

Validation of the Determinant-based Classification and Revision of the Atlanta Classification Systems for Acute Pancreatitis

Nelly G. Acevedo–Piedra,* Neftalí Moya–Hoyo,* Mónica Rey–Riveiro,* Santiago Gil,†
 Laura Sempere,* Juan Martínez,* Félix Lluís,* José Sánchez–Payá,§ and Enrique de–Madaria*

*Unidad de Patología Pancreática, †Servicio de Radiología, and §Servicio de Medicina Preventiva, Hospital General Universitario de Alicante, Alicante, Spain

BACKGROUND & AIMS: Two new classification systems for the severity of acute pancreatitis (AP) have been proposed, the determinant-based classification (DBC) and a revision of the Atlanta classification (RAC). Our aim was to validate and compare these classification systems.

METHODS: We analyzed data from adult patients with AP (543 episodes of AP in 459 patients) who were admitted to Hospital General Universitario de Alicante from December 2007 to February 2013. Imaging results were reviewed, and the classification systems were validated and compared in terms of outcomes.

RESULTS: Pancreatic necrosis was present in 66 of the patients (12%), peripancreatic necrosis in 109 (20%), walled-off necrosis in 61 (11%), acute peripancreatic fluid collections in 98 (18%), and pseudocysts in 19 (4%). Transient and persistent organ failures were present in 31 patients (6%) and 21 patients (4%), respectively. Sixteen patients (3%) died. On the basis of the DBC, 386 (71%), 131 (24%), 23 (4%), and 3 (0.6%) patients were determined to have mild, moderate, severe, or critical AP, respectively. On the basis of the RAC, 363 patients (67%), 160 patients (30%), and 20 patients (4%) were determined to have mild, moderately severe, or severe AP, respectively. The different categories of severity for each classification system were associated with statistically significant and clinically relevant differences in length of hospital stay, need for admission to the intensive care unit, nutritional support, invasive treatment, and in-hospital mortality. In comparing similar categories between the classification systems, no significant differences were found.

CONCLUSION: The DBC and the RAC accurately classify the severity of AP in subgroups of patients.

Keywords: Pancreas; Inflammation; Management; Infection.

See editorial on page 317.

Acute pancreatitis (AP) is a heterogeneous disease, ranging from mild cases to patients with high morbidity or even mortality. To describe the complications and course of AP, definitions are needed regarding local and systemic complications as well as a general description of the severity of the disease. Without a widely accepted standardized classification, comparative studies and clinical investigation are not possible between different centers. The Marseille classification^{1,2} and the Cambridge classification³ were early attempts to describe AP, but confusion regarding definitions in AP continued until the Atlanta classification. In 1992 an international symposium was held in Atlanta. Forty multidisciplinary internationally recognized experts in AP proposed a clinically based (opposed to previous morphology based) classification.⁴ Definitions were given regarding local (acute fluid collection, pancreatic

necrosis, acute pseudocyst, pancreatic abscess) and systemic (shock, pulmonary insufficiency, renal failure, and gastrointestinal bleeding) complications.⁴ Two categories of severity (mild and severe) were given (Table 1). The Atlanta classification was widely accepted, and in fact, the original publication is the most cited classic article in pancreatology.⁵

In the last decade, several authors have suggested the need for a revision of the Atlanta classification (RAC).^{6–11} New concepts in local complications have been described (peripancreatic fat necrosis,^{12–14} collections associated with pancreatic or peripancreatic necrosis^{15,16}). The nature and subtypes of organ failure

Abbreviations used in this paper: AP, acute pancreatitis; DBC, determinant-based classification; ICU, intensive care unit; RAC, revision of the Atlanta classification.

Table 1. Atlanta Classification, DBC, and RAC

Classification	Categories	Definition
Atlanta classification	Mild	No organ failure and no local complications
	Severe	Organ failure and/or local complications (pancreatic necrosis, abscess, or pseudocyst)
DBC	Mild	No (peri)pancreatic necrosis and no organ failure
	Moderate	Sterile (peri)pancreatic necrosis and/or transient organ failure
	Severe	Infected (peri)pancreatic necrosis or persistent organ failure
RAC	Critical	Infected (peri)pancreatic necrosis and persistent organ failure
	Mild	No organ failure and no local ^a /systemic complications ^b
	Moderately severe	Transient organ failure and/or local/systemic complications without persistent organ failure
	Severe	Persistent organ failure (single or multiple)

(Peri)pancreatic: peripancreatic fat necrosis and/or pancreatic necrosis; persistent organ failure: >48 h; transient organ failure: <48 h.

^aLocal complications: peripancreatic fluid collections, pancreatic and peripancreatic necrosis, pseudocyst, and walled-off necrosis.

^bSystemic complications without persistent organ failure: exacerbation of preexisting comorbidity, such as coronary artery disease or chronic lung disease, precipitated by AP.

have been better described because transient (<48 hours) and single (1 organ) organ failure have a much better prognosis than persistent (>48 hours)^{11,17,18} or multiple organ failure.^{9,11,19} Furthermore, the Atlanta classification system did not use a validated classification of organ failure. Mortality seems extremely high in the subgroup of patients associating organ failure and infected pancreatic necrosis.^{20–23} Finally, it has been suggested that 2 categories of severity (mild and severe) may be inaccurate in describing subgroups of patients with different outcomes.^{9,11,23} After 20 years from the Atlanta symposium, 2 new classifications have been very recently published, the determinant-based classification (DBC)²⁴ and the RAC²⁵ (Table 1). Severity in DBC is stratified in 4 categories according to the presence or not of (1) pancreatic/peripancreatic necrosis, (2) infection of pancreatic/peripancreatic necrosis, and (3) transient/persistent organ failure (Table 1). RAC defines 3 categories according to (1) local and/or systemic complications and (2) transient/persistent organ failure (Table 1). These systems are based on published data but also on expert opinion to combine current knowledge and generate the different severity categories. Many publications come from referral centers, so referral biases are frequent (more severe cases, a higher proportion of late complications). Thus a validation of these classifications is needed to verify that (1) the different categories describe different subgroups of patients and (2) the new systems give more accurate information than the former Atlanta classification. Our aim was to validate and compare those classifications in a non-referral consecutive cohort of patients with AP.

Methods

A post hoc analysis of a prospective cohort of patients (fluid therapy database²⁶) was undertaken. The study was approved by the ethics committee of our center. The original purpose of the study was to investigate the relationship between fluid therapy and outcome.

Consecutive adult (≥ 18 years) patients with AP admitted in our center between December 2007 and February 2013 were included. This period corresponded to the episodes of AP available for analysis at the time we decided to perform the study and was not based on sample size calculation. Diagnosis of AP was defined by at least 2 of the following criteria: (1) amylase level increase up to 3 times higher than the upper limit of normal, (2) abdominal pain, and (3) imaging compatible with AP. We excluded from analysis patients with chronic pancreatitis diagnosed during hospital admission. Epidemiologic, clinical, and outcome variables were prospectively collected. An expert radiologist (S.G.) who was blinded for clinical outcomes retrospectively reviewed imaging (mainly computed tomography scans; magnetic resonance imaging is scarcely used in our center to study local complications) to describe the new local complications defined in both classifications. The radiologist had data about timing between imaging and presentation of disease to allow a correct classification of local complications (acute collections versus pseudocysts, acute necrotic collections versus walled-off pancreatic necrosis). Eighteen patients had peripancreatic acute fluid collections ($n = 11$) or acute necrotic collections ($n = 7$) but did not have follow-up imaging after 4 weeks of admission, so it was not possible to ascertain whether pseudocyst or walled-off necrosis was present (missing data). Thus, in the 1993 Atlanta classification 11 patients were not possible to classify as mild or severe. To avoid unnecessary radiation exposure,²⁷ only patients with predicted severe AP (Acute Physiology and Chronic Health Evaluation II score ≥ 8 , C-reactive protein ≥ 150 mg/L at 48–72 hours, bedside index of severity in acute pancreatitis ≥ 3 , presence of persistent systemic inflammatory response syndrome), or with clinical suspicion of local complications underwent computed tomography scan. Patients without criteria for cross-sectional imaging and mild course of disease were considered as not having local complications. We investigated the clinical outcome according to the different categories of Atlanta classification, DBC and RAC. Outcome variables were need for nutritional support

Table 2. Local and Systemic Complications According to the DBC, the RAC, and the Atlanta Classification

Classification	Complication	Frequency, n (%)
DBC	(Peri)pancreatic necrosis	132 (24.3)
	Only pancreas	23 (4.2)
	Only peripancreatic tissue	66 (12.2)
	Pancreas and peripancreatic tissue	43 (7.9)
	Infected (peri)pancreatic necrosis	15 (2.8)
	Transient organ failure	31 (5.7)
	Persistent organ failure	21 (3.9)
RAC	Acute peripancreatic fluid collection	98 (18)
	Pancreatic pseudocyst	19 (3.5)
	Necrotizing pancreatitis	132 (24.3)
	Pancreatic parenchymal necrosis	66 (12.2)
	Peripancreatic necrosis	109 (20.1)
	Infected necrosis	15 (2.8)
	Acute necrotic collection	106 (19.6)
	Walled-off necrosis	61 (11.2)
	Transient organ failure	31 (5.7)
	Persistent organ failure	21 (3.9)
Atlanta classification	Acute fluid collection	146 (26.9)
	Pancreatic necrosis	27 (5)
	Acute pseudocyst	58 (10.7)
	Abscess	10 (1.8)
	Organ failure	52 (9.6)

(parenteral and/or enteral nutrition), invasive treatment (endoscopic drainage/necrosectomy, percutaneous drainage and/or surgery), intensive care unit (ICU) admission, length of hospital stay, and in-hospital mortality. We compared the severe plus critical categories of the DBC (both supposed to be associated with high morbidity and mortality, being maximal for the critical category) with the severe category of the RAC. Moderate and mild categories were directly compared between both classifications. We followed the STROBE statement for reporting data.²⁸

Statistical Analysis

Absolute and relative frequencies were used to describe qualitative variables, mean \pm standard deviation for age, and median (25th–75th percentile, range) for length of hospital stay. The χ^2 test was used to compare qualitative variables. The Mann–Whitney test or Kruskal–Wallis test was used to compare the different categories with quantitative end points (hospital stay).

Results

We analyzed 543 episodes of AP from 459 patients; mean age was 61.2 ± 18 years, and 274 (50.5%) were male. Only 4 patients were transferred from other centers. The etiology was associated with gallstones in 323 (59.5%), alcohol in 74 (13.6%), idiopathic in 73 (13.4%), and other causes in 73 (13.4%). Sixteen patients (2.9%) died; of them, 4 patients (25%) died because of pancreatitis-associated early sterile organ failure, 2

(12.5%) because of definitive pancreatic sepsis–associated organ failure, 3 (18.8%) because of late systemic inflammatory response syndrome and organ failure without definitive confirmation of pancreatic sepsis, 4 (25%) because of exacerbation of comorbid disease, and 3 (18.8%) because of extrapancreatic infection (acute cholangitis, pneumonia, and colonic perforation). Thirty-one patients (5.7%) needed invasive treatment, 12 (38.7%) of them required surgery, 7 (22.6%) received endoscopic drainage or endoscopic necrosectomy, and 22 (71%) underwent percutaneous drainage; 8 patients (25.8%) received at least 2 different invasive techniques. Ninety-two patients (16.9%) received nutritional support. Twenty-two patients (4.1%) were admitted in the ICU. Median length of hospital stay was 12 days (25th percentile, 8 days; 75th percentile, 18 days; range, 2–165 days). Local and systemic complications according to the different classifications are shown in Table 2. The incidence of acute peripancreatic fluid collections and peripancreatic necrosis was very similar (18% and 20%, respectively; Table 2). Peripancreatic necrosis was almost 2 times more frequent than parenchymal necrosis (Table 2). Parenchymal necrosis was more frequent according to the DBC and RAC definitions compared with the Atlanta classification (Table 2).

Fifteen patients had documented pancreatic or peripancreatic necrosis infection (positive culture); only 3 of them were complicated with persistent organ failure.

Outcomes according to the Atlanta classification, DBC, and RAC are shown in Table 3. All classifications had highly statistically significant differences among their categories regarding in-hospital mortality, need for invasive treatment, nutritional support, ICU admission,

Table 3. Outcomes According to the Atlanta Classification, DBC, and the RAC

Classification	Categories	In-hospital mortality, n (%)	Invasive treatment, n (%)	Nutritional support, n (%)	ICU admission, n (%)	Length of hospital stay (days)
Atlanta	Mild: 453 (85.2%)	0	6 (1.3)	43 (9.5)	1 (0.2)	11 (7–16)
	Severe: 79 (14.8%)	16 (20.3) ^a	25 (31.6) ^a	45 (57) ^a	21 (26.6) ^a	28 (21–46) ^a
DBC	Mild: 386 (71.1%)	0	2 (0.5)	22 (5.7)	1 (0.3)	10 (7–14)
	Moderate: 131 (24.1%)	0	20 (15.3)	58 (44.3)	9 (6.9)	19 (13–28)
	Severe: 23 (4.2%)	14 (60.9)	6 (26.1)	9 (39.1)	9 (39.1)	34 (21–76)
	Critical: 3 (0.6%)	2 (66.7) ^a	3 (100) ^a	3 (100) ^a	3 (100) ^a	55 ^{a,b}
RAC	Mild: 363 (66.9%)	0	2 (0.6)	17 (4.7)	1 (0.3)	10 (7–14)
	Moderately severe: 160 (29.5%)	0	24 (15)	67 (41.9)	10 (6.3)	18 (13–27)
	Severe: 20 (3.7%)	16 (80) ^a	5 (25) ^a	8 (40) ^a	11 (55) ^a	36 (21–134) ^a

NOTE. n = 543, 11 missing data in Atlanta classification (acute collections without follow-up imaging after 4 weeks and no organ failure). Data expressed as n (%) or median (25th–75th percentile) days. Percentage in categories: % of the global sample. Percentage in outcome variables: % within category.

^aP < .001 between categories.

^bLength of hospital stay was assessed only in surviving patients; in the critical category of the DBC, only 1 patient survived (length of hospital stay, 55 days).

and length of hospital stay (Table 3). In-hospital mortality among the severe and critical categories of the DBC was very similar. The comparison between DBC and RAC is shown in Table 4; no statistically significant differences were obtained.

Discussion

The ideal classification of AP should have the following characteristics: (1) include the most recent evidence from the published literature, (2) achieve consensus for issues not evidence-based, (3) provide definitions for the most important complications associated with worse outcome, and (4) define subgroups of patients with different outcome. Two classifications of AP have been recently published. The development of the DBC involved 3 steps.²⁴ First, the Auckland group performed a comprehensive review of available evidence and proposed the new classification.²³ The second step involved a global Web-based survey of pancreatologists with recent clinical publications regarding AP.²⁴ Finally, an international symposium was held in Kochi, India during the 2011 World Congress of the International

Association of Pancreatology to further discuss the proposed classification.²⁴ The final classification was very similar to the original proposal²⁴; the only important change was the more specific nature of local complications that influence prognosis (only considering pancreatic/peripancreatic necrosis). The DBC is focused basically on briefly defining pancreatic and peripancreatic necrosis, infected necrosis, organ failure (according to the SOFA score²⁹), and the categories of severity. DBC does not define other frequent complications of AP. According to our data, the different categories of the DBC accurately describe groups of patients with different outcomes. In our cohort of patients only 3 of 543 patients were classified in the critical category, and mortality among these patients was similar to the severe category. This distribution raises the question whether the critical category makes sense, at least in centers with low affluence of transferred patients such as ours. In a prospective study from India³⁰ that aimed to validate the DBC, data from 151 patients were analyzed. Twenty-one patients (14%) were categorized as mild, 63 (42%) as moderate, 59 (40%) as severe, and 8 (5%) as critical AP. The fact that only 14% of the patients were classified as mild AP (most patients have mild disease²⁷; in our

Table 4. Comparison Between DBC and RAC

Categories	Mortality, n (%)	Invasive treatment, n (%)	Nutritional support, n (%)	ICU admission, n (%)	Length of hospital stay (days)	
High morbidity and mortality categories	DBC: severe + critical (26)	16 (61.5)	9 (34.6)	12 (46.2)	12 (46.2)	36 (21–71)
	RAC: severe (20)	16 (80)	5 (25)	8 (40)	11 (55)	36 (21–134)
High morbidity–low mortality categories	DBC: moderate (131)	0	20 (15.3)	58 (44.3)	9 (6.9)	19 (13–28)
	RAC: moderately severe (160)	0	24 (15.1)	67 (42.1)	10 (6.3)	18 (13–27)
Low morbidity and mortality categories	DBC: mild (386)	0	2 (0.5)	22 (5.7)	1 (0.3)	10 (7–14)
	RAC: mild (363)	0	2 (0.6)	17 (4.7)	1 (0.3)	10 (7–14)

NOTE. n = 543. Data expressed as (n), n (%), or median (25th–75th percentile) days. Percentage in outcome variables: % within category. No statistically significant differences were observed.

sample, 71.1% of the patients had a mild course according to the DBC) raises the question whether data from referral centers have enough external validity to be applied in other centers. There is also a practical problem with increasing number of categories; a higher sample to achieve statistically significant results in clinical studies is needed if patients are stratified according to severity, and statistics are difficult if the number of cases is scarce in one of the categories.

RAC classification was generated by an iterative, Web-based consultation process led by a working group and incorporating responses from the members of various national and international pancreatic societies. All responses were reviewed by the working group, and the process was repeated by a Web-based approach.²⁵ The aim of the RAC classification is wider. It defines AP and its local and systemic complications, and it provides accurate radiologic descriptions and also a severity classification. Its 3 categories are associated with increasing morbidity, and mortality is restricted to the severe category. It has been criticized that the moderately severe category of the RAC includes local complications with different prognosis (particularly acute peripancreatic fluid collections, associated with better outcome than pancreatic necrosis)³¹; however, according to our data, the moderately severe category was clearly associated with a worse outcome than the mild category. Another issue is the somewhat confusing definition of exacerbation of preexistent comorbid disease in the RAC.²⁵ In our sample, 4 patients died as a result of exacerbation of previous pathologies (mainly heart diseases). Comorbidity is a well-known risk factor of death in AP.¹³ Probably some forms of exacerbation of comorbid disease should have been included in the severe category; in fact, we classified those patients who died as severe because of the development of persistent organ failure associated with previous disease.

It seems that the process of debate within that project changed dramatically from earlier drafts³²; thus the contribution of the working group and pancreatologists was more pronounced than in the DBC. In our study, the direct comparison between categories of both classifications (after unifying the severe and critical category of the DBC) yielded no significant differences.

We provide the frequency of the new local and systemic complications according to both classifications. Interestingly, 20% of the patients had peripancreatic necrosis, a complication that was even slightly more frequent than acute peripancreatic fluid collections. Most of the latter were reabsorbed, so true pseudocysts are infrequent. We classified acute necrotic collections of the peripancreatic tissue as acute fluid collections in the Atlanta classification and walled-off necrosis as pseudocysts; an important proportion of collections and pseudocysts in older literature^{33–35} were in fact acute necrotic collections and walled-off necrosis, arising from necrosis of the pancreas or peripancreatic tissues.

The number of patients who were admitted to the ICU was very low in our center. The explanation is that we have an intermediate care unit where patients with prediction of severity or with transient organ failure are managed by gastroenterologists; only patients who need vasoactive drugs, orotracheal intubation, or hemodialysis are managed in the ICU. The number of patients with persistent organ failure was very low; discrepancies with results from other centers³⁰ may be explained by the nonreferral population of our center.

The original cohort of patients was not designed to validate these classifications, and our study had a purely retrospective acquisition of data regarding imaging (local complications). On the other hand, we describe a wide cohort of patients without significant proportion of transferred patients, thus improving the external validity.

We conclude that both classifications describe different subgroups of patients in terms of outcomes. The critical category of the DBC includes a low number of patients and may not be useful to design studies because it increases the number of categories without a clear advantage. The RAC is a global description of most clinically relevant aspects of AP. The differences between early drafts and the final version of both classifications suggest that the process of debate has been more pronounced in the RAC.

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Reprint requests

Address requests for reprints to: Enrique de-Madaria, MD, PhD, Sección de Aparato Digestivo, Hospital General Universitario de Alicante, Calle Pintor Baeza s/n, Alicante 03010, Spain. e-mail: madaria@hotmail.com; fax: 34-965933468.

Conflicts of interest

The authors disclose no conflicts.