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A comparative study of severity scoring systems in acute pancreatitis

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Abstract
Objective: To investigate the prognostic and clinical usefulness of existing scoring systems in predicting the severity of acute pancreatitis (AP).
Methods: This prospective, observational clinical study included patients with diagnosed AP. Ranson's, bedside index for severity in acute pancreatitis (BISAP) and PANC 3 scoring systems were used to stratify the severity of disease. Scores from each model were compared to clinical severity. Sensitivity, specificity and accuracy were computed for each model. A $p<0.05$ was considered statistically significant.
Results: Of 54 patients, 25 patients had non-biliary (group I) and 29 patients had biliary pancreatitis (group II). Based on Ranson's scoring, 32% and 27.6% in group I and II were classified as severe pancreatitis whereas the calculated BISAP score predicted severe condition in 24% and 20.7% in group I and II (p=0.77). BISAP was the most accurate (78%) in predicting organ failure, followed by Ranson's (72%) and PANC 3 (65%). Accuracy of BISAP, Ranson's and PANC 3 scoring systems were 91%, 69% and 79.62%, respectively for predicting disease severity.
Conclusion: It was seen that BISAP was better than Ranson's in assessing organ failure, mortality and clinical severity in terms of sensitivity, specificity, PPV, NPV and accuracy.

Keywords: acute pancreatitis, BISAP, PANC3, accuracy

1. Introduction
Acute pancreatitis (AP) is an inflammatory process with a variable clinical course and most patients with AP present a mild disease that can be resolved spontaneously. However, despite critical care, 10%-20% of patients experience a severe attack with high mortality up to 30% [1, 2]. In case of mild to moderate pancreatitis, mortality is less than 5%, although, 30% of them develop secondary infection [3-4 weeks later than onset], which increases the mortality rate [3]. Ever since its establishment, the Atlanta Classification has been considered the global standard tool for the assessment of AP severity [4]. Nonetheless, with time and varying clinical representation, the Atlanta classification was revised with an emphasis on persistent organ failure in 2012 [5].

Therefore, it is of foremost importance to assess the severity and identify patients at risk for an early intensive therapy and timely intervention, and also, it has been shown to improve prognosis and survival.

In this context, various multi-factorial scoring systems including Ranson's [6] and Acute Physiology and Chronic Health Evaluation (APACHE)-II scores [7] have been validated and used for assessment of the severity of AP. However, due to their complex [8-10], a new prognostic scoring system, the Bedside Index for Severity in Acute Pancreatitis (BISAP), was recently proposed as an accurate and simple method for early identification of patients at risk of in-hospital mortality [11, 12]. Although various scoring models exist to clinically evaluate the severity of AP and organ failure, hitherto no single system has been considered ideal, thereby influencing surgeon's preference of choosing a method for prognostic assessment of AP. With this background, we performed a study to compare the accuracy of Ranson's criteria, BISAPs and PANC 3 scoring systems in predicting the severity of an attack of AP.

2. Methods
This prospective comparative observational clinical study was conducted from May 2015 to April 2017 in Sagar hospitals, a tertiary referral healthcare in Bangalore, India.

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The study protocol was approved by the institutional ethical committee. The diagnosis of Acute pancreatitis was made based on history, clinical examination, laboratory values of serum amylase and lipase, and imaging study – ultrasound of abdomen, to study the pancreas as well as to rule out or confirm biliary cause for pancreatitis. The presence of any 2 of the 3 criteria was diagnostic of pancreatitis.

Patients aged 18 years and above, diagnosed of AP (either first attack or recurrent attacks), presenting with acute onset of persistent severe epigastric pain, with or without radiation, and increased serum amylase and lipase levels were included. On the other hand, patients with pre-existing chronic pancreatitis or with co-existing local complications of pancreatitis, cardiac failure, liver failure, renal failure or any lung pathology were excluded.

2.1 Assessment of severity and associated complications
Ranson's, BISAPs and PANC 3 scoring systems were used to stratify the severity of disease, within 48 hours of admission (Table 1). The scores obtained from each of the scoring system were compared to the clinical severity, as defined by Revised Atlanta Classification 2012.

A score of ≥ 3 in first 48 hours for Ranson's and first 24 hours for BISAP indicated a likely severe pancreatitis condition.

Table 1: Description of parameters for BISAP and PANC 3 models

BISAPS	PANC 3
BUN	HCT
Mental status	BMI
SIRS	Chest X-Ray
Age	
Pleural effusion	

BMI: body mass index; BUN: blood urea nitrogen; HCT: haematocrit; SIRS:

Data pertaining to duration of nil per oral, absence, presence or persistence of organ failure, local complications, need for interventions, ICU care, in-hospital mortality and length of hospital stay was collected prospectively for each patient and clinical severity was assessed.

Organ failure was defined according to the Marshall scoring system. Respiratory (PaO2/FIO2), renal (serum creatinine) and cardiovascular organ (systolic blood pressure) functions were scored from 0-4. A score of 2 or more, involving one or more than 1 organ, which may be persistent, lasting for more than 48 hours or transient, lasting for not more than 48 hours was considered as organ failure. The clinical severity was assessed during the course in the hospital, according to Revised Atlanta classification 2012.

2.2 Statistical methods
Descriptive statistics was used to present continuous measurements as mean ± standard deviation (SD) and categorical measurements were presented as number and percentages (%). Student t test was used to compare parameters between two groups for continuous variables and Chi-square/ Fisher Exact test was used for categorical parameters. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were computed to find the diagnostic properties of Ranson's, BISAP and PANC 3 scoring to predict the severity of disease. SPSS 18.0, and R environment ver.3.2.2 were used for the analysis. A p<0.05 was considered as significant.

3. Results
A total of 54 patients (age range: 18 - 82 years) were included in the study, of which 25 patients had non-biliary (group I, mean age: 41.3±14.7 years) pancreatitis, and 29 patients had biliary pancreatitis (group II, mean age: 55.6±14.7 years). However, all the 54 patients were considered as a single group to draw inference regarding outcomes of the scoring systems.

It was seen that the disease was more common in men (n=35) than in women (n=19), although non-biliary pancreatitis was more common in men (76% vs. 55.2%), while biliary pancreatitis was more common in women (44.8% vs. 24%). Biochemical parameters for two groups are presented in Table 2.

Table 2: Demographic and biochemical characters in two groups of patients

Variables	Group I	Group II
PCV day1	39.93±6.31	39.67±5.80
PCV day2	36.57±6.91	36.79±5.84
TLC	14090.40±4959.24	12980.69±4972.59
BUN day 1	13.96±10.57	13.76±7.10
BUN day 2	15.84±12.3	15.24±7.06
RBS (mg/dl)	161.16±73.98	159.55±66.98
AST	106.68±167.02	207.31±200.02*
Calcium	8.46±0.88	8.71±0.67
Fluid sequestration	1201.80±669.53	1210.34±783.78
BMI (kg/m^2)	26.14±5.50	26.29±4.45

PCV: packed cell volume; TLC: total leukocyte count; BUN: blood urea nitrogen; RBS: random blood sugar; AST: aspartate aminotransferase; BMI: body mass index

Based on Ranson's scoring, 32% in group I and 27.6% in group II were classified as severe pancreatitis whereas the calculated BISAP score predicted severe condition in 24% of patients in group I and 20.7% in group II (P=0.77). It was seen that all 54 patients had a PANC 3 score of less than 3, suggesting that each of them would have mild or moderately severe pancreatitis. PANC 3 score did not predict any cases to be severe in our study (Table 3).

**Table 3:** Score code distribution among patients

Ranson's score code	Group I	Group II
Mild/ moderately severe (<3)	17 (68%)	21 (72.4%)
Severe pancreatitis (>/=3)	8 (32%)	8 (27.6%)
BISAP score		
Mild/moderately severe (<3)	19 (76%)	23 (79.3%)
Severe (>/=3)	6(24%)	6 (20.7%)
PANC 3 score		
Mild/moderately severe (<3)	25(100%)	29 (100%)
Severe (=3)	0 (0)	0(0)

As per revised Atlanta Classification 2012, 35 patients (64.8%) of 54 had mild pancreatitis, 8 (14.8%) had moderately severe and 11 (20.4%) had a severe disease (Table 4).

Table 4: Clinical (actual) severity analysis

Actual Severity	Group I	Group II
Not severe (mild + moderately severe)	19 (76%)	24 (82.7%)
Severe	6(24%)	5 (17.2%)

Among the three scoring systems, BISAP was the most accurate (78%) in predicting organ failure, with Ranson's having an accuracy of 72%, and PANC 3 depicted least accuracy (65%), Graph 1
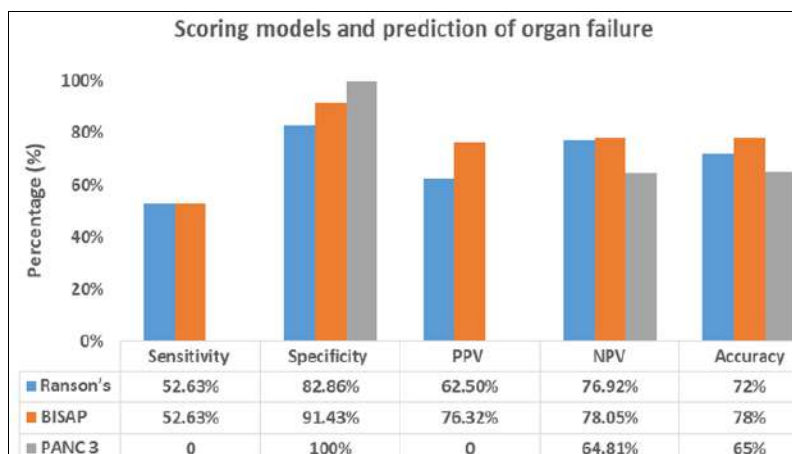
Graph 1: Performance of Ranson's, BISAP and PANC 3 for organ failure

As shown in graph 2, in terms of local complications, all three models were accurate; however, PANC 3 had the highest specificity (100%). PANC 3 was seen to be accurately scoring patients for mortality with highest specificity when compared to other two models (Graph 3).
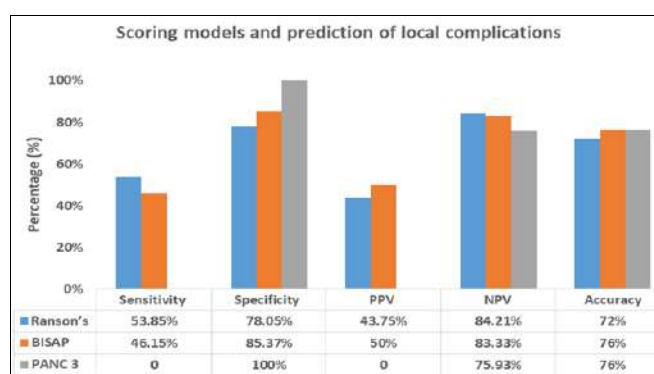
Graph 2: Performance of Ranson's, BISAP and PANC 3 for local complications
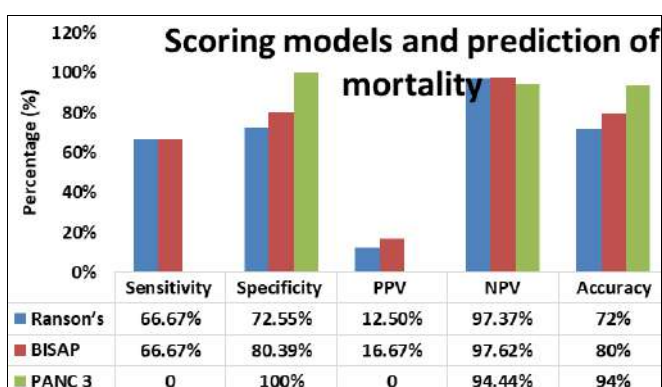
Graph 3: Performance of Ranson's, BISAP and PANC 3 for mortality

Local complications was present in 13 (24.1%) patients, which included pseudocyst, necrosis, ascites, walled off necrosis and recurrence, while 41 patients had no local complications (p=0.20).

Out of 11 patients, who had clinically severe pancreatitis, Ranson's score in 5 of them and BISAP score in 9 of them was more >/= 3. PANC 3 system did not predict severe pancreatitis in any cases (score < 3 in all 11 patients). BISAP score of >/= 3 predicted severity of acute pancreatitis significantly (p <0.0000) when compared to Ranson's score (p = 0.19) and PANC 3 (p value could not be calculated), Table 5.

Table 5: Correlation of Predicted scores with observed scores

Score	Actual severity		Total	p value
Ranson's	Severe	Not severe		
>/= 3	5	11	16	0.19
<3	6	32	38	
Total	11	43	54	
BISAPs				
>/= 3	9	3	12	<0.000*
<3	2	40	42	
Total	11	43	54	
PANC 3				
= 3	0	0	0	-
<3	11	43	54	
Total	11	43	54	

The performance of each scoring model as compared to actual severity of disease is presented in Table 6. The accuracy of BISAP, Ranson's and PANC 3 scoring systems were 91%, 69% and 79.62%, respectively for predicting the disease severity.

Table 6: Ranson's, BISAP and PANC 3 scores for predicting disease severity

Severity	Observation				
	Sensitivity	Specificity	PPV	NPV	Accuracy
RANSON score	45.45%	74.42%	31.25%	84.21%	69%
BISAP score	81.82%	93.02%	75%	95.24%	91%
PANC 3 score	0	100%	0	79.62%	79.62%

PPV: positive predictive value; NPV: negative predictive value

4. Discussion
Several markers have been validated for predicting the severity for management of acute pancreatitis [13]. It has been demonstrated that early recognition of a case can reduce the mortality rate associated with acute pancreatitis significantly and also improve outcome [14].

Multifactorial scoring systems such as Ranson's, Glasgow, APACHE II, CTSI, BISAP and PANC 3 are most commonly used wherein various clinical data such as age, etiology and obesity, blood urea nitrogen, lactate dehydrogenase, chronic health status and inflammatory markers are also used to predict the severity. However, owing to various risk factors considered in each model to define the severity, it is difficult to fully evaluate the actual sensitivity of the markers applied in prognosticating the course of the disease [15]. The ideal predictor of severity is described as being simple, highly sensitive, highly specific, safe, reproducible, cheap and can be rapidly performed [16]. The nature and purpose of this research work was to assess

the predictive accuracy of Ranson's criteria, BISAPs and PANC 3 scoring systems in predicting severity of an attack of acute pancreatitis.

A total of 54 patients with acute pancreatitis were prospectively studied and it was seen that majority of patients were men (64.8%). This is in conjunction with findings of other studies (62%) and it has been shown that alcohol is more common for pancreatitis in men [17]. In our study, it was also seen that, 43 (79.6%) patients had mild to moderately severe acute pancreatitis, while 11 (20.4%) patients had severe pancreatitis. 5 out of 11 and 9 out of 11 severe pancreatitis were correctly predicted by Ranson's score and BISAP, respectively. While, PANC 3 did not predict any severe cases.

It was seen that BISAP was the most accurate (78%) in predicting organ failure. Our results corroborate findings of studies reported elsewhere. A prospective study of 100 patients, done by, Lalithkumar *et al*. [18] showed that BISAP score had better specificity (95.35%), and diagnostic accuracy (92%) when compared to Ranson's model (74.42%, 88% respectively) [18]. Another retrospective study in 303 patients, by Park *et al*. [19]. showed that BISAP and Ranson's sensitivity for organ failure was 91.3% each, specificity was 85% and 71.4 %. PPV was 33.3 and 20.8, NPV was 99.2 and 99.0, respectively. It also showed that BISAP system predicts severity, death, and organ failure in acute pancreatitis better than Ranson's criteria. Results from current study supports the aforementioned findings.

Additionally, 13 patients in our study reported local complications like necrosis, ascites, pseudocyst, walled off necrosis and recurrence of the disease. Among the three models, Ranson's score had a higher sensitivity (53.85%) compared to BISAP (46.15%) whereas PANC3 had highest specificity for local complications (100%). BISAP and PANC 3 scoring models were accurate (76%) in predicting local complications. Park *et al*. [19] also showed that, for local complications (particularly necrosis), BISAP and Ranson's had a sensitivity of 22.5% and 32.5%, specificity of 79.5% and 66.5%, PPV of 14.3% and 12.9% and NPV of 87.1% and 86.6%, respectively.

Another report from Yadav *et al*. [15] also compared BISAP, Ranson's and CTSI in 119 patients prospectively, in predicting necrosis, mortality and severity. It was seen that BISAP and Ranson's were equally sensitive (89.4%) for determining necrosis, while specificity was higher in BISAP (95.8% versus 94.4%). The PPV was 93.3% and 91.3% for BISAP and Ranson's respectively, and NPV was 93.2% for both. The accuracy of BISAP was 93.4% whereas that of Ranson's was 92.7%.

In our study, for predicting mortality, Ranson's and BISAP scores had a sensitivity of 66.67% and highest specificity was seen for PANC 3 (100%). We observed that PANC 3 was most accurate in predicting mortality (94%). Comparable results were also reported by Park *et al*. [19] and Yadav *et al*. [15]. On the contrary, findings from another study, done by Koziel *et al*. reported that BISAP was more accurate in predicting mortality when compared to PANC 3 and Ranson's [20]. Furthermore, Singh V *et al*. [12], by a prospective study showed better accuracy with APACHE II compared to BISAP for predicting mortality.

In the current study, it was also seen that the BISAP score was most accurate amongst all three in predicting clinical severity with highest sensitivity of 81.82%, PPV and NPV of 75% and 95.24%, respectively. In agreement with our data, BISAP was seen to be better than Ranson's for predicting severity in terms of specificity, PPV, NPV and accuracy, in the study done by Park *et al*. [19]. On the other hand, when PANC 3 was compared with Ranson's in a study done by Fukuda *et al*. [21], for

predicting the severity of the disease, it was concluded that PANC 3 could be used to define the severity and predict acute pancreatitis, as a method to be used in combination with the Ranson's criteria owing to its high accuracy, positive predictive value and specificity. This hypothesis was further confirmed by Shah AS *et al*. [22], wherein PANC 3 was concluded to be a cost-effective, promising model for predicting severity allowing prompt treatment and early referral to higher centre.

Although, the various parameters in our study with regard to Ranson's, BISAP and PANC 3, for predicting organ failure, local complications, mortality and clinical severity, had resemblance to various studies comparing the various scoring systems, the sample size of our study was small to definitely predict which scoring system of the three is the best to accurately predict the clinical severity of acute pancreatitis.

In conclusion, we found that BISAP was better than Ranson's in assessing organ failure, local complications, mortality and clinical severity in terms of sensitivity, specificity, PPV, NPV and accuracy. BISAP was also better than PANC 3 in all parameters except specificity, which was highest for PANC 3, for predicting organ failure, local complications and mortality. However, the current data does not provide clear guidance on which models should be used in specific patient population and further studies with larger sample size are needed to clearly draw definite conclusions.

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