DATE: March 2019

OHSU HEALTH SYSTEM
OFFICE OF CLINICAL INTEGRATION AND EVIDENCE-BASED PRACTICE

GUIDELINE FOR THE MANAGEMENT OF ACUTE PANCREATITIS

Background: Acute pancreatitis is a leading cause of inpatient care within the United States, and is associated with significant morbidity and mortality.[1-2] The most common causes of acute pancreatitis remain gallstones and alcohol, which together comprise 80% of cases; the reminder of cases are due to less common causes, including drug reactions, pancreatic solid and cystic malignancies, and hypertriglyceridemia.[3] Patients with acute pancreatitis frequently experience abdominal pain, nausea, and vomiting, and the condition negatively impacts their quality of life.[4]

Prevalence: In the United States, more than 275,000 patients are hospitalized for acute pancreatitis annually, with a mortality rate that approaches 5%, even in those without severe disease. The incidence of acute pancreatitis ranges from 5 to 30 cases per 100,000, and there is evidence that the incidence has been rising in recent years.[5-7]

Risks: Acute pancreatitis is a common gastrointestinal condition that is associated with substantial suffering, morbidity, and cost to the health care system.[8] The overall case fatality rate for acute pancreatitis is roughly 5%, and is expectedly higher for more severe disease.[9] Despite improvements in access to care, imaging and interventional techniques, acute pancreatitis continues to be associated with significant morbidity and mortality.[10] The purpose of this guideline is to provide evidence-based recommendations for the management of acute pancreatitis.

Definitions:
Early Phase Acute Pancreatitis (AP): (within 1 week) Characterized by the systemic inflammatory response syndrome (SIRS) and / or organ failure;
Late Phase AP: (>1 week) Characterized by local complications.
Mild AP: Lacks both organ failure and local or systemic complications
Moderately Severe AP: Transient organ failure (organ failure of <2 days), local complications, and/or exacerbation of coexistent disease
Severe AP: Presence of persistent organ failure (organ failure that persists for >/2 days)
Chronic Pancreatitis: Loss of pancreatic function that develops gradually and worsens over time, resulting in permanent organ damage.
Local complications: Objective criteria based primarily on contrast-enhanced computed tomography; classified as acute peripancreatic fluid collections, pseudocyst, acute (pancreatic/peripancreatic) necrotic collection, and walled-off necrosis.

Guideline Eligibility Criteria: Adult patients with acute pancreatitis including, both early phase (within 1 week) and late phase (>1 week).

Guideline Exclusion Criteria: Adult patients with chronic pancreatitis and recurrent acute pancreatitis

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Clinical Practice Recommendations:

Diagnostic Criteria of Acute Pancreatitis:

- The diagnosis of AP is most often established by the presence of 2 of the 3 following criteria: (i) abdominal pain consistent with the disease, (ii) serum lipase greater than three times the upper limit of normal, and / or (iii) characteristic findings from abdominal imaging[11-12] **(Strong Recommendation, Moderate Quality of Evidence).**

Initial Assessment:

- The etiology of acute pancreatitis should be determined using detailed personal (i.e. previous acute pancreatitis, known gallstone disease, alcohol intake, medication and drug intake, known hyperlipidemia, trauma, recent invasive procedures such as ERCP) and family history of pancreatic disease, physical examination, laboratory serum tests (i.e. liver enzymes, calcium, triglycerides), and imaging (i.e. right upper quadrant ultrasonography)[13-14] **(Strong Recommendation, Moderate Quality of Evidence).**
- Transabdominal ultrasound should be strongly considered in all patients with first episode of acute pancreatitis[11] **(Strong Recommendation, Low Quality of Evidence)**.
- Contrast-enhanced computed tomography (CECT) of the pancreas should be reserved for patients in whom the diagnosis is unclear or who fail to improve clinically within the first 48 – 72 h after hospital admission or to evaluate complications[11-12] **(Strong Recommendation, Low Quality of Evidence).**

Diagnostic Approach:

- For imaging, the indication for initial CT assessment in acute pancreatitis can be: 1) diagnostic uncertainty, 2) confirmation of severity based on clinical predictors of severe acute pancreatitis, or 3) failure to respond to conservative treatment or in the setting of clinical deterioration. Optimal timing for initial CT assessment is at least 72-96 hours after onset of symptoms[8,13,22] **(Strong Recommendation, Moderate Quality of Evidence).**
- Follow up CT or MR in acute pancreatitis is indicated when there is a lack of clinical improvement, clinical deterioration, or especially when invasive intervention is considered[8,13,22] **(Strong Recommendation, Moderate Quality of Evidence).**

Risk Assessment:

- Risk assessment based on hemodynamic status and presence of organ failure should be performed to stratify patients into higher- and lower-risk categories to assist triage[11,13] **(Conditional Recommendation, Moderate Quality of Evidence)**.
- Transfer to intensive care unit (ICU) should be considered in patients identified as high risk with severe acute pancreatitis[13] **(Conditional Recommendation, Moderate Quality of Evidence)**.

Practice Implications:

- Utilize Sequential Organ Failure Assessment (SOFA) (Appendix A), Ranson's Criteria (Appendix B), or Acute Physiology and Chronic Health Assessment (APACHE) IV scoring systems (Appendix C) in conjunction with clinical judgement to determine disease severity.
- Early pancreatitis should be closely monitored for up to 48 hours

Initial Management

Intravenous Hydration:

- Use goal-directed therapy for fluid management[8] **(Conditional Recommendation, Very Low Quality Evidence).**
- Use Lactated Ringer's (LR) as the initial infusion solution for acute pancreatitis[13,15] **(Conditional Recommendation, Very Low Quality Evidence).**

- For patients in shock or with dehydration in the early phases of acute pancreatitis, short-time rapid fluid resuscitation is recommended. However, this should be carried out with great care in order to avoid excessive fluid infusion. For patients without dehydration, they should be monitored closely with an appropriate amount of fluid infusion. Patients with underlying cardiac or renal disease may warrant more conservative resuscitation[15] **(Conditional Recommendation, Very Low Quality Evidence).**

Antibiotics:

- Use of prophylactic antibiotics in patients with severe acute pancreatitis and necrotizing acute pancreatitis is not recommended[8, 18] **(Strong Recommendation, Moderate Quality Evidence)**.
- Infected necrosis should be considered in patients with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7 – 10 days of hospitalization. In these patients, either (i) initial CT-guided fine needed aspiration (FNA) for Gram stain and culture to guide use of appropriate antibiotics or (ii) empiric use of antibiotics without CT FNA should be given[11] **(Strong Recommendation, Low Quality Evidence)**.

Practice Implication

- Check Local Antibiotic Resistance Diagram when prescribing
- Use Piperacillin-tazobactam as first line treatment
- Recommend against empiric use of carbapenams
- Recommend ciprofloxacin + metronidazole for patients with well documented severe beta-lactam allergy

Endoscopic retrograde cholangiopancreatography (ERCP):

- In patients with acute biliary pancreatitis without cholangitis or evidence of obstruction, urgent ERCP is not recommended[8] **(Conditional Recommendation, Low Quality Evidence)**.
- Patients with acute pancreatitis and concurrent acute cholangitis should undergo ERCP within 24 hours of admission[16] **(Strong Recommendation, Moderate Quality Evidence)**.
- ERCP is not needed in most patients with gallstone pancreatitis who lack laboratory or clinical evidence of ongoing biliary obstruction[11,13] **(Strong Recommendation, Low Quality Evidence)**.
- In the absence of cholangitis and/or jaundice, MRCP or endoscopic ultrasound (EUS) rather than diagnostic ERCP should be used to screen for choledocholithiasis if highly suspected[11,17] **(Conditional Recommendation, Low Quality Evidence)**

Strategy to assign risk of choledocholithiasis in patients with symptomatic cholelithiasis based on clinical predictors: [19]

Predictors of choledocholithiasis	Very Strong	• CBD stone on transabdominal US • Clinical ascending cholangitis • Bilirubin >4 mg/dL
	Strong	• Dilated CBD on US (>6 mm with gallbladder in situ) • Bilirubin level 1.8-4 mg/dL
	Moderate	• Abnormal liver biochemical test other than bilirubin • Age older than 55 y

		• Clinical gallstone pancreatitis
Assigning a likelihood of choledocholithiasis based on clinical predicators • Presence of a very strong predictor – High • Present of both strong predictors – High • No predictors present – Low • All other patients - Intermediate		

Practice Implication

- Consult with Gastroenterology immediately if patient has acute pancreatitis and concurrent acute cholangitis, or if choledocholithiasis if highly suspected.

Nutritional Support:

- Early (within 24 hours) oral feeding should be started as tolerated[8,11,21] **(Strong Recommendation, Moderate Quality Evidence)**.
- Assess initial nutrition in acute pancreatitis to evaluate disease severity to direct nutrition therapy. Since disease severity may change quickly, reassess feeding tolerance and need for specialized nutrition therapy frequently[20] **(Consensus-Adapted)**.
- Specialized nutrition therapy should not be provided to patients with mild acute pancreatitis, recommend an oral diet as tolerated to patients instead. If an unexpected complication develops or there is failure to advance to oral diet within 7 days, then specialized nutrition therapy should be considered[8,11,20] **(Conditional Recommendation, Very Low Quality Evidence)**.
- Patients with moderate to severe acute pancreatitis should have a naso-/oroenteric tube placed and enteral started at a trophic rate and advanced to goal as fluid volume resuscitation is completed (within 24–48 hours of admission). Evidence has shown that nasogastric and nasoenteric have equal outcomes[8,20] **(Conditional Recommendation, Very Low Quality Evidence).**
- Initiate enteral nutrition with standard polymeric formula in patients with severe acute pancreatitis. Although promising, the data are currently insufficient to recommend placing a patient with severe acute pancreatitis on an immune-enhancing formulation at this time[20] **(Conditional Recommendation, Very Low Quality Evidence)**.
- Patients with severe acute pancreatitis who require nutrition therapy should be recommended enteral over parenteral nutrition whenever possible. If patient has not reached goal in 5 – 7 days on trophic feeding, then consider total parenteral nutrition[8,11,13,20] **(Conditional Recommendation, Low Quality Evidence)**.
- For the patient with severe acute pancreatitis, when enteral nutrition is not feasible, use of parenteral nutrition should be considered after one week from the onset of the pancreatitis episode[11,13,20] **(Consensus-Adapted)**.

Cholecystectomy:

- In patients with mild acute biliary pancreatitis, a cholecystectomy should be performed before discharge to prevent a recurrence of acute pancreatitis[8,11,13] **(Strong Recommendation, Moderate Quality Evidence)**.

Cross-Sectional Imaging:

- Follow-up CT or MRI in acute pancreatitis is indicated when there is a lack of clinical improvement or clinical deterioration, especially when invasive intervention is considered[11,13,22] **(Strong Recommendation, Moderate Quality Evidence)**.

Practice Implication

Generally routine single-phase contrast enhanced CT is adequate to assess local complications of pancreatitis. Multiphase pancreas CT should be reserved for suspected vascular complications (e.g. pseudoaneurysm, active bleeding, thrombosis, hemorrhage) or if malignancy is a possible etiology for pancreatitis (typically first episode in patients >45 years).

First line

- CT Abdomen and Pelvis with IV contrast
- CT Abdomen and Pelvis without IV contrast, if contraindicated

Second line

- MRI abdomen with or without IV contrast with MRCP

Drainage:

- For stable patients with proven or suspected infected necrotizing pancreatitis, invasive intervention (i.e. percutaneous catheter drainage, endoscopic transluminal drainage/necrosectomy, minimally invasive or open necrosectomy) should be delayed to allow liquefication of the contents and the development of a fibrous wall around the necrosis.[11,13] **(Strong Recommendation, Moderate Quality of Evidence).**
- In symptomatic patients with infected necrosis, minimally invasive methods of necrosectomy are preferred to open necrosectomy[11] **(Strong Recommendation, Low Quality Evidence)**.
- Endoscopic drainage of pancreatic fluid collections should be considered only after sufficient exclusion of alternative diagnoses, such as cystic pancreatic neoplasms and pseudoaneurysms[23] **(Strong Recommendation, Moderate Quality Evidence).**
- Recommend waiting for maturation of the cyst wall of PFCs until at least 4 weeks after initial presentation to allow the collection to become 'walled-off' before endoscopic intervention[23] **(Strong Recommendation, Moderate Quality Evidence)**.

Practice Implication

- Decisions about drainage should be made on a multidisciplinary basis with input from surgery, gastroenterology and radiology

Alcohol Counseling:

- Alcohol intervention during admission is recommended in patients with acute alcoholic pancreatitis[8] **(Strong Recommendation, Moderate Quality Evidence)**.

Practice Implication

- A multidisciplinary team approach should be used, utilizing your institution's resources, such as OHSU hospital's Improving Addiction Care Team (IMPACT) or organizational social workers specialized in alcohol abuse disorder

Pain Management:

- Use a multidisciplinary team approach to determine the appropriate pain management strategy utilizing shared-decision making with your patient. Appropriate strategies include oral, intravenous, and/or epidural analgesia[24] **(Conditional Recommendation, Very Low Quality Evidence)**.

Transfer Criteria:

- Patients admitted to OHSU with early phase acute pancreatitis (within one week) will be considered for transfer to Adventist and Tuality. Transfer will be facilitated by transfer center nurse and physician on duty, which will be based on patient condition and capability at partner site at time of transfer. See Capability Grid for Acute Pancreatitis to determine if transfer is possible. **(Consensus)**
- Patients admitted to Adventist and Tuality with acute pancreatitis will remain at site, unless there are services unavailable to care for patient. See Capability Grid for Acute Pancreatitis to determine if transfer if necessary. **(Consensus)**
    - If no bed is available for transfer, the following can be considered: (1) phone consult or (2) transfer to external hospital.

Practice Implication:

- If transfer is necessary, patient consent should be obtained and transfer expectations should be discussed in a clear, transparent manner to manage patient/family expectations.

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Capability Grid for Acute Pancreatitis

Capability of care at each OHSU Health System Hospital

	ICU	ERCP	EUS	General Surgery	IR	MRCP	Surgical Oncology	IMPACT
OHSU	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adventist	Yes	Yes	Limited*	Yes	Yes	Yes	No	No
Tuality	Yes	Yes	No	Yes	Limited*	Yes	No	No

*Limited number of clinicians provide this service at site, limiting days and times when service will be available

Quality Measures:

Process:

- % of patients with early vs. late phase pancreatitis
- % of patients with alcoholic acute pancreatitis
- # of USs
- # of CTs
- # of MRI
- Scoring system Utilization
- % of patients receiving fluid therapy
- Type of antibiotics prescribed
- Time when antibiotics was initiated
- # of ERCPs
- # of MRCPs
- Type of nutritional support received
- # of cholecystectomy
- # of patients receiving drainage
- Type of drainage used
- Referrals to Impact
- Analgesics prescribed

Outcome:

- Length of stay
- Readmissions
- Transfers between partner sites

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Guideline Preparation

This guideline was prepared by the Office of Clinical Integration (CI) and Evidence-Based Practice (EBP) in collaboration with content experts at Oregon Health and Science University.

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Development Process

This guideline was developed using the process outlined in the CI and EBP Manual (2016). The review summary documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing Internal and External Guidelines
   - Literature Review of Relevant Evidence
3. Critically Analyze the Evidence
4. Summarize the Evidence by preparing the guideline, and order sets

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **University of Pennsylvania's Trustworthy Guideline Rating Scale**. The summary of these guidelines are included in the evidence summary. The rating scale is based on the Institute of Medicine's "Standards for Developing Trustworthy Clinical Practice Guidelines" (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains. This scale evaluates a guideline's transparency, conflict of interest, development group, systematic review, supporting evidence, recommendations, external review and currency and updates. The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated).

The **GRADE (Grading of Recommendations, Assessment, Development and Evaluation)** criteria were utilized to evaluate the body of evidence used to make clinical recommendations. The table below defines how the quality of the evidence is rated and how a strong versus conditional recommendation is established. The evidence summary reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Recommendations for the guidelines were directed by the existing evidence, content experts, and consensus. Patient and family preference were included when possible. When evidence is lacking, options in care are provided in the guideline and the order sets that accompany the guideline.

Approval Process

Guidelines are reviewed and approved by the Content Expert Team, Office of CI and EBP, Knowledge Management and Therapeutics Committee, Professional Board, and other appropriate hospital committees as deemed appropriate for the guideline's intended use. Guidelines are reviewed and updated as necessary every 2 to 3 years within the Office of CI and EBP at OHSU. Content Expert Teams will be involved with every review and update.

Disclaimer

Guideline recommendations are made from the best evidence, clinical expertise and consensus, in addition to thoughtful consideration for the patients and families cared for within the Integrated Delivery System. When evidence was lacking or inconclusive, content experts made recommendations based on consensus. Expert consensus is implied when a reference is not otherwise indicated.

The guideline is not intended to impose standards of care preventing selective variation in practice that is necessary to meet the unique needs of individual patients. The physician must consider each patient and family's circumstance to make the ultimate judgment regarding best care.

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Appendix A. Sequential Organ Failure Assessment (SOFA)

Table 1

The Sequential Organ Failure Assessment (SOFA) score

SOFA score	1	2	3	4
Respiration[a]				
PaO_2/FIO_2 (mm Hg)	<400	<300	<220	<100
SaO_2/FIO_2	221-301	142-220	67-141	<67
Coagulation				
Platelets $\times 10^3/mm^3$	<150	<100	<50	<20
Liver				
Bilirubin (mg/dL)	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular[b]				
Hypotension	MAP <70	Dopamine ≤5 or dobutamine (any)	Dopamine >5 or norepinephrine ≤0.1	Dopamine >15 or norepinephrine >0.1
CNS				
Glasgow Coma Score	13-14	10-12	6-9	<6
Renal				
Creatinine (mg/dL) or urine output (mL/d)	1.2-1.9	2.0-3.4	3.5-4.9 or <500	>5.0 or <200

MAP, mean arterial pressure; CNS, central nervous system; SaO_2, peripheral arterial oxygen saturation.

[a] PaO_2/FIO_2 ratio was used preferentially. If not available, the SaO_2/FIO_2 ratio was used

[b] vasoactive mediations administered for at least 1 hr (dopamine and norepinephrine µmg/kg/min).

Reference: Jones, A. E., et al. (2009). "The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation." Critical Care Medicine 37(5): 1649-1654.

Appendix B. Ranson's Criteria

Criteria for acute pancreatitis not due to gallstones

At admission	*During the initial 48 h*
Age >55 y	Hematocrit fall >10 points
WBC >16,000/mm^3	BUN Elevation >5 mg/dL
Blood glucose >200 mg/dL	Serum calcium <8 mg/dL
Serum LDH >350 IU/L	Arterial PO^2 <60 mm Hg
Serum AST >250 U/dL	Base deficit >4 mEq/L
	Estimated fluid sequestration >6 L

Criteria for acute gallstone pancreatitis

At admission	
Age >70 y	Hematocrit fall >10 points
WBC >18,000/mm^3	BUN Elevation >2 mg/dL
Blood glucose >220 mg/dL	Serum calcium <8 mg/dL
Serum LDH >400 IU/L	Base deficit >5 mEq/L
Serum AST >250 U/dL	Estimated fluid sequestration >4 L

Risk Factors/Mortality

5% mortality risk with <2 signs
15-20% mortality risk with 3-4 signs
40% mortality risk with 5-6 signs
99% mortality risk with >7 signs

Reference: Ranson, J. H., et al. (1974). "Prognostic signs and the role of operative management in acute pancreatitis." Surgery, Gynecology & Obstetrics 139(1): 69-81.

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Appendix C. Acute Physiology and Chronic Health Assessment (APACHE) IV scoring system

Age (ans)	
Temperature (°C)	37
MAP (mmHg)	70
HR (/min)	80
RR (/min)	15
Mecanical Ventilation	○ No ○ Yes
FiO2 (%)	
pO2 (mmHg)	90
pCO2 (mmHg)	40
Arterial pH	7.4
Na+ (mEq/L)	140
Urine Output (mL/24h)	
Creatinine (mg/dL)	1
Urea (mEq/L)	4
BSL (mg/dL)	100
Albumin (g/L)	40
Bilirubin (mg/dL)	1
Ht (%)	40
WBC (x1000/mm3)	10
GCS :	☐ Not available
- Eyes	4. Spontaneous
- Verbal	5. Oriented
- Motor	6. On Command

Change values used for AaDO2 calculation

Chronic Health Condition :

☐ CRF / HD	☐ Lymphoma
☐ Cirrhosis	☐ Leukemia / Myeloma
☐ Hepatic Failure	☐ Immunosuppression
☐ Metastatic Carcinoma	☐ AIDS

Admission Information :

Pre-ICU LOS (days)	
Origin	Other
Readmission	◉ No ○ Yes
Emergency Surgery	◉ No ○ Yes

Admission Diagnosis :

○ Non operative ○ Postoperative

System

Diagnosis

Thrombolysis : ◉ No ○ Yes

Calculate

APACHE IV Score		/286
APS Score		/239
Estimated Mortality Rate		%
Estimated Length of Stay		days

Reference: Intensive Care Network. https://intensivecarenetwork.com/Calculators/Files/Apache4.html. Accessed on February 14, 2019