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Original Article

Predictors and outcomes of moderately severe acute pancreatitis – Evidence to reclassify

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ABSTRACT

Background/objectives: After the creation of the moderately severe acute pancreatitis (MSAP) category in the Revised Atlanta Classification in 2012, predictors to identify these patients early have not been identified. The MSAP category includes patients with (peri)pancreatic necrosis, fluid collections, and transient organ failure in the same category. However, these outcomes have not been studied to determine whether they result in similar outcomes to merit inclusion in the same severity.
Methods: Retrospective, review of 514 consecutive, direct admissions for acute pancreatitis from 2010 to 2013. Multivariate logistic regression identified predictors of MSAP.
Results: Persistent SIRS was the best prognostic marker of MSAP with AUC 0.72. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for persistent SIRS to predict MSAP are: 55%, 88%, 40%, 93%, and 84%. Patients with necrosis had significantly longer length of stay (LOS) ($p = 0.0001$) and higher rates of ICU admission ($p = 0.02$) compared with patients with transient organ failure. Compared to those with acute fluid collections, patients with necrosis had longer LOS ($p < 0.0001$), higher rates of ICU admission ($p = 0.0005$), required more interventions ($p = 0.001$), and demonstrated higher mortality (0.003).
Discussion: Moderately severe pancreatitis can be distinguished from mild pancreatitis on the basis of persistent SIRS but cannot be accurately distinguished from severe pancreatitis in the first 48 h (Peri) pancreatic necrosis demonstrates significantly more morbidity compared to the other components of MSAP of fluid collections and transient organ failure.
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1. Introduction

Acute pancreatitis (AP) encompasses a wide spectrum of disease severity from a brief, self-limited presentation to a fulminant progression to multi-organ failure and death. The original Atlanta classification in 1992 included local complications and organ failure under the classification of severe pancreatitis [1]. However the prognostic significance of resolving versus persistent organ failure was later demonstrated [2,3] and a new categorization of moderately severe acute pancreatitis (MSAP) was incorporated to the revised Atlanta classification of AP in 2012 [4]. MSAP was defined as AP with either transient organ failure (TOF) persisting no longer than 48 h, the presence of local complications including peripancreatic fluid collections and (peri)pancreatic necrosis, or exacerbation of co-morbidity. Patients with transient organ failure and local complications were previously included in the severe categorization of AP. Prior studies seeking to identify predictors of severity in AP have utilized the prior categorization of AP where patients currently classified as MSAP and severe acute pancreatitis (SAP) were both categorized as severe. Therefore, no studies to date have examined whether MSAP can be accurately distinguished from mild acute pancreatitis (MAP) early in the course of AP and whether MSAP can be distinguished from SAP before 48 h. The ability to clinically distinguish MSAP from MAP and SAP is meaningful as prior studies have shown MSAP is associated with significantly higher morbidity and need for intervention compared

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to MAP yet lacks the mortality associated with SAP [5–9]. The first aim of this study is to assess the ability of SIRS, BUN, and other readily available clinical and biochemical predictors within the first 48 h to distinguish moderate pancreatitis from mild and severe pancreatitis as defined by the revised Atlanta Classification.

Our second aim is to assess the validity of MSAP category by determining whether there are significant differences among the heterogeneous components (TOF, fluid collections, necrosis) in this new category that would merit further refinement of the MSAP category. While previous studies have demonstrated morbidity and mortality differs between mild, moderate, and severe pancreatitis – prior studies have not demonstrated whether transient organ failure, (peri)pancreatic necrosis, and the presence of fluid collections have similar outcomes that justify inclusion in the same category of severity.

2. Methods

Patients with acute pancreatitis were retrospectively identified through a search of the Mayo Clinic Rochester clinical database. All patients directly admitted to Mayo Clinic Rochester from November 2010 to December 2013 with acute pancreatitis were included in the study. Patients who were transferred to Mayo Clinic from another emergency room within 24 h of presentation were considered as direct admissions to our hospital and included in the study. Patients who were not admitted within 24 h to Mayo Clinic were excluded. The diagnosis of acute pancreatitis required 2 of the following 3 criteria: acute onset of upper abdominal pain consistent with pancreatic pain, amylase and/or lipase levels at least 3 times the upper limit of normal, or imaging evidence of pancreatic inflammation.

2.1. Data collection

Electronic medical records of patients included in this study were retrospectively reviewed and data regarding age, sex, BMI, length of hospital stay, hospital readmission, persistent organ failure, infected necrosis, need for intervention for (peri)pancreatic necrosis, and death were extracted. Systemic inflammatory response syndrome (SIRS) parameters after day 1 and day 2 were recorded. Laboratory parameters including hematocrit, white blood cell count (WBC), blood urea nitrogen (BUN), and creatinine during the first 48 h of admission extracted. These parameters were chosen to be included in our analysis as prior studies have demonstrated these to be predictive of severity in AP [10–14].

Patients were then stratified as mild, moderate or severe pancreatitis in accordance with revised Atlanta Classification. Mild pancreatitis lacked organ failure at any point or local complications. Moderate pancreatitis included patients with local complications defined as new peripancreatic fluid collections or (peri)pancreatic necrosis. The diagnosis of (peri)pancreatic necrosis was based on either contrast enhanced computed tomography (CECT) or magnetic resonance imaging (MRI) performed with gadolinium. Patients with transient organ failure lasting less than 48 h were also categorized as MSAP. The definition of organ failure included acutely elevated creatinine greater than 2 mg/dl after fluid resuscitation or any renal replacement therapy, a systolic blood pressure less than 90 mmHg after fluid resuscitation or any pressor support, or requirement of high flow oxygen by facemask, positive airway pressure ventilation, or intubation. Severe pancreatitis was defined as persistent organ failure beyond 48 h.

2.2. Statistical analysis

Descriptive data is presented as mean with standard deviations (SD) for continuous variables. Statistical analyses were performed using JMP and SAS statistical software (Cary, NC). Wilcoxon rank-sum test was used for comparisons of continuous variables. X^2 and Fisher's exact tests were used for comparisons of categorical variables. Univariate and multivariate logistic regression analysis was performed to investigate the connection between different dichotomous variables and continuous variables with MSAP. All reported *P* values are 2 sided with a $P < 0.05$ level of significance and odds ratios are presented with 95% confidence intervals. Assessment of the predictive accuracy of potential predictors were assessed by calculation of time specific area under receiver operating characteristic (ROC) curve on day 1 and day 2 of hospital admission.

3. Results

The analysis included 514 consecutive cases of acute pancreatitis directly admitted to Mayo Clinic Rochester from November 2010 to December 2013. Patient clinical characteristics are provided in Table 1. The mean age was 55.5 ± 18.6 years and 51% were male. The mean length of hospital stay (LOS) was 5.2 ± 9.4 days. 26 patients (5%) developed evidence of (peri)pancreatic necrosis. In-hospital mortality was 1% (5 patients died). Two patients died of multi-organ failure from SIRS after 2 and 7 days of admission. Another patient died of a cardiac arrest after 10 days in setting of renal failure. One patient died of septic shock as a result of hospital acquired pneumonia after 70 days of hospitalization. One patient died after a protracted hospital course requiring multiple debridements for infected necrosis with a drug resistant organism after 89 days of hospitalization.

According to the revised Atlanta Classification, 84% of patients were categorized as mild AP, 13% were categorized as MSAP, and 3% were categorized as SAP. 39% of patients demonstrated SIRS during the initial day of hospitalization and 20% of patients demonstrated persistent SIRS at 48 h.

3.1. Predictors to differentiate MSAP from MAP

We examined several laboratory and clinical parameters (age, sex, BMI, WBC, HCT, Cr, BUN, SIRS, WBC) for association with MSAP as several of these have been shown to have predictive value in predicting severity in AP based on prior studies [7–12]. Univariate analysis produced significant association of male sex, age ≥60 years, WBC $\geq 12 \times 10^9$/L on day 1 and day 2, HCT ≥44% on day 1 and day 2, BUN ≥23 mg/dl on day 1 and day 2, and creatinine on day 1 with MSAP. P values, odds ratios with 95% confidence intervals, and area under ROC curves are provided in Table 2.

Table 1
Patient characteristics.

	N (%)
Acute pancreatitis cases	514
Age, mean ± SD, y	55.5 ± 18.6
Women	250 (49)
BMI, mean ± SD	29.0 ± 7.2
Imaging (CT or MRI)	340 (66)
Etiology of pancreatitis	
Gallstones	180 (35)
Alcohol	90 (18)
Idiopathic	87 (17)
Post-ERCP	73 (14)
Hypertriglyceridemia	15 (3)
Pancreatic cancer	15 (3)
Hypercalcemia	6 (1)
Other	48 (9)

Y – years, BMI – body mass index.

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