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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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ABSTRACT

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) score, 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 local complication 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,

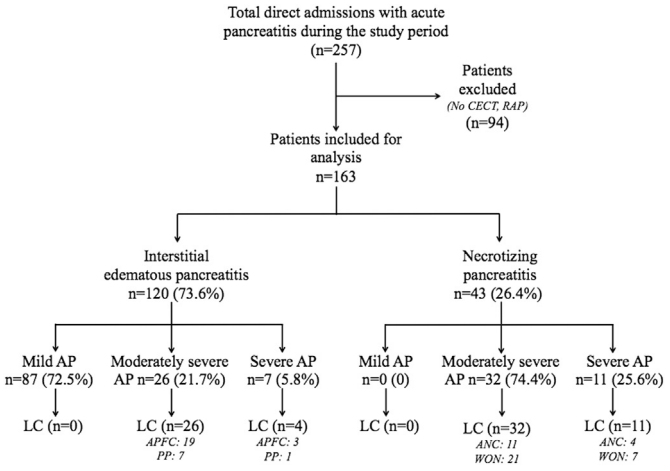

Fig. 1. Distribution of different categories of acute pancreatitis and local complications among the study subjects.

whichever was appropriate, was applied for comparisons. A 2-tailed '*p*' value of ≤0.05 was considered statistically significant.

4. Results

4.1. Patient characteristics

There were a total of 257 patients with acute pancreatitis directly admitted during the study period; out of which 94 were excluded, and data of 163 patients were analyzed. The clinical characteristics were similar for the patients from both study centers (Data not shown).

Fig. 1 shows the distribution of the patients with different disease categories and the associated local complications. 120 (73.6%) patients had interstitial AP while 43 (26.4%) necrotizing AP. Overall, 87 (53.4%) had MAP, 58 (35.6%) had MSAP and 18 (11.04%) had SAP. Seven patients with interstitial pancreatitis in this study had persistent single or multiorgan failure and were classified as having SAP. Categorization into MAP, MSAP and SAP could be completed in most patients by the end of 2 weeks, and in all patients by 3 weeks.

Table 1 shows the comparison of the baseline characteristics at the time of admission between the three groups of severity. Compared to MAP, patients with MSAP had a significantly higher mean (95% CI) BISAP score [1.2 (0.9–1.4) vs 1.6 (1.5–2.01); $p = 0.002$] at the time of admission; while hematocrit, BUN, serum creatinine, SIRS score and APACHE II scores were similar in both groups. When patients with SAP were compared with those with MSAP, mean (95% CI) BUN, serum creatinine and APACHE II scores were significantly higher in patients with SAP [64.9 (50.7–79.1) vs 24.9 (20.7–29.1), $p < 0.0001$; 3.5 (2.8–4.2) vs 0.9 (0.8–1.1), $p < 0.0001$ and 10.0 (7.2–12.7) vs 4.3 (3.1–5.5), $p = 0.001$ respectively].

The most common etiology was alcohol, which was seen in 66 (40.5%) patients, followed by gall-stones in 47 (28.8%) patients and drugs in 7 (4.3%) patients. Sodium valproate and azathioprine were the most common drugs responsible. Other etiologies included post-ERCP pancreatitis in 5 (3.1%) and pancreatic ascariasis in 1 (0.6%). An etiology could not be found in 37 (22.7%) patients.

4.2. Overall complications and outcomes

Fig. 1 shows the distribution of LCs among the different category of patients. Among the patients with ANP, the distribution of the type of necrosis in those with MSAP was pancreatic necrosis (PN) alone in 3, pancreatic with extrapancreatic (PN + EXPN) in 24 and only extrapancreatic (EXPN) in 5 patients; while in those with SAP it was PN in 2, and PN + EXPN in 9. The distribution of local complications as per Revised Atlanta definitions were: pancreatic and peripancreatic collections in 73 patients, splenic vein thrombosis in 9 and portal vein thrombosis in 3. No patients developed gastric outlet dysfunction and colonic necrosis. Other complications (that were not defined in the Revised Atlanta Classification) included significant pleural effusion in 5 patients, significant ascites in 7, splenic artery pseudoaneurysm in 2, and pancreatic ductal leak in 3 patients.

As shown in Fig. 1 and 22 patients (19 MSAP and 3 SAP) had APFC, 8 (7 MSAP and 1 SAP) had PP, 15 (11 MSAP and 4 SAP) had ANC and 28 (21 MSAP and 7 SAP) had WON. Among patients with (peri)pancreatic collections, 13 (11 MSAP and 2 SAP) required percutaneous drain (PCD), 11 (7 MSAP and 4 SAP) endoscopic drainage and 5 (4 MSAP and 1 SAP) required surgery (3 underwent previous PCD).

A total of 24 patients had OF, of which persistent OF was seen in 18 patients. Of these 18 patients 9 had MOF. Renal failure was seen in 11 patients, circulatory failure in 9 and respiratory failure in 5.

We also looked at the timing of development of POF and associated mortality (Fig. 2). Out of the 18 patients with SAP, 8 developed POF within the first week of AP. Three out of these 8 (37.5%) patients died after a mean (95% CI) of 3 (1.3–7.3) days after admission. Of the 10 patients who developed POF after 7 days, four (40%) died after a mean (95% CI) of 21.5 (14.4–28.6) days after admission.

Overall, eight patients (1 with MSAP and 7 with SAP) died in the hospital. The cause of death in the patients with POF within 7 days was MOF, while that for the patients with POF after 7 days were primary IN/sepsis with MOF in 4. The patient with MSAP who died had pre-existing coronary artery disease.

Table 1
Patient characteristics among different categories.

Characteristics at admission	Mild acute pancreatitis (MAP) ($n = 87$)	Moderately severe acute pancreatitis (MSAP) ($n = 58$)	Severe acute pancreatitis (SAP) ($n = 18$)
Duration of symptoms in hrs (mean; 95% CI)	18.7 (12.4–24.9)	20.9 (14.2–27.6)	12.1 (4.12–24.8)
Age in yrs. (mean; 95% CI)	40.6 (37.6–43.7)	35.7 (31.9–39.5)	45.5 (38.7–52.3)$^{\#}$
Male (*n*; %)	62 (71.3)	48 (82.6)	13 (72.2)
Hematocrit (mean; 95% CI)	38.8 (37.1–40.6)	38.1 (36.1–40.04)	38.7 (35.3–42)
BUN (mean; 95% CI)	20.3 (16.6–23.9)	24.9 (20.7–29.1)	64.9 (50.7–79.1)$^{\#\#}$
Serum creatinine (mean; 95% CI)	1.03 (0.9–1.1)	0.9 (0.8–1.1)	3.5 (2.8–4.2)$^{\#\#\#}$
SIRS score (mean; 95% CI)	2.1 (1.9–2.4)	2.3 (2.1–2.6)	2.3 (1.8–2.8)
BISAP score (mean; 95% CI)	1.2 (0.9–1.4)	1.6 (1.5–2.01)*	2.3 (1.8–2.8)
APACHE II score (mean; 95% CI)	3.9 (1.7–5.7)	4.3 (3.1–5.5)	10.0 (7.2–12.7)$^{\#\#\#\#}$

* indicates '*p*' value of 0.002, when compared with MAP.
$^{\#,\#\#,\#\#\#}$ and $^{\#\#\#\#}$ indicates '*p*' values of 0.022, <0.0001, <0.0001 and 0.001 respectively, when compared with MSAP.

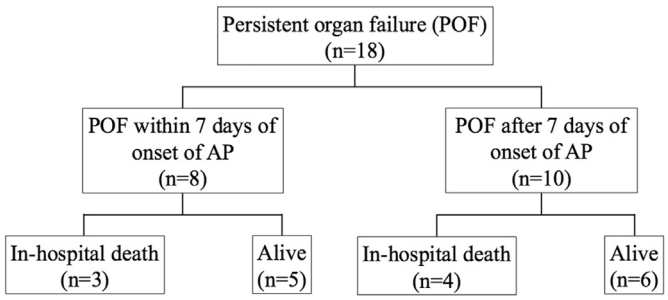

Fig. 2. Timing of persistent organ failure and associated mortality among patients with severe acute pancreatitis.

4.3. Comparison of outcomes between patients with MAP, MSAP and SAP

Table 2 shows the comparison of outcomes between patients in the three groups. Comparison of MSAP with MAP showed all study outcomes except mortality to be significantly higher in MSAP. 25 (43.1%) and 22 (37.9%) patients in the MSAP group required ICU care and LC specific interventions compared to 4 (4.6%) and 0 (0%) in MAP respectively. Indications of ICU care in MAP patients were pneumonia in 3 and sepsis in 1.

Comparison of SAP with MSAP showed that need for ICU care, days in ICU and in-hospital mortality were significantly higher in patients with SAP [15 (83.3%) vs 25 (45.5%), $p = 0.011$; 7.9 (4.8–10.9), vs 3.5 (2.7–5.1), $p = 0.041$ and 7 (38.9%) vs 1 (1.8%), $p = 0.0002$ respectively].

4.4. Distribution of infections among MAP, MSAP and SAP

In this study we looked for primary infected necrosis and extrapancreatic infections (pneumonia, UTI and sepsis). A total of 29 (17.8%) patients had infections. The distribution of infection among the different severity groups was: 5 (5.7%) in MAP, 15 (25.9%) in MSAP and 9 (50%) is SAP. A total of 13 (7.9%) patients had primary infected necrosis, 13 (7.9%) had pneumonia, 6 (3.7%) had UTI and 10 (6.1%) had sepsis. Primary infected necrosis was diagnosed after a mean (95%CI) of 15.6 (12.7–18.4) days.

As shown in Table 3, a significantly higher proportion of patients with MSAP and SAP had infections compared to MAP [15 (25.9%) vs 5 (5.7%); $p = 0.0009$)] and MSAP [9 (50%) vs 15 (25.9%); $p = 0.05$] respectively. The proportions of patients with infected necrosis were similar between MSAP and SAP [10 (17.2%) vs 3 (16.7%); $p = 1.0$]; while sepsis was seen in a significantly higher proportion of patients with SAP compared to MSAP [7 (38.9%) vs 2 (3.4%); $p = 0.002$]. The frequencies of pneumonia and UTI were similar in the three groups.

4.5. Comparison of outcomes between MSAP patients having primary IN and SAP

Ten (17.2%) patients with MSAP had IN. As shown in Table 4, all study outcomes including mortality among patients with MSAP who had primary IN were similar to those with SAP. Six patients with MSAP and primary IN required ICU care. The reasons for ICU admissions in these patients were: sepsis with transient renal failure ($n = 3$), and pneumonia ($n = 3$). The three patients with pneumonia did not have respiratory failure as defined by the Modified Marshall Scoring System.

5. Discussion

In this study we prospectively validated the clinical utility of the Revised Atlanta Classification. Severity of AP could be classified into three discrete categories (mild, moderate and severe) using the new definitions of the local complications. 87 (53.4%) patients had MAP, 58 (35.6%) had MSAP while 18 (11.04%) had SAP. We identified two subgroups of patients that need to be evaluated more elaborately in the context of the Revised Atlanta Classification. Firstly, patients who develop MOF within the first week of disease onset run a fulminant course with high mortality (37.5%). Secondly, patients having MSAP with primary IN may behave like SAP even in the absence of POF.

In view of the caveats in the Atlanta Classification from 1992, a revision of the definitions was long anticipated. The process of revision was initiated in 2007 and published as the Revised Atlanta Classification online in November 2012 and print version in early 2013 [8]. A major highlight of the revised classification is the CECT based definitions of pancreatic and peripancreatic collections, that distinguish between collections that contain only fluid content (APFC and PP) and those that contain a solid (necrotic) component with or without a fluid component (ANC and WON). APFCs are associated with interstitial edematous pancreatitis and often resolve spontaneously without intervention, with a small proportion that persists as PP. ANC and WON are associated with necrotizing pancreatitis and are prone to develop complications that may necessitate major interventions. PP and WON were categorized under the same category in the original Atlanta classification [4]; and most of fluid collections that were earlier treated as pancreatic pseudocysts were actually walled off necrosis. Furthermore, as opposed to the original Atlanta classification the Revised Atlanta Classification has categorized necrotizing pancreatitis into pancreatic, peripancreatic and both; and organ failure into transient (<48 h) and persistent (>48 h). Studies have shown that the outcomes for peripancreatic and pancreatic necrosis are different [15]; and patients with transient organ failure fares better than those with persistent organ failure [16]. Evaluation of AP in the context of these definitions can guide clinicians to monitor, triage and plan the best possible management strategy in an individualized manner.

Table 2
Difference in outcomes between MAP, MSAP and SAP.

Study outcomes	Mild acute pancreatitis (MAP) ($n = 87$)	Moderately severe acute pancreatitis (MSAP) ($n = 58$)	Severe acute pancreatitis (SAP) ($n = 18$)
Total hospital stay in days (mean; 95% CI)	6.7 (4.9–8.4)	10.6 (8.9–12.3)*	15.1 (10.7–19.5)
Need for ICU care (n; %)	4 (4.6)	25 (43.1)**	15 (83.3)#
Days in ICU (mean; 95% CI)	1.2 (0.9–3.4)	3.5 (2.7–5.1)***	7.9 (4.8–10.9)##
Need for LC specific interventions (n; %)	0 (0)	22 (37.9)****	6 (33.3)
In–hospital mortality (n; %)	0 (0)	1 (1.7)	7 (38.9)###

*, **, *** and **** indicates 'p' values of 0.0004, <0.0001, 0.0002 and 0.003 respectively when compared to MAP.
#,## and ### indicates 'p' values of 0.011, 0.041 and 0.0002 when compared to MSAP.

Table 3
Distribution of infections among different categories.

	Mild acute pancreatitis (MAP) ($n = 87$)	Moderately severe acute pancreatitis (MSAP) ($n = 58$)	Severe acute pancreatitis (SAP) ($n = 18$)
Overall infection (n; %)	5 (5.7)	15 (25.9)*	9 (50)#
Primary infected necrosis (n; %)	0 (0)	10 (17.2)**	3 (16.7)
Pneumonia (n; %)	3 (3.4)	7 (12.1)	3 (16.7)
Urinary tract infection (n; %)	2 (2.3)	2 (3.4)	2 (11.1)
Sepsis (n; %)	1 (1.1)	2 (3.4)	7 (38.9)##

* and ** indicates 'p' values of 0.0009 and 0.0002 respectively, when compared with MAP.
# and ## indicates 'p' values of 0.05 and 0.002 respectively, when compared with MSAP.

In the current study, the proportions of these collections were: APFC 22 (13.5%); PP 8 (4.9%); ANC 15 (9.2%) and WON 28 (17.2%) (Fig. 1). When classified according to the revised definitions, the frequency of PP was low, an observation also made in a recent retrospective study that compared the Revised Atlanta Classification with the recently described Determinant Based Classification [17]. In the absence of necrosis, majority of APFC eventually resolved and a small proportion persisted beyond 4 weeks and developed a well-defined surrounding wall to become PPs. On the other hand, (peri)pancreatic necrosis underwent liquefaction to form ANC (pancreatic, extrapancreatic and both), majority of which persisted beyond 4wks and developed a well-defined wall to become WONs. In the current study, 28/43 (65.1%) of ANCs persisted to become WONs.

The other major change in the revised classification was assessment of OF using the Modified Marshall score, which includes systolic blood pressure, serum creatinine value and PaO_2/FiO_2 [12]. Even though this system would facilitate uniform evaluation of OF, it would require testing for blood gases, which is usually not performed in every patient in routine clinical practice, more so at the community level. This could run the risk of underestimating early organ dysfunction. However, in the current study, since the patients were evaluated under a prospective study setting, we had a lower threshold for ordering arterial blood gas (ABG) analysis; therefore it was unlikely that we have missed any patients with respiratory dysfunction/failure.

Another development in the revised classification was the inclusion of a new category of AP, namely MSAP, which is characterized by presence of transient OF and/or LCs and/or systemic complications. The heterogeneity in the previously defined group of SAP led several workers to observe that a subgroup of SAP patients with only LCs (necrosis and local complications in the absence of POF) had high morbidity but low mortality (unlike in patients with OF). This new subgroup was formally proposed by Vege et al. in a study involving 207 patients, and was subsequently validated in further studies [18–21]. Gastric outlet dysfunction, splenic and portal vein thrombosis, and colonic perforations were also included as LCs in the Revised Atlanta Classification. The original and validation studies of MSAP looked primarily at differences in the outcomes between the MSAP and SAP groups; but did not explore into other complications like presence of infected necrosis and hospital acquired infections, which are known to impact outcomes [22]. In the current study, we defined LCs according to the revised classification; and also evaluated outcomes of the subgroup of patients with MSAP having IN separately and compared with patients having SAP. Even though broadly the patients could be classified into the three discrete categories, patients with MSAP who had IN had similar outcomes as those with SAP (Table 4). We also evaluated outcomes of patients who developed POF within the first seven days of AP. Mortality was high in this group of patients. Earlier studies had described this group as early severe acute pancreatitis (ESAP), which contributed to around one third of patients and was responsible for 42–44% of overall mortality [23,24]. In the current study, 37.5% of mortality was due to early persistent organ failure or ESAP.

Table 4
Difference in outcomes between MSAP with primary IN and SAP.

Study outcomes	Moderately severe acute pancreatitis (MSAP) with primary IN ($n = 10$)	Severe acute pancreatitis (SAP) ($n = 18$)	'p' value
Total hospital stay in days (mean; 95% CI)	14 (4.3–23.7)	15.1 (10.7–19.5)	0.84
Need for ICU care (n; %)	6 (60)	15 (83.3)	0.63
Days in ICU (mean; 95% CI)	3.5 (1.2–12.1)	7.9 (4.8–10.9)	0.35
Need for LC specific interventions (n; %)	5 (50)	6 (33.3)	0.39
In–hospital mortality (n; %)	1 (10)	7 (38.9)	0.11

Two recent studies, one retrospective [17] and the other prospective [25], have compared the Revised Atlanta Classification with the Determinant based (four-tier) classification of severity of AP; and both systems were found to reflect clinical outcomes with similar accuracy. The Determinant based classification contains a fourth category called critical AP (CAP) which is characterized by presence of IN with POF. This group is associated with a very high mortality (43%), compared to patients with organ failure and infected pancreatic necrosis alone (30% and 32% respectively) [26]. In the above-mentioned retrospective study, 3 (0.6%) patients had CAP while in the prospective study 17 (6.6%) had CAP. In the current study 3 (1.8%) patients had CAP, of which two died in-hospital. We opted not to compare CAP as a separate group in our study in view of the small sample size. The main outcomes of patients in the different severity groups in the present study was similar to that observed in the mild, moderately severe and severe categories in the prospective study by Nawaz H et al. [25].

The strengths of this study were prospective data collection from more than one center; inclusion of consecutive directly admitted patients with first episode of AP; exclusion of patients who did not have a CT scan done and patients with RAP. In the recent prospective validation study, 15% of the patients did not have CECT done, which increased the probability of missing local complications. We opted to exclude patients with RAP because many of these patients (especially those associated with alcohol) have underlying chronic pancreatitis. This could have skewed our observations. We also studied the prevalence of early POF (ESAP); and infection with associated outcomes (especially in the MSAP group). These two variables were not evaluated in the earlier and recent validation studies [17,19–21,25]. Our study had limitations too. Firstly, blood gases were not performed in patients who did not appear too sick and showed persistent improvement. However, the threshold for ordering blood gas analysis was low, therefore it was unlikely that patients with respiratory dysfunction/failure were missed. Secondly, the number of patients with infected necrosis ($n = 13$) and SAP ($n = 18$) were low. Thirdly, the number of MSAP with primary IN (whose outcomes were similar to those with SAP) was low ($n = 10$). A higher number could have reinforced our observations. Nevertheless, our data has identified a subgroup of patients that could potentially introduce heterogeneity to the MSAP category.

In conclusion, in this study we have prospectively validated the clinical utility of the Revised Atlanta Classification of AP. There appears to be some heterogeneity in the MSAP category that warrants further elaborate examination. Furthermore, patients with

ESAP could represent a subgroup that possibly needs to be dealt with separately in classification systems.

Conflict of interest

None.

Contribution of authors

Rupjyoti Talukdar conceived, designed and overlooked the study, analyzed the data, and drafted the manuscript.

Abhik Bhattacharyya and Bhavana Rao recorded patient data and followed up the patients in the study center in South India.

Mithun Sharma recorded patient data and followed up the patients in the study center in Northeast India.

D Nageshwar Reddy reviewed the manuscript and provided intellectual inputs.

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References

[1] Yadav D, Lowenfels AB. Trends in the epidemiology of the first attack of acute pancreatitis: a systematic review. Pancreas 2006;28:931–41.
[2] Talukdar R, Vege SS. Recent developments in acute pancreatitis. Clin Gastroenterol Hepatol 2009;7:S3–9.
[3] Petrov MS, Shanbhag S, Chakravarty M, Phillips AR, Windsor JA. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology 2010;139:813–20.
[4] Bradley 3rd EL. A clinically based classification system for acute pancreatitis: summary of the International Symposium on Acute Pancreatitis, Atlanta, GA September 11–13, 1992. Arch Surg 1993;128:586–90.
[5] Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006;101:2379–400.
[6] Bollen TL, Besselink MG, van Santvoort HC, Gooszen HG, van Leeuwen MS. Towards an update of the Atlanta Classification on Acute pancreatitis. Pancreas 2007;35:107–13.
[7] Bollen TL, van Santvoort HC, Besselink MG, van Leeuwen MS, Horvath KD, Freeny PC, et al. The Atlanta Classification of acute pancreatitis revisited. Br J Surg 2008;95:6–21.
[8] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11.
[9] Acute Pancreatitis Classification Working Group. Revision of the Atlanta classification of acute pancreatitis; 2008. http://www.pancreasclub.com/resources/AtlantaClassification.pdf.
[10] Sheu Y, Furlan A, Almusa O, Papachristou G, Bae KT. The Revised Atlanta Classification for acute pancreatitis: a CT imaging guide for radiologists. Emerg Radiol 2012;19:37–43.
[11] Thoeni RF. The Revised Atlanta Classification of acute pancreatitis: its importance for the radiologist and its effect on treatment. Radiology 2012;262:751–64.
[12] Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Crit Care Med 1995;23:1638–52.
[13] Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population-based study. Gut 2008;57:1698–703.
[14] Talukdar R, Nechutova H, Clemens M, Vege SS. Could rising in BUN predict future development of infected pancreatic necrosis? Pancreatology 2013;13:355–9.
[15] Bakker OJ, van Santvoort H, Besselink MG, Boermeester MA, van Eijck C, Dejong K, et al. Extrapancreatic necrosis without pancreatic parenchymal necrosis: a separate entity in necrotising pancreatitis? Gut 2013;62:1475–80.
[16] Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut 2004;53:1340–4.
[17] Acevedo-Piedra NG, Moya-Hoyo N, Rey-Riveiro M, Gil S, Sempere L, Martínez J, et al. Validation of the determinant-based classification and revision of the Atlanta classification systems for acute pancreatitis. Clin Gastroenterol Hepatol 2014;12:311–6.
[18] Vege SS, Gardner TB, Chari ST, Pearson RK, Clain JE, Petersen BT, et al. Low mortality and high morbidity in severe acute pancreatitis without organ failure: case for revising the Atlanta Classification to include ‘‘moderately severe acute pancreatitis.’’. Am J Gastroenterol 2009;104:710–5.
[19] Talukdar R, Clemens M, Vege SS. Moderately severe acute pancreatitis: prospective validation of this new subgroup of acute pancreatitis. Pancreas 2012;41:306–9.
[20] de-Madaria E, Soler-Sala G, Lopez-Font I, Zapater P, Martínez J, Gómez-Escolar L, et al. Pancreatology 2010;10:613–9.
[21] Thandassery RB, Yadav TD, Dutta U, Appasani S, Singh K, Kochhar R. Prospective validation of 4-category classification of acute pancreatitis severity. Pancreas 2013;42:392–6.
[22] Wu BU, Johannes RS, Kurtz S, Banks PA. The impact of hospital-acquired infection on outcome in acute pancreatitis. Gastroenterology 2008;135:816–20.
[23] Sharma M, Banerjee D, Garg PK. Characterization of newer subgroups of fulminant and subfulminant pancreatitis associated with a high early mortality. Am J Gastroenterol 2007;102:2688–95.
[24] Isenmann R, Rau B, Beger HG. Early severe acute pancreatitis: characteristics of a new subgroup. Pancreas 2001;22:274–8.
[25] Nawaz H, Mouzner R, Yadav D, Yabes JG, Slivka A, Whitcomb DC, et al. Revised Atlanta and determinant-based classification: application in a prospective cohort of acute pancreatitis patients. Am J Gastroenterol 2014;108:1911–7.
[26] Dellinger EP, Forsmark CE, Layer P, Lévy P, Maraví-Poma E, Petrov MS, et al. Determinant-based classification of acute pancreatitis severity: an international multidisciplinary consultation. Ann Surg 2012;256:875–80.