

Management of Acute Pancreatitis

A Best Practice in Surgery
Clinical Practice Guideline

Acute Pancreatitis

- The incidence of acute pancreatitis reported worldwide continues to increase
- Acute pancreatitis continues to be associated with significant morbidity and mortality
- Numerous CPGs have been developed but recent studies have shown significant areas of non-compliance with CPGs
- Chose to develop a Guideline at University of Toronto to ensure there is consistent and optimal care provided at all hospitals

Working Group Members

- Led by a working group consisting of:
 - John Marshall (General Surgery)
 - Avery Nathens (General Surgery)
 - Natalie Coburn (General Surgery)
 - Jan Friedrich (Critical Care)
 - Mohammed Bazaweer (Critical Care)
 - Gary May (Gastroenterology)
 - Josh Greenberg (Resident in General Surgery)
 - Jonathan Hsu (Medical Student)
 - Emily Pearsall (Manager)

Clinical Practice Guideline: Management of Acute Pancreatitis

Development of Acute Pancreatitis CPG

- 2 parts
 - Audit of current management of acute pancreatitis at 8 University of Toronto adult hospitals (2010-11)
 - Development of Practice Guidelines based on review of the literature and expert consensus
- Work done in tandem so we could assess compliance with proposed guideline recommendations

Acute Pancreatitis Audit

- Objective:
 - To identify whether there are gaps in the management of patients prior to implementation of a local CPG on the management of acute pancreatitis

Acute Pancreatitis Audit

- Retrospective audit of patients admitted between January, 2010 and December, 2011 with acute pancreatitis at 8 U of T affiliated hospitals
 - Included all patients admitted to the ICU (n=52)
 - A sample of patients admitted directly to the ward
 - Mean 31 patients (range 25-48 patients)/hospital
 - Diagnosis based on Atlanta Criteria
 - Patients transferred from another hospital were excluded

Development of the CPG

- Working group developed the research questions, analytical framework and decided upon the relevant clinical outcomes
- Scoping review with search term of *acute pancreatitis* and *guidelines* revealed 14 Clinical Practice Guidelines on this topic
- A systematic review of these guidelines published in 2010
- This systematic review was used as the basis of our CPG
- Further searches done using relevant search terms to update the evidence

Development of the CPG

- The working group reviewed the guidelines and associated evidence and developed recommendations based on best evidence, local practice and expert consensus
- Recommendations were sent to all general surgeons, gastroenterologists and critical care specialists at the University of Toronto for feedback

CPG Recommendations

1. Diagnosis of acute pancreatitis
2. Assessment of severity
3. Supportive care
4. Nutrition
5. Prophylactic antibiotics
6. Diagnosis and management of local complications of pancreatitis
7. Management of patients with gallstone pancreatitis

Diagnosis of acute pancreatitis: Recommendations

- Serum lipase preferred over serum amylase
 - Serum lipase remains elevated longer than serum amylase and therefore is more sensitive in patients who present late
 - No significant difference at day 1 but improved characteristics at day 2-3

Serum Lipase	85%	82%
Serum Amylase	85%	68%

- Performing both only marginally improves diagnosis
- A threefold elevation of serum lipase from the upper limit of normal is required to make the diagnosis of acute pancreatitis

Diagnosis of acute pancreatitis: Recommendations

Imaging:

- An ultrasound should be performed in all patients at baseline to evaluate the biliary tract
- CT scan should be performed selectively:
 - if another diagnosis is being strongly considered
 - in patients with suspected local complications of acute pancreatitis which usually occur 48-72 hours post-onset of symptoms
- Unless contraindicated (e.g. renal dysfunction), intravenous contrast should be given in order to assess for pancreatic necrosis
- 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

Diagnosis of acute pancreatitis: Current practice

	n	%
Total number of patients with AP	248	100%
Lipase only	56	22.6%
Amylase only	127	51.2%
Lipase and amylase	65	26.2%
Ultrasound within 48 hours of admission	174	70.2%
CT scan within 48 hours of admission	139	56.0%
CT scan and ultrasound within 48 hours of admission	86	34.6%
CRP measured	1	0.4%

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Assessment of severity: Recommendations

- A serum CRP ≥ 150 mg/dL at baseline or in the first 72 hours is suggestive of severe pancreatitis
 - Thus, serum CRP should be ordered
- APACHE II scores should be calculated on admission and daily for the first 72 hours after admission.
 - Score of 8 or higher at baseline or in the first 72 hours is suggestive of severe pancreatitis
- If a patient exhibits signs of persistent organ failure for > 48 hours despite adequate intravenous fluid resuscitation, it suggests severe pancreatitis

Supportive care: Recommendations

- Supportive care, including resuscitation with isotonic intravenous fluids like Ringer's Lactate, pain control, and mobilization should be the mainstay of treatment of patients with mild pancreatitis

Supportive care: Recommendations

- Consideration of transfer to a monitored unit should be made in patients with:
 1. Severe acute pancreatitis based on APACHE II Score > 8 , CRP > 150 mg/L, or organ dysfunction > 48 hours despite adequate resuscitation
 2. Evidence of present or evolving organ dysfunction:
 - Respiratory: $\text{PaO}_2/\text{FiO}_2 \leq 300$, or respiratory rate > 20
 - Cardiovascular: hypotension despite aggressive fluid resuscitation (systolic BP < 90 mm Hg off of inotropic support or drop of sBP > 40), need for vasopressors, or pH < 7.3
 - Renal: ≥ 1.5 fold increase in serum creatinine over 7 days, increase of ≥ 26.5 μmol in serum creatinine over 48 hours, urine output < 0.5 ml/kg/h for ≥ 6 hours

Supportive care: Recommendations

- Consideration of transfer to a monitored unit should be made in patients with:
 - Need for aggressive, ongoing fluid resuscitation
 - Evidence of severe haemoconcentration (Hb > 160, HCT > 0.500)
 - Patients with one or more of the above criteria and a BMI > 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

Supportive care: Supporting Evidence

- No high quality trials showing the benefit of aggressive fluid resuscitation
- Systematic review of 26 observation studies showed that patients with severe pancreatitis treated in an ICU had shorter duration of ICU stay and lower mortality

Nutrition: Recommendations

- Mild pancreatitis
 - Regular diet should be offered on admission
 - NPO unnecessary
 - Clear liquids to regular diet not necessary
- Severe pancreatitis
 - Enteral feeding is recommended over parenteral nutrition.
 - Enteral nutrition should be commenced as soon as possible following admission (within 48 hours).
 - Enteral feeding by nasojejunal tube is not superior to feeding by nasogastric feeding tube and often results in delays

Nutrition:

Supporting Evidence

- Multiple RCTs have shown that early oral/enteral feeding is not associated with adverse effects
 - Eckerwall et al also showed a decreased LOS (4 vs 6 days)
- Cochrane review
 - 8 RCTs comparing enteral to parenteral nutrition
 - Decreased mortality (RR 0.50, 95% CI 0.28-0.91)
 - Decreased multi-organ failure (RR 0.55, 95% CI 0.37-0.88)
 - Decreased operative interventions (RR 0.44, 95% CI 0.29-0.67)
 - Decreased septic complications (RR 0.74, 95% CI 0.40-1.35)

Nutrition: Current practice

	n	%
Non-ICU	196	
Regular diet on admission	0	0.0%*
NPO on admission	158	80.6%*
Average time to oral diet (d)	1.0	--
ICU	52	
NPO on admission	52	100%†
Average time to commencement of any nutrition (d)	3.2	--
Patients receiving EN	18	34.6%†
Mean time to start of EN (d)	7.5	--
Patients receiving PN	6	11.5%†
Mean time to start of PN (d)	14.8	--

Prophylactic antibiotics: Recommendations

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

Prophylactic antibiotics: Supporting evidence

- Cochrane review (2010)
 - 7 RCTs with 404 patients with necrotizing pancreatitis who received prophylactic antibiotics
 - No significant decrease in:
 - mortality (8.4% vs. 14.4%)
 - Infection (19.7% vs. 24.4%)
- Maravi Poma et al demonstrated a 3 fold increase in the incidence of local and systemic fungal infection in patients with prolonged treatment with prophylactic antibiotics

Prophylactic antibiotics: Current practice

Antibiotics	n	%
Non-ICU	196	
Patients receiving prophylactic antibiotics	50	25.5%*
ICU	52	
Patients receiving prophylactic antibiotics	25	48.1%†
Patients who underwent FNA prior to commencing antibiotics	1	2.7%†

Diagnosis & management of complications: Recommendations

- Patients 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 if:
 - There is extensive necrotizing pancreatitis
 - They show no clinical signs of improvement following appropriate initial management
 - They develop other complications

Diagnosis of complications: Recommendations

- Repeat CT scan should be considered if there is:
 - new (or unresolving) evidence of infection (eg: leukocytosis, fever) without a known source
 - new inability to tolerate oral/enteral feeds
 - change in haemodynamic status
 - evidence of bleeding

Diagnosis of complications:

Recommendations

- Role of FNA:
- 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.
- 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*

Management of complications: Recommendations

- Antibiotics should be prescribed
 - 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
 - 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*).

Management of complications: Recommendations

- Antibiotics should not be prescribed
 - Sterile necrosis based on negative FNA and/or stable clinical picture
 - 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 scan) is carried out

Management of complications: Recommendations

- 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
 - Surgical consultation should occur early, however, surgical intervention should be delayed until later in the course of disease whenever possible
 - Surgery should be considered for cases that fail less invasive approaches, but should be delayed long enough to allow demarcation of necrotic pancreatic tissue

Management of complications: Recommendations

- Pancreatic pseudocysts
 - Asymptomatic should be managed non-operatively
 - Symptomatic, infected, or those increasing in size on serial imaging, require intervention
 - Should be performed in a high volume center

Management of patients with gallstone pancreatitis: Recommendations

- ERCP should be performed early (within 24-48 hours) in patients with gallstone pancreatitis associated with bile duct obstruction or cholangitis
- In unstable patients with severe 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
- Cholecystectomy should be performed:
 - During the index admission in patients who have mild pancreatitis
 - Delayed until clinical resolution in patients who have severe pancreatitis

Management of patients with gallstone pancreatitis: Supporting evidence

- **Cochrane Review**
 - 5 RCTs with 644 patients with acute gallstone pancreatitis who were randomized to conservative Rx or early ERCP
 - No differences in mortality, or local or systemic outcomes
 - Patients with cholangitis or those with biliary obstructive had improved outcomes
- RCT in 50 patients with mild gallstone pancreatitis who were randomized laparoscopic cholecystectomy within 48 hours of admission vs after resolution of symptoms
 - Shorter stay: median stay of 3.5 days vs 5.8 days

Management of patients with gallstone pancreatitis: Recommendations

- If cholecystectomy cannot be performed during the index admission due to medical comorbidities, patients with gallstone pancreatitis should undergo ERCP with sphincterotomy prior to discharge.
- Evidence:
 - Prospective cohort study of 233 patients:
 - 37% recurrent gall stone disease at 30 days if no intervention vs 0% in those who underwent ERCP and sphincterotomy
 - Retrospective case series of 1,119 patients showed decrease in recurrence from 19% to 8%

Management of patients with gallstone pancreatitis: Current practice

	n	%
Patients with gallstone pancreatitis	106	
ERCP when indicated (radiographic CBD obstruction)	16	31%
Average time to ERCP (d)	3.1	--
Cholecystectomy on index admission	24	22.6% [‡]
ERCP + sphincterotomy for patients discharged without cholecystectomy	18	22.0% ^Δ

Take Home Messages

- Diagnosis: order Serum lipase only (not serum amylase) and Ultrasound (CT not required)
- Early feeding
 - Enteral feeds via NG tube in patients with severe pancreatitis rather than by jejunostomy
- No prophylactic antibiotics
- Confirm that there is infected necrosis by doing a FNA before starting antibiotics
- Avoid surgery in severe pancreatitis if possible
- Perform cholecystectomy prior to discharge in patients with gall stone induced pancreatitis. If not possible, do an ERCP and sphincterotomy