

Acute Pancreatitis severity scoring index: Prospective study to identify determinants in Pakistan

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¹ Analysis/Interpretation/Discussion

¹ Manuscript Writing

^{1,2} Critical Review

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Abstract

Introduction: The purpose of the study was to compare different parameters used in Ranson's Criteria, Bedside Index of Severity in Acute Pancreatitis (BISAP), Acute Physiology and Chronic Health Evaluation (APACHE-II), and modified computed tomography severity index (MCTSI) for predicting the severity of acute pancreatitis and formulate a new scoring system to assess the severity of acute pancreatitis based on their prognostic severity index in the local population.

Materials and Methods: This prospective pilot study was conducted at Rawalpindi Medical University allied hospitals from August 2019 to December 2019. All patients with a diagnosis of acute pancreatitis were included in the study through non-probability convenient sampling. Different scoring parameters were entered into standardized proforma.

Results: 100 patients were included in the pilot study with a mean age of 46.53 ± 15.324 . Among 24 parameters from APACHE-II, Ranson's, BISAP, and MCTSI, only 11 parameters, Pleural effusion (PE), Pancreatic necrosis (PN), LDH, serum Calcium (Sca⁺⁺), Pulse, GCS, MCTSI, Base deficit, Po₂, BUN-24 and BUN-48 were significantly related (at 10% level of significance) with the severity of acute pancreatitis. Similarly out of 24, 10 parameters AST, LDH, Sca⁺⁺, Pulse, PE, PN, Base deficit, MCTSI, Po₂, and BUN 48 were significantly covered more than 50% of the area in AUC analysis. Our proposed criteria based on 9 parameters LDH, Sca⁺⁺, Pulse, PE, PN, Base deficit, MCTSI, Po₂, and BUN 48 which were blowing by the two methods (ANOVA and ROC). The sensitivity and specificity were higher with our proposed criteria 93.1% and 60.6% respectively as compared to the Ranson's, modified Ranson, BISAP, and APACHE-II criteria.

Conclusion: The newly proposed criteria for the assessment of the severity of AP is superior as compared to old criteria.

Keywords: Acute Pancreatitis, Ranson's Criteria, Modified Ranson criteria, BISAP criteria, APACHE II criteria.

Introduction

Acute pancreatitis is a severe disease of the pancreas with significant morbidity and mortality. The worldwide annual incidence of acute pancreatitis is increasing and it is about 5 to 80 cases per year per 100,000. Its mortality is about 1 to 7% and can increase up to 20% depending upon disease severity. The increase in mortality directly related to organ failure.¹⁻³ Gallstone and alcohol abuse together responsible for 70-80% of all cases of acute pancreatitis.⁴⁻⁷ AP has an overall mortality of 5-10%. 80-90% cases are mild, self-limited with a fair outcome. The remaining 10-20% of cases with severe pancreatitis have variable pancreatic necrosis or organ failure and need ICU care with possible operative intervention and mortality rate of about 40%.¹⁴

Acute pancreatitis diagnosed based on two of the following three criteria:

1. Characteristic acute pancreatitis abdominal pain
2. Amylase and/or lipase serum levels at least three times upper limit of normal; and
3. Acute pancreatitis characteristic findings on abdominal ultrasonography and/or computerized tomography (CT) scan.

AP severity is classified as mild, moderately severe, and severe according to Atlanta classification 2012. Mild AP had neither local complications nor organ failure. Moderately severe acute pancreatitis had transient organ failure or local complications or both, and severe acute pancreatitis had persistent organ failure.^{8,15}

Different scoring systems based on clinical and biochemical data had been used for the past few decades. These include APACHE-II, Ranson's, BISAP, Glasgow-Imrie, and MCTSI. Each has its limitations like low sensitivity, specificity, and complexity as well as an inability to obtain a final score until 48 hours after admission.¹⁶

The rationale of this study is to compare different parameters used in Ranson's, BISAP, APACHE-II, and MCTSI for the severity of acute pancreatitis and design new criteria to assess the severity of AP at the local population because the etiology of acute pancreatitis is different as compared to western population, that may be cost-effective and more simple.^{17,18}

Objective: To compare parameters used in different scoring systems for the severity of acute pancreatitis and formulate a new scoring system for assessing the severity of acute pancreatitis in our population.

Materials and Methods

Study Design: Prospective study.

Setting: Rawalpindi Medical University and Allied Hospitals.

Period: Pilot study (6 months from July 2019 to December 2019)

Sample size: We validate our sample size for this pilot study through the WHO sensitivity specificity sample size calculator. Keeping sensitivity 93.1%, specificity 60.6%, the proportion of severe/moderate cases of AP (which is in our sample of 100 is observed) 29% and with precision 14%, the minimum sample size is 98 hence we include 100 patients for this pilot study.

Methods: All admitted patients with acute pancreatitis at Rawalpindi medical university allied hospitals were included in the study. Data collected through standardized Performa. All acute pancreatitis patients of either gender, having age over 12 years, reporting to the accident and emergency department, were included in the study. Informed consent was taken from all patients.

After the history and physical examination, laboratory investigations were sent at the time of admission, CBC, hematocrit, serum amylase and lipase, liver function test, kidney function test, serum electrolytes, LDH, ABG analysis, and blood sugar. All patients have abdominal ultrasonography at the time of admission and contrast-enhanced pancreatic protocol CT scan 2-7 days after symptoms onset.

Patients examined daily and investigations relevant to Ranson's, BISAP, and APACHE-II scores were noted. BISAP was calculated within the first 24 hours of admission and Ranson's score was evaluated within the first 48 hours of admission. Computed Tomography is carried out according to patient condition but preferably within two to seven days after admission.

Data Analysis Procedure: The collected data of diagnosed cases of AP were included and analyzed using SPSS version 23. AP patients classified according to Atlanta classification 2012. Pancreatic necrosis, need for ICU care and length of hospital stay were also observed. The final grade of AP was decided according to Atlanta 2012 classification. For the first part of our objective, we first examined thorough mean comparison (ANOVA), proportion comparison (Chi-square), and ROC from 24 parameters, how many were related to the severity of the disease in our sample. Then for the new index, we selected those parameters that were related to the severity of the

disease and also cover more than 50% area under the curve. Lastly, we calculated Ranson's score, Modified Ranson's score, BISAP, and APACHE II, and the sensitivity, specificity, and Area Under the Curve (AUC) were also calculated. We calculated the sensitivity, specificity, and AUC of our proposed criteria and found a better model through sensitivity, specificity comparison with different old criteria.

Results

Out of 100 cases, 53 were female and 47 were male. Only 10 patients were admitted to ICU for additional care. The average age of the patients was 46.53 ± 15.324 years ranged between 14 to 88 years of age. The patients having comorbid DM, HTN, and DM & HTN were 20%, 9%, and 10% respectively. Out of 100 patients, 75% biliary, 4% alcoholic, 5% post ERCP, 3% hyperlipidemia, and 1% tumor and 12% have other etiology.

We examined 24 parameters Sex, Age, White blood cells (WBC), Random blood sugar (RBS), Aspartate aminotransferase (AST), Lactic Acid Dehydrogenase (LDH), Hematocrit (HCT), Serum Calcium (SCa), Respiratory rate (RR), Pleural Effusion (PE), Pulse, GCS, Temperature, PN, MCTS1, Base deficit, Fluid Sequestration (FS), Po2, Ph. Arterial, Creatinine(Cr), BUN 24 hours, BUN 48 hours, MAP, Sodium(Na) and Potassium(K) in all selected patients and related the above parameters with the severity of the disease.

To test the relation between qualitative parameters and severity categories we used the chi-square test. Proportions of mild, moderate, and severe cases were not the same between patients having PE positive and negative with p-value 0.001. Similarly, there was no relation between PN and severity of the AP with p-value 0.000. The detail is mentioned in Table 1.

We compared all quantitative parameters between severity categories of the patients i.e. Mild, Moderate, and Severe through ANOVA. The mean values of 9 parameters LDH, Sca++, Pulse, GCS, MCTS1, Base deficit, Po2, BUN-24 and BUN-48 were significantly different between 3 categories having p-value 0.027, 0.001, 0.000, 0.000, 0.000, 0.008, 0.001, 0.017, 0.000. The reason behind the use of a 10% level of significance rather than 5% is that as this is a pilot study and the variable which is significant at 10%, at this stage, have very much chances of significant at 5% on final analysis with the higher number of cases.

Similarly, with the second method and for verification, we use Receiver Operative Curve (ROC) which gives us a second opinion regarding the relationship between parameters and the severity of the disease. Through the receiver operative curve, we also find the cut points (corner points) where the severity of AP is changed from one category to another. 10 out of 24 parameters AST, LDH, Sca++, Pulse, PE, PN, Base deficit, MCTS1, Po2 and BUN 48 have significantly covered the area under the curve with p-value 0.042, 0.072, 0.002, 0.015, 0.000, 0.001, 0.023, 0.000, 0.096 and 0.018 respectively. The detailed results of AUC analysis are mentioned in Table 3.

Based on the above analysis, we formed new criteria for the assessment of the severity of the disease. The new criteria were based on the 9 parameters PE, PN, LDH, Sca++, MCTS1, Base deficit, Po2, BUN 48, and Pulse, which were highlighted through both ANOVA and AUC analysis. The descriptive analysis of the selected parameters for the proposed criteria as mentioned in Table 4.

The AUC with proposed criteria (A) was 0.84 with a p-value of 0.000 whereas the sensitivity, specificity, PPV, and NPV were 93.1%, 60.6%, 53.5%, and 89.5% respectively. Interestingly, the cut off value in either case (proposed criteria A or in final proposed criteria) was observed 3.5 and the BUN-48 just strengthen the probabilities.

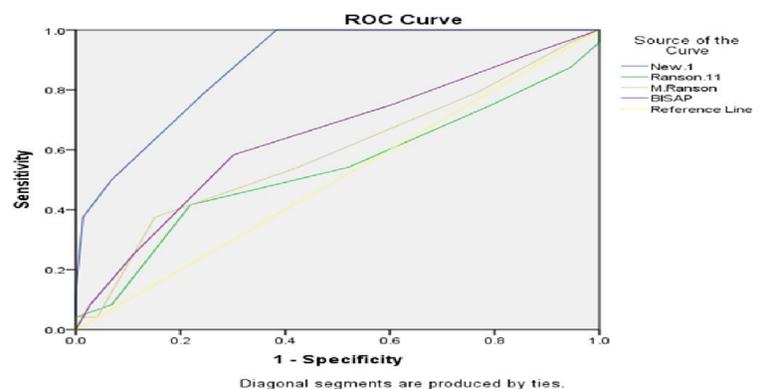


Figure 1: ROC Curve

Table 1: Relationship between qualitative parameters and severity of the disease

Variable	Categories	Severity of the disease			p-value
		Mild	Moderate	Severe	
PE	Yes	17	14	7	0.001
	No	54	7	1	
PN	No	56	12	0	0.000
	Less or equal to 30%	14	4	3	
	More than 30%	1	5	5	

Table 2: Mean comparison of quantitative parameters between different categories of AP with respect to the severity of the disease

Variable	Severity of the disease			P-value
	Mild (n=71)	Moderate (n=21)	Severe (n=8)	
LDH	487.90 ± 311.409	655.29 ± 519.611	818.63 ± 519.407	0.027
Serum Calcium	8.6577 ± 1.1591	7.5957 ± 1.0706	8.8263 ± 1.4376	0.001
MCTS1	3.04 ± 2.161	5.81 ± 2.600	8.25 ± 2.252	0.000
Base deficit	2.5827 ± 3.472	4.4095 ± 6.2195	10.9525 ± 21.9608	0.008
Po2	78.64 ± 11.17	76.76 ± 11.606	62.13 ± 12.276	0.001
BUN at 24 hours	15.2063 ± 5.2652	17.5067 ± 7.5316	22.9925 ± 18.1058	0.017
BUN at 48 hours	14.5669 ± 4.2094	17.7795 ± 6.9649	26.8763 ± 19.8948	0.000
Pulse	89.97 ± 9.823	93.00 ± 11.415	106.75 ± 15.709	0.000
GCS	14.99 ± 0.119	14.95 ± 0.218	14.5 ± 0.926	0.000

Table 3: Diagnostic accuracy of the parameters with respect of the severity of the disease

Variable	Cut off point	Area under the curve	Sensitivity	Specificity	P-value
PE	1	0.742	0.724	0.761	0.000
PN	More than 30%	0.665	0.345	0.986	0.01
LDH	473	0.615	0.552	0.577	0.072
Sca++	8.65	0.301	0.207	0.507	0.002
MCTS1	5	0.833	0.724	0.845	0.000
Base deficit	2.2	0.646	0.655	0.521	0.023
Po2	78.5	0.394	0.345	0.549	0.096
BUN 48	14.005	0.652	0.69	0.507	0.018
Pulse	89.5	0.656	0.655	0.507	0.015
AST	144.75	0.37	0.31	0.507	0.042

Table 4: Descriptive analysis of quantitative parameters used in proposed criteria

Parameters	Mean ± Standard deviation	Minimum	Maximum
LDH	549.51 ± 391.327	77	2013
Sca++	8.4482 ± 1.2348	5.7	11.68
MCTS1	4.04 ± 2.799	0	10
Base deficit	3.6359 ± 7.4624	-2	65
Po2	76.92 ± 12.079	42	100
BUN 48	16.2263 ± 7.8719	2.5	62
Pulse	91.95 ± 11.521	62	130

Table 5: Comparison of different criteria with the proposed criteria for measurement of severity of the disease

Criteria	Cut off point	Area	p-value	Sensitivity	Specificity
Ranson's	5.5	0.501	0.988	31%	76.1%
M.Ranson's	3.5	0.524	0.713	48.3%	54.9%
BISAP	5.5	0.711	0.001	62.1%	74.6%
APACHE II	9.5	0.636	0.033	62.1%	66.2%
Proposed criteria	3.5	0.848	0.000	93.1%	60.6%

Discussion

Acute pancreatitis is a common disease encountered by medical professionals all over the world. It is critical to identify those patients who have severe disease and benefit from early intensive care. In most cases of AP, it is very difficult to assess the severity clinically alone.

Various scoring systems incorporating clinical and biochemical criteria for severity assessment of AP have been in use for the last few decades. Among these, Ranson's et al. in 1970 included 11 measures⁹, Glasgow score (08 measures)¹⁰, MOSS score (12 measures), BISAP (05 measures), and APACHE II score (14 measures).¹¹ The sensitivity and specificity of these systems for predicting the severity of acute pancreatitis range between 55% and 90%, depending on the cut-off number and timing of scoring.¹² Limitations of these systems have been either a very low diagnostic accuracy of different parameters in 48 hours (Ranson and Glasgow scores) or the complexity of the scoring system itself (APACHE II). The APACHE-II score has not been developed specifically for acute pancreatitis but has been proven to be an early and reliable tool for organ failure.

Ranson's criteria have 11 parameters and recorded on admission and at 48 hrs, but its primary aim was to evaluate the early operative intervention in patients with AP. A composite score of 3 or more is used to classify a patient as having severe pancreatitis. In our study, the ROC analysis gives a very low AUC 50.1% with the best cutoff point 6 or more. On that cut point, sensitivity and specificity also not very impressive with 31% and 76.1% respectively.

The APACHE II score has the advantage to assess patients at any time during the illness but very cumbersome for routine clinical use. The sensitivity, specificity, and AUC were the best among the different old criteria to measure the sensitivity of the disease having 62.1%, 66.2%, and 63.6% respectively.

In this pilot study, we have 24 parameters from Ranson, BISAP, APACHE-II, MCTSI, and observed their correlation with the severity of acute pancreatitis.

We confirmed that different parameters can be used as a reliable marker for early stratification of the severity of acute pancreatitis.

In our pilot study, the mean age of the study population was 46.5 years with a slight female predominance. Out of 100 patients, 71 (mild), 21 (moderately severe) disease, and 7 have severe pancreatitis. Gall stone pancreatitis was found in 75 (75%) cases and alcoholic in only four cases. Nine parameters correlate with the severity of pancreatitis with a p-value <0.05. Among these pulse with mean 106 ± 15 in severe pancreatitis patients, pleural effusion was present in 7/8, LDH with 818 ± 519 in severe disease, were analysed at the arrival of patient in the hospital and base deficit with a mean 10.95 ± 21.96 , po_2 with mean 62 ± 12 , Sca with mean 8.82 ± 1.43 and BUN 48 with mean 26 ± 19 at 48 hours of admission. PN 30% or >30% were present in all severe pancreatitis patients and MCTSI with a mean 8.25 ± 2.25 score were assessed between 2-7 days after the patient in a hospital stay.

The proposed criteria are based on 9 parameters, most of them will be easily available when a patient with acute pancreatitis visited the emergency department. The proposed criteria cover 84% variation in the severity of the disease at the value 4 or more, which is significantly greater than 50% with p-value 0.000. The sensitivity, specificity, positive predictive value, and negative predictive value of the criteria is also higher as compared to the previously designed old criteria. Hence the proposed criteria are efficient, give a better result in less time, and cost-effective. We will validate our new criteria with a large sample in the future.

Conclusion

Based on our pilot sample, we conclude that it is necessary to design new and better criteria for our population as acute pancreatitis patients in our study, have a different proportion of etiology as compared to the western population. As this pilot study results show that our newly proposed criteria for the severity of AP are superior for our sample, hence we will be

able to design a better index when we observe the behavior of the parameters with a large sample data.

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