The Atlanta Classification, Revised Atlanta Classification, and Determinant-Based Classification of Acute Pancreatitis

Which Is Best at Stratifying Outcomes?

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Objectives: To determine which classification is more accurate in stratifying severity.

Methods: The study used a retrospective analysis of a prospective acute pancreatitis database (June 2005–December 2007). Acute pancreatitis severity was stratified according to the Atlanta classification (AC) 1992, the revised Atlanta classification (RAC) 2012, and the determinant-based classification (DBC) 2012. Receiver operating characteristic analysis (area under the curve) compared the accuracy of each classification. Logistic regression identified predictors of mortality.

Results: 338 patients were analyzed: 13% had persistent organ failure (POF) (>48 hours), of whom 37% had multisystem POF, and 11% had pancreatic necrosis, of whom 19% had infected necrosis. Mortality was 4.1%. For predicting mortality (area under the curve), the RAC (0.91) and DBC (0.92) were comparable ($P = 0.404$); both outperformed the AC (0.81) ($P < 0.001$). For intensive care unit admission, the RAC (0.85) and DBC (0.85) were comparable ($P = 0.949$); both outperformed the AC (0.79) ($P < 0.05$). There were 2 patients in the critical category of the DBC. Multisystem POF was an independent predictor of mortality (odds ratio, 75.0; 95% confidence interval, 13.7–410.6; $P < 0.001$), whereas single-system POF, sterile necrosis, and infected necrosis were not.

Conclusion: The RAC and DBC were generally comparable in stratifying severity. The paucity of patients in the critical category in the DBC limits its utility. Neither classification accounts for the impact of multisystem POF, which was the strongest predictor of mortality.

Key Words: acute pancreatitis, mortality, multisystem persistent organ failure, Atlanta classification, revised Atlanta classification, determinant-based classification

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The Atlanta Symposium in 1992 was the first major effort to develop a classification system for the severity of acute pancreatitis (AP) (Table 1).[1] Because the severe category in the Atlanta classification (AC) included subsets of patients with different morbidities and mortalities, it has been difficult for institutions to compare outcomes and for clinicians to determine which patients should be transferred to a referral center or an intensive care unit (ICU).

In 2012, the AC was revised using an iterative Web-based consultation process, with the goal of improving the assessment of severity of AP and clarifying the radiological descriptions of pancreatic and peripancreatic collections on cross-sectional imaging.[2] The revised Atlanta classification (RAC) included 3 categories of severity of AP: mild, moderately severe, and severe (Table 1). The category of moderately severe AP was deemed important to stratify patients with high morbidity but low mortality.[3,4] The category of severe AP was designed to include only those patients with both high morbidity and high mortality such that outcomes could now be properly compared and patients with the highest priority for transfer could be identified.

A subsequent severity classification system, the determinant-based classification (DBC), stratified severity of AP into 4 categories: mild, moderate, severe, and critical (Table 1).[5] The critical category was designed to more accurately identify those patients at the highest risk of death in AP. It was based on a meta-analysis of 14 studies conducted between 1986 and 2007 that concluded that the relative risk of death in AP doubled when organ failure and infected pancreatic necrosis were both present.[6]

Studies that have been published thus far have concluded that the RAC[7,8] and the DBC[9] are accurate for stratifying outcomes and both are superior to the AC.[10,11] Because these studies included unusually large numbers of patients who were either transferred,[10] had pancreatic necrosis,[9–11] or had persistent organ failure,[9,10] it is possible that these results were influenced by the inclusion of a disproportionate number of patients with severe AP. As a result, it remains unclear which classification is more accurate in assessing severity of AP. In addition, it remains unclear whether the category of severe AP in both the RAC and DBC still contains subsets of patients with different morbidities and mortalities such that it will continue to be difficult to compare outcomes and to stratify patients with the greatest need for intensive care.

The aims of this study are to clarify which classification system is more accurate in stratifying outcomes in AP and to determine whether the category of severe AP requires further stratification.

MATERIALS AND METHODS

The demographic, clinical, laboratory, and radiologic data for all patients directly admitted to our institution with a diagnosis of AP between June 2005 and December 2007 were collected for this study. Among patients who were admitted more than once to our institution, only the data from the first admission were included. Data for all patients were collected prospectively for 7 days or until discharge if fewer than 7 days. Medical records were reviewed and used to calculate a Charlson comorbidity score.[12] This study was approved by the Partners Institutional Review Board.

Acute pancreatitis was defined as 2 or more of the following: characteristic abdominal pain, serum amylase and/or lipase levels 3 or more times the upper limit of normal, and/or a contrast-enhanced computer tomography scan or magnetic resonance imaging within the first 7 days of hospitalization demonstrating characteristic changes of AP.

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TABLE 1. The AC (1992), the RAC (2012), and the DBC (2012) of AP

Classification	Criteria
AC	
Mild	No organ failure and no local complications
Severe	Organ failure* and/or local complications†
RAC	
Mild	No organ failure and no local or systemic complications
Moderately severe	Transient‡ organ failure§ and/or local‖ and/or systemic complications¶
Severe	Persistent# organ failure (single or multiple organ systems)
DBC	
Mild	No (peri)pancreatic necrosis and no organ failure
Moderate	Sterile necrosis and/or transient organ failure**
Severe	Infected necrosis or persistent organ failure
Critical	Infected necrosis and persistent organ failure

*Systolic blood pressure < 90 mm Hg, $PaO_2 \leq 60$ mm Hg, creatinine level ≥ 2 mg/dL, and gastrointestinal bleeding > 500 mL/24 h.

†Pancreatic necrosis, pancreatic abscess, or pseudocyst.

‡Transient organ failure: ≤48 hours.

§Systolic blood pressure ≤ 90 mm Hg, $PaO_2 \leq 60$ mm Hg, and creatinine level ≥ 2 mg/dL.

‖Acute peripancreatic fluid collection, pseudocyst, acute necrotic collection, or walled-off necrosis.

¶Exacerbation of preexisting comorbidity.

#Persistent organ failure: >48 hours.

**Requirement for inotropic support: $PaO_2/FIO_2 \leq 300$ mm Hg and creatinine level ≥ 2 mg/dL.

Organ failure was defined according to the criteria outlined in each severity classification (Table 1). Organ failure was assessed during the first 7 days of hospitalizations based on the most extreme laboratory value or clinical measurement in each 24-hour period. Transient organ failure was defined as a duration lasting 48 hours or less; persistent organ failure, greater than 48 hours.

Radiologic imaging was reviewed by an abdominal radiologist who was blinded to the purpose of the study to identify and characterize local complications including pancreatic necrosis. Patients who had no imaging studies were presumed to have had interstitial pancreatitis and no local complications. Infected necrosis was confirmed by fine-needle aspiration, by the initial aspiration at the time of insertion of a percutaneous drainage catheter before surgery, or by cultures obtained at the time of surgery.

The primary outcome was mortality. The secondary outcomes were admission to the ICU, ICU length of stay, and hospital length of stay (including outside hospital before transfer).

Statistical Analysis

All patients were classified according to each of the 3 severity classifications.[1,2,5] Mortality and ICU admission were binary variables. Intensive care unit length of stay and hospital length of stay were continuous variables. Intensive care unit length of stay was dichotomized using a threshold of 11 days (75th percentile). Hospital length of stay was dichotomized using a threshold of 7 days to allow receiver operating characteristic (area under the curve [AUC]) analysis. In several previous studies, the median hospital length of stay was shown to be 7 days or less in mild AP.[4,7,8,10]

The overall association between increasing severity and outcomes was analyzed using the Cochran-Armitage (binary variables) and Jonckheere-Terpstra (continuous variables) trend tests. Pairwise testing between severity grades within each classification was performed using Fisher exact test (binary variables) and the Kruskal-Wallis test (continuous variables). Independent predictors of mortality were identified using a binary logistic regression model. The following predictors were evaluated: age, Charlson

TABLE 2. Clinical Characteristics and Outcomes (N = 338 Patients)

Characteristic	n (%)
Age, median (IQR), y	52 (41–62.25)
Female	174 (51.5)
Etiology	
Biliary	102 (30.2)
Alcohol	71 (21.0)
Post-ERCP	47 (13.9)
Idiopathic	50 (14.8)
Other	68 (20.1)
AP Episode	
First	230 (68.0)
Second	33 (9.8)
Third or more	75 (22.2)
Admission Source	
Transferred from outside hospital	58 (17.2)
Organ Failure	
No organ failure	255 (75.5)
Organ failure	83 (24.5)
Cardiovascular	46 (55.4)
Renal	41 (49.4)
Respiratory	34 (41.0)
Transient organ failure	40 (11.8)
Persistent organ failure	43 (12.7)
Single system	27 (62.8)
Multisystem	16 (37.2)
Local Complications	
Interstitial pancreatitis	302 (89.3)
No fluid collections (confirmed by CT)	120 (39.7)
Acute (peri)pancreatic fluid collection (confirmed by CT)	46 (15.3)
No imaging (presumed interstitial)	136 (45.0)
Necrotizing pancreatitis	36 (10.7)
Sterile necrosis	29 (80.6)
Infected necrosis	7 (19.4)
Outcomes	
Mortality	14 (4.1)
Interstitial pancreatitis	7/302 (2.3)
Necrotizing pancreatitis	7/36 (19.4)
Sterile necrosis	6/29 (20.7)
Infected necrosis	1/7 (14.3)
ICU admission	55 (16.3)
ICU length of stay (n = 40), median (IQR), d	5 (1–11)
Hospital length of stay, median (IQR), d	4 (2–8)

CT indicates computed tomography; ERCP, endoscopic retrograde cholangiopancreatography.

comorbidity score, transient and persistent organ failure, and sterile and infected necrosis. Organ failure and necrosis were included as they were the primary determinants of severity in the classification systems being compared in this study. The Charlson comorbidity score was included to control for patients' overall health. A second logistic regression model evaluated age, Charlson comorbidity score, single-system and multisystem persistent organ failure, and sterile and infected necrosis.

Receiver operating characteristic analysis was performed to determine the areas under the curve and evaluate accuracy of each classification system for predicting each outcome. For each outcome, the AUC of each classification was compared to determine which (if any) was most accurate.

RESULTS

There were a total of 397 consecutive admissions for AP between June 2005 and December 2007. Fifty-nine repeat admissions (involving 42 patients) were excluded resulting in a final study cohort composed of 338 patients. The clinical characteristics and outcomes of the study cohort are listed in Table 2: 58 (17.2%) were transferred from an outside hospital, 43 (12.7%) had persistent organ failure of whom 16 (37.2%) had multisystem persistent organ failure, and 36 (10.7%) had necrotizing pancreatitis of whom 7 (19.4%) had infected necrosis.

There were 14 (4.1%) deaths. Mortality was higher in necrotizing (19.4%) compared with interstitial (2.3%) AP (Fisher exact $P < 0.001$). However, there was no difference in mortality between sterile (20.7%) and infected (14.3%) necrosis (Fisher exact $P = 1.000$). The median ICU length of stay was 5 (interquartile range [IQR], 1–11) days, and the median hospital length of stay was 4 (IQR, 2–8) days.

Table 3 stratifies the outcomes in the 3 classification systems. In the AC, severe AP was associated with greater mortality (Fisher exact $P < 0.001$), ICU admission (Fisher exact $P < 0.001$), and longer hospital length of stay (Kruskal-Wallis $P < 0.001$) but not longer ICU length of stay (Kruskal-Wallis $P = 0.116$) than mild AP. In the RAC, trend tests showed that higher AP severity grades were associated with greater mortality (Cochran-Armitage $P < 0.001$), ICU admissions (Cochran-Armitage $P < 0.001$), and longer hospital length of stay (Jonckheere-Terpstra $P < 0.001$) but not longer ICU length of stay (Jonckheere-Terpstra $P = 0.315$). All pairwise comparisons between severity grades were significant for mortality and ICU admission (Fisher exact $P < 0.001$). Pairwise comparisons for hospital length of stay were significant only between mild and moderate AP (Kruskal-Wallis $P < 0.001$). No pairwise comparisons

TABLE 3. Stratification of Outcomes in the 3 Classification Systems

	Classification System				
	AC				
Outcomes	**Mild**	**Moderate**	**Severe**		***P****
N (%)	202 (60)		136 (40)		
Mortality, n (%)	0 (0)		14 (10)		<0.001†
ICU admission, n (%)	6 (3)		49 (36)		<0.001†
ICU LOS (n = 55), median (IQR), d	1.5 (1–9)		5 (2–13)		0.116‡
Hospital LOS, median (IQR), d	3 (2–5)		8 (4–16)		<0.001†
	RAC				
	Mild	**Moderate**	**Severe**		***P****
N (%)	202 (60)	93 (27)	43 (13)		
Mortality, n (%)	0 (0)	3 (3)	11 (26)		<0.001†
ICU admission, n (%)	6 (3)	20 (22)	29 (67)		<0.001†
ICU LOS (n = 55), median (IQR), d	1.5 (1–9)	6 (1–13)	5 (2–13)		0.315‡
Hospital LOS, median (IQR), d	3 (2–5)	8 (4–16)	9 (4–20)		<0.001§
	DBC				
	Mild	**Moderate**	**Severe**	**Critical**	***P****
N (%)	242 (71)	48 (14)	46 (14)	2 (0.6)	
Mortality, n (%)	0 (0)	3 (6)	10 (22)	1 (50)	<0.001‖
ICU admission, n (%)	9 (4)	15 (31)	29 (63)	2 (100)	<0.001‖
ICU LOS (n = 55), median (IQR), d	1 (1–9)	6 (1–10)	5 (2–12)	66 (21-n/a)	0.039¶
Hospital LOS, median (IQR), d	4 (2–6)	9 (3–16)	10.5 (4–20)	69 (27-n/a)	<0.001#

*Cochran-Armitage and Jonckheere-Terpstra tests of trend for categorical and continuous variables, respectively.

†All pairwise comparisons were significant.

‡No pairwise comparisons were significant.

§Mild versus moderate was significant.

‖Mild versus moderate and moderate versus severe were significant.

¶Severe versus critical was significant.

#Mild versus moderate and severe versus critical were significant.

LOS indicates length of stay; n/a, not available.

TABLE 4. Predictive Accuracy of Each Classification System for Clinical Outcomes (ROC Analysis)

	Classification System, AUC (95% CI)		
Outcome	**AC 1992**	**RAC**	**DBC**
Mortality*	0.81 (0.77–0.85)	0.91 (0.88–0.94)	0.92 (0.88–0.94)
ICU admission†	0.79 (0.75–0.83)	0.85 (0.81–0.89)	0.85 (0.81–0.89)
ICU LOS > 11 d‡ (75th percentile)	0.57 (0.43–0.70)	0.59 (0.44–0.72)	0.64 (0.50–0.76)
Hospital LOS > 7 d§	0.76 (0.71–0.81)	0.77 (0.72–0.81)	0.72 (0.67–0.77)

*Both RAC and DBC were more accurate than AC 1992 ($P < 0.001$). There was no difference between RAC and DBC ($P = 0.404$).

†Both RAC ($P < 0.001$) and DBC ($P = 0.004$) were more accurate than AC 1992. There was no difference between RAC and DBC ($P = 0.949$).

‡There was no difference between AC 1992 and RAC ($P = 0.844$) and between AC 1992 and DBC ($P = 0.433$). There was no difference between RAC and DBC ($P = 0.289$).

§RAC ($P = 0.011$) was more accurate than DBC. There was no difference between AC 1992 and RAC ($P = 0.397$) and between AC 1992 and DBC ($P = 0.059$).

LOS indicates length of stay; ROC, receiver operating characteristic.

were significant for ICU length of stay (Kruskal-Wallis $P > 0.05$). In the DBC, trend tests showed that higher AP severity grades were associated with greater mortality (Cochran-Armitage $P < 0.001$), ICU admissions (Cochran-Armitage $P < 0.001$), and longer hospital length of stay (Jonckheere-Terpstra $P < 0.001$) and ICU length of stay (Jonckheere-Terpstra $P < 0.039$). Pairwise comparisons for mortality and ICU admission were significant between mild and moderate and between moderate and severe (Fisher exact $P < 0.05$). For ICU length of stay, comparison between severe and critical was significant (Kruskal-Wallis $P = 0.017$). For hospital length of stay, comparisons between mild and moderate (Kruskal-Wallis $P < 0.001$) and severe and critical (Kruskal-Wallis $P = 0.028$) were significant. Overall, trend tests and pairwise comparisons showed that higher severity grades were generally associated with worse outcomes in all 3 classifications.

Table 4 shows the predictive accuracy of each classification system for clinical outcomes. The RAC and DBC were more accurate than the AC for predicting mortality ($P < 0.001$) and ICU admission ($P < 0.005$), but there was no difference between the RAC and DBC ($P > 0.400$). There was no difference among the 3 classifications in predicting ICU length of stay greater than 11 days ($P > 0.200$). The RAC was more accurate than the DBC for predicting hospital length of stay greater than 7 days ($P = 0.011$), but there was no difference between the AC and RAC ($P = 0.397$) or the AC and DBC ($P = 0.059$).

Table 5 shows mortality in patients stratified by degree of organ failure. Patients with persistent organ failure (11/43, 25.6%) had a higher mortality than those with no organ failure (0%) ($P < 0.001$) and transient organ failure (3/40, 7.5%) ($P = 0.039$). There was no mortality attributable to AP in the absence of persistent organ failure, even in the presence of sterile and infected necrosis. The 3 deaths among patients with transient organ failure were due to preexisting comorbid disease (two with hepatic failure and one with duodenal adenocarcinoma). Binary logistic regression controlling for age and Charlson comorbidity score demonstrated that persistent organ failure (odds ratio [OR], 19.6; 95% confidence interval [CI], 4.6–83.5; $P < 0.001$) and sterile necrosis (OR, 5.9; 95% CI, 1.3–27.3; $P = 0.022$) were independent risk factors for mortality, but infected necrosis was not ($P = 0.448$). Among the patients with persistent organ failure, mortality in multisystem persistent organ failure (9/16, 56.3%) was significantly higher than in those with single-system persistent organ failure (2/27, 7.4%) ($P = 0.001$). A second binary logistic regression model controlling for age and Charlson comorbidity score demonstrated that multisystem persistent organ failure was an independent predictor of mortality (OR, 75.0; 95% CI, 13.7–410.6; $P < 0.001$), whereas single-system persistent organ failure ($P = 0.102$), sterile necrosis ($P = 0.143$), and infected necrosis ($P = 0.977$) were not.

DISCUSSION

This study compared the accuracy of 3 different AP severity classifications for predicting important outcomes using a large prospective database. The RAC and DBC were essentially equivalent in predicting mortality, need for admission to the ICU, ICU length of stay, and hospital length of stay. Both were more accurate for predicting mortality and ICU admission than the AC.

TABLE 5. Mortality Stratified by Degree of Organ Failure

	n	Mortality, n (%)
All patients, N	338	14 (4.1)
No OF*	255	0 (0)
Interstitial pancreatitis	242	0 (0)
Sterile necrosis	10	0 (0)
Infected necrosis	3	0 (0)
Transient OF*	40	3 (7.5)†
Interstitial pancreatitis	33	3 (9.1)†
Sterile necrosis	5	0 (0)
Infected necrosis	2	0 (0)
Persistent OF*	43	11 (25.6)
Interstitial pancreatitis	27	4 (14.8)
Sterile necrosis	14	6 (42.9)
Infected necrosis	2	1 (50.0)
Single system	27	2 (7.4)‡
Multisystem	16	9 (56.3)‡

*Cochran-Armitage trend test. Pairwise comparisons: mortality in persistent OF was greater than in transient OF ($P = 0.039$) and no OF ($P < 0.001$), and mortality in transient OF was greater than in no OF ($P = 0.002$).

†Three deaths due to comorbid disease: 2 patients with hepatic failure and 1 patient with duodenal adenocarcinoma.

‡Mortality in multisystem persistent OF was significantly greater than in single-system persistent OF ($P = 0.001$).

OF indicates organ failure.

This study also demonstrates that all patients with persistent organ failure do not have the same risk of mortality and should be further stratified. In particular, those with multisystem persistent organ failure experienced a significantly higher mortality than those with single-system persistent organ failure (7.4% vs 56.3%, respectively) ($P = 0.001$) (Table 5). Regression analysis demonstrated that multisystem persistent organ failure was a stronger predictor of mortality than single-system persistent organ failure, sterile necrosis, or infected necrosis. The results of our study suggest that patients classified as having severe AP on the basis of persistent organ failure should be further stratified by the presence or absence of multisystem persistent organ failure.

The primary difference between the RAC and DBC is the importance accorded to infected necrosis in predicting mortality. The DBC was largely based on the results of a meta- analysis that showed comparable mortality rates associated with organ failure and infected necrosis and a doubling of the risk of mortality when both were present.[6] In this study, infected necrosis was not an independent risk factor for mortality. One potential explanation for this difference is that the management of infected necrosis has improved. For example, urgent surgical debridement was the standard of care for patients with infected necrosis for many decades, but this has been shown to be associated with high mortality.[13] Consensus guidelines now advocate delaying debridement for as long as possible to allow acute necrotic collections to organize into walled-off necrosis and employing a "step-up" approach with percutaneous, endoscopic, and/or minimally invasive surgical drainage as needed.[14] As a result, the impact of infected necrosis on morbidity and mortality, particularly in the absence of persistent organ failure, may be diminishing. In this study, among the 5 patients with infected necrosis in the absence of persistent organ failure (Table 5), the median time to intervention was 42 days (IQR, 20–45 days), and there were no deaths. In addition, in a recent large prospective study of 447 patients with pancreatic necrosis, persistent organ failure in the first week was a much stronger predictor of mortality than infected necrosis.[15]

There seem to be several disadvantages of the DBC. First, in this study and in a previous study,[11] there was a paucity of patients in the critical category, thereby diminishing its usefulness. Second, the criteria for severe AP are the presence of either persistent organ failure or infected necrosis without persistent organ failure. In this study, all 5 patients with infected necrosis in the absence of persistent organ failure survived. Therefore, the category of severe AP likely contains 2 subsets of patients with different mortalities. Third, because infected necrosis develops in the majority of patients after the first 7 to 10 days of hospitalization,[16–19] the DBC cannot be used during the first week for stratifying patients for intensive care.

The primary strength of this study is that the data were collected prospectively. This minimized missing data and enabled the inclusion of patients transferred from outside institutions. The primary limitation in this study was that some patients did not undergo any imaging studies during their admission or outpatient follow-up. These patients were presumed to have interstitial disease, but the presence of necrosis could not be excluded. However, it is unlikely that patients with clinically significant pancreatic necrosis would not have undergone abdominal imaging given the frequent use of imaging in AP.[20] A second limitation is that this study represents the experience of a single referral center, potentially limiting the generalizability of its conclusions.

A potential limitation was that the inclusion of transferred patients, who generally have a higher morbidity and mortality than patients directly admitted to a hospital,[21] may have introduced a selection bias. Similar to our primary analysis, a subset analysis of patients directly admitted to our hospital showed that the RAC and DBC were essentially equivalent and superior to AC for predicting outcomes in AP (data not shown), suggesting that the inclusion of transferred patients did not confound the results.

In conclusion, the RAC and DBC were generally equivalent and superior to the AC for predicting outcomes in AP. The results of this study support the use of the 3-tiered RAC rather than the 4-tiered DBC. Both classifications fail to account for the impact of multisystem persistent organ failure, which was the strongest predictor of mortality in this study. Patients with persistent organ failure should be further stratified by the presence or absence of multisystem persistent organ failure.

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