Review Article

Acute Pancreatitis: A Review of Innovations in Diagnosis, Severity Prediction, and Prognostic Scoring System

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ABSTRACT

An inflammatory disease of the pancreas with a variety of clinical manifestations is called acute pancreatitis. It is among the most frequent reasons for hospital admission due to stomach discomfort. Numerous people suffer from acute pancreatitis, a condition with a diverse origin, clinical presentation, and examination profile. For the aim of appropriate therapy and mortality prevention, identifying patients with pancreatitis who are at risk of severe illness and death is an essential first step. Many multifactorial scoring systems are described in order to forecast the severity. This review provides an overview of available multifactorial scoring systems for predicting severe acute pancreatitis.

Keywords: Acute pancreatitis, Scoring system, Severity prediction.

INTRODUCTION

Pancreas

The pancreas is a soft, lobulated, greyish pink gland that is located posterior to the stomach at the level of the second lumbar vertebra. It is 12–15 cm long and weighs around 80g. [1] The pancreas serves a dual role, to promote both exocrine and endocrine functions. In its exocrine role, the organ releases digestive enzymes and bicarbonate into the small intestine to facilitate food digestion. This involves the production of pancreatic juice by acinar cells, which is then transported to the duodenum through the main pancreatic duct and, in some cases, the accessory pancreatic duct. On the endocrine side, the pancreatic islets of Langerhans release hormones, such as insulin and glucagon, directly into the bloodstream. These hormones play a crucial role in regulating blood sugar levels and ensuring overall balance in energy metabolism and digestion processes. [2]

Acute pancreatitis

An acute inflammatory condition of the pancreas with varied involvement of adjacent organs is called acute pancreatitis (AP). Recently, two distinct stages of AP have been identified: (I) the early phase, which occurs during the first week of the disease and is marked by organ failure and/or a systemic inflammatory response syndrome (SIRS); and (II) the late phase, which occurs beyond one week and is characterized by local problems. [3]

The Atlanta classification broadly classifies acute pancreatitis into two categories. These are:

- The initial inflammation of the pancreatic parenchyma and surrounding peri-pancreatic tissue is the hallmark of interstitial edematous acute pancreatitis.
- Necrotizing acute pancreatitis is distinguished by necrosis of the peri-pancreatic and pancreatic parenchyma.

Based on the severity of the disease, acute pancreatitis is divided into the following types;

- In mild acute pancreatitis, there is the absence of local or systemic complications and organ failure.
- In moderately severe acute pancreatitis are local complications with or without organic failure for less than 48 hours.
- In severe acute pancreatitis, there is persistent organ failure for more than 48 hours with the involvement of one or more than one organ. [4]

The diagnosis of acute presentation is simple, but the major challenge is predicting the progression of the disease course and outcome. The duration of the disease is essential in determining the level of care.[5] The mortality of acute pancreas ranges from 3% in patients with mild edematous pancreatitis to as high as 20% in patients with pancreatic necrosis. [6]

Etiology

Acute pancreatitis is caused by various factors, including gallstones, alcohol use, hypertriglyceridemia, drug-induced pancreatitis, idiopathic, post-procedural, ampullary stenosis, autoimmune pancreatitis, viral infections, bacterial infections, smoking, trauma, congenital anomalies, genetic disorders, hypercalcemia, parasitic infections, renal disease, toxins, and vasculitis. The occurrence of each etiology varies across geographic

regions and socioeconomic strata. Treatment options include endoscopic retrograde cholangiopancreatography or abdominal surgery, ampullary stenosis, autoimmune pancreatitis, viral infections, bacterial infections, smoking, trauma, congenital anomalies, genetic disorders, hypercalcemia, parasitic infections, renal disease, and toxins. [7, 8, 9]

Clinical presentations

Symptoms

According to the standard definition of AP, stomach discomfort is a crucial component in the diagnosis of AP. The epigastric region or the right upper quadrant is typically the site of acute, persistent pain that frequently radiates to the back.[10-12] The typical symptom of gallstone pancreatitis is sudden, intense discomfort, while the pain caused by alcoholic, metabolic, and genetic pancreatitis is less severe and poorly localized. [13] Nausea and vomiting are frequently related to pain.

Signs

Findings of a physical examination might vary and include fever, hypotension, guarding, intense pain in the stomach, and respiratory distress. Patients who have modest abdominal palpation might experience discomfort in the area around their stomachs. Frequently, patients want to lie supine to ease their discomfort because they are restless. When necrotizing pancreatitis develops, the exudates from a necrotic pancreas may migrate through the falciform ligament down into the retroperitoneum. This can cause bruising in the flank (Grey-Turner' sign) or the periumbilical area (Cullen's sign).[14]

Diagnosis

The 2012 Revised Atlanta Classification specifies that two out of the three following criteria must be met in order to diagnose acute pancreatitis: (1) Pancreatitis-related stomach discomfort; (2) Amylase and/or Lipase levels in the serum that are at least three times higher than normal; or (3) Imaging results (MRI, ultrasonography, or contrast-enhanced CT) that are consistent with acute pancreatitis. The severity of acute pancreatitis is classified as mild, moderate or severe. Mild when there are no local or systemic complications present; moderate in case of local (e.g., peripancreatic fluid collections) or systemic complications (e.g., exacerbation of chronic disease) or transient organ failure (<48 hours) and severe in case of persistent organ failure (>48 hours). [15]

Complications of acute pancreatitis

Peripancreatic fluid collection

Pancreatitis frequently results in acute peripancreatic fluid collections (APFCs) or pancreatic fluid collections (PFCs), particularly when the condition is acute. Pseudocysts have been linked to 5–15% of pancreatitis episodes that have necessitated in-patient stays; the majority of these instances are linked to spontaneous remission. [16,17] Pseudocysts, necrotic collections, and even abscesses are examples of walled-off, chronic collections that may emerge from acute collections if they fail to clear off on their own. [18]

Pseudocyst

Pseudocysts are collections that form over the course of three to four weeks and are enclosed by a non-epithelial network of granulation tissue. The majority of acute pseudocysts will go away on their own, but if they fail to, they might get worse and cause bleeding, rupture, infections, or other problems**.** [19, 20] Collections of pus or infected fluid that form in close proximity to or contact with the pancreas in the context of pancreatitis or trauma are known as pancreatic abscesses. This abscess is linked to a wider spectrum of problems and may seem walled off and thicker walled on CECT. [21] The primary cause of pancreatic pseudocyst development is alcohol-related pancreatitis, accounting for over 70% of cases, particularly in nations with higher alcohol use rates. [22]

Pancreatic necrosis

Acute pancreatitis may lead to a late consequence called pancreatic necrosis, which kills pancreatic tissue and impairs organ function. Necrosis that is infected and sterile are the two varieties. Sterile necrosis is brought on by severe inflammation and abnormal blood flow in the pancreas and happens in the absence of bacterial infection. On the other side, bacterial colonization of the necrotic tissue results in infected necrosis**.** [23]

Abdominal Compartment Syndrome

A cavity's internal pressure might rise, like in the case of the abdomen (ACS), leading to organ damage or malfunction is known as compartment syndrome. Generally speaking, abdominal pressure is less than 10 mmHg; standards state that abdominal hypertension occurs when the pressure is more than 12 mmHg and abdominal compartment syndrome occurs when the pressure exceeds 20 mmHg. Consequently, there is evidence of organ malfunction or injury. [24] When intra-abdominal pressure increases to a point where it compromises the function of organs and tissues, abdominal compartment syndrome (ACS) develops. An intra-abdominal pressure of 5-7 mmHg is considered normal. Above 19 mmHg, the intraabdominal pressure is deemed abnormal and causes ACS. [25,26] Individuals often experience dyspnea or dyspnea, dysuria, stomach discomfort and distention, elevated blood pressure, deterioration in mental state, and oliguria. [27, 28]

Intestinal Obstruction & Ileus

Blocking the regular flow of luminal materials through the gastrointestinal system is known as intestinal obstruction, and it can be brought on by either an intraluminal or extrinsic mechanism. [29] Intestinal blockage and paralytic ileus are uncommon obstructive consequences in acute pancreatitis. Furthermore, a duodenal blockage resulting from severe acute pancreatitis involving the duodenum may have a functional origin or a combination of structural and functional elements. The incidence ranges around from

1 to 4 percent. In summary, it is critical to recognize the uncommon but potentially fatal obstructive consequences of acute pancreatitis, which need for immediate medical attention. [30]

Prediction of severity of acute pancreatitis

Patients at a moderate or elevated risk of complications can be identified by using the severity prediction of acute pancreatitis. The Acute Physiology and Chronic Health Eval-auction II (APACHE-II), Ranson score, modified Glasgow/Imrie score, SIRS criteria, Bedside Index for the Severity in Acute Pancreatitis, and Harmless Acute Pancreatitis Score are among the several scoring systems that integrate clinical and laboratory findings to evaluate the likelihood of a severe disease course. Single laboratory parameters, such as C reactive protein (CRP), can also be used. [31] Although the specific clinical presentation of the illness complicates bedside evaluation and invalidates the predictive validity of prognostic ratings, several writers sought to address the organ failure to better evaluate the severity of the disease. Several prognostic ratings linked to organ failure, including Marshall [32], MOF/Goris [33], and SOFA [34], were developed in this context. In addition to the aforementioned scoring systems, it has been discovered that various types of pancreatic enzymes, such as trypsinogen, and several systemic inflammatory markers, such as procalcitonin, TNF-α, red cell distribution width (RDW), interleukin (IL)-1, IL-6, TNF-α, and C-reactive protein (CRP), are also good and promising predictors of the severity of AP, particularly in the early stages of the illness. [35-40]

Glasgow score

Blamey et al. developed the Glasgow pancreatitis score in 1984 as a predictive measure to determine the severity of AP. Imrie's Glasgow score appears to be more accurate than Ranson's for both alcohol- and biliary-related acute pancreatitis, with a sensitivity range of 56%–85% when assessing severe acute pancreatitis. [41] It is also known as the Imrie score, and it may be completed by patients within 24 hours of their admission. It comprises eight of the eleven elements that make up the Ranson's criterion. Regardless of the cause, the Glasgow score is a useful predictive measure for mortality. [42]

This scoring system includes following components:

1) age > 55 years, 2) serum albumin < 32 g/l (3.2 g/dl), 3) arterial PO2 on room air < 8 kPa (60 mm Hg), 4) serum calcium < 2 mmols/l (8 mg/dl), 5) blood glucose > 10.0 mmols/l (180 mg/dl), 6) serum LDH > 600 units/l, 7) serum urea nitrogen > 16.1 mmols/l (45 mg/dl), 8) WBC count > 15×109 /l (15×103 /microliter). Each variable in this scoring system has 1 point. Cut-off for severe AP is ≥ 2 points, and scores above 3 also indicate that the patient is likely to require admission to intensive care (ICU). [43]

Kiat et al. confirmed that the method is user-friendly and comparable to the Ranson score in predicting AP severity with an AUC of 0.78.[44] Buxbaum et al. found that the Glasgow score has an AUC of 0.73 for predicting AP severity.[45]

Thaddaeus Tan Jun Kiat's GS showed a sensitivity of 76.8%, specificity of 69.2%, PPV of 25.8%, and NPV of 95.5%, with a diagnostic odds ratio of 7.44 and overall accuracy of 70.1%. [46]

Glasgow Score exceeded other pancreatitis-specific rating systems. It is less effective in predicting death, but it is still an effective indicator of the severity of the disease. Nevertheless, it suffers from the 48-hour calculation lag, much like Ranson's score performed. While a high score can identify patients at risk of death and severe pancreatitis, its sensitivity and specificity persist to be poor. [47]

BISAP (bedside index of severity in acute pancreatitis) score

The scoring system, while user-friendly, has only undergone validation for predicting mortality.[48] This score is one of the most accurate and applicable in everyday clinical practice because of the simplicity and the capability to predict severity, death, and organ failure. [49]

BISAP scoring system includes following components:

BUN > 25 mg/dl, impaired mental status (Glasgow coma scale < 15), SIRS (it is defined as two or more of the following: 1) temperature of >38.0 °C or 24 breaths/min or PaCO2 < 32 mm Hg, 3) pulse > 90 beats/min, 4) WBC 12,000 cells/mm3 or > 10% immature bands), age > 60 years, pleural effusion detected on chest radiograph. It is a reliable scoring system to predict severity and organ failure within 24 hours of admission. [50]

Cut-off value of BISAP score for prediction of severe AP is ≥ 2. [51] Another meta-analysis showed that a BISAP score of 3 is reliable to identify the high-risk AP. [52] BISAP score showed mortality of < 2% when score: 0–2 and > 15% when score: 3–5. [53] One study from China demonstrated that the best cut-off value for BISAP is 2 for predicting pancreatic necrosis and organ failure, and 3 for predicting mortality. [54]

Mention must be of Papachristou GI, et al. who conducted a prospective study in 2010 to compare BISAP and SIRS scoring systems with the available “traditional” systems i.e. Ranson’s system, APACHE-II, CTSI in predict severe AP, necrosis, and mortality in AP patients . The study concluded that the BISAP score was a precise instrument to predict risk factors in AP patients with added advantage of ease of use and early predictability**.** [55]

Zhang J, et al. conducted a study from 2010 to 2013 in China to compare BISAP scores and Atlanta classification in for the purpose of assessing the disease severity of acute pancreatitis. scoring may be of great utility for the purpose of classifying patients of acute pancreatitis based on risk and predicting the clinical course and prognosis. [56]

Gompertz M, et al. published a retrospective review in 2012 in 128 patients with acute pancreatitis. The BISAP, APACHE II and Balthazar scoring system was used to check the severity. A statistically significant correlation was found was

among BISAP scores and duration of hospital stay. The study concluded that BISAP system of scoring was an important tool for predicting SAP. Moreover, all the parameters were on the first day of hospital. The sensitivity and specificity were better in BISAP compared to APACHE II and Balthazar systems. [57]

An earlier study by Ye JF, et al. (2017) conducted to see consistency of BISAP, Modified Early Warning Score (MEWS), serum Ca2+, and red cell distribution width (RDW) in predicting acute pancreatitis severity. Univariate analysis, was done which showed that the BISAP, MEWS and serum Ca2+ had good predictive capacity to detect the severity of AP (P-value<0.001), whereas RDW was not associated with good prediction The study concluded that BISAP and serum Ca2+ have high predictive value for the severity of AP. [58]

This score is also able to identify patients at increased risk of mortality prior to the onset of organ failure. Papachristou et al also demonstrated that main advantages of BISAP score were its high accuracy rate and usefulness for predicting the severity within 24 h of hospital admission. [59] However, lack of some parameters including etiology, presence of recurrent attack of AP, and obesity are the disadvantages of this score. Some authors tried to insert obesity into the BISAP score; however, they also indicated that prospective clinical trials with large populations are required to describe the exact association between BISAP score and obesity. [60]

Management

Nonsurgical treatment

Bowel rest, hydration, and pain management are the three main treatments for pancreatitis. While most patients with mild pancreatitis need to be hospitalized, some may be managed as outpatients. For outpatients, oral opioids should be used to relieve pain while clear fluids should be used to maintain nutrition and hydration. [61] General guidelines recommend early fluid resuscitation, starting with 250 - 500 mL/hr. [62] with the goal of maintaining urine output at ≈0.5 mL/kg/hr. if there is no acute kidney injury. [63] Administering more oxygen also helps, particularly for people who are elderly. Another crucial component of treating early AP is analgesia; manage glycemia—a blood sugar level of greater than 180 mg/dL upon admission in a patient who is not diabetic is linked to a higher mortality rate. [64]

Fluid resuscitation

Fluid flows into the third space as a result of pancreatic inflammation and the ensuing systemic inflammatory response. In extreme situations, this might lead to hypoperfusion, hypovolemia, and eventually organ failure. A sufficient amount of fluid resuscitation is required to stop this cascade. A few RCTs considered the kind of fluids. Colloids are generally avoided in critically sick patients since there is little evidence that they are beneficial, and hydroxyethyl starch may even increase mortality. [65]

Nutritional therapy:

Following a reduction in stomach discomfort, oral feeding may be resumed in patients with mild pancreatitis. Supportive nutrition is recommended 48 hours following the beginning of severe AP. There is little doubt that enteral nutritional assistance is preferable. If oral feeding is not tolerated, a polymeric or elemental formulation may be employed, and a nasogastric or Nasojejunal tube may be implanted. Improved gut blood flow, preservation of mucosal surface immunity, reduction of microbial translocation, preservation of physical gut barrier function, and maintenance of gut-associated lymphoid tissue bulk and function are all benefits of enteral feeding. [66,67]. In 25% of cases, these variables lead to enhanced outcomes, less SIRS, fewer infectious complications, and inclusive pain relief. [68, 69] As a second-line treatment for acute pancreatitis, parenteral nourishment can be given. If nutritional supplementation is necessary and Nasojejunal tube feeding is not tolerated. Immunonutrients such as glutamine and omega-3 fatty acids given to parenteral formulations can help individuals with acute pancreatitis have better prognoses. Parenteral immunonutrition lowered the risk of infectious complications by a large margin. [70]

Antibiotic therapy:

As a second-line treatment for acute pancreatitis, parenteral nourishment can be given. if nutritional supplementation is necessary and nasojejunal tube feeding is not tolerated. Immunonutrients such as glutamine and omega-3 fatty acids given to parenteral formulations can help individuals with acute pancreatitis have better prognoses. Parenteral immunonutrition lowered the risk of infectious complications by a large margin. [71, 72]

Surgical management:

When a patient experiences complications resulting from AP, such as abdominal compartment syndrome, persistent acute bleeding, intestinal ischemia, or acute necrotizing cholecystitis, surgery is recommended. Lower mortality is achieved by postponing surgical operations for a duration of four weeks or more from the commencement of the condition. [73, 74] Demarcation of necrosis happens with late surgery, minimizing damage to important tissues. Necrosectomy is therefore more successful and bleeding is reduced during late surgery. A new meta-analysis evaluated the timing of surgical interventions at three distinct cut-off periods (72 hours, 12 days, and 30 days) and contrasted late surgery to early surgery. The benefit of late surgery for survival was seen at all cut-off points.[75] Drainage or neurectomy is not usually advised if emergency surgery is required sooner for other reasons.[76,77]Although they need more treatments, less invasive surgical techniques like video-assisted retroperitoneal debridement (VARD) and trans gastric endoscopic neurectomy reduce the incidence of new-onset postoperative organ failure.[74] Pseudocyst spontaneous resolution occurs in a third of patients with a pseudocyst.[78] Symptomatic pseudocysts can be

successfully decompressed by endoscopic cyst gastrostomy with endoscopic ultrasound guidance . [79] After a staggered course of therapy, open neurectomy is still a viable therapeutic choice for severe pancreatic necrosis, according to the recently released World Society for Emergency Surgery for the therapy of Severe Pancreatitis.[74]

CONCLUSION

Acute pancreatitis requires prompt diagnosis, severity stratification, and clinical judgment for proper management. The Revised Atlanta Classification, BISAP SCORE, and Glasgow score are commonly used for diagnosis and severity assessment. New approaches like fluid resuscitation, antibiotic use, nutritional support, and necrosis treatment have been introduced but not widely adopted.

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