Original Article

ISSN (O): 2663-8347; ISSN (P): 2663-8339

Comparison of Multifactor Vs Independent Marker in Predicting Severity of Acute Pancreatitis

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Abstract

Background: Acute pancreatitis (AP) is an inflammatory process with a highly variable clinical course. This study was conducted to compare the multifactor vs independent marker in predicting the severity of acute pancreatitis. **Subjects and Methods:** The present study comprised of 50 patients of acute pancreatitis. In all patients, reactive protein (CRP), Interleukin-6 (IL-6), PMN-Elastase (PMN-E), Procalcitonin (PCT), RANSON"s score, GLASGOW score, APACHE-II score, APACHE-O score and Balthazar's CTSI score was recorded. **Results:** There were 45 males and 5 females in the study. There were 12 (22.64%) obese patients in this study. The age of the patients was a significant indicator to discriminate or predict patients with mild or severe pancreatitis. With an AUROC of 0.6004, it was found that age was a poor predictor of the severity of acute pancreatitis. Obesity of the patients was a significant indicator to discriminate or predict patients with mild or severe pancreatitis. With an AUROC of 0.6004, it was found that age is a poor predictor of the severity of acute pancreatitis. Organ failure at admission is more likely to reflect severe cases, it is found to be a poor predictor of severity in acute pancreatitis. The mean CTSI score in the study was 3.57 (SD 2.64), with a median of 2 and ranged from 1 to 10. It was higher in severe pancreatitis and a CTSI score of >=3 was significantly associated with patients with acute pancreatitis by bivariate analysis. **Conclusion:** The authors found that overall, CRP was the best predictor, followed by IL-6, CTSI score, PCT, Glasgow, Ranson's and APACHE-II. PMN-Elastase, Age, obesity and organ failure at admission are poor predictors of severity of acute pancreatitis.

Keywords: Acute Pancreatitis, APACHE-II, Scoring systems

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Received: 15 April 2020 **Revised: 29 May 2020** **Accepted: 11 June 2020** **Published: 30 June 2020**

Introduction

Acute pancreatitis (AP) is an inflammatory process with a highly variable clinical course.[1] Most patients with AP have a mild disease that resolves spontaneously without sequelae. However, 10%-20% of patients experience a severe attack with high mortality of up to 30%.[2] This high-risk group of patients may benefit from aggressive fluid resuscitation, close monitoring for the development of organ failure, proper administration of antibiotics and specific therapeutic procedures, such as endoscopic sphincterotomy and radiologic intervention. Therefore, early assessment of the severity and identification of patients at risk is essential for first intensive therapy and timely response and has been shown to improve prognosis and survival.[3]

Most patients with acute pancreatitis have a mild form of the disease that will respond to supportive treatment. Approximately 20% of affected individuals will develop a severe clinical course in association with the development of a systemic inflammatory response syndrome (SIRS), multiple organ failure (MOF), and on occasion, death. Severe attacks of pancreatitis are associated with prolonged hospitalization, significant morbidity, and mortality ranging between 30% and 50%.[4]

The AP classification criteria established by the 1992 Atlanta International Symposium used Acute Physiology and Chronic Health Evaluation (APACHE) II scores ≥8 and Ranson scores ≥3 as early markers of SAP. Subsequently, many guidelines have also recommended using APACHE II and Ranson scores to assess disease severity at 24-48 h after admission.[5] Moreover, specific instructions recommend using computed tomography severity index (CTSI) scores ≥3, C-reactive protein (CRP) levels ≥150 mg/L and hematocrit (HCT) levels ≥44 to predict SAP. Recently, procalcitonin (PCT), Cr and blood urea nitrogen (BUN) have been used to predict SAP and mortality.[6] This study was conducted to compare the

multifactor vs independent marker in predicting the severity of acute pancreatitis.

Subjects and Methods

The present study was conducted in the Department of Surgical Gastroenterology. It consisted of comprised of 50 patients of acute pancreatitis of both genders. All patients were informed regarding the study and their written consent was obtained. Ethical clearance was obtained from the institutional ethical committee.

Inclusion criteria were all patients who present with acute pancreatitis with the above diagnostic tests and patients who came within 72 hours of the onset of symptoms. Exclusion criteria were all patients who came more than 72 hours after the start of symptoms.

Data such as name, age, gender etc. were recorded. A detailed general and systemic examination were done in all patients. All the patients were subjected to complete blood counts (CBC), S. electrolytes, chest x-ray, USG, contrast-enhanced CT Scan abdomen, C-reactive protein (CRP), Interleukin-6 (IL-6), PMN-Elastase (PMN-E), Procalcitonin (PCT). In all patients, RANSON"s score, GLASGOW score, APACHE-II score, APACHE-O score and Balthazar's CTSI score were recorded. Results thus obtained were subjected to statistical analysis. A P-value of less than 0.05 was considered significant.

Results

Table 1: Sex distribution

Total- 50		
Gender	**Male**	**Female**
Number	45	5

[Table 1] shows that there were 45 males and 5 females in the study.

Table 2: Obesity distribution

Obesity	Number	Percentage
Obese	12	22.64
Non-Obese	41	77.36
Total	53	100

[Table 2] shows that there were 12 (22.64%) obese patients in this study.

[Figure 1] shows that the age of the patients was a significant indicator to discriminate or predict patients with mild or severe pancreatitis. With an AUROC (Area Under ROC) of 0.6004, it was found that age was a poor predictor of the severity of acute pancreatitis.

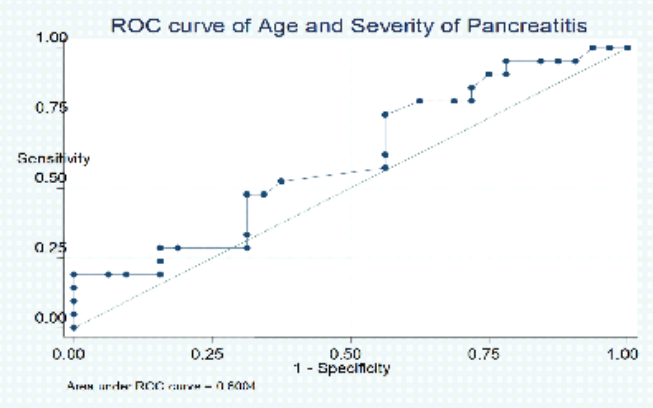

Figure 1: Accuracy of Age as predictors

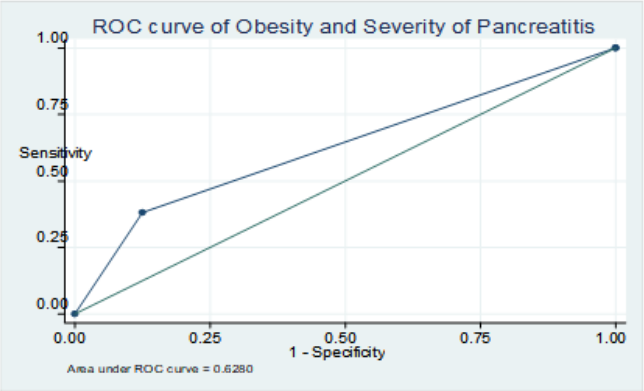

Figure 2: Obesity as a predictor

[Figure 2] shows that the obesity of the patients was a significant indicator to discriminate or predict patients with mild or severe pancreatitis. With an AUROC (Area under ROC) of 0.6004, it was found that age is a poor predictor of the severity of acute pancreatitis.

[Figure 3] shows that although bivariate analysis demonstrated that Organ failure at admission is more likely to reflect severe cases, it is found to be a poor predictor of severity in acute pancreatitis, when plotted on a ROC with an AUC of 0.6429.

[Figure 4] shows that the Ranson's score at 48 hours after admission of the patients in the study ranged from 0 to 6 with a mean (SD) of 1.68 (1.68) and a median of 1. It was higher in severe pancreatitis and a score of >=3 was significantly associated with severe pancreatitis by bivariate analysis. The area under the ROC for a Ranson's score of >=3 was 0.7783 for predicting the severity of pancreatitis. The sensitivity,

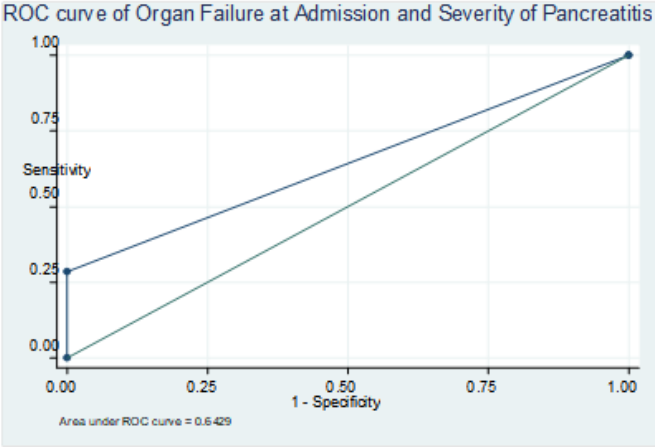

Figure 3: Organ failure at admission

specificity, PPV, NPV and overall accuracy of Ranson's score >=3 in predicting the severity of pancreatitis was 62, 94, 87, 79, and 81%, respectively.

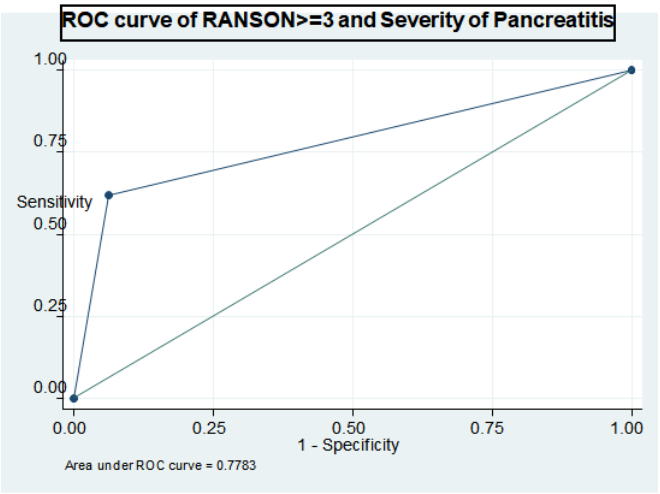

Figure 4: Ranson's scoring system

[Figure 5] shows that the Glasgow score of the patients in the study ranged from 0 to 5 with a mean (SD) of 1.38 (1.43) and a median of 1. It was higher in severe pancreatitis and a score of >=3 was significantly associated with patients with acute pancreatitis by bivariate analysis. The area under the ROC for a Glasgow score of >=3 was 0.7463 for predicting the severity of pancreatitis. The sensitivity, specificity, PPV, NPV and overall accuracy of Ranson's rating>=3 in predicting the severity of pancreatitis was 52, 97, 92, 76 and 79%, respectively. With a cut off >=2, the AUROC was 0.82, with a sensitivity of 76% and NPV of 83%.

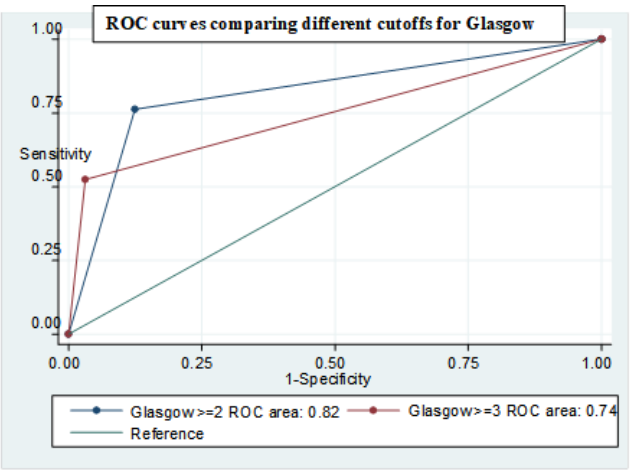

Figure 5: Glasgow scoring system

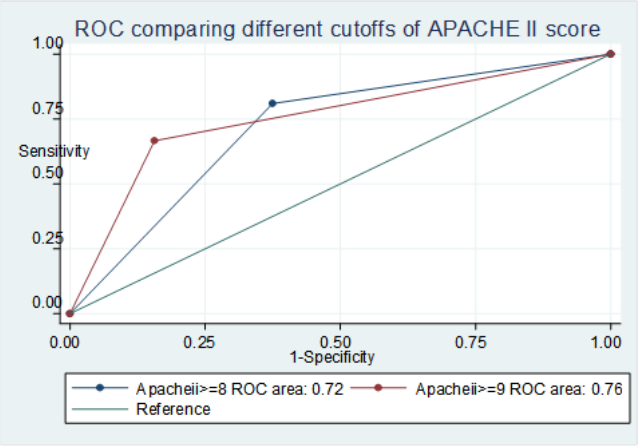

Figure 6: Apache-II scoring system

[Figure 6] shows that the total APACHE-II score of the patients in the study ranged from 4 to 20 with a mean (SD) of 8.28 (3.24) and a median of 8. Bivariate analysis showed APACHE-II score to be higher in severe pancreatitis and a score of >=8 was significantly associated with acute pancreatitis. The AUROC for an APACHE-II score of >=8 was 0.7173 for predicting the severity of pancreatitis. The sensitivity, specificity, PPV, NPV and overall accuracy of APACHE-II score >=8 in predicting the severity of pancreatitis was 81, 63, 59, 83 and 70%, respectively. With a cutoff of >=9, the AUROC was increased to 0.7552 and overall accuracy of 77%.

[Figure 7] shows that the APACHE-O score of the patients in the study ranged from 4 to 22 with a mean (SD) of 8.79 (3.58) and a median of 8. It higher in severe pancreatitis and

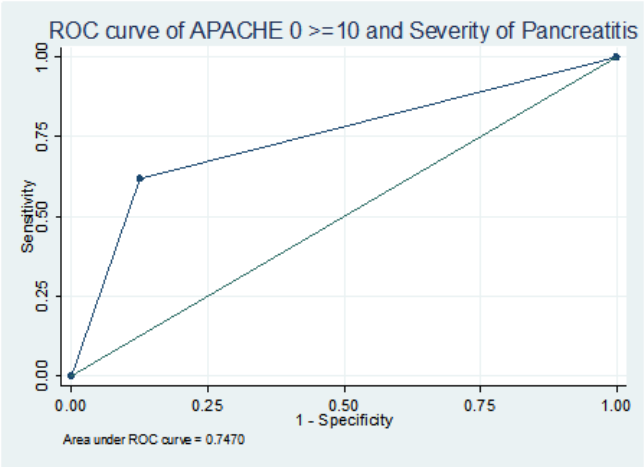

Figure 7: Apache-O scoring system

an APACHE-O score of >=10 was significantly associated with acute pancreatitis by bivariate analysis. The AUROC for an APACHE-O score of >=10 was 0.7068 for predicting the severity of pancreatitis. The sensitivity, specificity, PPV, NPV and overall accuracy of APACHE-O rating>=10 in predicting the severity of pancreatitis was 62, 88, 76, 78 and 77%, respectively.

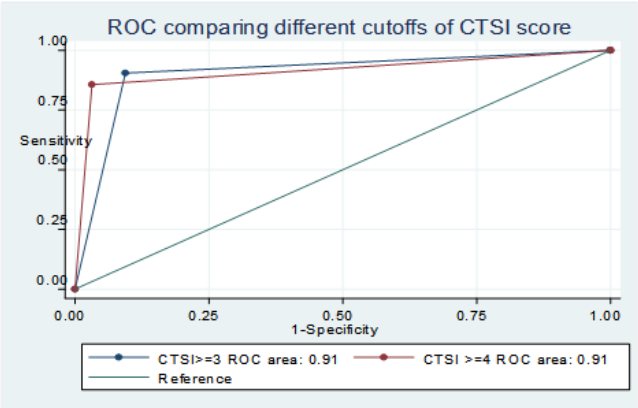

Figure 8: Balthazar's CTSI scoring system

[Figure 8] shows that the mean CTSI score in the study was 3.57 (SD 2.64) with a median of 2 and ranged from 1 to 10. It was higher in severe pancreatitis and a CTSI score of >=3 was significantly associated with patients with acute pancreatitis by bivariate analysis. The area under the ROC for a CTSI score of >=3 was 0.9055 for predicting the severity of pancreatitis. The sensitivity, specificity, PPV, NPV and overall accuracy of CTSI score >=3 in predicting the severity of pancreatitis was 90, 91, 86, 94, and 91%, respectively. With a cut of >=4, the AUROC was marginally better with 0.9129 with sensitivity and overall accuracy of 95 and 92%, respectively.

Table 3: Comparison of other predictors

Variable	AUC-ROC	STD error	95% CI Lower upper
CRP	0.9754	0.0183	0.93959 1.00000
IL-6	0.9539	0.0292	0.89660 1.00000
PMN-E	0.4301	0.0850	0.26343 0.59669
PCT	0.8110	0.0562	0.70090 0.92112

[Table 3] shows that among the biochemical markers, CRP was the best predictor of severity. Except for PMN-Elastase, all the biochemical markers are shown to be good predictors. PMN-Elastase was reasonable in discriminating diseased from ordinary but was a very poor predictor of the severity of pancreatitis. Overall, CRP was found to be the best predictor, followed by IL-6 and PCT.

[Table 4] shows that there was a significant difference in variables in mild and severe acute pancreatitis patients (P< 0.05).

Discussion

The pathophysiology of acute pancreatitis is usually considered in 3 phases. Phase I- Premature activation of trypsin within pancreatic acinar cells. Phase II- Intra pancreatic inflammation and phase III- Extra pancreatic inflammation.[7] In some instances, the various pathways that contribute to increased intrapancreatic and extrapancreatic inflammation result in what is generally termed systemic inflammatory response syndrome (SIRS).[8] In 20-30%, it predisposes to multiple organ dysfunction and/or pancreatic necrosis. The factors that determine severity are not clearly understood but appear to involve a balance between pro-inflammatory and anti-inflammatory factors.[9] This study was conducted to compare the multifactor vs independent marker in predicting the severity of acute pancreatitis.

In our study, there were 50 patients, of whom 45 were males and 5 were females. Cho et al,[10] found that of 161 patients, 21 (13%) were classified as severe AP, and 3 (1.9%) died. Statistically significant cutoff values for prediction of severe AP were Ranson $\geq$ 3, BISAP $\geq$ 2, APACHE-**II** $\geq$ 8, CTSI $\geq$ 3, and CRP24 $\geq$ 21.4. AUCs for Ranson, BISAP, APACHE-**II**, CTSI, and CRP 24 in predicting severe AP were 0.69 (95%ci: 0.62-0.76), 0.74 (95%ci: 0.66-0.80),

Table 4: Comparison of variables

Variable	Mild Pancreatitis (N=32)	Severe Pancreatitis (N=18)	P-value
Age	34.72 ± 12.73	42 ± 16.93	0.08
Obesity (n, %)	4 (12.50%)	8 (38.10%)	0.05
RANSON	0.84±0.95	2.95±1.77	0.0000
RANSON 3 (n, %)	2(6.25)	13(61.90)	<0.001
GLASGOW	0.66±0.79	2.48±1.50	0.0000
GLASGOW	1(3.13)	11(52.38)	<0.001
APACHE-II	6.94±2.09	10.33±3.64	0.0001
APACHE-II ≥8 (n, %)	12(37.50)	17(80.95)	0.002
APACHE-O	7.34±2.10	11±4.24	0.0001
APACHE-O≥10	4(12.50)	13(61.90)	<0.001
CTSI	1.90±0.44	6.15±2.54	0.0000
CTSI≥3 (n, %)	3(9.38)	19(90.48)	<0.001
CRP	44.35±53.04	174.80±14.55	0.0000
IL-6	129.63±319.(	1166.76±818.	0.0000
PMN-E	3.89±1087	3.99±2.75	0.88
PCT (n, %)	4(12.50)	12(57.14)	<0.001

0.78 (95%ci: 0.70-0.84), 0.69 (95%ci: 0.61-0.76), and 0.68 (95%ci: 0.57-0.78), respectively. APACHE-**II** demonstrated the highest accuracy for the prediction of severe AP. However, no statistically significant pairwise differences were observed between APACHE-II and the other scoring systems, including CRP.

In patients with acute pancreatitis, early gradation of disease severity is essential to provide optimum supportive care in intensive units, high dependency units or wards, especially with limited health-care resources as well as to plan for appropriate interventional procedures viz ERCP in biliary pancreatitis. About 50% of deaths occur within 1 week of the attack, mostly from multi-organ dysfunction syndrome. Various single markers have been tested to replace the multifactor systems, of which the most successful has been C-reactive protein.

We found that there were 12 (22.64%) obese patients in this study. We found that age of the patients was a significant indicator to discriminate or predict patients with mild or severe pancreatitis. With an AUROC of 0.6004, it was found that age was a poor predictor of the severity of acute pancreatitis. Obesity of the patients was a significant indicator to discriminate or predict patients with mild or severe pancreatitis. Organ failure at admission is more likely to reflect severe cases, it is found to be a poor predictor of severity in acute pancreatitis when plotted on a ROC with an AUC of 0.6429.

Ranson's score at 48 hours after admission of the patients in the study ranged from 0 to 6 with a mean (SD) of 1.68 (1.68) and a median of 1. It was higher in severe pancreatitis and a score of >=3 was significantly associated with acute pancreatitis by bivariate analysis.

Glasgow score of the patients in the study ranged from 0 to 5 with a mean (SD) of 1.38 (1.43) and a median of 1. It was higher in severe pancreatitis and a score of >=3 was significantly associated with patients with acute pancreatitis by bivariate analysis. The total APACHE-II score of the patients in the study ranged from 4 to 20 with a mean (SD) of 8.28 (3.24) and a median of 8. Bivariate analysis showed APACHE-II score to be higher in severe pancreatitis and a score of >=8 was significantly associated with acute pancreatitis.

The APACHE-O score of the patients in the study ranged from 4 to 22 with a mean (SD) of 8.79 (3.58) and a median of 8. It higher in severe pancreatitis and an APACHE-O score of >=10 was significantly associated with acute pancreatitis by bivariate analysis. The mean CTSI score in the study was 3.57 (SD 2.64) with a median of 2 and ranged from 1 to 10. It was higher in severe pancreatitis and a CTSI score of >=3 was significantly associated with patients with acute pancreatitis by bivariate analysis. The biochemical markers, CRP was the best predictor of severity. Except for PMN-Elastase, all the biochemical markers are shown to be good predictors. PMN-Elastase was reasonable in discriminating diseased from ordinary but was a very poor predictor of the severity of pancreatitis. Overall, CRP was found to be the best predictor, followed by IL-6 and PCT. There was a significant difference in variables in mild and severe acute pancreatitis patients (P< 0.05).

It is hard to identify severe cases earlier than 2–3 days of symptom onset, by which time the network of pathophysiological mechanisms leading to multi-organ dysfunction syndrome is established. An ideal prognostic system would be based on a single test and have a high negative predictive value and should also be universally available, reproducible and non-expensive. Existing methods rely on clinical-biochemical multifactor scoring systems, some of which involve cumbersome calculation.[11]

Conclusion

The authors found that overall, CRP was the best predictor, followed by IL-6, CTSI score, PCT, Glasgow, Ranson's and APACHE-II. PMN-Elastase, Age, obesity and organ failure at admission are poor predictors of severity of acute pancreatitis.

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How to cite this article: Bada VC. Comparison of Multifactor Vs Independent Marker in Predicting Severity of Acute Pancreatitis. Acad. J Surg. 2020;3(1):136-141.

DOI: dx.doi.org/10.47008/ajs/2020.3.1.30

Source of Support: Nil, **Conflict of Interest:** None declared.