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Original article

Management and outcomes of acute pancreatitis patients over the last decade: A US tertiary-center experience

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ABSTRACT

Background/objectives: Acute pancreatitis (AP) management remains largely supportive and can be challenging in patients with severe disease. This study aims to describe a ten-year US tertiary-center experience in managing AP patients.

Methods: Clinical management and outcomes of 400 prospectively enrolled AP patients stratified by the Revised Atlanta Classification were analyzed; trends in management between early (2004–2008) and late enrollment phase (2009–2014) were assessed.

Results: Fifty-two% of patients were classified as mild AP (MAP); moderately severe (MoAP) and severe (SAP) grades contained 23.5% and 24.5% of participants. Intravenous fluid administration during the first 24 h (MAP 3.7, MoAP 4.7, and SAP 4.8 L), need for ICU (6%, 23%, 93%), and nutritional support (7%, 51%, 90%) increased significantly with greater AP severity ($p < 0.001$). One hundred fifty five (39%) patients developed necrotizing AP, of which 41% received prophylactic antibiotics, and 44% underwent pancreatic drainage/debridement. Prophylactic antibiotics (58% vs. 27%) and interventions (63% vs. 27%) were noted more frequently in SAP than MoAP ($p < 0.001$). Enteral nutrition (18% vs. 30%) and minimally invasive pancreatic interventions (19% vs. 41%) were more commonly used in the late phase ($p < 0.05$). The overall median length of hospitalization was 7 days reaching 29 days in SAP group. Mortality was 5%; all deaths occurred in SAP group.

Conclusions: This study provides an extensive report on clinical management of AP and its trends overtime. Pancreatic intervention is required in less than 50% of patients with necrotizing pancreatitis. Utilization of enteral nutrition and minimally invasive pancreatic interventions has been increasing over time.

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1. Introduction

Acute pancreatitis (AP) is an inflammatory process of the pancreas characterized by sudden onset and highly variable clinical course. With 270,000 annual admissions in the United States, AP is the leading gastrointestinal-related reason that people enter the hospital [1]. The economic burden of AP exceeds 2.5 billion US dollars per year [2,3]. Most AP patients have a mild disease course with focal interstitial inflammation of the pancreatic parenchyma and rapid restoration of homeostasis. However, about 20% of individuals who experience an episode of AP develop systemic inflammatory response syndrome (SIRS) and subsequent organ dysfunction. This group of AP patients typically requires intensive care unit (ICU) management, prolonged hospitalization, and has a mortality rate as high as 30% [4].

Recent advances have been made in classifying the severity of AP. After an extended period of expert discussion, two updated classification systems were published: the Revised Atlanta (RAC) [5], and the Determinant-based Classification of Severity [6]. The

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RAC categorizes AP patients as mild, moderate, or severe and the DBC stratifies them to 4 groups: mild, moderate, severe and critical, based on various clinical parameters. Very few studies have compared clinical outcomes in AP patients by RAC and/or DBC severity grades [7–9]. Nonetheless, there is paucity of empiric data on management of AP patients grouped according to the RAC/DBC.

The goal of our study is to examine numerous aspects of management and clinical outcomes in a sizable, prospectively-enrolled cohort of AP patients from a U.S. tertiary center that are categorized according to the RAC. Based on the assessment of our cohort, we will describe management trends of AP over the last decade.

2. Methods

2.1. Study design and patients

The Severity of Acute Pancreatitis/Pancreatitis-associated Risk Of Organ Failure (SAPS/PROOF) is an observational cohort study conducted at the University of Pittsburgh Medical Center (UPMC) that aims to assess risks, biomarkers, and outcomes in AP [10,11]. Patients have been prospectively enrolled in two chronological phases. The first phase began in 2004 and lasted until early 2008. The second phase began in 2009 and remains ongoing. Patients included in this report were enrolled until 2014. The Institutional Review Board at the University of Pittsburgh approved the study protocol (IRB protocol ID PRO08010374). All participants signed a written informed consent form prior to enrollment. For seriously ill patients unable to provide consent, the next of keen was contacted. At a later point, when patients' clinical condition improved, they were also informed about the study and signed informed consent. Only AP patients captured relatively early in the disease course (within 72 h from onset) were included in the study. Based on our retrospective review of electronic medical records, approximately 45% of all AP patients admitted or transferred to our institution were enrolled in the study. The percentage of AP patients requiring ICU admission was similar between all comers and our prospective enrolled cohort.

At the time of patient enrollment, detailed questionnaires on demographics and clinical characteristics were collected. Close monitoring of the clinical course including laboratory and imaging tests, therapeutic approaches and disease outcomes were recorded on a prospective daily basis for the first week and then weekly in case of prolonged hospitalization. Therefore, in the present report data on demographics, laboratory measurements, clinical course, management therapies, and outcomes were all abstracted prospectively. Detailed data on specific parameters of treatment required for this manuscript, such as the volume of intravenous fluid (IVF) administered, prophylactic antibiotics, and interventions for walled-off necrosis (WON), were retrospectively collected from electronic medical record review by participating physicians. The major criterion for transferring AP patients to our institution was the development of moderately severe or severe disease. For patients with mild AP the two main etiologies for transfers were need for ERCP or nutritional support. Outside hospital medical records of patients transferred to our institution were retrieved and reviewed. For all transferred patients, disease onset was considered the original presentation at the outside hospital.

RAC was utilized because it focuses on the early, dynamic nature of AP compared to DBC [8]. Study patients were retrospectively assigned a severity grade based on the RAC system [5].

2.2. Computerized tomography

Contrast-enhanced computerized tomography (CECT) scans were performed upon the discretion of the primary treatment team. Initial and follow-up CECT scans were reviewed retrospectively by two abdominal radiologists with subspecialty training (AD, AF), who were blinded to patients' outcomes. RAC definitions were used for local complications [5].

2.3. Definitions

The diagnosis of AP was defined as the presence of at least two of the three following criteria: 1) Epigastric abdominal pain that is typical of AP, 2) Serum amylase or lipase elevated to greater than three times the upper limit of normal, and/or 3) CT scan (or less commonly magnetic resonance imaging [MRI]) findings consistent with AP [12].

Organ failure was defined using the modified Marshall scoring system involving cardiovascular (systolic blood pressure <90, not fluid responsive, or pH < 7.3), respiratory (PaO_2 mmHg/FiO_2<300), or renal system derangements (serum creatinine >1.8 mg/dL) [5]. Single organ failure was determined by the involvement of a single system, whereas multiple organ failure was designated by the presence of organ failure in two or more systems [5]. Transient organ failure was assigned to duration of less than 48 h, while persistent organ failure was described if organ failure lasted longer than 48 h.

Local complications were defined using RAC terminology [5]. AP was morphologically classified as 'interstitial' when only pancreatic edema and/or peripancreatic stranding were present. AP was categorized as 'necrotizing' when parenchymal and/or peripancreatic tissue necrosis developed. Pancreatic necrosis was determined by the lack of pancreatic gland enhancement on CECT scan or by direct identification of necrosis upon laparotomy. Peripancreatic necrosis was defined by the presence of heterogeneous areas of non-enhancement on CECT scan that contain non-liquefied, ill-defined components, nodular areas of increased peripancreatic fat attenuation with visual density higher than simple fluid and considerably higher than simple stranding without pancreatic necrosis. Infected necrosis was diagnosed by the presence of extraluminal gas in the pancreatic or peripancreatic tissues on CECT scan, or by positive Gram staining and/or cultures after fine-needle aspiration or necrosis debridement [13]. Extrapancreatic infections included bacteremia, sepsis of unknown origin, and *Clostridium difficile* colitis, as well as respiratory, urinary, or biliary tract infections. These infections developed during hospitalization and were diagnosed based on a combination of clinical symptoms, imaging studies, and laboratory tests (e.g. blood and/or urine cultures, stool *Clostridium difficile* toxin testing).

Severe AP (SAP) based on RAC was defined as persistent organ failure in one or more physiologic systems [14,15]. Moderately severe disease (MoAP) included a mixed group of the following criteria: transient organ failure, exacerbation of baseline comorbidities, and/or local complications including pancreatic and peripancreatic necrosis. It is important to mention that necrosis, sterile or infected, in the absence of persistent organ failure was classified as MoAP according to RAC. Thus, patients with infected pancreatic necrosis and no organ failure were classified as MoAP. Mild AP (MAP) was selected by the absence of any systemic or local complications.

The SIRS score and serum blood urea nitrogen (BUN) levels were recorded on admission and at 48 h. The SIRS score was calculated based on the presence of the following criteria: 1) temperature above 38C° (100.4 °F) or below 36 °C (96.8 °F), 2) heart rate greater than 90 beats per minute, 3) respiratory rate higher than 20 breaths per minute or PaCO2 less than or equal to 32 mm Hg or ventilator use, and 4) white blood cell (WBC) count higher than 12,000/μL or lower than 4000/μL or the presence of over 10% immature (band)

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