ORIGINAL RESEARCH PAPER

Volume-8 | Issue-3 | March-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF 24 HOUR APACHE-II, BISAP AND POP SCORES IN PREDICTING OUTCOMES IN ACUTE PANCREATITIS

General Surgery

Dr. Sami Anwar Khan — Former Resident, Department of General Surgery, SMS medical college and attached hospitals, Jaipur-302001, Rajasthan, India.

Dr. Selvakumar Balakrishnan* — Former Resident, Department of General Surgery, SMS medical college and attached hospitals, Jaipur-302001, Rajasthan, India. *Corresponding Author

Dr. Shalu Gupta — Professor & unit head, Department of General Surgery, SMS medical college and attached hospitals, Jaipur-302001, Rajasthan, India.

ABSTRACT

Acute Pancreatitis(AP) is a disease of variable clinical presentation, with an uneventful course in a majority and a significantly morbid course(severe AP) in about 20% cases1. In severe AP, the mortality is about 20 - 25%2. Predicting patients likely to develop severe AP at admission and early intensive care(ICU) likely leads to a better therapeutic outcome as a > 24hours delay in ICU shifting leads to a four-fold increase in mortality5. The multifactorial Acute Physiology and Chronic Health Evaluation(APACHE) – II score is widely considered the "gold standard"6 against which newer systems are evaluated. Recently two new simple systems appear promising in initial studies: the bedside index of severity assessment in acute pancreatitis(BISAP) and the pancreatitis-outcome prognostication(POP) score8,9,10. We compared these three scores to find out which score predicts closest to outcomes of AP. It was found that BISAP and POP scores can predict the adverse outcomes of AP viz., persistent organ failure, Panctratic Necrosis or in-hospital mortality as accurately as APACHE-II score. The cut-offs of these scores that definitively predict a given adverse outcome needs to be established in further studies. Of the 3 outcomes, Pancreatic Necrosis was less accurately predicted by all the 3 scores as compared to persistent organ failure or mortality.

KEYWORDS

Acute Pancreatitis, APACHE-II, BISAP, POP

INTRODUCTION

Acute Pancreatitis(AP) is a disease of variable clinical presentation, with an uneventful course in a majority and a significantly morbid course(severe AP) in about 20% cases[1]. In severe AP, the mortality is about 20 - 25%[2] occuring in 2 peaks: *early* (within the first 2 weeks) determined by persistence of organ failure >48h(Persistent OF) in the first week[3], and *late*(after 2 weeks), determined chiefly by the presence of pancreatic necrosis(PNec)[4] which increases the risk of sepsis and delayed organ dysfunction manifold. Predicting patients likely to develop severe AP at admission and early intensive care(ICU) likely leads to a better therapeutic outcome as a > 24hours delay in ICU shifting leads to a four-fold increase in mortality[5].

The multifactorial Acute Physiology and Chronic Health Evaluation(APACHE) – II score is widely considered the "gold standard"[6] against which newer systems are evaluated. The APACHE-II system is accurate in predicting mortality and has many advantages but, in reality, even in developed countries, it is rarely used in clinical practice[7] mainly due to its many variables and complex computation. Hence the search for newer, simpler systems of equivalent accuracy continued.

Recently two new simple systems appear promising in initial studies: the bedside index of severity assessment in acute pancreatitis (BISAP) and the pancreatitis-outcome prognostication (POP) score[8,9,10]. Both were proposed in contrasting settings: the BISAP score based in community hospitals and the POP score in ICUs. Both these systems have a few variables, easy to remember and compute at the bedside within 24 hours. The versatility of both systems can be proved beyond doubt only when studied in different populations. Hence we planned to prospectively study the predictive accuracy of these 2 systems in comparison to APACHE- II score in AP cases admitted to a tertiary care center in North India.

METHODS

Ours was a hospital-based prospective observational study of AP patients admitted to our hospital in the year 2012 and having any two of the three features: characteristic abdominal pain, S. Amylase and/or Lipase >3 times normal or AP on CECT scan within 7 days of admission. The study design was approved by the Institute Ethics Committee and Medical Research Council. Consent of participation of each patient was got in the native language(hindi).

A pre-designed data collection proforma was used within 24 hours of admission, to collect clinical and lab details needed to compute the 3 scores. The APACHE-II, the BISAP and the POP scores were then computed as mentioned[8,10]. If a lab test needed to compute one of the scores was not available with the patient, zero was put against that test while computing a given score. Unless contraindicated, each patient underwent a CECT scan of the abdomen between the 3rd and 7th day of admission.

Each patient was observed for development of Persistent OF in the first week, defined as persistent failure in any one of the 3 systems viz., respiratory(PaO2 < 60 mm in room air/need for mechanical ventilation), cardiovascular(Systolic BP <90 mm Hg after resuscitation/ need for inotropic support) and renal(S.Creatinine >2.0 mg/dl after resuscitation). Presence PNec was assessed from the CT scan, if it was done for a given patient. Each patient was followed up until discharge from hospital or death in hospital.

While analyzing the data, continuous and discrete variables were expressed as mean +/- standard deviation and proportions respectively. Comparative analysis was done using the 'Independent Samples t test'/'One-way ANOVA test' for continuous variables and the 'Pearson Chi-square test' for discrete variables.

The predictive accuracy of APACHE-II, BISAP and POP scores were analysed using receiver-operator characteristic(ROC) curve and expressed as area under the curve(AUC). No pre-determined cut-offs of each score for the AP outcomes were used. Sensitivity and specificity were determined at the cut-off with maximum Youden's index for each score for any given outcome. Comparison of ROC curves of various scores for a given outcome was done by the method devised by *Delong et al*[11].

The software SPSS version 20.0(IBM Technologies) was used for majority of the analysis. The MedCalc software version 12.2.1 (www.medcalc.org) was used for ROC curve analysis. A p value < 0.05 was considered significant.

RESULTS

A total of 130 cases of AP were included. Mean age was 42.66 years with maximum contribution in the 21-40 years category(50%). Male/female ratio stood at 1.5. Alcohol abuse was the most common etiology(41.5%), followed by gallstone disease(35.4%) and

idiopathic(17.7%). Among the lab data for calculation of the scores, S. Calcium was not available in 42 cases(32.31%), Arterial Blood Gas analysis in 19 cases(14.62%) and Chest X ray in 7 cases(5.4%). Hence, BISAP score was the most accurately calculated score(complete data in 123 cases; 94.61%) in our study(See Table 1).

Table 1. Basic characteristics and outcomes of acute pancreatitis (AP) cases in our study

Variable		Number
Sample size	130	
Age(in years)		
	Mean +/- SD#	42.66 +/- 15.14
Age Categories		
	21-40 years	65 (50.0%)
	41-60 years	46 (35.4%)
Sex		
	Males(M)	77(59.2%)
	Females(F)	53(40.8%)
	M:F	1.5:1
Etiology		
	Alcohol abuse	54(41.5%)
	Gallstone disease	46(35.4%)
	Idiopathic	23(17.7%)
	Others	7(5.4%)
Patients with complete data for score calculation		
	APACHE II score	111(85.3%)
	BISAP score	123(94.6%)
	POP score	78(60.0%)
Persistent organ failure(Persistent OF)		
	Present	24(18.5%)
	Absent	106(81.5%)
Pancreatic necrosis(PNec)*		
	Present	32(27.4%)
	Absent	85(72.6%)
In-hospital mortality		
	Overall	16(12.3%)
	In Persistent OF	14/24(58.3%)
	Without Persistent OF	2/106 (1.9%)
	In PNec	8/32 (25.0%)
	Without PNec	2/85 (2.4%)
Hospital Stay(in days)		
	Mean +/- SD	8.2 +/- 7.2

SD – Standard Deviation; *Excluding the 13 patients in whom CECT abdomen could not be done.

24/130(18.5%) patients developed Persistent OF, with the respiratory system being the most common failing organ system(24/24; 100%) and 15/24(62.5%) patients having atleast 2 failing organ systems. CECT scan was done in 117/130(90%) cases, with 27.4%(32/117) showing evidence of PNec. The overall in-hospital mortality rate of AP cases was 12.3%(16/130) in our study. The factors significantly associated with mortality were Persistent OF, PNec, inability to do CECT scan, female sex, shifting to ICU. Etiology and age did not affect mortality. The overall mean hospital stay was 8.2 days, being significantly longer only in the presence of Pnec.

The mean APACHE-II score among survivors was 4.17+/-3.42 and that among non-survivors was 12.25+/-5.64. The corresponding mean BISAP scores were 0.88+/-0.87 and 2.63+/-1.03 and mean POP scores, 7.54+/-3.64 and 13.44+/-6.18. The APACHE-II, BISAP and POP scores, all had a significantly higher mean score with a worse outcome viz., Persistent OF or PNec or death($p < 0.0001$ in all cases)

On ROC curve analysis, all the 3 scores, APACHE-II, BISAP and POP scores were able to significantly predict each of the 3 outcomes of AP viz., Persistent OF, PNec and in-hospital mortality(See Figure 1). For Persistent OF, the AUC of APACHE-II score was the highest whereas, for PNec and in-hospital mortality, the AUC of BISAP score was the highest. However, the differences in AUCs of the scores were not significant for any outcome(See Table 2).

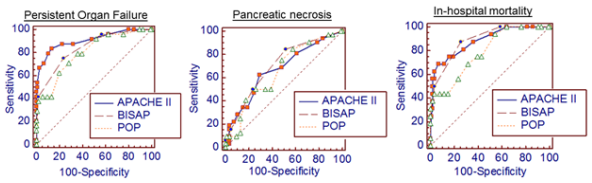

Figure 1. ROC curves of APACHE-II, BISAP and POP scores for each outcome of acute pancreatitis.

Table 2. Predictive abilities of APACHE-II, BISAP and POP scores.

The score	AUC# (95%CI)	Cut-off*	Sensitivity (95%CI)	Specificity (95%CI)
Persistent Organ Failure(AUC difference, pairwise, between all 3 scores – $p > 0.05$)				
APACHE-II	0.906(0.843-0.950)	>6	83.3(62.6-95.3)	86.8(78.8-92.6)
BISAP	0.839(0.764-0.898)	>1	75.0(53.3-90.2)	76.4(67.2-84.1)
POP	0.800(0.721-0.865)	>8	79.2(57.8-92.9)	64.2(54.3-73.2)
Pancreatic Necrosis(AUC difference, pairwise, between all 3 scores – $p > 0.05$)				
APACHE-II	0.668(0.575-0.753)	>4	62.5(43.7-78.9)	70.6(59.7-80.0)
BISAP	0.701(0.610-0.782)	>0	84.4(67.2-94.7)	48.2(37.3-59.3)
POP	0.657(0.563-0.742)	>6	75.0(56.6-88.5)	65.8(40.7-62.7)
In-hospital mortality (AUC difference, pairwise, between all 3 scores – $p > 0.05$)				
APACHE-II	0.882(0.814-0.932)	>9	68.8(41.3-89.0)	93.0(86.6-96.9)
BISAP	0.889(0.822-0.937)	>1	87.5(61.7-98.4)	74.6(65.6-82.3)
POP	0.789(0.708-0.855)	>14	43.8(19.8-70.1)	96.5(91.3-99.0)

Area Under the Curve;
*the score cut-off value with the best sensitivity and specificity (maximum Youden's index)

APACHE-II score predicted Persistent OF, PNec and in-hospital mortality best at cut-offs of >6, >4 and >9(See Table 2). BISAP score predicted the outcomes in the same order, best at cut-offs of >1, >0 and >1, while POP score at cut-offs of >8, >6 and >14, respectively. All the 3 scores predicted PNec significantly less accurately than Persistent OF or in-hospital death($p<0.05$).

DISCUSSION

The mean age of AP patients was 42.66 years with the 21-40 year age group contributing half of the sample. This is consistent with other studies on AP from Asia which report a mean age in the range of 30-48 years[12-14]; in contrast, studies from the West have a higher mean age in the range of 51-57 years[8,9,15-17] with 41-60 years as the most common age group[18]. Our study had a M:F ratio of 1.5:1; other studies from Asia show a M:F ratio in the range of 1.3 – 2.7:1[12-14]. Western studies show M:F ratio of about 1:1[15-17], with some studies even showing a female preponderance[19,20].

Etiology of AP depends on the predominant age and sex of the study sample as well as social habits of the population studied. Some studies have reported alcohol abuse as the leading cause[12,17], whereas others have reported gallstone disease as the leading etiology[8,9,16,19,20]. The predominant etiology of AP was alcohol abuse followed by gallstone disease in our study.

Most authors studying prognostic scores in AP do not mention details regarding completeness of data collection for their scores[10,14,15,17,19,20]. Wu et al, mentioned availability of complete data in 96.8% cases for BISAP score against 2.2% cases for APACHE-II score[8]. BISAP score was the most accurately calculated score in our study, probably due to simple parameters needed for BISAP without the need for an ABG.

Persistent OF was present in 18.5% cases in our study, consistent with

recent studies report persistent OF in AP cases in the range of 19.5 – 26%[9,15,16]. Respiratory system was the most common organ to fail in our study and 62.5% patients of persistent OF having failure of atleast 2 organs. Mofleh, in his systematic review[21], stated that the failing organs in their order of frequency were respiratory(39.1-63.0%), cardiovascular(23.0-37.7%), hepatic(20.7%) and renal(5.8-13%) and failure of atleast 2 organs occured in 35-66% patients with organ failure.

PNec was present in 27.4% cases of AP who got a CECT scan done. This is higher than PNec rates of 14 and 19% reported recently[9,15]. In our study, 90% patients got a CECT scan done, similar to reported rates(67% - 100%) of getting a CECT scan in AP cases[9,15,17]. In-hospital mortality rate was high(12.3%) in our study as compared to recent studies which report a mortality rate in the range of 3.5 – 5.9%[9,15,16], except one study which reported a mortality rate of 13%[17].

As expected, mortality rate was significantly higher in patients developing persistent OF(58.3% vs 1.9%; p <0.000001) or PNec(25% vs 2.4%; p=0.00002). Surprisingly, female sex was associated with a higher mortality rate(20.8% vs 6.5%; p=0.015), despite there being no differences in the rates of persistent OF or PNec based on sex. Age and etiology did not affect mortality rate, in contrast to studies showing a higher mortality in older age[22] and in idiopathic etiology[2].

All the 3 scores had a higher mean score when a worse outcome occurred and were able to significantly predict each of the outcomes. Also the differences between AUC of the scores for any given outcome was not significant. The inference is that BISAP and POP scores, needing just 5 and 6 variables, are able to predict the poor outcomes of AP as reliably as APACHE-II score, which needs 14 variables. This is an important advance in the scoring systems of AP and is consistent with other studies on BISAP[15,19,23,24] and POP scores[14,17].

The cut-offs of the APACHE-II, BISAP and the POP scores for predicting the adverse outcomes of AP are not well established and vary in literature, as seen in Table 3. Lower cut-offs have a higher sensitivity but poor specificity, leading to over-treatment, while higher cut-offs have a high specificity with a low sensitivity, missing cases that could potentially develop an adverse outcome. The ideal cut-off of BISAP and POP scores for predicting persistent OF, PNec and mortality need to be estimated in larger prospective studies.

Table 3. Best predictive cut-offs of APACHE-II, BISAP and POP scores for the various outcomes of Acute pancreatitis.

Score	Outcome	Study	AUC	Cut-off	Sensitivity	Specificity
APACHE – II	Persistent Organ Failure	Current study	0.906	>6*	83%	87%
				>7	79%	89%
		Mounzer et al[25]	0.71 – 0.74	7(or >6)	84 – 97%	44 – 71%
		Papachristou et al[15]	0.78	>7	70%	72%
	Pancreatic Necrosis	Current study	0.668	>4*	63%	71%
				>7	34%	85%
				>8	28%	89%
		Dambrauskas et al[17]	0.79	>8	64%	84%
	Mortality	Current study	0.882	>9*	69%	93%
				>7	75%	84%
				>8	69%	89%
		Dambrauskas et al[17]	0.93	>9	92%	86%
		Papachristou et al[15]	0.94	>7	100%	66%
		Fan et al[14]	0.93	14(or >13)	90%	85%
BISAP	Persistent Organ Failure	Current study	0.839	>1*	75%	76%
				>2	42%	98%
		Papachristou et al[15]	0.81	>2	38%	92%
		Mounzer et al[25]	0.69 – 0.72	2(or >1)	61-62%	76-84%
	Pancreatic Necrosis	Current study	0.701	>0*	84%	48%
				>1	50%	77%
				>2	16%	98%
		Papachristou et al[15]	0.78	>2	33%	91%
	Mortality	Current study	0.889	>1*	84%	48%
				>2	50%	97%
		Wu et al[8]	0.82	>2	50%	93%
		Singh et al[9]	0.82	>2	71%	83%
		Papachristou et al[15]	0.82	>2	57%	88%
POP	Persistent Organ Failure	Current study	0.800	>8*	79%	64%
				>9	71%	72%
		Mounzer et al[25]	0.64-0.67	9(or >8)	46-57%	76-80%
	Pancreatic Necrosis	Current study	0.657	>6*	75%	52%
				>8	50%	74%
		Dambrauskas et al[17]	0.71	>8	52%	93%
	Mortality	Current study	0.789	>14*	44%	97%
				>13	44%	85%
		Fan et al[14]	0.96	>/=14(or >13)	90%	92%
		Dambrauskas et al[17]	0.86	>5	83%	71%

*the cut-off values with maximum Youden's index in our study.

All the 3 scores studied in this study are based on clinical parameters and predicted persistent OF and mortality significantly better than PNec. Other studies too have proven clinical scores like APACHE-II to be unreliable in predicting PNec[26]. Fan et al[14] showed Balthazar CT score to be superior(as compared to clinical scores) in predicting local complications of AP(viz., PNec) but inferior in predicting MODS and mortality.

CONCLUSION

BISAP and POP scores can predict the adverse outcomes of AP viz., persistent OF, PNec or in-hospital mortality as accurately as APACHE-II score. The cut-offs of these scores that definitively predict a given adverse outcome need to be established in further studies. Of the 3 outcomes, PNec was less accurately predicted by all the 3 scores as compared to persistent OF or mortality.

LIMITATIONS

POP score calculation was affected by lack of S.Calcium reports with 32.31% cases. The clinical course and delayed death of patients after discharge from hospital was not followed up in the study.

REFERENCES

1. Isenmann R, Beger HG. Natural history of acute pancreatitis and the role of infection. Baillieres Best Pract Res Clin Gastroenterol 1999; 13: 291-301.
2. Pitchumoni CS, Patel NM, Shah P. Factors influencing mortality in acute pancreatitis: can we alter them? J Clin Gastroenterol 2006; 12: 5068-70.
3. 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.
4. Beger HG, Bittner R, Block S, Buchler M. Bacterial contamination of pancreatic necrosis. A prospective study. Gastroenterology 1986; 91: 433-8.
5. Brivet FG, Emilie D, Galanaud P. Pro- and anti-inflammatory cytokines during acute severe pancreatitis: an early and sustained response, although unpredictable of death. Parisian Study Group on Acute Pancreatitis. Crit Care Med 1999; 27: 749-55.
6. Dervenis C, Johnson CD, Bassi C, Bradley E, Imrie CW, McMahon MJ, Modlin I. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini consensus conference. Int J Pancreatol. 1999;25:195-210.
7. Toh SK, Phillips S, Johnson CD. A prospective audit against national standards of the presentation and management of acute pancreatitis in the South of England. Gut. 2000 Feb;46(2):239-43.
8. 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.
9. Singh VK, Wu BU, Bollen TL, Repas K, Maurer R, Johannes RS et al. A prospective evaluation of the bedside index for severity in acute pancreatitis score in assessing mortality and intermediate markers of severity in acute pancreatitis. Am J Gastroenterol. 2009; 104: 966-71.
10. Harrison DA, D'Amico G, Singer M. The Pancreatitis Outcome Prediction (POP) Score: a new prognostic index for patients with severe acute pancreatitis. Crit Care Med. 2007; 35(7): 1703-8.
11. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988 Sep;44(3):837-45.
12. Baig SJ, Rahed A, Sen S.A prospective study of the aetiology, severity and outcome of acute pancreatitis in Eastern India. Trop Gastroenterol. 2008 Jan-Mar;29(1):20-2.
13. Barreto SG, Rodrigues J. Comparison of APACHE II and Imrie Scoring Systems in predicting the severity of Acute Pancreatitis. World J Emerg Surg. 2007 Dec 9;2:33.
14. Fan JY, Huang ZW, Guo J. 4 scoring systems for prognostic evaluation of patients with severe acute pancreatitis: Receiver operating characteristic curve analysis. J Chin Integr Med. 2009; 7(1): 34-40.
15. Papachristou GI, Muddana V, Yadav D, O'Connell M, Sanders MK, Slivka A et al. Comparison of BISAP, Ranson's, APACHE-II and CTSI scores in predicting Organ Failure, Complications and Mortality in Acute Pancreatitis. Am J Gatroenterol 2010; 105: 435-41.
16. Mofidi R, Duff MD, Wigmore SJ, Madhavan KK, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br J Surg. 2006 Jun ;93(6) :738-44.
17. Dambrauskas Z, Gulbinas A, Pundzius J, Barauskas G. Value of different prognostic systems and biological markers for predicting severity and progression of acute pancreatitis. Scand J Gastroenterol 2010Aug;45(7-8):959-70.
18. Toouli J, Brooke-Smith M, Bassi C, Carr-Locke D, Telford J, Freeny P et al. Guidelines for the management of acute pancreatitis. J Gastroenterol Hepatol 2002 Feb; 17(s1): S15–S39
19. Surco Y, Huerta Mercado J, Pinto J, Piscoya A, De Los Ríos R, Prochazka R et al. Early prediction of severity in acute pancreatitis. [Article in Spanish] Rev Gastroenterol Peru. 2012 Jul-Sep;32(3):241-50.
20. Guzmán Calderon E, Montes Teves P, Monge Salgado E. Bisap-O: obesity included in score BISAP to improve prediction of severity in acute pancreatitis. [Article in Spanish] Rev Gastroenterol Peru. 2012 Jul-Sep;32(3):251-6.
21. Mofleh IA. Severe acute pancreatitis: Pathogenetic aspects and prognostic factors. World J Gasteroenterol 2008;14(5): 675-84.
22. Mann DV, Hershman MJ, Hittinger R, Glazer G. Multicentre audit of death from acute pancreatitis. Br J Surg 1994; 81: 890–3.
23. Gompertz M, Fernández L, Lara I, Miranda JP, Mancilla C, Berger Z. Bedside index for severity in acute pancreatitis (BISAP) score as predictor of clinical outcome in acute pancreatitis: Retrospective review of 128 patients.[Article in Spanish] Rev Med Chil. 2012 Aug;140(8):977-83.
24. Bezmarević M, Kostić Z, Jovanović M, Micković S, Mirković D, Soldatović I et al. Procalcitonin and BISAP score versus C-reactive protein and APACHE II score in early assessment of severity and outcome of acute pancreatitis. Vojnosanit Pregl. 2012 May;69(5):425-31.
25. Mounzer R, Langmead CJ, Wu BU, Evans AC, Bishehsari F, Muddana V et al. Comparison of existing clinical scoring systems to predict persistent organ failure in patients with acute pancreatitis. Gastroenterology. 2012 Jun;142(7):1476-82.
26. Khan AA, Parekh D, Cho Y, Ruiz R, Selby RR, Jabbour N et al. Improved prediction of outcome in patients with severe acute pancreatitis by the APACHE II score at 48 hours after hospital admission compared with the APACHE II score at admission. Acute Physiology and Chronic Health Evaluation. Arch Surg. 2002 Oct;137(10):1136-40.