Guidelines

for the Management of

Acute Pancreatitis

By

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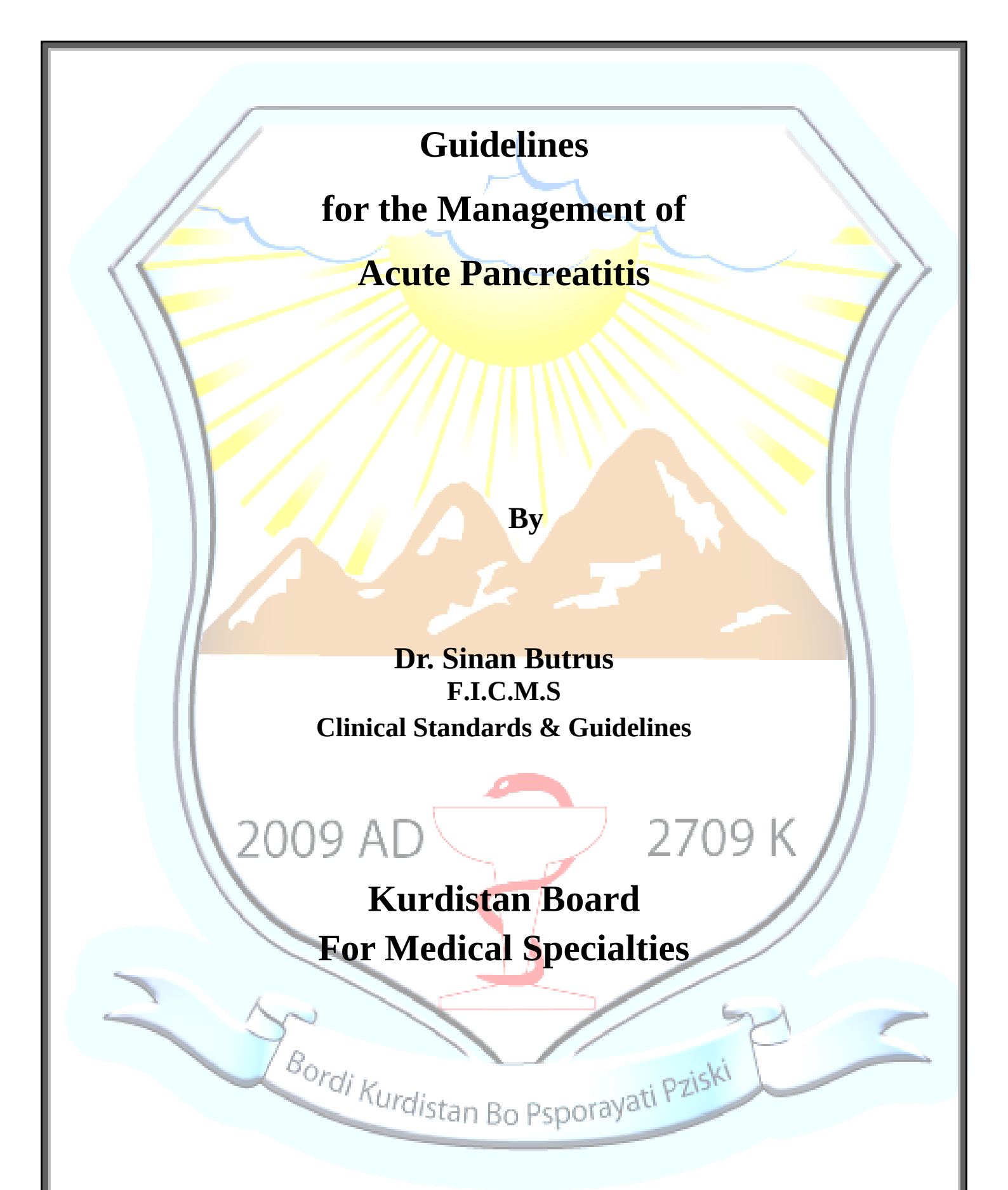
F.I.C.M.S
Clinical Standards & Guidelines



Kurdistan Board
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A. Acute Pancreatitis AP: Diagnosis and etiology

1. The definition of acute pancreatitis AP is based on the fulfillment of '2 out of 3' of the following criteria:

a. clinical (upper abdominal pain) consistent with the disease,

b. laboratory (serum amylase &/or lipase >3x upper limit of normal)

c. imaging (CT, MRI, and ultrasonography) criteria.

2. On admission, the etiology of acute pancreatitis should be determined using *detailed personal history* (i.e. previous acute pancreatitis, known gallstone disease, alcohol intake, medication & drug intake, hyperlipidemia, trauma, recent invasive procedures such as ERCP and family history of pancreatic disease), together with *physical examination*, *laboratory* serum tests; liver enzymes, calcium, lipid profile. (In the absence of gallstones and/or history of significant history of alcohol use, a serum triglyceride should be obtained and considered the etiology if >1,000 mg/dl) & *imaging* (i.e. right upper quadrant ultrasonography) should be performed in all patients with AP

3. In patients considered to have idiopathic acute pancreatitis, after negative routine work-up for biliary etiology, endoscopic ultrasonography (EUS) is recommended as the first step to assess for occult microlithiasis, neoplasms and chronic pancreatitis. If EUS is negative, MRCP is advised as a second step to identify rare morphologic abnormalities.

Genetic counseling should be considered if etiology remains unidentified, especially after a second attack of idiopathic pancreatitis, young patients (<30 years old) if no cause is evident & family history of pancreatic disease or type 1 diabetes mellitus is present.

B. Prognostication/prediction of severity

Risk assessment should be performed to stratify patients into higher- and lower-risk categories to assist triage, such as admission to ICU

4. Look for *Systemic Inflammatory Response Syndrome* (SIRS) to predict severe acute pancreatitis at admission and at 48 hours manifested by:

-Body temperature < 36 °C (96.8 °F) or > 38 °C (100.4 °F)

-Heart rate > 90 beats per minute

-Tachypnea (high respiratory rate) > 20 breaths per minute; or, an arterial partial pressure of carbon dioxide < 4.3 kPa (32 mmHg)

-WBC count<4000 cells/mm³ ($4x10^9$ cells/L) or >12,000 cells/mm³ ($12x10^9$ cells/L); or the presence of > 10% immature neutrophils- band forms.

(Band forms > 3% is called bandemia or a "left-shift.")

** When two or more of these criteria are met with or without evidence of infection, patients may be diagnosed with "SIRS*."

** Patients with SIRS and acute organ dysfunction may be termed severe SIRS*

** Several potential risk factors of severity and measurements related to the acute pancreatitis that may reflect severity should be recorded and evaluated prospectively; including age, body mass index, hematocrit, APACHE II scores, and serum levels of C-reactive protein (which is most predictive at 48-72 hours after onset of disease).*

5. A 3-dimension approach is advised to predict outcome of acute pancreatitis:
combining host risk factors (e.g. age, co-morbidity, and body mass index),
clinical risk stratification (e.g. persistent SIRS)
monitoring response to initial therapy (persistent SIRS, blood urea & creatinine).

C. Imaging

6. The indication for initial CT assessment in acute pancreatitis is:
diagnostic uncertainties, confirmation of severity based on clinical predictors of sever AP, failure to respond to conservative treatment or in the setting of clinical deterioration.

7. Optimal timing for initial CT assessment is at least 72-96 hours after onset of symptoms.

8. 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.

D. Fluid therapy

9. No medication has been shown to be effective in treating AP but early oxygen supplementation to maintain an arterial saturation >95% & early aggressive fluid resuscitation within the first 24 hours of admission (as it is associated with decreased rates of persistent SIRS and organ failure but may have little benefit then after).

10. Preferably; use Ringer's lactate at a rate of 5-10 ml/kg/h until resuscitation goals are reached; a total infusion of 2500-4000 ml within the first 24 h might be needed to reach these goals unless cardiovascular &/or renal co-morbidities exist.
Fluid requirements should be reassessed at frequent intervals within 6 hr of admission and for the next 24 – 48 h.

11. Assess the response to fluid resuscitation based on one or more of the following:
a) clinical targets of heart rate <120/min, mean arterial pressure between 65-85 mmHg (8.7-11.3 kPa), and urinary output > 0.5-1ml/kg/h
b) invasive clinical targets of stroke volume variation, and intrathoracic blood volume determination,
c) biochemical targets of hematocrit 35-44% & reduction of the blood urea nitrogen.

E. Intensive care management

12. Patient should be managed in ICU if diagnosed with sever or predictive serious AP having one or more of the following parameters identified at admission (guidelines of the Society of Critical Care Medicine SCCM):
(1) systolic arterial pressure <80 mmHg (<10.7 kPa) or mean arterial pressure <60 mmHg (<8.0 kPa) or diastolic arterial pressure >120 mmHg (>16 kPa);
(2) pulse <40 or >150 beats/min; (3) respiratory rate >35 breaths/min;
(4) paO_2 <50 mmHg (<6.7 kPa); (5) pH < 7.1 or >7.7;
(6) S. sodium <110 mmol/l or >170 mmol/l; (7) S. potassium <2.0 mmol/l or >7.0 mmol/l; (8) serum glucose >800 mg/dl (>44.4 mmol/L); (9) serum calcium>15 mg/dl (>3.75 mmol/L);
(10) anuria; (11) coma;
Furthermore, patient with severe acute pancreatitis as defined by the revised Atlanta Classification (i.e. persistent organ failure) should be managed in ICU.

13. Intra-abdominal hypertension (IAH) is defined by an ongoing or repeated pathologic increase in intra-abdominal pressure >12 mmHg. IAH occurs in 60-80% of patients with severe acute pancreatitis & is graded as follows:
grade I: intra-abdominal pressure 12-15 mmHg *grade II:* 16-20 mmHg
grade III: 21-25mmHg *grade IV:* >25mmHg
Abdominal compartment syndrome (ACS) is defined as a sustained intra-abdominal pressure > 20 mmHg (with or without abdominal arterial perfusion pressure < 60 mmHg) that is associated with new onset organ failure.
IAH & ACS in patients with severe acute pancreatitis contributed to gut barrier failure with significantly greater endotoxin levels &can be managed medically through:
(I) Hollow-viscera volume: nasogastric drainage, prokinetics, rectal tubes or if necessary endoscopic decompression.
(II) Intra/extra vascular fluid: volume resuscitation on demand, if volume overloaded either ultrafiltration or diuretics can be employed.
(III) Abdominal wall expansion: adequate analgesia and sedation to decrease abdominal muscle tone, if necessary neuromuscular blockade.
Invasive treatment & decompression for ACS in acute pancreatitis is indicated in patients with a sustained intra-abdominal pressure >25 mmHg with new onset organ failure refractory to medical therapy and nasogastric/rectal decompression.

F. Preventing infectious complications

14. Antibiotics should be given only for an extra-pancreatic infection like cholangitis, catheter-acquired infections, bacteremia, urinary tract infections & pneumonia.
Routine use of prophylactic antibiotics in patients with severe AP is not recommended nor for the prevention of infectious complications.
However; selective gut decontamination may have some benefits in preventing infectious complications in acute pancreatitis.
Also; routine administration of antifungal agents along with prophylactic or therapeutic antibiotics is not recommended
15. 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 needle aspiration (FNA) for Gram stain and culture to guide use of appropriate antibiotics or
(ii) empiric use of antibiotics known to penetrate pancreatic necrosis, without CT FNA should be given
In patients with infected necrosis, antibiotics such as carbapenems, quinolones, and metronidazole, may be useful in delaying or sometimes totally avoiding intervention, thus decreasing morbidity and mortality.

G. Nutritional support

16. The need to place the pancreas at rest until complete resolution of AP has no longer seems imperative as bowel rest is associated with intestinal mucosal atrophy and increased infectious complications because of bacterial translocation from the gut. Oral feeding early in the course of AP is associated with shorter hospital stay, decreased infectious complications, decreased morbidity and decreased mortality.

17. Oral feeding in predicted mild pancreatitis with a low-fat solid diet appears as safe as a clear liquid diet & can be started once abdominal pain is decreasing and inflammatory markers are improving

18. Enteral tube feeding should be the primary therapy in patients with predicted severe acute pancreatitis who require nutritional support.

Parenteral nutrition can be administered as second-line therapy only if nasojejunal tube feeding is not tolerated, not available, or not meeting caloric requirements and nutritional support is required.

19. Nasogastric delivery and nasojejunal delivery of enteral feeding appear comparable in efficacy and safety & either elemental or polymeric enteral nutrition formulations can be used.

H. Biliary tract management

20. ERCP is not indicated in predicted mild biliary pancreatitis without cholangitis.

ERCP is probably not indicated in predicted severe biliary pancreatitis without cholangitis.

ERCP is probably indicated in biliary pancreatitis with common bile duct obstruction.

ERCP is indicated urgently in patients with biliary pancreatitis and cholangitis within 24 hours of admission

Pancreatic duct stents and/or postprocedure rectal non-steroidal anti-inflammatory drug (NSAID) suppositories should be utilized to lower the risk of severe post-ERCP pancreatitis in high-risk patients

21. Magnetic resonance cholangiopancreatography (MRCP) & endoscopic ultrasound (EUS) may salvage a proportion of ERCPs that would otherwise be performed for suspected common bile duct stones in patients with biliary pancreatitis who do not have cholangitis or jaundice without influencing the clinical course.

EUS is superior to MRCP in excluding the presence of small (<5mm) gallstones but MRCP is less invasive, less operator-dependent and probably more widely available than EUS. Therefore; there is no clear superiority for either over other.

I. Indications for intervention in necrotizing pancreatitis

22. Asymptomatic pseudocysts and pancreatic and/or extrapancreatic necrosis do not warrant intervention regardless of size, location, and/or extension.

Common indications for intervention (either radiological, endoscopical or surgical) in necrotizing pancreatitis are:

(a) Clinical suspicion or documented infected necrotizing pancreatitis with clinical deterioration, preferably when the necrosis has become walled-off,

(b) In the absence of documented infected necrotizing pancreatitis, ongoing organ failure for several weeks after the onset of acute pancreatitis, preferably when the necrosis has become walled-off.

(c) Less common indications for intervention are: abdominal compartment syndrome ongoing acute bleeding, bowel ischemia, ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect from large walled-off necrosis (arbitrarily >4-8 weeks after onset of pancreatitis).

23. In symptomatic patients with infected necrosis, minimally invasive methods of necrosectomy are preferred to open necrosectomy

24. In stable patients with infected necrosis, surgical, radiologic &/or endoscopic intervention or drainage should be delayed preferably for more than 4 weeks to allow liquefaction of the contents and the development of a fibrous wall around the necrosis (walled-off necrosis).
25. Routine percutaneous fine needle aspiration of peri-pancreatic collections to detect bacteria is not indicated, because clinical signs (i.e. persistent fever, increasing inflammatory markers) and imaging signs (i.e. gas in peripancreatic collections) are accurate predictors of infected necrosis in the majority of patients, besides, fine needle aspiration (FNA) has its own risk of false-negative results.

J. Timing of intervention in necrotizing pancreatitis

26. For patients with proven or suspected infected necrotizing pancreatitis, invasive intervention should be delayed where possible until at least 4 weeks after initial presentation to allow the collection to become 'walled-off'.
Surgical necrosectomy should ideally be delayed until collections have become walled-off, typically 4 weeks after the onset of pancreatitis, in all patients with complications of necrosis, earlier or delayed intervention has no clear benefit.

K. Intervention strategies in necrotizing pancreatitis

27. The optimal interventional strategy for patients with suspected or confirmed infected necrotizing pancreatitis is initial image-guided percutaneous (retroperitoneal) catheter drainage or endoscopic transluminal drainage followed, if necessary by endoscopic or surgical necrosectomy.

L. Timing of cholecystectomy (or endoscopic sphincterotomy)

28. In patients with mild AP & gallstones; cholecystectomy during admission for mild biliary pancreatitis appears safe and is recommended as interval cholecystectomy after mild biliary pancreatitis is associated with a substantial risk of readmission for recurrent biliary events, especially recurrent biliary pancreatitis.
29. Cholecystectomy should be delayed in unstable patients & those with pancreatic necrosis or peripancreatic collections until stabilization of the medical condition of the patient & the collections either resolve or if they persist beyond 6 weeks at which time cholecystectomy can be performed safely.
31. In patients with biliary pancreatitis who have undergone sphincterotomy and are fit for surgery, cholecystectomy is advised, because ERCP and sphincterotomy prevent recurrence of biliary pancreatitis but not gallstone related gallbladder disease, i.e. biliary colic and cholecystitis.

Further Reading

1. The onset of acute pancreatitis is defined as the time of onset of abdominal pain.
2. Because of its limitations in sensitivity, specificity, positive and negative predictive value, serum amylase alone cannot be used reliably for the diagnosis of AP and serum lipase is preferred as it remains elevated longer than amylase & it is more specific as the pancreas is the only source of lipase).
Serum amylase and lipase activities, while important in the diagnosis of "acute pancreatitis," are not of any clinical importance in defining the severity of acute pancreatitis

3. Two distinct phases of AP can be identified:
(i) Early (within 1 week), characterized by the systemic inflammatory response syndrome (SIRS) and / or organ failure.
(ii) Late (> 1 week), characterized by local complications defined as peripancreatic fluid collections, pseudocysts, pancreatic and peripancreatic necrosis (sterile or infected), and walled-off necrosis WOPN (sterile or infected- formerly known as pancreatic abscess). Isolated extrapancreatic necrosis is also included under the term necrotizing pancreatitis.
4. The rationale for early aggressive hydration in AP arises from observation of the frequent hypovolemia that occurs from multiple factors affecting patients with AP, including vomiting, reduced oral intake, third spacing of fluids, increased respiratory losses, and diaphoresis. Researchers hypothesize that a combination of microangiopathic effects and edema of the inflamed pancreas decreases blood flow, leading to increased cellular death, necrosis, and ongoing release of pancreatic enzymes activating numerous cascades. Inflammation also increases vascular permeability leading to increased third space fluid losses and worsening of pancreatic hypoperfusion that leads to increased pancreatic necrosis and cell death.
Early aggressive intravenous fluid resuscitation provides micro- and macrocirculatory support that can prevent serious complications such as pancreatic necrosis.
Hydration with a lactated Ringer's solution is more beneficial, resulting in fewer patients developing SIRS as compared with patients receiving (0.9%) normal saline, although both are isotonic crystalloid solutions, normal saline given in large volumes may lead to the development of a non-anion gap hyperchloremic metabolic acidosis
Organ failure is defined in accordance with the Marshall scoring system as score >2 for at least one of these three organ systems: respiratory (PaO_2 < 60 mm Hg);
renal (serum creatinine creatinine >2 mg/dl after rehydration); and
cardiovascular (systolic blood pressure < 90 mm Hg mm Hg).
The modified Marshall score (which includes the Glasgow coma score, platelet count, serum bilirubin) can be determined at presentation and daily thereafter so that a comparison can be made with the Marshall scoring system.
Multi-system organ failure is defined as two or more organs failing over the same 2- 3 day period.
Moderately severe acute pancreatitis is defined by the presence of transient organ failure lasting < 48 h or systematic or local complications such as pancreatic necrosis in the absence of persistent organ failure.
Severe AP is defined entirely on the presence of persistent organ failure >48 hr using the (modified Marshall scoring system for organ dysfunction).
To be considered as having persistent organ failure (i.e. >48 hours), a patient requires persistent evidence of organ failure (one or more organ systems) on at least one occasion on 3 consecutive days.
Interstitial Edematous Pancreatitis (IEP) demonstrates diffuse or localized enlargement of the pancreas and normal, homogeneous enhancement of the pancreatic parenchyma. The presence of solid components in these fluid collections is indicative

of peripancreatic necrosis, excludes the diagnosis of IEP, and the process should be termed necrotizing pancreatitis

Acute peripancreatic fluid collection is fluid collections without solid components arising in patients during the first 4 weeks with IEP. It could be sterile or infected.

Acute pseudocyst is a fluid collection persisting for more than four weeks, arising from an attack of acute pancreatitis

Pancreatic necrosis is defined as diffuse or focal areas of nonviable pancreatic parenchyma > 3 cm in size or > 30% of the pancreas.

Pancreatic necrosis can be sterile or infected.

Marshall Scoring System

	Score				
Organ system	**1**	**2**	**3**	**4**	**5**
Respiratory (PO_2/FIO_2)	>400	301-400	201-300	101-200	<101
Renal S.creatinine µmol/l S.creatinine mg/dl	 ≤134 ≤1.4	 134-169 1.4-1.8	 170-310 1.9-3.6	 311-439 3.6-4.9	 >439 >4.9
Cardiovascular(systolic B. pressure, mmHg)	> 90	< 90 Fluid responsive	< 90 Fluid responsive	< 90 pH<7.3	< 90 pH<7.2

The Revised Atlanta Criteria define organ failure as a score of 2 or more for one of these organ systems using the modified Marshall scoring system.

Practically and rather than calculating a Marshal score (which may be complex for the busy clinician), relying on the older Atlanta definitions would be as useful as well.

Atlanta Revision (2013)

Mild acute pancreatitis	**Moderately severe acute pancreatitis**	**Severe acute pancreatitis**
Absence of organ failure Absence of local complications	1.Local complications AND / OR 2. Transient organ failure < 48 hr	*Persistent organ failure > 48 hr
*Persistent organ failure is now defined by a Modified Marshal Score		

Clinical findings associated with a severe course for initial risk assessment

Patient characteristics

Age > 55 years Obesity (BMI > 30 kg/m^2)

Altered mental status Co-morbid disease

The systemic inflammatory response syndrome(SIRS) Presence of ≥2 of the following:

Pulse > 90 beats / min Temperature > 38° C or < 36° C

Respirations > 20 / min or $PaCO_2$ > 32 mm Hg

WBC count > 12,000 or < 4,000 cells/mm^3 or > 10 % immature neutrophils (bands)

Laboratory findings

BUN > 20 mg/dl or Rising BUN or Elevated creatinine

HCT > 44 % or Rising HCT

Radiology findings

Pleural effusion. Pulmonary infiltrates. Multiple/extensive extrapancreatic collections

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