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Acute Pancreatitis: Presentation and Risk Assessment

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1. Introduction

Acute pancreatitis is the third most common gastrointestinal disease diagnosis at hospital discharge. (Browse 2003) Although many etiologies exist, the most common causes worldwide are gallstone disease and excessive alcohol consumption. However, one-third of pancreatitis cases have no association with alcohol, no associated biliary tract disease, and no pancreatic duct obstruction, and are thus labelled idiopathic. Despite a documented increase in the overall incidence of acute pancreatitis in several countries, disease related mortality has progressively declined over the years. This improvement is in part due to advances in disease management, including better diagnostics and treatment modalities. (Baron 2001)

Acute pancreatitis is a pathological condition in which activated pancreatic enzymes leak into the substance of the pancreas and initiate auto-digestion of the gland. Most episodes of acute pancreatitis are mild and self-limiting and do not require aggressive intervention. In marked contrast, approximately one fifth of patients develop severe acute pancreatitis which is associated with a mortality rate that can exceed 30%. (Bradley and Dexter 2010).

Pancreatitis occurs with equal frequency in men and women, despite the common association of gallstones with female gender. Although the peak incidence of pancreatitis is in the fourth and fifth decades of life, it can occur at any age.

2. Signs and symptoms

The most common presenting symptom of acute pancreatitis is pain. Typically the discomfort begins suddenly, high in the epigastrium, and steadily increases in severity until movement is intentionally limited and respiratory excursion is reduced. It is often unrelenting and may radiate through to the back, classically just to left of mid-line. Frequently, a complex of nausea, vomiting and retching accompanies the abdominal pain. Although many acute abdominal conditions can cause nausea, and vomiting, pancreatitis is often associated with a specific pattern of persistent nausea between cyclical bouts of emesis without nausea prior to initiation of the pain. (Mergener and Baillie 1998)

Many patients report having eaten an unusually large meal or drunk alcohol an hour or so before the pain began (Mergener and Baillie 1998). When the pain is severe, any movement

of the lower chest wall and abdomen exacerbates the discomfort, often resulting in rapid shallow breathing and a sensation of dyspnea. In advanced cases, patients may develop tetanic muscle twitches, cramps and spasms related to associated hypocalcemia associated with the development of intra-abdominal fat necrosis. (Browse 2003)

As the condition progresses, retroperitoneal inflammation and trans-capillary leak reduce intravascular volume resulting in tachycardia with peripheral vasoconstriction generating a pale skin tone and diaphoresis. A paralytic intestinal ileus may develop, resulting in abdominal distension, a quiet abdomen to auscultation, and aggravation of nausea. Advanced cases may be associated with retroperitoneal haemorrhage, causing bruising and discoloration in the left flank (Grey Turner's sign) and around the umbilicus (Cullen's sign); both are late signs of extensive inflammatory destruction of the pancreas and peri-pancreatic tissues. (Dickson et al 1984)

Physical findings often consist of tenderness to palpation in the upper abdomen and abdominal distension, with severe cases producing diffuse abdominal guarding with discrete epigastric fullness secondary inflammatory exudate present in the lesser sac. Over time, this collection can organize, resulting in the formation of a pancreatic pseudocyst or lesser sac abscess. (Browse 2003)

3. Laboratory assessment, risk assessment and prognostic systems

Multiple risk assessment and classification systems have been developed over the years to assist in the clinical assessment of patients presenting with acute pancreatitis. These systems have been formulated in an attempt to predict the severity of a given episode of pancreatitis, and therefore aid in directing disease- appropriate management plans. Notable tools include the Atlanta Classification, Ranson's Criteria, the Acute Physiology and Chronic Health Evaluation (APACHE) II systems, and the Balthazar CT Severity Index (CTSI). (Brisinda, Vanella et al. 2011)

3.1 Biochemical values used for prognostication

Biochemical markers, including serum amylase and lipase, have been traditionally utilized in the diagnosis of acute pancreatitis. Newer indices have been reported to yield higher correlations with the presence of pancreatitis and have demonstrated improved prognostic value. (Gates 1999)

3.1.1 Serum amylase and lipase

Serum amylase and lipase levels are the most commonly obtained biochemical markers of pancreatic disease, particularly for evaluation of the presence of acute pancreatitis. However, the utility of these enzyme markers is complicated by significant limitations, including low sensitivity and specificity (Young 1989). In aggregate, there are many causes of elevated serum amylase levels, and amylase levels may only be moderately elevated or even normal in proven cases of acute pancreatitis of all degrees of severity (Clavien et al. 1989).

While an amylase level of three times the upper limit of normal is often recommended to support a clinical diagnosis of acute pancreatitis, the magnitude of the observed

hyperamylasemia has limited direct correlation with disease severity (Clavien et al. 1989). Furthermore, after reaching a peak serum concentration, the subsequent return of amylase levels to previously normal levels does not necessarily correlate with resolution of clinical illness, limiting the value of serial measurements (Young 1989). If hyperamylasemia temporally persists in conjunction with clinical symptoms, consideration should be given to the presence of a pseudocyst or peri-pancreatic abscess. Clinical studies have demonstrated that serum amylase levels can be normal in one-fifth of diseased patients, elevated in one-quarter of well patients, and that the magnitude of serum elevation has poor statistical correlation with disease severity or ultimate prognosis. (Vissers, Abu-Laban et al. 1999)

Serum lipase is the acinar enzyme most often recommended to replace or supplement amylase levels for the diagnosis of acute pancreatitis. At a cut-off of five times the upper limit of normal, an elevated lipase is virtually diagnostic for pancreatitis, approaching 100% specificity; however, its sensitivity is limited to 60% (Kazmierczak et al. 1993). Given these considerations, using a multiple of twice the upper limit of normal may offer high specificity without significantly compromising sensitivity. Although few studies have examined the prognostic value of elevated lipase levels in acute pancreatitis, most suggest poor correlation with disease severity, similar to amylase. (Vissers, Abu-Laban et al. 1999)

Simultaneous measurements of both serum lipase and amylase have not been shown to improve diagnostic accuracy, and no advantage has been demonstrated over assaying lipase alone (Viel et al. 1990). While serum lipase measurements are comparable to amylase in terms of speed, cost, and availability, evidence suggests that lipase is the more accurate assay for acute pancreatitis (Clave et al. 1995). As a result, in institutions where both tests are available, it is recommended that lipase replace amylase as the initial enzymatic test for acute pancreatitis. Regardless of the marker employed, it is important to appreciate that the absolute levels of neither amylase nor lipase have prognostic value in established disease. (Vissers, Abu-Laban et al. 1999)

3.1.2 Blood Urea Nitrogen (BUN)

Some studies have demonstrated that an elevated Blood Urea Nitrogen (BUN) level at admission and subsequent temporal increases in BUN levels during the initial 24 hours of hospitalization are independent risk factors for mortality in acute pancreatitis (Wu et al. 2009). Serial BUN measurements have also been shown to provide prognostic accuracy comparable to the more complex APACHE II score for early prediction of in-hospital mortality (Papachristou et al. 2010). Among patients with an elevated BUN value at admission (>20 mg/dL), a decrease of at least 5 mg/dL at 24 hours is associated with a reduced risk of in-hospital death. In contrast, among patients with a normal BUN value at admission, even modest increases in the BUN level (≥ 2mg/dL) are associated with an increased risk of mortality (Wu, Bakker et al. 2011). Due to its correlation with outcome, an algorithm based on early changes in BUN level has been developed to aid clinicians in evaluating patient responses to early resuscitation efforts in pancreatitis. (Wu, Bakker et al. 2011)

3.1.3 Coagulation parameters: D-dimer and tissue factor

Coagulation disorders are known to occur in the early phase of severe acute pancreatitis and the D-dimer of fibrinogen is a commonly used clinical parameter to assess the hemostatic

system (Salomone et al. 2003). Studies have demonstrated that serum D-dimer levels significantly differ between pancreatitis patients with and without key clinical differentiators such as the progression to multiple organ dysfunction syndromes, the eventual need for surgical intervention, and the development of both pancreatic and secondary infection (Radenkovic et al. 2009). Furthermore, serum D-dimer levels have been demonstrated to correlate well with two traditional markers of severity in acute pancreatitis, namely the APACHE II score and C-reactive protein serum levels (Papachristou, Whitcomb 2004). As such, the D-dimer assay may be a useful, easy, and inexpensive early prognostic marker of the evolution and complications of acute pancreatitis. (Ke, Ni et al. 2011) Several studies have demonstrated elevated levels of circulating Tissue factor (TF) to be present in patients presenting with acute pancreatitis (Yasuda et al. 2009). Furthermore, a weak statistical correlation between assayed serum TF levels and disease severity has been observed (Yasuda et al. 2009). Further studies will be required to characterize this relationship. (Andersson, Axelsson et al. 2010)

3.1.4 C-reactive protein (CRP)

C-reactive protein (CRP) is an acute phase reactant that is elevated in several inflammatory conditions and serves as a non-specific marker for inflammation (Wilson et al 1989). In acute pancreatitis, CRP levels commonly peak on the 3rd or 4th day after symptom onset, with 48-hour values of 150 mg/dL often accepted as a predictor of subsequent disease severity (Dervenis et al. 1999). It has been demonstrated that peak CRP levels of ≥210 mg/dL can differentiate severe acute pancreatitis from milder forms with a sensitivity of 83-84% and a specificity of 74-85%. (Wilson et al. 1989) Similar studies have shown that high CRP levels have an overall accuracy of 93% in detecting pancreatic necrosis. CRP levels are easy to measure, widely available, and relatively inexpensive to perform. One disadvantage of CRP is its delayed serum peak (48-72 hours), although this delay is also inherent in other methods used for severity assessment in acute pancreatitis such as the Ranson criteria. (Yadav, Agarwal et al. 2002)

3.1.5 Hemoconcentration

Recently, hemoconcentration has been identified as a strong risk factor and an early marker for the develpment of necrotizing pancreatitis and organ failure (Baillargeon, Ramagopal et al. 1998). Admission hematocrit (Hct) ≥ 47 and failure of admission Hct to decrease by 24 h represent strong risk factors for the development of severe pancreatitis. (Yadav, Agarwal et al. 2002). The sensitivity of hematocrit as a marker for necrotizing pancreatitis is 72% at admission and increases to 94% at 24 hours; specificity is 83 and 69%, respectively. (Baillargeon, Ramagopal et al. 1998)

The relationship between hemoconcentration and the development of pancreatic necrosis has been studied extensively in experimental animal models (Hotz et al. 1995). These studies have shown that early hemoconcentration in acute pancreatitis contributes significantly to the impairment of the pancreatic microcirculation and to the subsequent progression to pancreatic necrosis (Hotz et al. 1995). Patients presenting with an elevated admission hematocrit or those demonstrating an admission hematocrit that does not decrease by 24 hours are at high risk for complications (Brown, Orav et al. 2000). Consideration in this

patient cohort should be given to early intensive care unit admission for vigorous fluid resuscitation, supportive care, and continous hemodynamic monitorring. In contrast, patients who do not exhibit these criteria may have a lower likelihood of developing severe pancreatitis and could represent a group that requires less intensive care. (Brown, Orav et al. 2000)

3.1.6 Interleukins and procalcitonin

Interleukins, particularly IL-6 and IL-8, have been identified as serum markers of disease severity in acute pancreatitis (Heath et al. 1993 and Rau et al 1997). Although predictive accuracies have varied in several clinical studies, meta-analyses performed to assess their utility in predicting severe acute pancreatitis have demonstrated promising correlations. (Gregoric, Sijacki et al. 2010)

IL-6 is a cytokine produced by a wide variety of cell types, including macrophages (Xing et al 1994). It drives the hepatic acute phase response and as such may be one biochemical step closer than CRP to the underlying inflammatory process in acute pancreatitis. Serum levels of IL-6 in patents with severe pancreatitis can be elevated as early as five hours after admission; pooled sensitivities range between 81.0% and 83.6%, specificities between 75.6 and 85.3%, and odds ratios of between 3. 43 and 4.90 in predicting disease severity (Aoun, Chen et al. 2009). IL-8 serum levels also have been found to correlate with pancreatitis, with pooled sensitivities identified between 65.8 and 70.9% and specificities of 66.5% and 91.3% for days 1 and 2 of disease presentation. (Aoun, Chen et al. 2009)

Procalcitonin (PCT) is the inactive propeptide of the hormone calcitonin, which is involved in calcium homeostasis (Assicot et al. 1993). In patients with acute pancreatitis, PCT has been shown to predict the subsequent development of infected pancreatic necrosis and has been demonstrated to be a predictor of severity and organ failure in patients with acute pancreatitis (Riche et al. 2003). Sensitivity analyses performed on multiple studies have demonstrated that a serum PCT value greater than 0.5 ng/mL is an accurate predictor of severe acute pancreatitis (Mofidi, Suttie et al. 2009). In studies where daily serum PCT levels were measured, it was noted that patients who subsequently developed infected pancreatic necrosis had a sustained increase in serum PCT levels and that the degree of PCT increase reflected the severity of systemic inflammation and progresion to multiorgan dysfunction (Rau et al. 1997). Furthermore, it has been observed that serum PCT levels tend to decrease with clinical improvment (Rau et al. 1997).

The identification of pancreatic necrosis is clinically important because patients with sterile pancreatic necrosis are often treated with supportive care only, whereas infected pancreatic necrosis generally requires surgical or radiologic intervention (Büchler et al. 2000). Infected pancreatic necrosis is classically diagnosed by microbial culture of material obtained using image-guided FNA of pancreatic tissue. Unlike FNA, the measurement of PCT is non-invasive and is not hindered by the potential for image-directed sampling error. Furthermore, PCT levels are not affected by antifungal and antimicrobial systemic coverage, and remain elevated in infected pancreatic necrosis (Rau et al. 1997). However, it is important to note that PCT is a nonspecific marker of infectious complications in critically ill patients, and as a result other infective foci need to be excluded carefully when interpreting PCT measurements in pancreatitis.. (Mofidi, Suttie et al. 2009)

3.2 Systems based risk models

3.2.1 Atlanta classification

Most recent attempt to standardize severity criteria in acute pancreatitis The 1992 Atlanta Symposium was convened to standardize severity criteria and nomenclature in acute pancreatitis (Bradley 1993). A major step forward at the time was the establishment of a universal definition of severe pancreatitis. Objective criteria of severity and outcome were defined by both local and systemic parameters (Table 1.) In addition, universal standards to define "predicted severe" pancreatitis were adopted based on the two most popular scoring systems, namely the Ranson criteria and the Acute Physiology and Chronic Health Evaluation II (APACHE II) criteria. "Predicted severe" pancreatitis was defined as either a score of three or more in Ranson criteria, or eight or more in APACHE-II criteria. (Gates 1999)

Severity Criteria	**Definitions**
Organ Failure	
Cardiovascular	Systolic blood pressure < 90 mm Hg (after resuscitation)
Respiratory	PaO_2 < 60mmHg (8 kPa)
Renal	Serum creatinine > 177 µmol/l (2mg/dl) after resuscitation
Gastrointestinal Haemorrhage	>500 ml/ 24h
Systemic Complications	
Coagulation System	Platelet count < 100 × 109/l
	Fibrinogen level < 1g/l
	Fibrin split products >80µg/mL
Metabolic	Corrected serum calcium < 1.85 mmol/l (7.5 mg/dl) serum lactate levels > 5mmol/l
Local Complications	
Acute fluid collections	Occur early in the natural history of acute pancreatitis and lack a fibrous capsule
Pseudocyst	Occurs at least 4 weeks after the onset of symptoms and has a fibrous capsule
Pancreatic abscess	A localised collection of pus containing little or no necrotic pancreatic material
Pancreatic necrosis	Pathological features : diffuse or focal area of nonviable pancreas that maybe associated with peripancreatic fat necrosis CT features : an area of non-enhancing pancreas measuring > 3 cm in diameter or 30% of pancreatic tissue

Table 1. Atlanta Classification for Severe Pancreatitis

Threshold scores for assignment of "predicted severe" pancreatitis

≥ 3 Ranson criteria
≥ 8 APACHE II criteria

Although the Atlanta Classification has proven useful, a more thorough classification system could incorporate assessment of clinical severity with more objective measurements of anatomic pathology in and around the pancreas. In addition, the Atlanta Classification fails to differentiate between the two discrete peaks in mortality (early and late) observed with pancreatitis. (Brisinda, Vanella et al. 2011)

3.2.2 Ranson criteria

Ranson proposed the first numerical grading system for acute pancreatitis in 1974, focusing on several commonly observed clinical and hematochemical variables (Ranson et al. 1974). With an increased number of risk factors present, there is a corresponding increase in mortality rate (Ranson et al. 1974). In patients with less than three positive signs no significant associated mortality is observed, whereas in patients with at least six signs the mortality rate is over 50% (Ranson 1995). Furthermore, individuals with a score greater than six often develop necrotising pancreatitis (Ranson 1995). This system is particularly useful at the two extremes of the scale, with less discriminating power between; correlation with severity of disease or the eventual development of necrosis in patients with a score of 3-5 is deficient. (Brisinda, Vanella et al. 2011)

At admission	**During initial 48 hours**
Age > 55 years	Hematocrit decrease > 10%
White blood cell count > 16000/µl	Blood urea nitrogen increase >5mg/dl (>1.8 mmol/l)
Serum glucose level > 200 mg/dl (>11.1 mmol/l)	Calcium < 8 mg/dl (<2 mmol/l)
Serum lactate dehydrogenase > 350 IU/l	PaO2 < 60 mmHg
Aspartate Aminotransferase > 250 IU/l	Base deficit > 4 mEq/l
	Fluid sequestration > 6 l

Table 2. Ranson criteria for non- gallstone pancreatitis

At admission	**During initial 48 hours**
Age > 70 years	Hematocrit decrease > 10%
White blood cell count > 18000/µl	Blood urea nitrogen increase >5mg/dl (>1.8 mmol/l)
Serum glucose level > 220 mg/dl (>12.2 mmol/l)	Calcium < 8 mg/dl (<2 mmol/l)
Serum lactate dehydrogenase > 400 IU/l	PaO2 < 60 mmHg
Aspartate Aminotransferase > 250 IU/l	Base deficit > 5 mEq/l
	Fluid sequestration > 4 l

Table 3. Ranson criteria for gallstone pancreatitis

The Ranson scoring system was derived from statistical analysis of multiple clinical and laboratory parameters from consecutive patients who were tested for significant correlation with disease outcome (Ranson et al. 1974). The result was an 11-point conglomerate of predictive factors, five of which were to be obtained on admission and the remaining six within 48 hours of presentation. Because the first group of patients analysed had a preponderance of alcohol-associated disease, a second analysis was later performed with patients manifesting gallstone pancreatitis. (Ranson et al. 1974) Thus, two separate Ranson criteria currently exist for gallstone and non-gallstone pancreatitis, as illustrated above.

The Ranson scoring system has important merits, along with some deficits. Clear benefits include its ease of use and its clinical correlation, with an estimated sensitivity of 72%, specificity of 76%, positive predictive value of 51%, and negative predictive value of 89. (Gates 1999)

However, many physicians inappropriately apply the non-gallstone criteria to patients with gallstone pancreatitis, which accounts for a third of all cases of acute pancreatitis. Furthermore, patients are often incorrectly classified as having "predicted mild" pancreatitis before 48 hours; using the Ranson criteria, patients may only be classified as "predicted severe" or "pending" pancreatitis before the 48 hour mark. Importantly, the Ranson criteria have not been validated for continued temporal monitoring of the patient's condition. A repeat assessment with the criteria at say, 72 hours, cannot be accurately interpreted with the tool. It is also important to note that the Ranson criteria have not been validated for used in children. (Gates 1999)

3.2.3 Glasgow criteria

The Glasgow criteria (Imrie) were originally introduced in the late 1970's and early 1980'sand have since been modified three times. (Imrie et al. 1978). The original Glasgow, or modified system, has been used for the prediction of mortality, and like the Ranson, performs well. It yields an estimated sensitivity of 63%, specificity of 84%, positive predictive value of 52%, and negative predictive value of 89% (Steinberg 1990). When

Variables for the Glasgow Scoring System
Age > 55 years
White blood cell count > 15000 /µl
PaO2 < 60 mmHg (8 kPa)
Serum lactate dehydrogenase > 600 units/l
Serum aspartate aminotransferase > 200 units/l[a]
Serum albumin < 32g/l
Serum calcium < 2 mmol/l
Serum glucose > 10 mmol/l
Serum urea > 16 mmol/l

[a] Removed from revised Glasgow outcome score.
Each variable has a binary score of 0 or 1. The outcome score is derived from the sum of all variables at 48 hours after presentation.

Table 4. Glasgow (Imrie) severity scoring system for acute pancreatitis

Physiologic Variable	High Abnormal Range				Low Abnormal Range					
	+4	+3	+2	+1	0	+1	+2	+3	+4	Points
Temperature (rectal °C)	>41	39-40.9		38.538.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9	
Mean Arterial Pressure (mmHg)	≥160	130-159	110-129		70-109		50-69		≤49	
Heart Rate	≥180	140-179	110-139		70-109		55-69	40-54	≤39	
Respiratory Rate	≥50	35-49		24-34	12-24	10-11	6-9		≤5	
Oxygenation: A-a DO_2 or P_aO_2 (mmHg) FiO_2 > 0.5 record A-a DO_2 FiO_2 < 0.5 record P_aO_2	≥500	350-499	200-349		< 200 P_aO_2 > 70	P_aO_2 61-70		P_aO_2 55-60	P_aO_2 < 55	
Arterial pH (preferred) Serum HCO_3 (venous mEq/l) **(not preferred, may use if no ABGs)**	≥7.7 ≥52	7.6-7.69 41-51.9		7.5-7.59 32-40.9	7.33-7.49 22-31.9		7.25-7.32 18-21.9	7.15-7.24 15-17.9	<7.15 <15	
Serum Sodium (mEq/l)	≥180	160-171	155-159	150-154	130-149		120-129	111-119	≤110	
Serum Potassium (mEq/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5	
Serum Creatinine (mg/dl) Double point score for acute renal failure	≥3.5	2-3.4	1.4-1.9		0.6-1.4		<0.6			

Table 5. Continued

Physiologic Variable	High Abnormal Range						
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9
White Blood Count (total/mm^3) (in 100s)	≥40		20-39.9	15-19.9	3-14.9		1-2.9
Glasgow Coma Score (GCS) Score = 15 minus actual GCS							
Total Acute Physiology Score (sum of above 12 points)							
Age points (years) ≤44= 0; 45 – 54 = 2; 55 – 64 = 3; 65 – 74 = 5; ≥75 = 6							
Chronic Health Points (see below)							
Total APACHE II Score (Add together points from A + B + C)							

Chronic Health Points: If the patient has a history of severe organ system insuffiency or is immunocompromis
points as follows:
2 points for nonoperative or emergency postoperative patients
2 points for elective postoperative patients
Liver insufficiency: Biopsy proven cirrhosis; Documented portal hypertension; Episodes of past upper GI bleed
hypertension; Prior episodes of hepatic failure / encephalopathy / coma. ***Cardiovascular*:** New York Heart As
Respiratory: Chronic restrictive, obstructive or vascular disease resulting in severe exercise restriction, i.e. una
household duties; Documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hyp
respirator dependency. ***Renal***: Receiving chronic dialysis. *Immunosuppression*: The patient has received therapy
infection e.g. immunosuppression, chemotherapy, radiation, long term or recent high dose steroids, or has a di
advanced to suppress resistance to infection, e.g. leukemia, lymphoma, AIDS.

Table 5. Acute Physiology and Chronic Health Evaluation II (APACHE-II) Worksheet Adapted fro
829. (Knaus, Draper et al. 1985)

compared to Ranson, it may be less sensitive while adding increased specificity. Any Glasgow data point may be scored at any time during the first 48 hours of presentation, but like Ranson, the Glasgow system is not valid for repeat measurements beyond 48 hours and cannot be applied to children (Gates 199). During the initial 48 hours, a patient may be classified only as having "severe" or "pending" pancreatitis. (Gates 1999)

3.2.4 Acute Physiology and Chronic Health Evaluation II (APACHE-II)

The Acute Physiology and Chronic Health Evaluation II (APACHE-II) assessment has become popular more recently. The system is comparatively complex and more difficult to perform because 12 different physiologic measurements are used (Larvin 1989). The higher the total score, the more severe the episode of acute pancreatitis, which corresponds to an increase in predicted morbidity and mortality (Wilson et al. 1990). One major advantage of the APACHE-II numeric system compared with other systems is that it can be used throughout the patient's hospital course, aiding evaluation and monitoring of response to therapy. (Knaus, Draper et al. 1985)

The APACHE-II system was developed as a general measure of disease severity and not specifically as a tool for describing acute pancreatitis. Each physiologic parameter is weighted from 0 to 4, and an aggregate score is tabulated (Knaus, Draper et al. 1985). Unlike the Ranson and Glasgow criteria, APACHE-II can provide a valid prediction of mild pancreatitis on admission. The APACHE-II is valid for repeated measures throughout hospitalization and it represents a universal measurement of disease severity, obviating the need for a separate score for acute pancreatitis. The APACHE II performs very well as a prognostic tool, with sensitivity and specificity rates of 75% and 92% respectively (Wilson et al. 1990).

3.2.5 Bedside Index for Severity in Acute Pancreatitis (BISAP)

A newer prognostic scoring system, the Bedside Index for Severity in Acute Pancreatitis (BISAP) has been proposed as an accurate method for early identification of patients at risk for in-hospital mortality (Wu, Johannes et al. 2008). The BISAP combines findings of physical examination, vital signs, routine laboratory data, and imaging studies to derive a five-point score (Wu, Johannes et al. 2008).

Individual Components of the BISAP Scoring System
BUN > 25mg/dl
Impaired mental status (Glasgow Coma Scale Score < 15)
Age > 60 years
Pleural effusion detected on imaging
SIRS, ≥ 2 or more of the following: Temperature <36°C or >38°C Respiratory Rate >20 breaths/min or $PaCO_2$ <32 mmHg Pulse > 90 beats/min WBC count > 12,000 or <4,000 cells/mm^3 or >10% immature neutrophils (bands

Adapted from *Gut* 57(12): 1698-1703 (Wu, Johannes et al. 2008)

Table 6. BISAP Scoring System

The BISAP uses five ordinal points: urea nitrogen (BUN) >25 mg/dl, impaired mental status as defined by evidence of disorientation or alteration in mental status, presence of Systemic Inflammatory Response Syndrome (SIRS), age > 60 years, and the presence or absence of pleural effusions (Singh, Wu et al. 2009).

SIRS is defined by the presence of ≥ 2 of the following criteria:

Pulse >90 beats/min, respirations >20/min or $PaCO_2$ <32 mmHg, temperature >38°C of <36°C, WBC count > 12,000 or <4,000 cells/mm^3 or >10% immature neutrophils (bands).

The presence of each variable contributes one point to a total 5-point score, and is obtained within 24 hours of admission; there is no requirement for additional computation, and the assessment of mental status is the only subjective parameter involved. It should be noted, however, that the SIRS criterion is a composite parameter that involves four separate but related criteria. Essentially, the BISAP is an eight-variable system cumulatively applied to calculate five points. (Wu, Johannes et al. 2008)

Studies have demonstrated that the BISAP score can predict mortality risk (Wu, Johannes et al. 2008). Studies have demonstrated that a BISAP score ≥ 3 is associated with higher mortality when compared to scores < 3; high specificity and negative predictive values were observed using these ordinal values (Wu, Johannes et al. 2008). Furthermore, it has been shown that BISAP scores ≥ 3 predict the development of organ failure, persistent organ failure, and the evolution of pancreatic necrosis. (Singh, Wu et al. 2009)

The key advantages of the BISAP include its relative ease of use and application of parameters that are commonly obtained either at presentation or within 24 hours of presentation (Wu, Johannes et al. 2008). The score appears generalizable, having been initially formulated and validated using a large number of patients across 389 hospitals, reflecting a broad spectrum of health-care delivery. (Singh, Wu et al. 2009)

The BISAP score cannot readily distinguish transient organ dysfunction from more persistent organ dysfunction at 24 hours (sensitivity of 38%, specificity 92%, PPV 58%, and NPV 84%), an important clinical distinction since the latter group suffers the majority of morbidity and mortality in acute pancreatitis (Zimmerman et al. 1994). The BISAP score may prove more useful in the triage of patients to levels of care intensity on initial evaluation rather than being used to predict the development of persistent organ failure and its consequences. (Papachristou, Muddana et al. 2010)

In summary, the BISAP score is a reliable prognostic tool enabling classification of patients with acute pancreatitis into mild or severe groups, and its components are clinically relevant and easy to obtain. It is important to recognize that an inherent limitation of all such scoring systems is their conversion of continuous variables into binary values of equal weight and thus fail to capture synergistic or multiplicative effects based on interactions of interdependent systems.

3.3 Imaging based risk models

3.3.1 Ultrasonography

Ultrasonography (US) may be useful in the early assessment of acute pancreatitis to evaluate the biliary system for the presence of gallstones or common bile ductal stones. However, US

use is often technically limited to applications in the early staging of acute pancreatitis due to the presence of overlying bowel gas secondary to paralytic intestinal ileus. In aggregate, abnormal US findings are seen in 33-90% of patients with acute pancreatitis; a diffusely enlarged and hypoechoic gland is consistent with interstitial edema, while extrapancreatic fluid collections (e.g., lesser sac, anterior pararenal space) can be detected in patients with severe disease. (Balthazar 2002)

3.3.2 Computed Tomography (CT)

Most of the clinical and laboratory parameters discussed thus far are applied to evaluate the systemic effects of pancreatitis, and only indirectly infer the presence and degree of pancreatic damage. The use of Computed Tomography (CT) in acute pancreatitis has increased in the last decade as it offers improved anatomic visualization, direct assessment of the extent of parenchymal injury, and identification of local complications (Dervenis et al. 1999). The CT Severity Index (CTSI) derived by Balthazar et al. has become the standard objective assessment for the description of CT findings in acute pancreatitis. (Balthazar 2002)

The first described CT grading index was based on radiographic images obtained without the addition of intravenous (IV) contrast (Hill et al. 1982). Using the scoring system, it was demonstrated that patients with high grade pancreatic damage (grades D or E) had a mortality rate of 14% and a morbidity rate of 54%, as compared with no mortality and a morbidity rate of only 4% in lesser affected patients (groups A, B or C.) Due to the lack of IV contrast, its main drawback was an inability to reliably depict pancreatic necrosis (Balthazar, Robinson et al. 1990).

A major significant improvement has been achieved in early CT grading systems with the introduction of an incremental contrast bolus CT technique (Kivisaari et al. 1983). Contrast-enhanced CT has been used effectively to directly characterize and quantify pancreatic parenchymal injury. Investigators have shown that the attenuation values of pancreatic parenchyma during an intravenous contrast bolus study can be used as an indicator of pancreatic necrosis and as a predictor of disease severity (Dervenis et al. 1999).

Patients with mild interstitial pancreatitis have an intact but vasodilated capillary network and therefore exhibit uniform enhancement of the pancreatic gland (Balthazar 2002). To the contrary, areas of diminished or no enhancement are indicative of decreased blood flow and reveal pancreatic zones of ischemia or necrosis (Balthazar 2002). An excellent correlation has been documented between necrosis, length of hospitalization, development of complications, and death. Furthermore, the extent of pancreatic necrosis has also been proven to be of clinical importance with prognostic and therapeutic implications (Vitellas et al. 1999). Studies have shown that patients with less than 30% necrosis exhibited no mortality and a 48% morbidity rate, while larger areas of necrosis (30-50% and >50%) were associated with morbidity rates of 75-100% and mortality rates of 11-25% (Balthazar, Robinson et al. 1990).

The CT Severity Index (CTSI) was designed to improve the early prognostic value of CT in cases of acute pancreatitis and is based on IV contrast-enhanced imaging (Balthazar, Robinson et al. 1990). The grading and allocation of points takes into consideration the CT grade as well as the extent of necrosis and is illustrated in the table below. It has been

demonstrated that a statistically significant correlation exists between morbidity and mortality and the CTSI score (Balthazar, Robinson et al. 1990). Studies have shown that patients with a severity index of 0 or 1 exhibit a 0% mortality rate and no morbidity, while patients with a severity index of 2 had no mortality and a 4% morbidity rate (Balthazar, Robinson et al. 1990). In contrast, a severity index of 7-10 yields a 17% mortality rate and a 92% complication rate. (Balthazar, Robinson et al. 1990) In a clinical study comparing BISAP, Ranson criteria, APACHE-II, and CTSI, CTSI was the most accurate in predicting pancreatic necrosis. (Papachristou, Muddana et al. 2010)

CT grade	**Grade Points**	**Necrosis (in percentage)**	**Necrosis Points**	**CT severity index[b]**
Normal (A)	0	0	0	0
Focal, diffuse enlargement, contour irregularity, inhomogenous attenuation (B)	1	0	0	1
B + peripancreatic haziness/strand densities (C)	2	< 30	2	4
B + C + one ill-defined peripancreatic fluid collection (D)	3	30 - 50	4	7
B + C + two ill-defined peripancreatic fluid collections (E)	4	< 50	6	10

[a] Balthazar

[b] Grade points are added to points assigned for percentage of necrosis.

Table 7. Computed Tomography Severity Index[a]

Adapted from Eur J Gastroenterol Hepatol 23(7): 541-551 (Brisinda, Vanella et al. 2011) of presentation may show only equivocal findings of pancreatitis, and that CT scans obtained 3 days after clinical onset yield higher accuracy in the depiction of pancreatic necrosis (Vitellas et al. 1999). Thus, it is recommended that when the clinical diagnosis of pancreatitis is in doubt, an initial early CT be used to confirm the clinical suspicion or to help detect alternative acute abdominal conditions that mimic acute pancreatitis. For staging, however, more reliable results are obtained with the use of intravenous bolus contrast-enhanced CT performed 48-72 hours after the onset of an acute attack of pancreatitis. (Balthazar 2002)

It appears that the CTSI is an anatomically oriented scoring system that aids in identifying local complications from pancreatitis, while clinical scores, such as the APACHE-II, may be superior for predicting associated organ failure and systemic complications (Lankisch et al. 2000). In patients with predicted severe disease or those manifesting a severe clinical course within the first 48 hours of presentation, the CTSI appears superior to other scoring systems in predicting overall pancreatitis severity and pancreatic necrosis. (Chatzicostas, Roussomoustakaki et al. 2003) At present, it appears that clinical scores are the best way to stratify the immediate management of acute pancreatitis, particularly the requirement for intensive care, and that the value of CT is greater in evaluating intermediate term management. (Alhajeri and Erwin 2008)

3.3.3 Magnetic Resonance Imaging (MRI)

The development of high field strength magnetic resonance imaging (MRI), rapid gradient-echo breath hold techniques, and fat suppression methodologies has made MR imaging an excellent alternative imaging modality to aid in the evaluation of patients with acute pancreatitis (Lecesne et al. 1999). It is particularly useful in patients who cannot receive iodinated contrast material due to allergic reactions or renal insufficiency. Gadolinium-enhanced T1 weighted gradient-echo MR images can depict pancreatic necrosis as areas of non-enhanced parenchyma (Fulcher, Turner 1999). Fat-suppression images are also helpful in defining subtle, diffuse, or focal parenchymal abnormalities. T2 weighted images can accurately depict fluid collections, pseudocysts, and areas of haemorrhage. (Balthazar 2002)

4. Conclusion

Acute pancreatitis is a dynamic entity with varying degrees of severity. Most episodes of acute pancreatitis are generally mild, but up to a third of cases may progress to severe pancreatitis. This is associated with a significant increase in associated mortality and complications. The key to effectively managing the patient with an episode of acute pancreatitis is early identification and diagnosis, followed by an appropriate assessment of severity. Appropriate evaluation of severity and prognosis is of great help in aiding the clinician in administering appropriate care. The clinician needs to be able to determine which patients will benefit from invasive intervention or transfer to a critical care unit, with the availability of its attendant intensive laboratory and cardiorespiratory monitoring.

A variety of prognostication systems for acute pancreatitis have been developed over the years to better categorize disease severity and predict clinical outcomes. There are three commonly employed types of predictors of the severity of acute pancreatitis: individual biological markers, multi-parameter scorings systems, and imaging-based systems. Within each category there are several individual systems, each with unique advantages and disadvantages. Given the currently available tools, the majority of patients presenting with acute pancreatitis will benefit from a rational and informed combination of these complimentary but distinct systems. In an era where intensive and invasive techniques are available to manage the local and systemic complications of pancreatitis, the ability to appropriately identify patients who will benefit from these interventions in a timely fashion is an important adjunct to their care.

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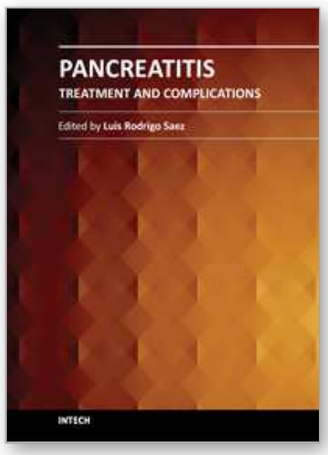

Pancreatitis - Treatment and Complications
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Pancreatitis may be acute or chronic. Although they can be caused by similar aetiologies, they tend to follow distinct natural histories. Around 80% of acute pancreatitis (AP) diagnoses occur as secondary to gallstone disease and alcohol misuse. This disease is commonly associated with the sudden onset of upper abdominal that is usually severe enough to warrant the patient seeking urgent medical attention. Overall, 10 to 25% of AP episodes are classified as severe, leading to an associated mortality rate of 7 to 30%. Treatment is conservative and consists of general medical support performed by experienced teams, sometimes in ICUs. Although most cases of acute pancreatitis are uncomplicated and resolve spontaneously, the presence of complications has significant prognostic importance. Necrosis, hemorrhage, and infection convey rates of up to 25%, 50%, and 80% mortality, respectively. Other complications such as pseudocyst formation, pseudoaneurysm formation, or venous thrombosis increase morbidity and mortality to a lesser degree. The presence of pancreatic infection must be avoided.

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