SEVERE ACUTE PANCREATITIS (SAP) REVIEW OF LITERATURE

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Abstract: *In acute pancreatitis, infection of pancreatic or peripancreatic necrosis is the most important risk factor, determining the patientsş outcome. The mortality in patients with hemorrhagic necrotizing (severe) pancreatitis is of 10-24%. Pancreatic necrosis develops within the first 4 days after the onset of the disease. Infections occur in 40-70% of patients with SAP. The incidence of pancreatic infection is of 24, 36 and 71% in the first, second, and third weeks respectively. The detection of the infection of pancreatic or peripancreatic necrosis is reliably by ultrasound or by CT (computer tomography) guided fine needle puncture, followed by bacterial determination in culture. The surgery in acute pancreatitis is indicated in patients with SAP and proven infection. In SAP, which occurs in 15- 20% of the patients, is still a life threatening disease with mortality rates of up to 60% in old patients, with comorbidities. In the early phase, in the first 4 days in evolutions, the release of pancreatic enzymes and vasoactive substances leads to cardiovascular, pulmonary and renal disturbances. In the second phase of SAP, septic complications are the major cause of death.*

Cuvinte cheie: *pancreatita acută, necroza pancreatică infectată*

Rezumat: *În pancreatita acută (PA) infecţia necrozei pancreatice sau a ţesutului peripancreatic reprezintă cel mai important factor de risc, determinând evoluţia pacienţilor. Mortalitatea la pacienţii cu pancreatită acută necrotico-hemoragică severă (PAS) este de 10-24%. Necroza pancreatică apare în primele patru zile de la debutul bolii. În PAS, infecţia apare în 40-70% din cazuri. Incidenţa infecţiei pancreatice în prima, a doua şi a treia săptămână este de 24, 36, respectiv 71%. Identificarea infecţiei pancreatice şi peripancreatice este realizabilă prin examinarea CT (computer tomograf), ecografie, prin puncţia ghidată ultrasonografic sau CT urmată de analiza bacteriologică a punctatului. Tratamentul chirurgical este indicat în PA la pacienţii cu PAS şi infecţie dovedită. PAS este întâlnită la 15-20% din pacienţii cu PA şi este o afecţiune cu risc vital, având o rată a mortalităţii de până la 60% la pacienţii vârstnici cu comorbidităţi. În faza incipientă a evoluţiei bolii, în primele 4 zile, eliberarea enzimelor pancreatice şi a substanţelor vasoactive determină tulburări sistemice cardiovasculare, pulmonare şi renale. În faza a 2-a a evoluţiei, complicaţiile septice sunt cauzele majore ale mortalităţii.*

Most patients with acute pancreatitis have severe abdominal pain, vomiting, nausea and sometimes present cardiocirculatory shock. The diagnosis of acute pancreatitis can be made in presence of elevated serum lipase levels, abdominal pain and vomiting. The specificity of amylase and lipase levels is in the range of 90%. Once the diagnosis of acute pancreatitis (AP) is established, the question arrives whether or not the course in gallstone disease. Early severity difference between mild or SAP has been shown to be of clinical value for intensive care beds and for indication to urgent ERCP or other interventional treatment.(1,2)

It is difficult to have on admission a distinction about severity of AP, because the serum lipase cannot be used to determine disease severity. The initial clinical assessment by on experienced gastroenterologist or surgeon there are several prognostic markers and scoring systems that help to have a different diagnosis between SAP and mild acute pancreatitis. In presence of organ failure (a fall in pO_2 – oxygen partial pressure - or a rise of serum creatinine levels) according to the Ranson score or the Imrie score, in all extrapancreatic complication develops (ARDS, acute renal insufficiency) or in presence of pancreatic, peripancreatic necrosis, extensive acute pancreatitis, confirmed by contrast enhanced CT scan, the course of AP is more likely to be severe.(1,2)

Reasoning that the presence of necrotic tissue was not always an indication for its removal, particularly in cases where removal carries significant risk (severe comorbidities), the nonoperative management (percutan drainage under CT image) of SAP is considered. Pancreatic necrosis remains the most severe form with evolution to majority of mortality cases related to AP. In the majority of mortalities in patients with SAP, this is associated with MSOF (multiply organ failure).(3) The lock of contrast enhancement of the pancreatic gland in CT-control, indicating disruption of normal pancreatic microcirculation, correlates with the findings of necrosis at surgery.(4)

More studies have demonstrated that pancreatic necrosis develops. Over a couple of days (4 days) and however remains stable during a given episode of AP, and the demarcation of necrosis evolves two to three weeks after onset of pancreatitis.(5) The natural evolution of PA proceeds in two phases. In the early phase, which occurs in the first 4 days after the onset of pancreatic inflammation, the release of pancreatic enzymes and vasoactive substances leads to cardiovascular, pulmonary and renal disturbances.(6)

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Patients with SAP are rarely lost during this early phase, but in SAP organ failure is common and often occurs in the absence of infection, in presence of systemic toxic phase caused by the release of inflammatory mediators or citokines induces organ failure. The second phase at the end of the second week, is dominated by sepsis and septic shock, because the presence of infection of pancreatic necrosis.(6) In natural evolution of AP, infection might occur at any moment.(7)

Development of pancreatic necrosis (PN) in AP, with pancreatic infection (IPN)

More clinical studies analyzed the time pattern of the occurrence of pancreatic necrosis.(5) Serum levels of C reactive protein (CRP) were measured to determine whether they were >120 mg/l reported to be a reliable indicator of pancreatic necrosis. Based on these levels, pancreatic necrosis was present in 46% within the first 24 h, and after 48, 72 and 96 h after clinical manifestation of disease, the percentage of pancreatic or peripancreatic necrosis had increased to 70, 97 and 100% respectively. Only patients with necrosis are at risk for developing infection.(8) In the studies of Berger et al. the pancreatic infection in patients with SAP was 39,4% undergoing surgery, and 23,8% of the patients had infected necrosis after one week of evolution.(6) If the patients were operated in the second week after the onset of AP, the infection was present in 36%, and if the surgery was undergoing in the third week, this complication was present in 71% and , in contrast, patients with surgical operation in fourth week had on infection rate of 32,5%.(6) After these studies, the conclusion was that patients with acute necrotizing pancreatitis have highest risk for infection in the third week after onset of disease.(9,10)

C- Reactive Protein (CRP)

As a prognostic marker, an elevated C-Reactive Protein (CRP) concentration, greater than 130 mg/l indicates that the disease has a complicated course. The sensibility of the CRP test is 85% in the first 72 h after the onset of symptoms. Detection of elevated CRP levels is sensitive for SAP, but it is not specific for the disease and other cause of inflammation.(11,12)

Procalcitonin

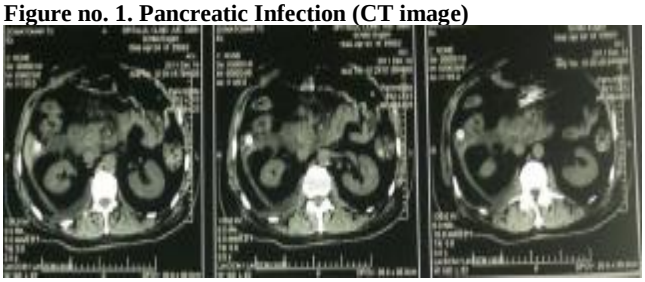
The CRP level in AP is an indicator for presence and evolution of inflammation, but not for presence of abscess. The procalcitonin is another marker that has been evaluated as a prognostic indicator for pancreatitis. Proinflammatory citokines as well as bacterial lipopolisacharides strongly induce the synthesis on release of procalcitonin during inflammation. Several clinical studies have attempted to show a correlation with disease severity in pancreatitis. A recent meta-analysis indicates that procalcitonin cannot be regarded as a reliable marker for assessing the severity of pancreatitis.(13) Whereas a European multicenter trial has presented somewhat more promising results.(14)

The role of CT and magnetic resonance imaging in AP

Dynamic contrast – enhanced CT (DCT) is the imaging modality for staging AP and for detecting complications.(1,4) DCT detect the pancreatic necrosis with 87% sensitivity and an overall detection rate of 90%.

The morphologic severity of acute pancreatitis can be determined using o CT severity index (CTSI), initially developed by Balthazar et al., and extended to monitor organ failure by Silverman and Banks in 2004.(15,16,17,18,19) Although CT remains the gold standard MRI has also been used in several studies for imaging AP. MRI is highly suited for the detection of vascular complications, such as venous thrombosis. A recent study reported that MRI detected severe acute pancreatitis with 83% sensitivity (58-96%) and 91% specificity (68-98%), whereas the sensitivity for CT was 78% (52-93%) and its specificity 86% (63-96%).(20,21,22,23,24)

Figure no. 1. Pancreatic Infection (CT image)



The role of APACHE II, CTSI Scores, RANSON's, BISAP in predicting organ failure, complications, mortality and classification of the severity of Acute Pancreatitis

Identification of patients at risk for SAP early in the course of AP is an important step to guiding management and improving outcomes. A new prognostic scoring system, the bedside index for severity in AP (BISAP), has been proposed as an accurate method for early identification of patients at risk for intra-hospital mortality. The Ranson's score represented a major advance in evaluating the severity of AP and has been used for over three decades to asses AP severity.(25) This score is moderately accurate in classifying patients in terms of severity, but has the disadvantage of requiring a full 48 h to be completed, missing a potentially valuable early therapeutic window.(25) In USA, the most commonly used prediction scoring system for clinical research in AP is the APACHE II, and this score is an accurate as Ranson's score and can be administered on any day.(26) Recent, a new prognostic scoring system, the bedside index for severity in AP (BISAP) has been proposed as an accurate method for early identification of patients at risk for in-hospital mortality.(27) The BISAP uses five points: urea nitrogen (BUN) > 25 mg/dl, impaired mental status by evidence of disorientation or disturbance in mental status, presence of the SIRS, age > 60 years and pleural effusions.(28)

Surgical treatment in SAP

Sterile pancreatic necrosis

The development of pancreatic parenchymal and/or extrapancreatic necrosis is the critical feature determining the prognosis of AP. Patients with documented sterile necrosis are indication for manage solely by intensive medical support.(29) and sterile pancreatic necrosis, even when accompanied by organ failure, was not an absolute indication for surgery, with mortality rates lower than 10% in nonoperative management.(30,31,32)

Infected pancreatic necrosis (IPN)

In contrast to the now largely resolved controversies surrounding sterile necrosis, there has been relatively little disagreement regarding the necessity for surgical debridement and drainage of IPN. The principal area of discussion in IPN has centered over the precise form of surgical drainage after necrosectomy – whether it should be open, semiclosed or closed.(29,30,31,32,33,34,35) More recently, operative alternatives to the traditional transabdominal approach for debridement, and drainage of IPN have described, both retroperitoneal and laparoscopic approaches have been reported, with acceptable results in very selected cases.(36,37,38) With the advent of programmatic debridement and drainage of documented IPN, surgical mortality rates for this condition were lowered to less than 15%.(31,39,40)

The rationale for the surgical debridement of pancreatic necrosis is based on two principles. The first is to remove the necrotic pancreatic tissue as well as pancreatogenic

ascites out of the peritoneal cavity and the lesser sac. Secondly, as much viable pancreatic tissue as possible should be preserved, because the remaining pancreatic parenchyma strongly influences the quality of long-term results conserving the endo- and exocrine pancreatic function.(40,41)

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