, or increasing in size on serial imaging, and should be performed in a high volume centre.

A pancreatic pseudocyst is a collection of pancreatic juice (either direct leakage from the inflamed gland or disruption of the pancreatic duct) enclosed by a non-epithelialized wall of granulation or fibrous tissue. They usually occur more than 4 weeks after onset of acute pancreatitis, and contain pancreatic enzyme-rich fluid. They are most often sterile but can become infected^{50 112}. Fifty per cent of all pseudocysts resolve spontaneously^{113 114}. Neither size nor duration of the pseudocyst are predictive of the natural course^{115 116}. Clinical signs of sepsis, or the presence of air bubbles in a pseudocyst indicates potential infection. At this point, aspiration of the fluid with gram stain, culture, and sensitivities is indicated. The most common bacteria cultured in an infected pseudocyst are enteric microorganisms, such as *Escherichia coli*, *Bacteroides species*, *Enterobacter species*, *Klebsiella species* and *Streptococcus faecalis*, as well as other gram positive organisms such as *Staphylococcus epidermidis* and *Staphylococcus aureus*^{95 96}. General indications for intervention are symptomatic pseudocysts, complications from a pseudocyst, or increasing size on serial imaging¹¹⁷⁻¹²⁰. Many options are available for management of pancreatic pseudocysts including percutaneous, endoscopic, or surgical drainage (open and laparoscopic), and creation of a cystogastrostomy (endoscopic or surgical). These procedures should be performed at high volume centres with integrated multidisciplinary teams.

7. Management of Patients with Gallstone Pancreatitis

7.1 Endoscopic retrograde cholangiopancreatography (ERCP) should be performed early (within 24-48 hours) in patients with acute gallstone pancreatitis associated with bile duct obstruction or cholangitis. In unstable patients with severe acute gallstone pancreatitis and associated bile duct obstruction or cholangitis, placement of a percutaneous transhepatic gallbladder drainage tube should be considered if ERCP is not safely feasible.

A 2012 Cochrane meta-analysis¹²¹ included RCTs comparing early routine ERCP versus early conservative management with or without selective use of ERCP in patients with suspected acute gallstone pancreatitis. There were five RCTs with 644 patients. Overall, there were no statistically significant differences between the two treatment strategies in mortality (RR 0.74, 95% CI 0.18 to 3.03), local or systemic complications as defined by the Atlanta Classification (RR 0.86, 95% CI 0.52 to 1.43; and RR 0.59, 95% CI 0.31 to 1.11 respectively). Among trials that included patients with cholangitis, the early routine ERCP strategy significantly reduced mortality (RR 0.20, 95% CI 0.06 to 0.68), local and systemic complications as defined by the Atlanta Classification (RR 0.45, 95% CI 0.20 to 0.99; and RR 0.37, 95% CI 0.18 to 0.78 respectively). Among trials that included patients with biliary obstruction, the early routine ERCP strategy was associated with a significant reduction in local complications as defined by authors of the primary study (RR 0.54, 95% CI 0.32 to 0.91), and a non-significant trend towards reduction of local and systemic complications as defined by the Atlanta Classification (RR 0.53, 95% CI 0.26 to 1.07; and RR 0.56, 95% CI 0.30 to 1.02 respectively). ERCP complications were infrequent.

In a prospective, randomized trial from China (n = 101), patients with severe gallstone pancreatitis were randomized to early treatment (within 72 hours of onset) with ERCP or image-guided percutaneous transhepatic gallbladder drainage (PTGD)¹²². Success rates were comparable between the ERCP and PTGD (92% and 96%, respectively), and 4 month mortality, local complication, and systemic complications did not differ significantly, with p-values of 0.80, 0.59, and 0.51, respectively. Wu *et al.* concluded that PTGD is a safe, effective, and minimally invasive option which should be considered for all patients with severe gallstone pancreatitis who are poor candidates for or who are unable to tolerate ERCP¹²².

7.2 Cholecystectomy should be performed during the index admission in patients who have mild acute pancreatitis and should be delayed until clinical resolution in patients who have severe acute pancreatitis.

A systematic review of 8 cohort studies (n = 948) and 1 RCT (n = 50) revealed that while the readmission rate for gallstone disease in patients admitted for gallstone pancreatitis and discharged without cholecystectomy was 18% within the first 58 days post discharge, it was 0% in the cohort who underwent index admission cholecystectomy ($p < 0.0001$)¹²³. This is supported by several retrospective studies which also cite significantly higher recurrence rates of gallstone disease (between 15 and 32%) in patients who do not undergo index admission cholecystectomy¹²⁴⁻¹²⁶. The majority of these recurrent attacks occur prior to the time of interval cholecystectomy^{125 126}.

In a randomized controlled trial which included 50 patients with mild gallstone pancreatitis, laparoscopic cholecystectomy performed within 48 hours of admission resulted in a shorter hospital stay (mean 3.5 days, 95% CI 2.7 to 4.3 days; median 3 days, IQR 2 to 4 days) than one performed after resolution of pain and laboratory abnormalities (mean 5.8 days, 95% CI 3.8 to 7.9 days; median 4 days, IQR 4 to 6 days [$p = 0.0016$])¹²⁷. A second study demonstrated the same findings, with a significant reduction in the total length of stay from 7 to 5 days ($p < 0.001$)¹²⁶.

While studies have demonstrated no increase in complication rate or mortality in gallstone pancreatitis undergoing early versus late cholecystectomy^{123 128}, special consideration should be given to patients admitted for severe necrotizing pancreatitis and/or requiring ICU admission. In this patient population, delaying cholecystectomy for at least 3 weeks may be reasonable because of an increased risk of infection¹²⁹.

7.3 If cholecystectomy is contraindicated in patients because of medical comorbidities, ERCP and sphincterotomy should be considered prior to discharge in patients with acute gall stone pancreatitis.

High recurrence rates of gallstone disease in patients admitted for gallstone pancreatitis and discharged without cholecystectomy has prompted several studies looking at the effectiveness of ERCP and sphincterotomy to reduce this risk. In a prospective study of 233 patients with gallstone pancreatitis, a subgroup analysis of patients discharged without undergoing cholecystectomy revealed that 37% of patients discharged with no intervention had recurrent gallstone disease within 30 days, compared to 0% recurrence in those patients undergoing ERCP and sphincterotomy alone ($p = 0.019$)¹²⁴. In a retrospective analysis of 1,119 patients admitted for gallstone pancreatitis, Hwang et al. (2013) showed a reduction of recurrent gallstone disease from 17% to 8% ($p < 0.001$) with ERCP and sphincterotomy alone, as opposed to no intervention in individuals discharged home without cholecystectomy¹²⁵. A systematic review of 8 cohort studies and 1 RCT demonstrated a similar reduction in biliary events from 24% to 10% ($p < 0.001$) when patients not undergoing index admission cholecystectomy underwent ERCP and sphincterotomy prior to discharge¹²³. These data strongly support the consideration of ERCP with sphincterotomy for patients unable to tolerate surgery on the index admission due to co-morbidities or deconditioning.

All data regarding the use of ERCP with sphincterotomy to prevent recurrent complications of gallstone disease have been generated in patients with mild to moderate acute gallstone pancreatitis, and currently, there is a lack of evidence on which to base definitive recommendations for management of patients with severe and complicated gallstone pancreatitis.

Section 4. Grading of Recommendations

Guideline Recommendation	Strength of Evidence	Guideline Recommendation
Serum lipase should be performed in all patients with a suspected diagnosis of acute pancreatitis.	Moderate High	Weak
An ultrasound should be performed in all patients at baseline to evaluate the biliary tract to determine if the patient has gall stones and/or a stone in the common bile duct.	High	Strong
An MRCP is recommended only in patients in whom there is elevation of liver enzymes, and the common bile duct is either not visualized adequately or is found to be normal on ultrasound.	High	Strong
A CT scan should be performed selectively when (1) a broad differential diagnosis which includes acute pancreatitis must be narrowed or (2) in patients with acute pancreatitis and a suspected local complication of (e.g. peritonitis, signs of shock, suggestive ultrasound findings).	Low-Moderate	Strong
CRP should be performed at admission and for the first 72 hours after admission.	Low-Moderate	Weak
APACHE II scores should be calculated on admission and daily for the first 72 hours after admission.	Moderate	Weak
The diagnosis of severe acute pancreatitis should be made if the patient has a serum CRP \geq 150 mg/dL at baseline or in the first 72 hours; APACHE score of 8 or higher at baseline or in the first 72 hours; or exhibits signs of persistent organ failure for > 48 hours despite adequate intravenous fluid resuscitation.	Moderate	Strong
Supportive care, including resuscitation with isotonic intravenous fluids like Ringer's Lactate, pain control, and mobilization, should be the mainstay of treatment for patients with mild acute pancreatitis.	Low	Strong
Careful consideration of transfer to a monitored unit should be made in patients with: <ul style="list-style-type: none"> Severe acute pancreatitis based on APACHE II Score > 8, CRP > 150 mg/L, or organ dysfunction > 48 hours despite adequate resuscitation Evidence of present or evolving organ dysfunction: Need for aggressive, ongoing fluid resuscitation. 	Low	Strong
Patients with mild acute pancreatitis should receive a regular diet on admission. If patients initially are unable to tolerate an oral diet due to abdominal pain, nausea, vomiting, or ileus, they may be allowed to self-advance their diet from NPO to a regular diet as tolerated.	High	Strong
In patients with severe acute pancreatitis, enteral nutrition should be commenced as soon as possible following admission (within 48 hours).	High	Strong
Prophylactic antibiotics are not recommended.	High	Strong
Patients with 1) extensive necrotizing acute pancreatitis, 2) who	Moderate	Weak

Guideline Recommendation	Strength of Evidence	Guideline Recommendation
show no clinical signs of improvement following appropriate initial management, or 3) who develop other complications should be managed in institutions which have on site, or access to, therapeutic endoscopy, interventional radiology, surgeons, and intensivists with expertise in dealing with severe acute pancreatitis.		
Follow-up CT scans should be based on the clinical status of the patient and not performed routinely at regular intervals.	Low	Strong
Patients with acute peri-pancreatic fluid collections with no radiological or clinical suspicion of sepsis should be observed, and image-guided FNA should be avoided due to the risk of introducing infection into a sterile collection.	Moderate	Weak
When there is radiological or clinical suspicion of infected necrosis in patients with acute necrotic collections (ANCs) or walled-off pancreatic necrosis (WOPN), image-guided fine needle aspirate (FNA) with culture should be performed to distinguish infected from sterile necrosis.	Moderate	Strong
Sterile necrosis based on negative FNA and/or stable clinical picture should be managed non-operatively, and antibiotics are not indicated. For unstable patients in whom sepsis is suspected but no source has been identified, treatment with broad spectrum antibiotics on speculation may be indicated while an appropriate work up (bacterial and fungal cultures, CT scan) is carried out.	Moderate	Weak
In patients with FNA-confirmed infections of acute necrotic collections (ANCs) or walled-off pancreatic collections (WOPN), a step-up approach of antibiotics, image-guided drainage, followed by surgical intervention, if necessary, is indicated.	Moderate	Strong
Pancreatic pseudocysts which are asymptomatic should be managed non-operatively. Intervention is indicated in pseudocysts which are symptomatic, infected, or increasing in size on serial imaging.	Moderate	Strong
ERCP should be performed early (within 24-48 hours) in patients with acute gallstone pancreatitis associated with bile duct obstruction or cholangitis. In unstable patients with severe acute gallstone pancreatitis and associated bile duct obstruction or cholangitis, placement of a percutaneous transhepatic gallbladder drainage tube should be considered if ERCP is not safely feasible.	Moderate-high	Strong
Cholecystectomy should be performed during the index admission in patients who have mild acute pancreatitis and delayed until clinical resolution in patients who have severe acute pancreatitis.	Moderate	Strong
If cholecystectomy cannot be performed during the index admission due to medical comorbidities, patients with acute gallstone pancreatitis should undergo ERCP with sphincterotomy prior to discharge.	low	Weak

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