Comparative Analysis of Scoring Systems for Predicting Mortality in Acute Pancreatitis

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ABSTRACT

Background: In the view of need for early identification of cases of Acute Pancreatitis [AP] who may end up dying in spite of rigorous treatment measures, many scores have been proposed claiming to be superior in doing so. This study compares 5 newer scores which are possible to be assessed in first few hours of admission with mortality as outcome.

Methods: It's a retrospective study of 200 consecutive cases of first episodes of AP in a tertiary care centre in India. Scores were compared at their optimal cut off values by sensitivity, specificity, Positive and Negative predictive Values and Odds ratios.

Results: This study showed maximum sensitivity of mortality prediction by HAPS, but best PPV by CTSI. Best specificity was achievable by HAPS.

Conclusion: The newer scores have a reliable predictive capability for mortality outcome at earlier stage of management, irrespective of severity of AP.

Key words: acute pancreatitis, scores, prediction of mortality

INTRODUCTION

Acute pancreatitis [AP] is a common disease with an incidence of 5 – 80 per 100,000 members of the population worldwide (1), although it exhibits wide variation in its geographic distribution and it has shown a steady increase in recent decades. Biliary tract stones and alcohol account for 80-90% cases of AP (2). Other causes include hypertriglyceridemia, hypercalcemia, post-endoscopic retrograde cholangio-pancreatography [ERCP] and drug-induced pancreatitis, but they are much less common. The clinical course of AP is usually mild and often resolves without sequelae. Nonetheless, between 10 and 20 % of patients experience a severe AP attack (3), resulting in an intense inflammatory response, a variety of local and systemic complications, a prolonged hospital course, significant morbidity and mortality. In such patients, the acute inflamma-

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tory response may progress to Systemic Inflammatory Response Syndrome [SIRS], multiorgan failure, and / or pancreatic necrosis. However, the individual patient response to pancreatic injury is highly variable and often unpredictable. A mortality of approximately 1% among all AP but so high as 20% to 30% among those with severe acute pancreatitis [SAP] is documented in literature (4).

Clinical biomarkers that predict the development of these life-threatening complications are important to help guide patient triage and management. However, no simple test or group of tests have proven to perform reliably in stratifying the cases on the severity basis. Since the morbidity and mortality of AP differ markedly between mild and severe disease [mild < 5% vs severe 20–25%], it is very important to assess severity as early as possible. Multiple clinical criteria, biochemical parameters and imaging criteria have been used for this purpose.

Ranson, in 1974, proposed a score of objective parameters predicting the severity of AP, which has been modified by few [Imri, Banks, etc]. This score was proven to predict the outcome to optimal capacity, but had the drawback of requiring 48 hours to assess thus losing the critical time frame of management to improve the outcome if the score is high. In a large population study, modified Ranson's score has shown to have sensitivity of 75%, specificity of 77%, Positive Predictive Value [PPV] 49% and Negative Predictive value [NPV] 91% for the mortality prediction (5). In 1989, Larvin et al first proposed that Acute Physiology and Chronic Health Enquiry score [APACHE II], had 77% prediction of outcome which was even better as 88% at 48 hours (6). APACHE II had the advantages of consideration of major physiological risk factors, serial 24-hourly assessment giving better prediction and disadvantage being a lengthy and non-pancreatitis-specific score, thus important measures such as pancreatic injury and significant regional complications are missed. Many other scores, such as Simplified Acute Physiology [SAP] score, Medical Research Council [MRC], Pancreatitis Outcome Prediction [POP] Score, Japanese Severity score [JSS], Modified Glasgow Score [MGS], etc have been proposed since then, but very few have been proven as good predictors of morbidity and mortality after comparison with standard Ranson's and APACHE II.

Here, the study aimed to compare the mortality prediction capabilities of five newer scores which are possible to be assessed in first few hours of admission - Bedside Index for Severity in Acute Pancreatitis [BISAP], Modified Marshall's Score [MMS], Systemic

Inflammatory Response Syndrome Score [SIRSS], Harmless Acute Pancreatitis Score [HAPS] and CT Severity Index [CTSI] [Modified Balthazar's score].

METHODS

This is a retrospective observational study in a prospectively collected data of consecutive cases of first episodes of AP from November 2019 to November 2020 in a tertiary care centre in India. Inclusion criteria was first episode of confirmed cases of AP admitted in the hospital. Cases with underlying chronic or traumatic pancreatitis, congenital malformations of pancreaticobiliary tract, malignancies of hepato-pancreaticobiliary system, immunosuppression due to concurrent ailment or medication, pregnancy, known history of coagulative disorders or a recent history of myocardial infarction or cerebral infarction, treatment terminated for nonmedical reasons and incomplete data files were excluded. Five scores, viz BISAP, MMS, SIRSS, HAPS and CTSI were calculated at the time of admission in cases of AP at their first presentation. Annexure 1 shows the details of the components of scores. The cases were triaged as per revised Atlanta Classification and treated as per standard protocol of International Association of Pancreatology/ American Pancreatic Association guidelines (7).

All analyses were conducted in SAS 9.4. Bivariate relationship was assessed between categorical score variables and mortality outcome using odds ratios [OR] calculated based on Pearson's chi-squared [χ^2]-test. By plotting Receiver-operator curves for mortality, AUC estimates at 95% Confidence Interval for all the scores were compared. The AUC ranges were, by convention, between 1.0 [perfect separation of the 2 groups by the test] and 0.5 [no ability of the test to distinguish between the 2 groups]. The optimal cut offs were derived using Youden's Index at highest sensitivity and specificity. Furthermore, PPV and NPV for different cut offs were evaluated.

RESULTS

Among the 200 patients fulfilling inclusion criteria, 162 were males and 38 were females diagnosed with AP. Most of them [86%] were less than 50 years of age. Aetiology of pancreatitis in our population has been depicted in *table 1*. Overall mortality was reported in 24 [12%] of the patients.

Receiver operating curves [ROC] yielded highest values of Area under Curve [AUC] for HAPS as 0.96 [0.91-1.00] followed by SIRSS 0.92 [0.86-0.97], as

Table 1 - Aetiology of Pancreatitis

Causes	Number of cases	Percentage
Alcohol	113	56.5
Biliary	28	14
Both	4	2
Other	58	29

shown in table 2 and figure 1. Least AUC values were observed for CTSI score, 0.78 [0.70-0.87]. Using chi-squared test, odds ratio and 95% confidence intervals were also estimated for all scores for predicting mortality. HAPS score yielded an odds ratio of 52.7 [12.3-225.2] while CTSI score yielded an odds ratio of 1.53 [1.26-1.85].

As shown in table 3, on comparing the sensitivity, specificity, PPV and NPV for all the scores under study, HAPS score presented a sensitivity of 91.7% and a specificity of 93.8% which was comparable to MMS, but BISAP presented with best specificity of 98.3%.

Applying optimal cut off to the sample size, the number of patients with MMS ≥ 3 was 22 [11%], SIRSS ≥ 3 was 42 [21%], BISAP ≥ 3 was 19 [9.5%], HAPS ≥ 2 was 33 [16.5%] and CTSI ≥ 6 was 89 [44.5%]. All 17 patients with a HAPS of 3 died. However, only 25% of

Table 2 - Comparison of AUC and ORs of the scores

AUC of different scoring systems for mortality			
Parameter	Area	95% Wald Confidence intervals	
		Lower limit	Upper limit
HAPS	0.9582	0.9105	1
SIRSS	0.9169	0.8622	0.9716
BISAP	0.8203	0.7034	0.9373
MMS	0.7962	0.69	0.9023
CTSI	0.7836	0.6964	0.8709

OR for Mortality stratified by different scores (95%)			
Parameter	Odds ratio	95% Wald Confidence intervals	
		Lower limit	Upper limit
HAPS	52.697	12.33	225.228
SIRSS	11.695	5.16	26.508
BISAP	7.775	3.596	16.811
MMS	4.261	2.344	7.746
CTSI	1.525	1.259	1.848

Table 3 - Efficiencies of the scores

Parameter	Sensitivity	Specificity	PPV	NPV
HAPS	91.7	93.8	33.3	1.2
SIRS	83.3	87.5	52.4	2.5
BISAP	66.7	98.3	15.8	4.4
MMS	54.2	94.9	40.9	6.2
CTSI	87.5	61.4	76.4	2.7

Figure 1 - Graphic presentation of ROC curves of the scores

patients had a mortality event among patients with a CTSI score ≥ 8 . For SIRSS ≥ 3 , 48% reported mortality while for BISAP score of ≥ 3 had 84% of patients died. On the other hand, among patients who died, 5 patients had a BISAP of 1. Odds of predicting mortality were the highest for HAPS followed by SIRSS.

All the statistical analyses in this study are deduced and certified by Statistician who is a co-author of the study.

DISCUSSION

In this study, the newer multifactorial scores are compared which are not yet universally accepted for morbidity and mortality prediction in AP. Though there have been discrete studies proving superiority of individual scores in this list for predicting outcome over the traditional scores with proven efficacy such as Ranson's, APACHE II or modified Glasgow Score, to the best of our knowledge, there is no literature comparing these scores, which can be assessed within few hours of admission, with each other. Keeping the null hypothesis as none of these scores had better predictability of mortality over others, results negated it after analysing the AUC and odds ratios for each score coming to

conclusion that HAPS had the best discriminative abilities followed closely by SIRSS. The overall mortality in our sample size was 12% which was higher than a previous American study (8), but almost same as another study in a heavy intake tertiary care centre in India (9).

AP occurs when pancreatic enzymes are prematurely activated inside the pancreas leading to autodigestion of the gland and local inflammation. These enzymes can also reach the bloodstream, triggering the inflammatory cascade, which leads to the SIRS. Multiorgan dysfunction syndrome, the extent of pancreatic necrosis, infection, and sepsis are the major determinants of mortality in AP. Thus, 5 multifactorial scoring systems were selected which take these elements into consideration and as a result, are very much likely to predict the mortality.

For simplified understanding of these five scores, the summary of their components, advantages and flaws is shown in *Annexure 1*.

There are multiple comparative studies of these scores with traditional scores showing competitive efficacies.

BISAP has a component as SIRSS, so its efficacy parallels SIRSS. Majority of the literature has shown BISAP to have a very accurate mortality prediction (10). An Indian study performed in Uttar Pradesh with a cohort of 72 patients, had shown BISAP to have sensitivity of 100% for prediction of mortality while it was compared with APACHE II, SIRSS, CTSI and individual markers like procalcitonin, CRP, etc (9). On

the other hand, our study has shown a sensitivity of 66.7% for outcome of mortality at the cut off of 3. BISAP has been shown to be the best predictor of mortality when compared to CTSI and SIRSS in another Indian study with a sample size of 105 (11). Another recent study conducted in China has shown that BISAP and Ranson's score have comparable ability [no statistically significant difference] in predicting overall outcome [SAP, local complications, organ failure and mortality] of patients with AP (12). This study of 442 subjects has also concluded that combination of BISAP with HAPS can better help predict the prognosis of AP patients. HAPS on its own has shown a sensitivity of 98% and specificity of 77% for detecting disease severity (13). This study showed moderate agreement and positive correlation between HAPS and Ranson's score with kappa= 0.77 at $p < 0.001$.

CTSI has been primarily designed to identify the need for intervention in local complications. It, being a purely radiological score, with no clinical or biochemical /haematological component, hasn't shown comparable correlation with mortality in previous literature as good as Ranson's, APACHE II or BISAP (9,14,8), but it has conclusively shown superiority in more accurately diagnosing clinically severe disease and better correlate with pancreatic infection and the need for intervention (15).

Though SIRSS and MMS have been widely used in AP management, there is a very scarce literature about their prediction abilities with mortality as outcome. SIRSS at intervals of 24 hours shows a trend in the

Annexure 1

Score	Components	Strengths	Weaknesses
MMS	1. PaO ₂ /FiO ₂ 2. Serum creatinine 3. Systolic Blood pressure	1. Easy and early derivation possible 2. Assesses Multi organ involvement	1. Doesn't assess immune response of the body
SIRSS	1. Pulse 2. Respiration 3. Temperature 4. WBC count	1. Higher component of clinical factors, thus easy to assess 2. Can be calculated even in clinically suspected cases, even before diagnosis, within an hour of admission	1. Nonspecific nature of the scoring 2. Comorbidities are not taken into consideration
BISAP	1. Blood urea nitrogen (BUN) 2. Impairment of mental status 3. Systemic inflammatory response syndrome (SIRS) score 4. Age 5. Pleural effusion	1. Simplicity of derivation 2. Detects immune response to injury 3. considers old age and dependent systemic changes	1. cannot easily distinguish transient organ dysfunction from persistent organ dysfunction at 24 hrs
HAPS	1. Hematocrit 2. Serum creatinine 3. Rebound tenderness or guarding	1. Only 3 factors are needed for assessment 2. Involves basic laboratory tests, possible to be calculated within 30 minutes of admission	Not a good score for severe cases of AP, rather useful in triaging non-severe cases of AP (Talukdar et al., 2014)
CTSI	CT grade of pancreatitis + Necrosis score	Directly assesses morphologic severity of necrosis and inflammation	1. Costly investigation and CT is not indicated in very mild cases of AP 2. Claimed to be solely not reliable, needs one or the other clinical criteria 3. Based on local complications and has the drawback of not reflecting the systemic inflammatory response.

management outcome and disease progress. Persistent organ dysfunction is correlated with persistently raised SIRSS 48 hours apart, which indirectly points towards grave outcome, thus indicative of mortality (16,17). MMS is used for stratification in revised Atlanta classification in 2012 on the basis of respiratory, renal and cardiovascular systems as indicative of multiorgan dysfunction in SAP.

This study has several strengths. The first is that specific scores were selected for comparison which can be performed within the first few hours of diagnosis and admission, thus its logically intriguing to find out the best predictors in early hours. Second is exclusion of chronic pancreatitis and other comorbid conditions which had different behaviour of presentation than isolated acute pancreatitis. The limitation of all scoring systems discussed here may be that they convert continuous variables into binary values of equal weight and fail to capture multiplicative effects based on the interactions of interdependent systems. Another limitation was that the morbidity status in short or long term couldn't be evaluated and stratification of the cases based on severity in view of inadequacy of the available data in those contexts, plus the extended scoring advantage of serial assessments is not taken into consideration e.g., SIRSS at 48 hours adds up in prediction of mortality by defining persistent organ dysfunction as against transient (16).

CONCLUSION

This study showed maximum sensitivity of mortality prediction by HAPS, but best PPV by CTSI. Best specificity was achievable by HAPS. With our study and previously available literature, it can be concluded that newer scores have a reliable predictive capability for mortality outcome at earlier stage of management, irrespective of severity of AP.

Conflict of interest

All author declare that they have no conflict of interest.

Ethical approval

Institutional ethical clearance was obtained prior to the study.

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