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Review Article

PANCREATITIS PRESENTATION AND MANAGEMENT

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Abstract:

Introduction: Pancreatitis is a medical condition that is defined as the ongoing inflammation in the pancreas that occurs together with autodigestion of the pancreatic tissue, which is a result of erratic activation of the trypsin enzyme with resultant activation of zymogen within the pancreatic tissue. Patients with pancreatitis could even progress to develop a case of severe acute pancreatitis. The commonly used definition among clinicians is that of a severe acute pancreatitis that comes together with failure of multiple body organs along with the development of systemic inflammatory response syndrome. In most patients with acute pancreatitis, the presence of necrotic foci is usually noticed within the tissue of the inflamed pancreas. Located in the retroperitoneum, the pancreas organ is greatly saved from developing injuries due to either environmental factors mechanical factors. Severe cases of acute pancreatitis could have many underlying etiologies with gallbladder stones and alcoholism being the most causes of pancreatitis in most patients. In the vast majority of patients who develop acute pancreatitis, the clinical condition will regress without developing severe complications. On the other hand, in a smaller number of patients, acute pancreatitis could lead to the development of severe and possibly fatal complications with mortality rates that reach up to twenty-five percent. Highest mortality rates are usually found among patients with acute pancreatitis who need to be hospitalized and admitted to the intensive care unit for a period that is more than fourteen days. **Aim of work:** In this review, we will discuss pancreatitis presentation and management. **Methodology:** We did a systematic search for pancreatitis presentation and management using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles. **Conclusions:** Severe acute pancreatitis is associated with significantly high mortality rates. This study is a qualitative review of the recent medical literature. Unfortunately, it is difficult to encompass the whole amount of knowledge over such topic of severe acute pancreatitis in the literature. We have included the relatively more influential studies in this review based on our inclusion criteria. Severe acute pancreatitis remains to be a subject of grey areas in its surgical management albeit new studies have been recorded since the origin of the latest UK guidelines for management of acute pancreatitis and severe acute pancreatitis. We do encourage the conduction of furthermore recent studies in this surgical topic with an aim to further reduce the associated mortality with severe acute pancreatitis.

Key words: pancreatitis, presentation, management, surgical options.

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INTRODUCTION:

Pancreatitis is a medical condition that is defined as the ongoing inflammation in the pancreas that occurs together with autodigestion of the pancreatic tissue, which is a result of erratic activation of the trypsin enzyme with resultant activation of zymogen within the pancreatic tissue. [1-2] Patients with pancreatitis could even progress to develop a case of severe acute pancreatitis. The commonly used definition among clinicians is that of a severe acute pancreatitis that comes together with failure of multiple body organs along with the development of systemic inflammatory response syndrome. In most patients with acute pancreatitis, the presence of necrotic foci is usually noticed within the tissue of the inflamed pancreas. [3-4] Located in the retroperitoneum, the pancreas organ is greatly saved from developing injuries due to either environmental factors mechanical factors. Severe cases of acute pancreatitis could have many underlying etiologies with gallbladder stones and alcoholism being the most causes of pancreatitis in most patients. In the vast majority of patients who develop acute pancreatitis, the clinical condition will regress without developing severe complications. On the other hand, in a smaller number of patients, acute pancreatitis could lead to the development of severe and possibly fatal complications with mortality rates that reach up to twenty-five percent. Highest mortality rates are usually found among patients with acute pancreatitis who need to be hospitalized and admitted to the intensive care unit for a period that is more than fourteen days. [5]

Multiple previously-published studies have shown recent declines in mortality rates among patients with acute pancreatitis. [6] Moreover, previous research have found that mortality rates following acute pancreatitis can differ among different populations of patients and are significantly affected by social and economic disparities among different groups of patients. [7]

In this thorough review we will look at the main principles of pathophysiology, categorization and surgical intervention in patients who have severe acute pancreatitis. We will also examine the recent shift in paradigm in the treatment of patients with severe acute pancreatitis. We will also discuss the most recent evidence regarding pancreatitis presentation and management guideline developed by the British Society of Gastroenterology. [8] There will also be a lot of discussion about whether patients with severe acute pancreatitis should undergo invasive surgical interventions or not.

METHODOLOGY:

We did a systematic search for pancreatitis presentation and management using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: pancreatitis, presentation, management, surgical options.

Epidemiology and pathogenesis

The British Society of Gastroenterology has released their report in which they stated that the incidence rates of acute pancreatitis in the United Kingdom have ranged between 150 and 420 cases per million person-years, with incidence rates significantly increasing over the last ten years. In addition, they concluded that up to twenty percent of patients with acute pancreatitis will finally develop severe acute pancreatitis. Many patients whose disease is complicated with severe acute pancreatitis were recorded in the patient's registries and the medical literature, but still, the pathophysiology behind the mechanisms responsible for this complication remains to be not clearly understood and an area of debate among researchers. The rate of developing severe acute pancreatitis among patients with acute pancreatitis can be significantly elevated because of many predisposing factors that include genetic predisposition, certain environmental exposures and having some metabolic factors. In developed countries, the commonest underlying etiologies include gallbladder stones and alcoholism. These two etiologies alone are generally responsible for up to eighty-five percent of cases of acute pancreatitis. Alcohol drinks generally lower the trypsin activation threshold within the pancreatic tissue, leading to the development of necrosis of the pancreatic tissue. [9] In fact, multiple risk factors even increase the rates of developing acute pancreatitis among patients with gallbladder stones and/or alcoholism. These factors include older age, sex, high BMI, number of attempts to cannulate the papilla of pancreatic duct poor emptying, which all significantly elevate the rate of developing acute pancreatitis.

Several adaptive mechanisms and protecting mechanisms have been discovered to lead to significant reductions in the rates of developing acute pancreatitis. On the other hand, the presence of dysfunctions within these adaptive mechanisms or protecting mechanisms will significantly increase the risk of developing acute pancreatitis, and make

individuals highly susceptible for developing the disease and even turning into a case of severe acute pancreatitis. previous research studies have discovered the presence of certain genetic variations that can potentially lead to significant losses of these previously mentioned adaptive mechanisms. These include cymtripsin C [CTRC], human cationic trypsinogen [PRSS1], carboxypeptidase A1 [CPA1] and serine protease inhibitor, Kazal type 1 [SPINK1] mutations. [10] The ductal cells of the pancreas could express sensors within the luminal surface of the pancreas like protease-activated receptors 1 and 2 [PAR1, PAR2] that can detect trypsin and the presence of its activity. These are among the main factors that provide protective mechanisms. Other possible molecules that are involved in this pathway include P2X, ligand-gated ion channel 4 [P2X4], P2Y purinoreceptor 2 [P2Y2], and P2X ligand-gated ion channel 7 [P2X7] and act by recognizing the concentrations of calcium. When these molecules are turned on, the fluids secretion will lead to flushing of the damaging fluid out of the pancreas and into the duodenum. The presence of dysfunctions in these molecular receptors could potentially lead to insufficient protective mechanisms, therefore significantly rising the rates of developing severe acute pancreatitis in a patient with acute pancreatitis. A previous study that was published by Papachristou et al suggested that a single nucleotide polymorphism in the gene that produces monocyte chemoattractant protein-1, can potentially lead to a systemic inflammatory response leading to severe acute pancreatitis which will be associated with high mortality rates. [11]

In addition, mutations in the cystic fibrosis transmembrane conductance regulator [CFTR] gene, which are usually found among patients with cystic fibrosis, have also been found to significantly elevate the vulnerability of individuals to develop acute pancreatitis. In a previous study that was published by Pezzilli et al, about twelve percent of patients who were diagnosed with acute pancreatitis had been found to have CFTR gene mutations.

Outlining severity

Two different systems to score the clinical severity of acute pancreatitis have been published in the medical literature. These two scoring systems are the Revised Atlanta criteria and the Determinant-based Classification. Both scoring systems are based on both local factors and systemic factors. The British Society of Gastroenterology generally recommends the use of the Revised Atlanta criteria to predict the

severity of clinical condition of patients with acute pancreatitis. The Revised Atlanta criteria depend mainly on a multifactorial scoring system and predictive factors of severity of the condition. [12]

Based on the Revised Atlanta criteria, during the first twenty-four hours of the onset of acute pancreatitis clinical manifestations, the indicators that will predict the severity of the condition include: the presence of high suspicion based on clinical picture, the presence of abnormally high BMI and obesity, the detection of pleural effusions and the elevation of the Acute Physiology and Chronic Health Evaluation II [APACHEII] Score. After twenty-four hours have already passed, the indicators that will predict the severity of acute pancreatitis include: continuous and progressing failure of multiple organs and/or an Imrie score that is higher than three. A worse severity score is also usually predicted when levels of C-reactive protein are higher than 150 mg/L or when levels of biomarkers like interleukin (IL)-8, IL-6, IL-10, procalcitonin and IL-1 beta-receptor antagonist are significantly elevated.

Other more recent scoring systems have been developed to estimate the severity of acute pancreatitis. Of these recent systems, the most famous ones are the Ranson scoring system and the Imrie scoring system. Both these scoring systems have a sensitivity that can reach eighty percent at the first forty-eight hours following the onset of clinical manifestations of acute pancreatitis. Such scoring systems can help in the identification of patients who might need more strict observation and admission to an intensive care unit to monitor progression and prevent the development of a severe acute pancreatitis. A more recent scoring system for the severity of acute pancreatitis is the Determinant based system which measures actual severity. This scoring system of severity was primarily developed following the introduction of the newer advanced imaging modalities and aims at achieving a better detection of the risk of developing organ failure in patients who have acute pancreatitis and are susceptible to developing severe acute pancreatitis. This severity scoring system is dependent on the accurate identification of either sterile or infected necrosis of the pancreas and the presence of any signs of organ failure. levels of serum biomarkers like urinary trypsin activation peptide and serum amyloid A have also been studied as possible markers that could potentially be used for the early prediction of the severity of severe acute pancreatitis. [13]

Surgical management of necrotizing pancreatitis

The principle of applying surgical interventions for the management of acute necrotizing pancreatitis necessitate the application of intensive care management, identification of any possible infections and if required, proper debridement of any infected necrotic tissues. Invasive surgical operations that are used for patients with severe acute pancreatitis may be indicated in cases of biliary pancreatitis, infected necrosis of the pancreas, massive pancreatic hemorrhage, sterile necrosis of the pancreas, drainage of an abscess in the pancreas and symptomatic organized necrosis of the pancreas. The current recommendation is that a confirmed diagnosis of a case of biliary pancreatitis will necessitate performing a laparoscopic cholecystectomy immediately at diagnosis or within fourteen days following the diagnosis. This is thought to cause relief of the obstruction and thus will enhance chances of achieving complete recovery of patients with severe acute pancreatitis without having to perform other surgical interventions which could be associated with significantly higher risks of developing complications.

Initial management plan of patients who develop severe acute pancreatitis must consist of continuous strict monitoring of the patients because they have significantly high risk of developing a superadded bacterial infection within the necrotic pancreatic tissue. Bacterial infections generally occurs three to seven percent of patients who develop acute pancreatitis. On the other hand, about ten to fifty percent of patients who have necrosis of the pancreatic tissue will eventually develop a superadded bacterial infection. In these cases that develop a superadded infection, the infection classically manifests following two or three weeks of the primary onset of acute pancreatitis. Based on this, several randomized controlled clinical studies have investigated the potential role of using prophylactic antibiotics in patients with acute pancreatitis to prevent the development of a superadded infection. However, results of all these trials are still inconclusive, making this issue a controversial issue with many debates. [14]

Making a definitive diagnosis of acute pancreatitis complicated by an infection needs performing CT imaging whether with or without having a positive fine needle aspiration for bacteriology. Patients who suffer from continuous pain or features that are suspicious of the presence of an underlying sepsis with higher than thirty percent necrotic tissues, which could be confirmed radiologically, must immediately get a fine needle aspiration to confirm the presence of

an infection. Without receiving proper treatment, mortality of these acute pancreatitis patients can be significantly high and even reach eighty percent of cases. [15]

Before the official release of the British Society of Gastroenterology guidelines, the common recommendation was that acute pancreatitis cases that have infected necrotic tissues are indicated to undergo surgical intervention or interventional drainage. when less than thirty percent of the pancreatic tissue contains necrotic tissues with fluid collections, this can be treated with performing minimally invasive necrosectomy. Recent studies have shown that surgical interventions, in such cases, can be safely avoided. A meta-analysis that was published by by Mouli et al concluded that sixty-four percent of cases that were diagnosed with acute pancreatitis followed by infected necrosis of pancreatic tissue had successful recovery following conservative management with mortality that is about twelve percent of cases. The current paradigm is shifting towards the application of conservative approaches in such patients instead of undergoing surgical operations. [16]

Surgery in pancreatic necrosectomy should often be delayed for fourteen days to be able to allow the demarcation of the necrosom, unless the case can be treated completely by eliminating of the underlying etiology, such as in the cases of cholecystectomy for the treatment of gallbladder stone induced acute pancreatitis with infected pancreatic necrosis.

Early surgical intervention is usually only opted in cases of confirmed infected necrotizing pancreatitis. Actually, mortality rates of up to sixty-five percent have been found with early surgical interventions in cases of severe acute pancreatitis. Patients with severe necrotizing pancreatitis could thus eventually undergo surgical debridement with the ideal time being set at the third or fourth week following the onset of acute pancreatitis.

The choice of surgical procedure is currently very debatable and is usually dependent on the facilities and surgical ability of the surgeon who will be performing the procedure. The current interventional procedures used include the use of standard surgical open necrosectomy, endoscopic necrosectomy or minimally invasive necrosectomy.

This approach to remove the infected necrotic pancreatic tissue was associated with a significantly higher rate of complications with studies finding

between thirty-four percent to ninety-five percent of procedures end up with severe complications. Mortality results in several research studies are between six percent and fifty percent. based on these findings of previous studies, one could explain why the interest in open necrosectomy is decreasing. It is also noticed in the recent medical literature that preference is changing to favor safer procedures with minimally invasive necrosectomy. In a study that was conducted by Bakker et al, endoscopic necrosectomy was shown to cause significantly better outcomes regarding pro-inflammatory response and clinical end point identified by recording IL-6 levels that were found to decline following endoscopic procedures when they were compared to open surgery with significant values on correlation. Castellanos et al [17] concluded that all patients who underwent trans-lumbar retroperitoneal endoscopy had good outcomes following the procedure. They were noticed to avoid subsequent surgical interventions for debridement. Similar research studies have shown significantly high success rates.

The NICE guidelines list two subtypes of endoscopic necrosectomies, these two are the percutaneous retroperitoneal endoscopic necrosectomy and the endoscopic trans-luminal necrosectomy. In a previous interview done with Baron, despite the presence of a risk of complications, with proper experience, ninety percent of patients with acute pancreatitis may have complete recovery of the necrotizing pancreatitis following undergoing endoscopic necrosectomy. However, this procedure must be only performed in specialized centers. [18]

Sileikis et al, on the other hand, found that performing minimally invasive necrosectomy is reported as being the best choice for treating necrotizing pancreatitis. Such patients have relatively lower risks of complications including decreased incidence of bacteremia, multiple organs failure and post-surgical complications. They also have a decreased operating table to discharge time. Unfortunately, as with the endoscopic approach, the procedure needs multiple specialized settings in order to be able to resect the whole necrosom.

The current paradigm is shifting towards the use of a step-up approach, where catheterization for drainage is later followed by video-scopic assisted retroperitoneal debridement. van Stantvoort et al found that when compared to primary open necrosectomy, this step-up approach led to significantly less complications. The removal of pressure and infected fluid from around the pancreas together with the use of intravenous antibiotics can

prevent further invasive management and any remaining necrotic tissue would be removed by the patient's own immune system. [19] videoscopic assisted retroperitoneal debridement tends to follow the initial drainage if the symptomatology persists.

CONCLUSIONS:

Severe acute pancreatitis is associated with significantly high mortality rates. This study is a qualitative review of the recent medical literature. Unfortunately, it is difficult to encompass the whole amount of knowledge over such topic of severe acute pancreatitis in the literature. We have included the relatively more influential studies in this review based on our inclusion criteria. Severe acute pancreatitis remains to be a subject of grey areas in its surgical management albeit new studies have been recorded since the origin of the latest UK guidelines for management of acute pancreatitis and severe acute pancreatitis. We do encourage the conduction of further more recent studies in this surgical topic with an aim to further reduce the associated mortality with severe acute pancreatitis.

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