

Original Article

Determinant-based classification and revised Atlanta classification: differences between in categorization of moderate acute pancreatitis

Baoju Qi^{1,2}, Feng Cao¹, Jian Liu¹, Diangang Liu¹, Ang Li¹, Kuo Liang¹, Fei Li¹

¹Department of General Surgery, Xuanwu Hospital Capital Medical University, Beijing, China; ²Department of Anorectal Surgery, People's Hospital of Beijing Daxing District, Beijing, China

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Abstract: Determinant-based classification (DBC) and revised Atlanta classification (RAC) are two new systems of acute pancreatitis (AP) severity classification. The difference between them is in classification of moderate AP (MAP). Therefore, we aimed to explore the practical value of RAC and DBC systems in classifying MAP. A total of 321 patients with MAP were included and assigned to RAC (n = 167) and DBC (n = 154) groups. Each group was further divided into three subgroups: local complication only, transient organ failure only, and both. Outcome variables including in-hospital mortality, intensive care unit (ICU) admission, surgery for infected pancreatic necrosis (IPN), length of ICU stay and hospital stay were compared among the three subgroups in each group. Meantime, patients in the RAC group were divided into infected group and sterile group and possible predictors and risk factors for infection were investigated. No significant differences were observed in MAP patients characteristics between the two groups except in infected necrosis ($P = 0.000$). According to the MAP criterion of RAC, the ICU admission ($P = 0.000$), surgery for IPN ($P = 0.000$), and ICU stay ($P = 0.012$) were significantly different among the three subgroups. For the MAP criterion of DBC, no significant differences were found among the three subgroups. In addition, we found that (peri) pancreatic necrosis, Ranson score, CT score, and organ function failure were possible predictors and risk factors for patients with infection. RAC system has higher heterogeneity than DBC system when used to classify MAP.

Keywords: Acute pancreatitis, moderate acute pancreatitis, determinant-based classification, revised Atlanta classification

Introduction

Acute pancreatitis (AP) is a frequent gastrointestinal disorder, and its incidence has been progressively increasing [1]. The clinical outcomes rang from uneventful and mild to fatal [2, 3]. It has been estimated that the mortality can be as high as 30% in patients with severe AP [4]. Therefore, accurate classification of AP is very important in clinical research and practice because patients with severe AP always have significantly worse outcomes than those with mild AP [5]. Atlanta classification, proposed in 1992 [6], was a widely-accepted classification for AP for more than two decades. However, this classification has several limitations. For example, some scholars believe that the score of at least eight points based on Acute Physiology and Chronic Health Examina-

tion (APACHE) II score is not a good predictor for severe AP on admission to hospital [7]. In addition, the Atlanta classification only defines organ failure without mentioning the duration of the organ failure. Recent studies have shown that persistent (>48 hours) early organ failure is a marker for subsequent death or local complications [8].

Recently, two new classification systems were proposed, the Determinant-Based Classification (DBC) [9] and the Revision of the Atlanta Classification (RAC) [10, 11]. The difference between RAC and DBC lies in stratification of AP. The severity of AP is stratified in four categories based on DBC (mild, moderate, severe, and critical AP), and while is stratified in three categories based on RAC, namely, mild, moderately and severe AP. DBC is mainly focused on

RAC and DBC in classification of MAP

Table 1. Characteristics of patients with MAP

Characteristics	RAC (n = 167)	DBC (n = 154)	P value
Age, median (range), years	49 (36-59)	50 (36-58)	0.302
Male, no (%)	111 (66.5%)	109 (70.8%)	0.406
Etiology, no (%)			
Biliary	82 (49.1%)	77 (50%)	0.872
Alcohol abuse	21 (12.6%)	19 (12.3%)	0.949
High triglyceride	33 (19.7%)	28 (18.2%)	0.719
Others	31 (18.6%)	30 (19.5%)	0.834
BMI on admission	25.8 (22.8-29.6)	25.7 (22.8-29.5)	0.122
Transfers from other hospitals, no (%)	33 (19.8%)	31 (20.1%)	0.934
WBC ($\times 10^9/L$)	11.9 (9.4-14.8)	11.8 (9.3-14.7)	0.647
Hematocrit (%)	41.5 (37.3-45.1)	42.0 (37.4-45.2)	0.342
C-reaction protein on admission	83.8 (19.8-211.2)	86.4 (20.1-214.1)	0.712
Organ failure, no (%)			
Multiple organ failure	13 (7.8%)	12 (7.8%)	0.998
Solitary organ failure	65 (38.9%)	62 (40.3%)	0.807
Transient organ failure	78 (46.7%)	74 (48.1%)	0.809
Local complication, no (%)			
Pancreatic necrosis	57 (34.1%)	55 (35.7%)	0.766
Perpancreatic necrosis	62 (37.1%)	60 (39.0%)	0.735
Fluid collection	149 (89.2%)	145 (94.2%)	0.112
Infected necrosis	42 (25.1%)	0 (0.0%)	0.000

MAP, moderate acute pancreatitis; RAC, Revision of the Atlanta classification; DBC, Determinant-Based classification; BMI, body mass index; WBC, white blood cell.

the presence of (peri) pancreatic necrosis, the status (sterile or infected) and the duration of organ failure (transient or persistent). In contrast, RAC concerns on local and/or systemic complications and transient/persistent organ failure. Although the DBC and the RAC could accurately classify the severity of AP in subgroups of patients, accumulating evidence has suggested that there was inconsistent application of standards and practices on clinical outcomes [12-14].

The most obvious difference between the two systems exists in the classification of moderate AP (MAP). Previous studies were focused on the comparison between the two entire systems [15]. However, little information is available about classifying patients with MAP in clinical according to the different systems. Therefore, in the present study, we aimed to explore the practical value of RAC and DBC systems in classifying MAP patients in clinical. Our study might provide novel explanation for such differences between RAC and DBC.

Materials and methods

Patients

The study was approved by the ethics committee of Xuanwu Hospital of Capital Medical University. A prospective database of AP was used to check the categories of different classification systems. Consecutive adult (>18 years) patients with AP (n = 321) admitted in our center between January 2012 and December 2015 were included in this study. AP was diagnosed with the occurrence of at least two of the following criteria: (i) amylase level is at least three times higher than the upper limit of the normal level; (ii) clinical findings of abdominal pain; (iii) imaging results suggestive AP. We collected the following data from the prospective database: Patient demographics, etiology, hematology parameters, presence of infectious complications, and organ failure. In addition, all components of the APACHE II scoring system and the Ranson scoring system were recorded upon admission.

RAC and DBC in classification of MAP

Table 2. Clinical outcomes of MAP stratified by classification system

		Local complication only	Transient organ failure only	Both	P value
RAC	Number of patients	89	18	60	
	Mortality, n (%)	4 (4.5%)	0 (0%)	2 (3.3%)	0.640
	ICU admission, n (%)	12 (13.4%)	6 (33.3%)	26 (43.3%)	0.000
	Surgery for IPN, n (%)	13 (14.6%)	0 (0%)	29 (48.3%)	0.000
	ICU stay, median days (IQR)	3 (2-11)	6 (2-19)	7 (3-21)	0.012
	Hospital stay, median days (IQR)	9 (6-21)	8 (6-15)	11 (8-27)	0.052
	Number of patients	80	39	35	
DBC	Mortality, n (%)	0 (0%)	0 (0%)	0 (0%)	1.000
	ICU admission, n (%)	3 (3.8%)	4 (10.3%)	4 (11.4%)	0.231
	Surgery for IPN, n (%)	0 (0%)	0 (0%)	0 (0%)	1.000
	ICU stay, median days (IQR)	3 (1-8)	4 (2-12)	5 (2-16)	0.059
	Hospital stay, median days (IQR)	7 (5-18)	8 (5-15)	9 (6-21)	0.126

MAP, moderate acute pancreatitis; RAC, Revision of the Atlanta classification; DBC, Determinant-Based classification; ICU, intensive care unit; IPN, infected pancreatic necrosis; Local complication including (per) pancreatic necrosis and/or fluid collection.

Grouping

Patients were divided into two groups according to different classification systems. One group was classified based on RAC MAP criteria and the other group was classified based on DBC MAP criteria (**Table 2**). Based on DBC classification system, patients were grouped into local complication only, transient organ failure only, and both groups. According to RAC classification system, the patients were also divided into local complication only, transient organ failure only, and both groups. Outcome variables in the two groups were as follows: in-hospital mortality, intensive care unit (ICU) admission, surgery for infected pancreatic necrosis (IPN) (e.g. open pancreatic necrosectomy, retroperitoneal pancreatic necrosectomy, or primary percutaneous catheter drainage), length of ICU stay and hospital stay.

Statistical analysis

Continuous variables were shown as median and range, and while categorical variables were summarized using frequencies and percentages. Mann-Whitney test was used to determine differences. Data were compared by chi-square analysis, Fisher's exact test, or linear-by-linear association test. A value of $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS for Windows version 21.0 (SPSS, Chicago, IL, USA).

Results

A total of 321 patients (220 males, medium 49.5 years) with AP were enrolled in this study. The etiology of AP included biliary, alcohol abuse, high triglyceride and others. There were a total of 64 patients who were transferred from other hospitals. As shown in **Table 1**, there were 167 patients and 154 patients were respectively assigned to RAC and DBC groups. No significant differences were found in ages, sex ratio, the etiology of AP, BMI, numbers of transfers from other hospitals, hematology parameters, organ failure, and local complication between the two groups. However, we found that there were 42 cases with infected necrosis in RAC group and none in DBC group, and there was a significant difference between the two groups ($P = 0.000$).

Among the 167 patients in RAC group, 89 patients only had local complications, 18 patients only had transient organ failure, and 60 patients had both (**Table 2**). As shown in the Table, we found that there were statistical differences in ICU admission ($P = 0.000$), surgery for IPN ($P = 0.000$), and length of ICU stay ($P = 0.012$) among the three subgroups, and while there were no significant differences in mortality ($P = 0.640$) and length of hospital stay ($P = 0.052$). Meantime, there were 80, 39, and 35 patients with only local complications, transient organ failure, and both according to

RAC and DBC in classification of MAP

Table 3. Possible predictors for infection in MAP patients based on RAC

	Infected (n = 42)	Sterile (n = 107)	P value
Age, median (range), years	50 (37-59)	49 (36-59)	0.873
Male, no (%)	29	82	0.339
Etiology, no (%)			0.950
Biliary	22 (52.4%)	57 (53.3%)	
Alcohol abuse	6 (14.3%)	14 (13.1%)	
High triglyceride	9 (21.4%)	20 (18.7%)	
Others	5 (11.9%)	16 (14.9%)	
BMI on admission	25.6 (22.5-29.3)	25.9 (22.5-29.7)	0.412
WBC ($\times 10^9/L$)	12.1 (9.7-14.9)	11.4 (9.2-14.6)	0.658
C-reaction protein	84.2 (21.8-243.2)	83.0 (19.6-211.0)	0.717
Serum creatinine	76.1 (42.2-91.4)	76.2 (39.4-96.4)	0.891
(Peri) pancreatic necrosis	40	79	0.003
Organ failure	24	36	0.009
APACHE II score	7 (4-9)	7 (4-9)	0.657
Ranson score	3 (1-4)	2 (1-4)	0.031
K ⁺ (mmol/L)	4.0 (3.8-4.3)	4.1 (3.8-4.4)	0.219
Serum lactate dehydrogenase	277.0 (183.3-392.3)	270.3 (179.6-390.1)	0.424
Serum urea nitrogen	5.0 (3.6-6.4)	5.2 (3.7-6.4)	0.075
CT severity index			0.000
0-3	12 (28.6%)	53 (49.5%)	
4-6	15 (35.7%)	49 (45.8%)	
7-10	15 (35.7%)	5 (4.7%)	

MAP, moderate acute pancreatitis; RAC, Revision of the Atlanta classification; BMI, body mass index; APACHE, Acute Physiology and Chronic Health Examination; CT, computed tomography.

DBC system, respectively. No significant differences were found among the three groups with respect to mortality ($P = 1.000$), ICU admission ($P = 0.231$), surgery for IPN ($P = 1.000$), ICU stay ($P = 0.059$), and hospital stay ($P = 0.126$). The results indicated that RAC system had higher variability than DBC system.

To further explore the underlying reason, patients in the RAC group were divided into two subgroups: Infected group (n = 42) and sterile group (n = 107). We found that the pancreas (pancreatic) necrosis ($P = 0.003$), organ failure ($P = 0.009$), Ranson score ($P = 0.031$), and CT score ($P = 0.000$) were significantly different between the two subgroups (Table 3). As shown in Table 4, univariate and multivariate regression analysis were performed to evaluate relevant risk factors, and the results revealed that pancreas (pancreatic) necrosis, organ failure, Ranson score, and CT score were all the risk factors of AP patients with infection, either using univariate or multivariate regression analysis. The results demonstrated

that the appearance of these factors, either alone, or in combination with one or more factors, indicated the occurrence of infection in patients (Table 4).

Discussion

In the present study, we explored the practical value of RAC and DBC systems in classifying MAP. The results showed that there was significant difference in infected necrosis of MAP patients between the two groups. In addition, we found that, the ICU admission, surgery for IPN, and ICU stay were significantly different among the three subcategories according to the MAP criterion of RAC, and while no significant differences were observed according to the MAP criterion of DBC. Therefore, our results indicated that RAC system had higher heterogeneity than DBC system when used to classify MAP and infection might be responsible for the heterogeneity.

In 1992 Atlanta classification system, AP was divided into two categories: mild and severe.

RAC and DBC in classification of MAP

Table 4. Risk factors for MAP patients with infection based on RAC

	Univariate analysis		Multivariate regression analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
(Peri) pancreatic necrosis	1.34 (1.21-3.55)	0.011	1.41 (1.19-3.71)	0.010
Ranson score	2.44 (1.87-4.59)	0.009	2.49 (1.91-4.66)	0.008
Organ failure	1.80 (1.19-3.36)	0.003	1.91 (1.23-3.51)	0.002
CT severity index (0~3/4~6/>7)	5.46 (3.48-8.81)	0.001	5.51 (3.39-8.73)	0.000

MAP, moderate acute pancreatitis; OR, odds ratio; CI, confidence interval.

Recognizing the limitation of the Atlanta classification [16, 17], two international classifications, RAC and DBC systems, have been recently proposed [18-20]. However, there has been a lot of controversy regarding the application value of RAC and DBC classification systems [13, 21-25]. Haq Nawaz *et al.* [13] compared 1992 Atlanta classification system, 2012 RAC system, and DBA system. The study prospectively enrolled 256 cases of AP and compared some indexes that could reflect the severity of the disease, including mortality rate, ICU stay, intervention, and hospital stay. Compared to the Atlanta classification system, RAC and DBC could better predict the mortality rate, ICU admission, and duration of AP patients with higher classification and more severe disease. DBC system can better predict whether or not intervention is necessary, while RAC can better predict the days of hospital stay. Thandassery *et al.* compared DBC and RAC systems, and concluded that DBC was superior to RAC [26]. However, Acevedo-Piedra *et al.* [14] found that the number of days of hospitalization, ICU stays, nutritional support, invasive treatment, and mortality rate were similar in both RAC and DBC systems. The results suggested both of the classification systems can accurately classify AP based on the severity of the disease. Guo *et al.* [12] further classified each of the RAC and DBC categories into different subgroups. The results suggested that DBC classification system cannot accurately reflect the prognosis, and RAC classification system has more advantages than DBC classification system in clinical.

Compared to the 1992 Atlanta classification system, the concept of MAP appears in the two systems. As a new category, MAP is an issue that needs to be further explored. For both RAC and DBC systems, the classification of MAP contains three subcategories including local

complications only, organ function obstacles only, and the combination. However, the definitions of local complications are different in the two systems. In the RAC system, local complications included acute peripancreatic fluid collection (APFC), acute necrotic collection (ANC), walled-off necrosis (WON), and pancreatic pseudocyst, and each of the complications can be infected or sterile [10, 11]. In contrast, for the DBC system, local complication only includes aseptic necrosis [27], which might be responsible for the inconsistency in predicting the clinical intervention and prognosis in AP patients. To further confirm the differences between RAC and DBC with respect to the MAP criterion, we enrolled a total of 321 patients with MAP and assigned the patients to RAC group and DBC group. From our data, we found that there were no significant differences in MAP patients' characteristics between the two groups except in infected necrosis, indicating that infection might be involved in the differences between RAC and DBC.

It has been well demonstrated that infection is a key factor that affects the prognosis of AP, and is also an important indication for surgical intervention [28-31]. Considering the important roles of infection in AP, we further divided the two systems into three subgroups: Local complication only, transient organ failure only, and both. Outcome variables including in-hospital mortality, ICU admission, surgery for IPN, length of ICU stay and hospital stay were compared among the three subgroups in each group. As indicated in our results, we observed that no significant differences were found among the three subgroups according to MAP criterion of DBC. Interestingly, there were significant differences in ICU admission, surgery for IPN, and ICU stay based on the MAP criterion of RAC. These results revealed that RAC had higher heterogeneity than DBC system when used to clas-

sify MAP. Based on these data, we assumed that infection might be responsible for the heterogeneity. The reasons underlying the infection for the heterogeneity can be understood by different classification of MAP local complications. In our study, the local complications of MAP in RAC system included two types: infected and sterile. Infection is not an impact fact for MAP determination based on RAC system. In contrast, in DBC system, sterile necrosis was classified into MAP and infected necrosis was classified into severe or critical AP. In order to better define the symptoms of RAC moderately severe AP patients, possible predictors and risk factors for infection were investigated. We identified that the pancreas (pancreatic) necrosis, Ranson score, CT score, and organ failure were indicators for infection, implying that pancreas (pancreatic) necrosis, higher Ranson score, higher CT score, and organ failure may indicate poor prognosis.

In conclusion, our results suggest that RAC system has higher heterogeneity than the DBC system with respect to classification of MAP, which should be noted when using RAC to classify AP.

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Disclosure of conflict of interest

None.

Address correspondence to: Fei Li, Department of General Surgery, Xuanwu Hospital Capital Medical University, 45, Changchun Street, Xicheng District, Beijing 100053, China. E-mail: FeiLisdykdx@163.com

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RAC and DBC in classification of MAP

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