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Original article

Clinical utility of the Revised Atlanta Classification of acute pancreatitis in a prospective cohort: Have all loose ends been tied?☆

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A B S T R A C T

Background and aim: Revision of the Atlanta classification for acute pancreatitis (AP) was long awaited. The Revised Atlanta Classification has been recently proposed. In this study, we aim to prospectively evaluate and validate the clinical utility of the new definitions.

Patient and methods: 163 consecutive patients with AP were followed till death/6 mths after discharge. AP was categorized as mild (MAP) (no local complication[LC] and organ failure[OF]), moderate (MSAP)(transient OF and/or local/systemic complication but no persistent OF) and severe (SAP) AP (persistent OF). LC included acute peripancreatic fluid collections, pseudocyst, acute necrotic collection, walled-off necrosis, gastric outlet dysfunction, splenic/portal vein thrombosis, and colonic necrosis. Baseline characteristics (age/gender/hematocrit/BUN/SIRS/BISAP) and outcomes (total hospital stay/need for ICU care/ICU days/primary infected (peri)pancreatic necrosis[IN]/in-hospital death) were compared.

Results: 43 (26.4%) patients had ANP, 87 (53.4%) patients had MAP, 58 (35.6%) MSAP and 18 (11.04%) SAP. Among the baseline characteristics, BISAP score was significantly higher in MSAP compared to MAP [1.6 (1.5–2.01) vs 1.2 (1.9–2.4); $p = 0.002$]; and BUN was significantly higher in SAP compared to MSAP[64.9 (50.7–79.1) vs 24.9 (20.7–29.1); $p < 0.0001$]. All outcomes except mortality were significantly higher in MSAP compared to MAP. Need for ICU care (83.3%vs43.1%; $p = 0.01$), total ICU days[7.9 (4.8–10.9) vs 3.5 (2.7–5.1); $p = 0.04$] and mortality (38.9%vs1.7%; $p = 0.0002$) was significantly more in SAP compared to MSAP. 8/18 (44.4%) patients had POF within seven days of disease onset (early OF). This was associated with 37.5% of total in-hospital mortality. Patients with MSAP who had primary IN ($n = 10$) had similar outcomes as SAP.

Conclusions: This study prospectively validates the clinical utility of the Revised Atlanta definitions of AP. However, MSAP patients with primary infected necrosis may behave as SAP. Furthermore, patients with early severe acute pancreatitis (early OF) could represent a subgroup that needs to be dealt with separately in classification systems.

1. Introduction

In spite of generation of robust data from experimental acute pancreatitis (AP), the natural history of clinical AP still eludes complete understanding. The incidence of AP has been increasing globally [1,2]. Even though the overall mortality (5%) has remained stable, a recent meta-analysis has shown that mortality among patients with infected necrosis and persistent organ failure (POF) reaches 43% [2,3]. Therefore, it becomes important to categorize patients with different severity grades in a homogenous manner in order to triage and prognosticate. The Atlanta Classification from 1992 was the first systematic attempt to categorize the severity of

Abbreviations: AP, Acute pancreatitis; POF, persistent organ failure; ULN, upper limit of normal; CP, chronic pancreatitis; CECT, contrast enhanced computed tomography; BMI, body mass index; HCT, hematocrit; BUN, blood urea nitrogen; SIRS, systemic inflammatory response syndrome; BISAP, bedside index of severity of acute pancreatitis; APACHE, acute physiology and chronic health evaluation; ICU, intensive care unit; MAP, mild acute pancreatitis; MSAP, moderately acute severe pancreatitis; SAP, severe acute pancreatitis; APFC, acute pancreatic fluid collection; PP, pancreatic pseudocyst; ANC, acute necrotic collection; WON, walled-off necrosis; IN, infected necrosis; CI, confidence interval; PN, pancreatic necrosis; EXPN, extrapanceatic necrosis; PCD, percutaneous drainage.

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AP [4]. Even though the Atlanta classification was widely practiced initially at research and clinical levels, it became evident that several issues were not addressed optimally [5]. Eventually it turned out that the nomenclatures proposed in the classification were not followed uniformly; and several new terminologies (eg. organized necrosis) came up with advances in technology and better understanding of the pathophysiology [6,7]. These discrepancies demanded a revision of the Atlanta Classification.

The endeavor to revise the classification began in 2007, and has been recently published after revisions and modifications [8]. The revised classification incorporated modern concepts of the disease, addressed areas of confusion, and provided more homogeneous definitions of complications (local and systemic) that would enable improvement in clinical evaluation, data reporting in a standardized manner and assist evaluation of new treatment. The classification was based on a web based consultation process with members of 11 national and international pancreatic societies. Responses of the members were incorporated in the revisions of the document and the process was repeated until the fourth version was finally published. Prior to publication of the final version, the methodology was published in the Pancreas Club website and radiological aspects were also published by different authors [9–11]. The inclusion of the moderately severe AP (MSAP) category was made at the time of the fourth revision. Since the Revised Atlanta Classification was generated through a web based consultation process, its validity in clinical practice needs to be prospectively evaluated in different populations.

In this study we evaluate the clinical utility of the definitions proposed in the Revised Atlanta Classification in a prospectively followed cohort.

2. Patients and methods

This study was conducted at two academic hospitals in southern and northeastern India. Institutional review board approvals were obtained prior to the study and informed consent was taken from the patients/relatives (whenever the patient was unable to consent). Consecutive directly admitted patients over 18yrs with a primary diagnosis of first episode of AP were enrolled from August 2011 to October 2012, and prospectively followed for at least six months after discharge or till death, whichever was earlier. Diagnosis of AP was made if the patient fulfilled two of the following criteria: a) abdominal pain characteristic of AP; b) serum amylase/lipase values of more than three times the upper limit of normal (ULN); and c) imaging evidence of AP. Exclusion criteria were: a) recurrent AP; and b) patient who did not get a CT scan. AP was defined as interstitial and necrotizing based on CECT appearance, as per the Revised Atlanta definitions. Interstitial AP was considered when there was a relatively homogenous enhancement by intravenous contrast agent and peripancreatic tissue showed some inflammatory changes or haziness and mild stranding. Necrotizing AP was considered when there was lack of enhancement of pancreatic parenchyma and/or heterogeneous and non-liquid density of varying degrees in different locations (intra- and/or extrapancreatic) with or without a well-defined encapsulating wall. One radiologist each, who was not aware of the clinical status read CT scans in the two study centers.

For all the enrolled patients, the following parameters were recorded at admission in an electronic database: duration of symptoms, age, gender, body mass index (BMI), hematocrit (HCT), serum creatinine, blood urea nitrogen (BUN), systemic inflammatory response syndrome (SIRS), bedside index of severity of acute pancreatitis (BISAP) score, and APACHE II score. Patients received 175–200 ml/h of normal saline after diagnosis and initial clinical evaluation. Once the initial blood reports were available, the fluid volume was titrated based on the hematocrit and was monitored based on urine output. Besides this, patients were given analgesics as required; and early oral/enteral nutrition was attempted as per the clinical condition. All major events during hospitalization and follow-up period, including development of organ failure (transient and persistent), development of infections (urinary tract infection, pneumonia, infected (peri)pancreatic necrosis[IN] and sepsis), development of pleural effusion and ascites, development of venous thrombosis and arterial pseudoaneurysms, and development of gastric outlet dysfunctions and colonic necrosis were recorded. Outcomes that were studied included: total hospital stay, need for care in the intensive care unit (ICU), total days in the ICU, development of primary infected necrosis (IN), need for organ failure specific interventions (radiological, endoscopic or surgical drainage/necrosectomy) and in-hospital mortality. Patients were categorized into mild, moderately severe and severe AP as defined in the Revised Atlanta Classification, after these were published in 2013. Definitions of the different severity categories were: a) mild AP (MAP): AP without organ failure, local and systemic complications, b) moderately severe AP (MSAP): AP with OF that resolved within 48 h (transient OF) and/or local or systemic complications without persistent OF, and c) severe AP (SAP): AP with persistent OF (OF>48 h). LCs, as defined according the revised Atlanta definitions, included acute peripancreatic fluid collection (APFC), pancreatic pseudocyst (PP), acute necrotic collection (ANC), walled-off necrosis (WON), gastric outlet dysfunction, splenic and portal vein thrombosis, and colonic necrosis. Systemic complications included worsening of pre-existing coronary artery disease and chronic lung disease.

Organ dysfunction was evaluated according to the Modified Marshall scoring system [12]. Organ failure was defined as the presence of a score of 2 or more in any one system (respiratory, renal and cardiovascular). SIRS was considered to be present if two or more of the following were present: heart rate $\geq$ 90/min; respiratory rate $\geq$ 20/min; temperature <36° or >38 °C; and total leucocyte count of <4000/mm^3 or >12,000/mm^3. BISAP [13] was defined as BUN > 20 mg/dL, impaired mental status (Glasgow coma score <15), SIRS $\geq$ 2, age > 60 yrs and pleural effusion; and a score of 1 was given to each of the above. The APACHE II score was calculated with an automated online calculator.

Primary IN was defined as bacterial and/or fungal infections of necrotic pancreatic parenchyma or peripancreatic collections that developed prior to any radiological and/or surgical and/or endoscopic interventions [14]. Presence of primary IN was suspected if the patients with local complications had continuous fever and persistent leukocytosis beyond 2 weeks of onset and was generally not doing well despite appropriate aggressive management. Confirmation was done by the computed tomographic (CT) evidence of free air within the necrotic tissue or peripancreatic collections. Microbiological confirmation was made by culture of samples obtained during interventions for the LCs (radiological/endoscopic/surgical) drainage.

3. Statistical analysis

A database was generated in Excel for Mac 2011 (Version 14.2.3) and all statistical analyses were conducted in the JMP statistical software (Version 9; Cary NC). Continuous variables are presented as mean (95% confidence interval [CI]) while categorical variables are presented as percentage. Continuous data were tested for normal distribution prior to statistical analysis (Goodness-to-fit test) and were compared using the Student's '*t*' test. For categorical variables, a 2 × 2 contingency table was constructed, and the χ [2] test (with Yates correction if indicated), or the Fisher's exact test,

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