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Comparison of modified Glasgow-Imrie, Ranson, and Apache II scoring systems in predicting the severity of acute pancreatitis

Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search

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ABSTRACT:

Aim: The course of acute pancreatitis is variable with patients at risk of poor outcomes. The purpose of this study was to compare Modified Glasgow-Imrie, Ranson, and APACHE II scoring systems in predicting the severity of acute pancreatitis.

Material and Methods: After a brief history, clinical examination and qualifying inclusion criteria, 70 patients (41 women, 29 men) diagnosed with acute pancreatitis were included in the study. The three scores were calculated for each patient and evaluated for their role in the assessment of specific outcomes.

Results: 34.3% patients were diagnosed with severe acute pancreatitis, while 65.7% patients had mild acute pancreatitis. A strong positive correlation was found between all the prognostic scores and the severity of disease. In the prediction of the severity of disease according to AUC, it was found that Glasgow-Imrie score had an AUC of 0.864 (0.756–0.973), followed very closely by APACHE II score with an AUC of 0.863 (0.758–0.968). APACHE II had the highest sensitivity (79.17%) in predicting severity while Glasgow-Imrie score was the most specific (97.83%) of all the scores. Patients with a Glasgow-Imrie score above the cut-off value of 3 had more complications and a longer hospital stay.

Conclusion: The Glasgow-Imrie score was comparable to APACHE II score and better than Ranson score statistically in predicting the severity of acute pancreatitis. Its administration in predicting the severity of acute pancreatitis is recommended.

KEYWORDS: APACHE II, Glasgow-Imrie, prognostic scores, Ranson, severe acute pancreatitis

ABBREVIATIONS

ANC – Acute necrotic collection
AP – Acute Pancreatitis
APACHE II – Acute Physiology and Chronic Health Evaluation II
APFC – Acute peripancreatic fluid collection
AUC – Area Under the Curve
CECT – Contrast-Enhanced Computed Tomography
HDU – High Dependency Unit
ICU – Intensive Care Unit
NPV – Negative Predictive Value
PPV – Positive Predictive Value
ROC – Receiver Operating Characteristic
USG – Ultrasonography

INTRODUCTION

Acute Pancreatitis (AP) is an inflammation of the pancreatic and peripancreatic tissue with the clinical course ranging from a mild, self-limiting disease in most patients to severe, multiple organ dysfunction in very few [1–3]. AP occurs due to an abnormal activation of pancreatic enzymes resulting in the autodigestion of the pancreatic parenchyma [4]. This leads to a local as well as systemic inflammatory response. There is a release of pro-inflammatory cytokines and anti-inflammatory mediators. All these mediators cause increased permeability and damage to the microcirculation of the pancreas [5]. The cascade of inflammation is self-limiting in approximately 80–90% of all patients. However, in the remaining few, there is a massive release of inflammatory mediators into the systemic circulation leading to a multiple organ dysfunction syndrome and rarely, death of the patient [1].

Confirmation of AP is done by history, clinical findings, and raised levels of pancreatic enzymes in the plasma. Rise of amylase or lipase of more than 3 times its normal levels is confirmatory of the diagnosis of AP [6]. To evaluate the pancreas, contrast-enhanced computed tomography (CECT) is the best modality for imaging, especially for the assessment of complications such as sterile or infected peripancreatic fluid collections, pancreatic necrosis, pancreatic pseudocyst, pancreatic-pleural fistulas, and vascular complications [7–9]. Surgical intervention may sometimes be needed for these complications. Image-guided aspiration or necrosectomy may be performed in infected pancreatic necrosis. Surgical debridement and drainage may also be needed in pancreatic abscesses if it fails to respond to percutaneous catheter drainage and antibiotics. Pseudocysts may rarely require drainage by laparoscopic and endoscopic means [10].

The variable course of the disease ranging from mild AP to severe AP with a high rate of mortality in the severe form, necessitates early and accurate prediction of severity to strategize its management [1]. A thorough assessment of the severity of disease is also important to predict prolonged hospitalization, complications, and to prevent mortality.

The severity of AP was divided into 3 categories by the Revised Atlanta classification (2012) [11]. When organ failure or local or systemic

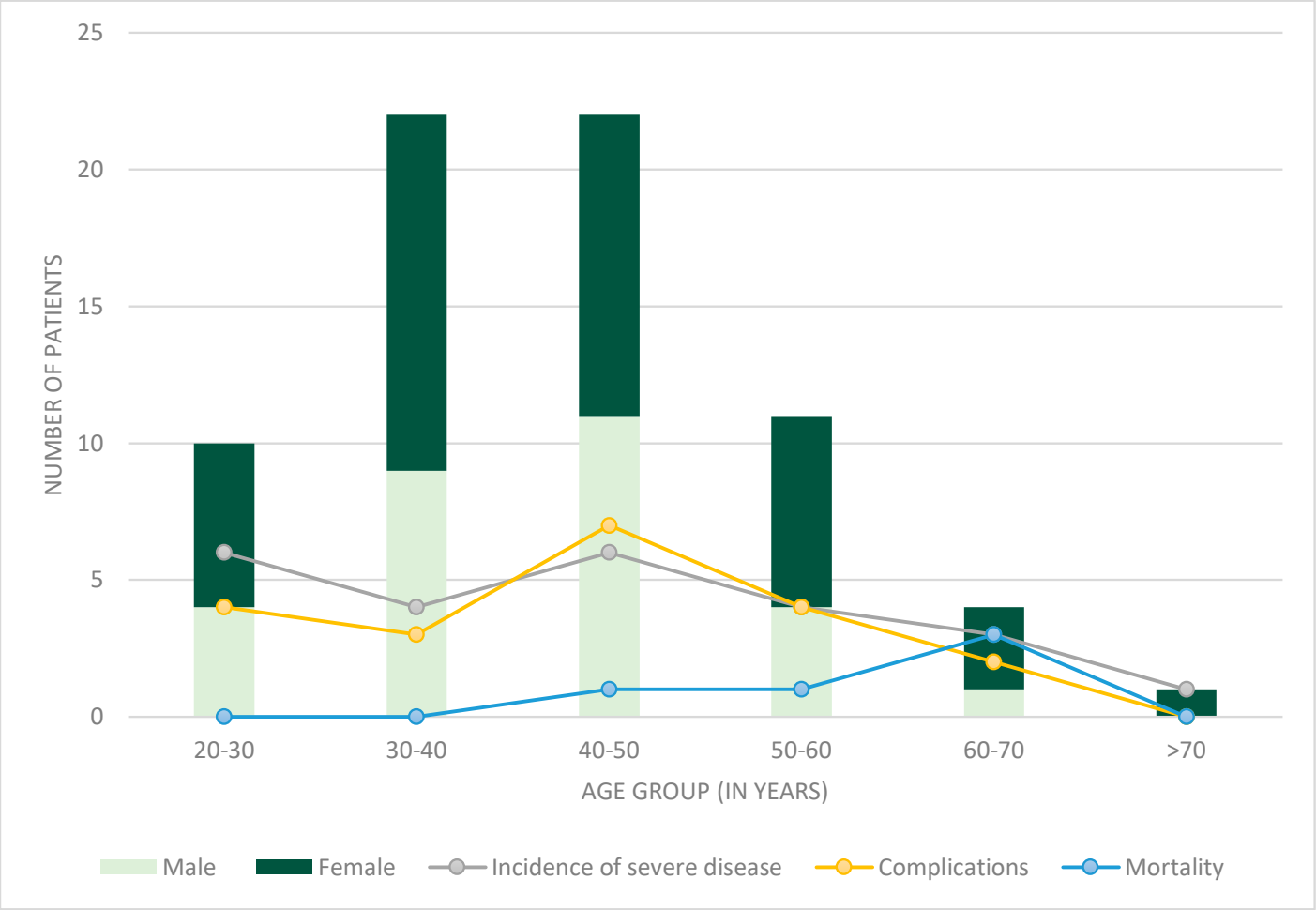

Fig. 1. Demographic features and incidence of severe disease, mortality and complications.

complications were absent, it was classified as mild AP. Transient organ failure that resolved within 48 h was classified as moderately severe AP. Persistent organ failure for ≥ 48 h was termed severe AP.

Several prognostic markers have been developed for severity grading in AP. Multifactorial scoring systems that take into account clinical and biochemical criteria for severity stratification have been used for the past many years. These include the criteria described by Ranson in the 1970s [12, 13], the Acute Physiology and Chronic Health Evaluation (APACHE II) score in 1981 [1, 14], and the modified Glasgow-Imrie score in 1984 [15]. Various studies have been conducted in the past to identify the best predictor of severity in AP but with conflicting results and thus no ideal single method for assessing the severity in AP.

This study was conducted to find out a scoring system that provides an early as well as accurate prediction of the severity of the disease. A prognostic score that is easy to calculate and convenient to use for practical purposes, is desired. The scores were evaluated for their assessment of severity, complication rates, mortality and length of hospital stay in case of AP.

MATERIAL AND METHODS

With the approval of the Ethics Committee, a prospective observational study was carried out on patients who were clinically suspected to have AP, in the Department of General and Minimally Invasive Surgery at Atal Bihari Vajpayee Institute of Medical Sciences & Dr. Ram Manohar Lohia Hospital, New Delhi, India between the 1st November 2018 and 31st March 2020.

Inclusion criteria

All patients aged > 18 years who presented to our centre and diagnosed as AP were included in the study. The diagnostic criteria were the presence of any 2 out of the following three criteria – (a) history of pain in the abdomen radiating to the back and relieved on bending forward associated with tenderness/guarding in the upper abdomen, (b) elevation over 3 times the upper normal limit of serum amylase (normal range – 30 to 110 U/L)/serum lipase (normal range – 23 to 300 U/L), and (c) radiographic evidence – USG (Ultrasonography) or CECT findings suggestive of AP such as pancreatic oedema, pancreatic necrosis, peripancreatic fluid collections.

Exclusion criteria

The exclusion criteria were – (a) recurrent AP, (b) chronic pancreatitis (± calcific), and (c) patients not willing to participate in the study.

A total of 70 patients diagnosed with AP were included in the study after taking an informed and written consent from the patient. A detailed history was taken and clinical examination was carried out as per written proforma. All the biochemical parameters were

Tab. I. Incidence of severe AP, mortality, complications, and length of hospital stay stratified among different scoring systems.

SCORE	PATIENTS WITH AP % (N)	SEVERE AP % (N)	MORTALITY % (N)	COMPLICATIONS % (N)	MEAN LENGTH OF HOSPITAL STAY (DAYS)
Ranson Score					
<3	72.9 (51)	10 (7)	-	11.4 (8)	5.46
≥3	27.1 (19)	24.3 (17)	7.1 (5)	17.1 (12)	8.10
Total	100 (70)	34.3 (24)	7.1 (5)	28.6 (20)	6.21
Glasgow-Imrie Score					
<3	72.9 (51)	8.6 (6)	-	12.9 (9)	5.77
≥3	27.1 (19)	25.7 (18)	7.1 (5	15.7 (11	7.59
Total	100 (70)	34.3 (24)	7.1 (5)	28.6 (20)	6.21
APACHE II Score					
<8	68.6 (48)	7.1 (5)	1.4 (1)	10 (7)	5.13
≥8	31.4 (22)	27.2 (19)	5.7 (4)	18.6 (13)	8.43
Total	100 (70)	34.3 (24)	7.1 (5)	28.6 (20)	6.21

Tab. II. Sensitivity, Specificity, PPV, NPV, and Accuracy of different scoring systems for severe AP.

	SENSITIVITY	SPECIFICITY	PPV	NPV	ACCURACY
Ranson Score	70.83	95.65	89.47	86.27	87.14
Glasgow-Imrie Score	75	97.83	94.74	88.24	90.00
APACHE II	79.17	93.48	86.36	89.58	88.57

PPV – Positive Predictive Value; NPV – Negative Predictive Value. All values are expressed in percentage.

noted at the time of admission and after 48 hours of admission. Severity of the disease was classified as per Atlanta Classification at 48 hours after admission. The modified Marshall score was used to assess organ failure [16, 17]. CECT of the abdomen was done after 72 hours of admission in all patients with moderate or severe AP. The modified Glasgow-Imrie score, Ranson score and APACHE II score were calculated. The outcome measures were severity, mortality, complications and length of hospital stay. All patients were followed up in the outpatient department at 3 months.

Statistics

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were presented in numbers and percentages (%) and continuous variables were presented as mean ± SD and median. The scores were correlated with the outcomes, that is, severity, mortality, complications and length of hospital stay statistically using two-by-two contingency tables, odds ratio, Chi-square test, Fisher's Exact test & Mann-Whitney-U test. A P-value of < 0.05 was considered statistically significant. Predictive accuracy of each score was determined by AUC (Area Under the Curve) in the ROC (Receiver Operating Characteristic) analysis.

RESULTS

Epidemiology

The mean and median age of the patients included was 41.6 years and 40 years respectively. The oldest patient was 72 years old and the youngest person was 23 years old. There were 62.8% (n = 44) of patients in the range of 30–50 years. A female predominance with a 1.41:1 ratio i.e. 58.6% females (n = 41) and 41.4% males (n = 29) was observed. The mean age was 40.7 years in males and 42.2 years in females. The most common aetiology was gall stones (77.14%), followed by alcohol intake (17.14%). The cause for the rest 5.71% of patients was idiopathic.

The incidence of severe disease in the study group was 34.3% (n = 24) as calculated by the Revised Atlanta criteria [11]. The remaining, 65.71% (n = 46) of the patients had a mild form of AP. The complications that were encountered were acute peripancreatic fluid collection (APFC) and acute necrotic collection (ANC) with an incidence of 28.6% (n = 20). Of the 15 patients with APFC, 80% (n = 12) had a spontaneous resolution of the collection at the 3-month follow-up. Only 3 patients had a persistent fluid collection in the form of pseudocyst. All 3 underwent surgical intervention in the form of internal drainage. Four out of the 5 patients with ANC died. Only 1 patient with a walled-off necrosis underwent surgical intervention after his 3-month follow-up. Surgical intervention was done for persistent symptoms in only 5.7% (n = 4) of patients, all of whom had severe AP.

Patients were also stratified by the type of organ failure according to the modified Marshall scoring system [16, 17]. Out of the 24 patients who had severe AP, 17 patients had only a single organ system failure and 7 had multiple organ failure persistent beyond 48 hours. Majority of patients with persistent single organ failure had an acute kidney injury reflected by their raised serum creatinine.

The mean and median length of hospital stay was 6.2 days (+ 2.9 days) and 5 days respectively. The mean length of hospital stay was

Tab. III. Extent of correlation of scores with the outcomes.

SCORES	SEVERITY	MORTALITY	COMPLICATIONS	LENGTH OF STAY
Ranson	53.43[a]	****	9.21[a]	6 *versus* 8 days
	(P < 0.0001) [b]	(P = 0.001) [c]	(P = 0.0009) [b]	(P < 0.001) [d]
Glasgow-	135[a]	****	6.42[a]	6 *versus* 8 days
-Imrie Score	(P < 0.0001) [b]	(P = 0.001) [c]	(P = 0.0009) [b]	(P = 0.020) [d]
APACHE II	54.47[a]	10.44[a]	8.46[a]	5 *versus* 8 days
	(P < 0.0001) [b]	(P = 0.031) [c]	(P = 0.0001) [b]	(P < 0.001) [d]

[a] Odds ratio; [b] Chi-square test; [c] Fisher's exact test; [d] Mann-Whitney test; significance was tested at 5%.**** Odds ratio not calculated.

Tab. IV. AUC of different scores in predicting severity, mortality, and complications.

AUC (95% CI)	SEVERITY	MORTALITY	COMPLICATIONS
Ranson Score	**0.832**[a] (0.716–0.949)[b]	**0.892** (0.809–0.975)	**0.730** (0.588–0.872)
	(0.059)[c]	(0.044)	(0.073)
Glasgow-Imrie Score	**0.864** (0.756–0.973)	**0.892** (0.809–0.975)	**0.695** (0.549–0.841)
	(0.055)	(0.108)	(0.075)
APACHE II	**0.863** (0.758–0.968)	**0.762** (0.547–0.976)	**0.735** (0.596–0.874)
	(0.054)	(0.110)	(0.071)

[a] Area under the curve; [b] Confidence Interval; [c] Standard Error.

longer in patients with a severe disease (8.1 days + 3 days) as compared to those with a mild form of the disease (5.2 days + 2 days). There was a mortality of 7.14% (n = 5) and in all cases where mortality was confirmed, the disease was of severe type. The mean age of mortality was 57.6 (+ 10.7) years. Fig. 1. shows the distribution of the three outcomes – severity, mortality and complications – stratified by age groups and gender.

Prognostic scores

As shown in Tab. I., it was observed that out of all patients, 34.3% (n = 24) had a severe form of the disease. In this subset, 24.3% (n = 17) had a Ranson score above its cut-off value, that is ≥3. Similarly, 25.7% (n = 18) had a Glasgow Imrie score ≥3 and 27.2% (n = 19) of the patients had an APACHE II score ≥ 8, i.e. above their respective cut-off values.

Mortality as an outcome was observed in 7.1% (n = 5) of the cases. All 5 cases had a Ranson and Glasgow-Imrie score of more than their cut-off values of 3. Out of these 5 cases, only 4 had an APACHE II score above its cut-off value of 8.

Complications were observed in 28.6% (n = 20) of the cases where 17.1% (n = 12) had a Ranson score ≥3, 15.7% (n = 11) had a Glasgow-Imrie score ≥3, and 18.6% (n = 13) had an APACHE II score ≥8.

The mean length of hospital stay was found to be 6.2 days (3.3 to 9.1 days) with a longer length of stay observed in patients with a score above the cut-off value for each scoring system.

Tab. I. depicts the cross-tabulations among the scoring systems and the outcomes.

The sensitivity, specificity, PPV (Positive Predictive Value), NPV (Negative Predictive Value) and accuracy for predicting the incidence of severe disease is depicted in Tab. II. It was observed that APACHE II score had the highest sensitivity, of 79.17%, in terms of the incidence of severe disease. Ranson and Glasgow-Imrie scores had a sensitivity of 70.83% and 75% respectively. Among the three scores, Glasgow-Imrie had the highest specificity, of 97.83%. Ranson and APACHE II had a specificity of 95.65% and 93.62% respectively.

In Tab. III., the degree of association between the outcomes and the categories of the scoring systems has been shown. The Chi-square test showed that the incidence of severe disease was higher with all the three scoring systems when a value higher than the cut-off was attained. Glasgow-Imrie score had the strongest correlation in predicting the severity of AP with an odds ratio of 135. Similar observations were made in terms of mortality and complications. As there was no mortality when the score was less than the cut-off value, the odds ratio for Ranson and Glasgow-Imrie scores could not be calculated. However, by Fisher's exact test there was significant evidence (P < 0.05) of higher mortality in the group with a score above the cut-off values. APACHE II score had an odds ratio of 10.44 and P = 0.031 (significant) by Fisher's exact test in predicting mortality.

In predicting complications, a comparable odds ratio of 9.21, 6.42, and 8.46 was found for the Ranson, Glasgow-Imrie, and APACHE II scores respectively, indicating that the three scores were almost equivalent in predicting complications.

From the results of the Mann-Whitney U test, it could be concluded that the mean length of hospital stay was significantly higher for patients with a score above the cut-off value.

In the prediction of the severity of the disease according to AUC (with 95% Confidence Interval) in the ROC curve, it was found that Glasgow-Imrie score had an AUC of 0.864 (0.756– 0.973), followed very closely by APACHE II score with an AUC of 0.863 (0.758 –0.968). Ranson score had an AUC of 0.832 (0.716–0.949). Similarly, the ROC curves were plotted for mortality and complications, and their AUC was calculated as depicted in Table 4.

The area under the ROC curve (AUC) is an indicator of the probability of correct or accurate prediction by the test of severity, mortality, complications. An AUC of 1 represents a perfect test whereas an AUC of 0.5 represents a worthless test.

Fig. 2. depicts different ROC curves. Since the incidence of mortality above the cut-off values for Ranson and Glasgow-Imrie score are equal, the ROC curves overlap each other, and thus have an equal AUC of 0.892 (0.809–0.975). APACHE II had an AUC of 0.762 (0.547–0.976) which is less than the other 2 scoring systems.

DISCUSSION

The wide variability in the clinical course of AP ranging from a mild form to multiple organ failure and death led to the development of various prognostic scores to assess the disease severity. In this study, an analysis of the scoring systems against the outcomes was done to tag the most appropriate scoring system for predicting the outcomes studied.

APACHE II score had the highest sensitivity – of 79.17% – in predicting the severity of AP followed by Glasgow-Imrie and Ranson scoring systems with a sensitivity of 75% and 70.83% respectively (Tab. II.). The high sensitivity of APACHE II could be attributed to the greater number of physiological parameters needed to calculate it, as compared to the other two scores. APACHE II score also had a very high accuracy as well as NPV making it suitable to rule out a severe form of AP rather than predicting it. Serial calculation of APACHE II at regular intervals would probably make it even more sensitive and specific to predict the severity in AP. Marco Simoes et al. reported a similar high sensitivity (79.4%), NPV (91.2%) and AUC (0.861) for APACHE II score [18].

Glasgow-Imrie score was the most specific of all the scores. The difference in the sensitivity of Glasgow-Imrie score and APACHE II was not high. The odds of having severe AP were high when the score was higher than the cut-off value, as depicted by a significantly high odds ratio. Although the AUC for Glasgow-Imrie score was the highest of all three scores, it was comparable to the AUC of APACHE II score. Both scores were equally good predictors of severity of pancreatitis but the difference in the ability of the two scores i.e., Glasgow-Imrie and APACHE II, to predict the severity of disease was negligible.

The two scores were thus comparable to each other in predicting the severity of disease. However, the ease of calculation of Glasgow-Imrie score makes it a more favourite choice. Ranson score was the least useful in predicting the severity of AP in our study. The findings were consistent with the study by Savio G. Barreto in which the author concluded that APACHE II and Glasgow-Imrie scores were comparable to each other in predicting the severity of AP [19].

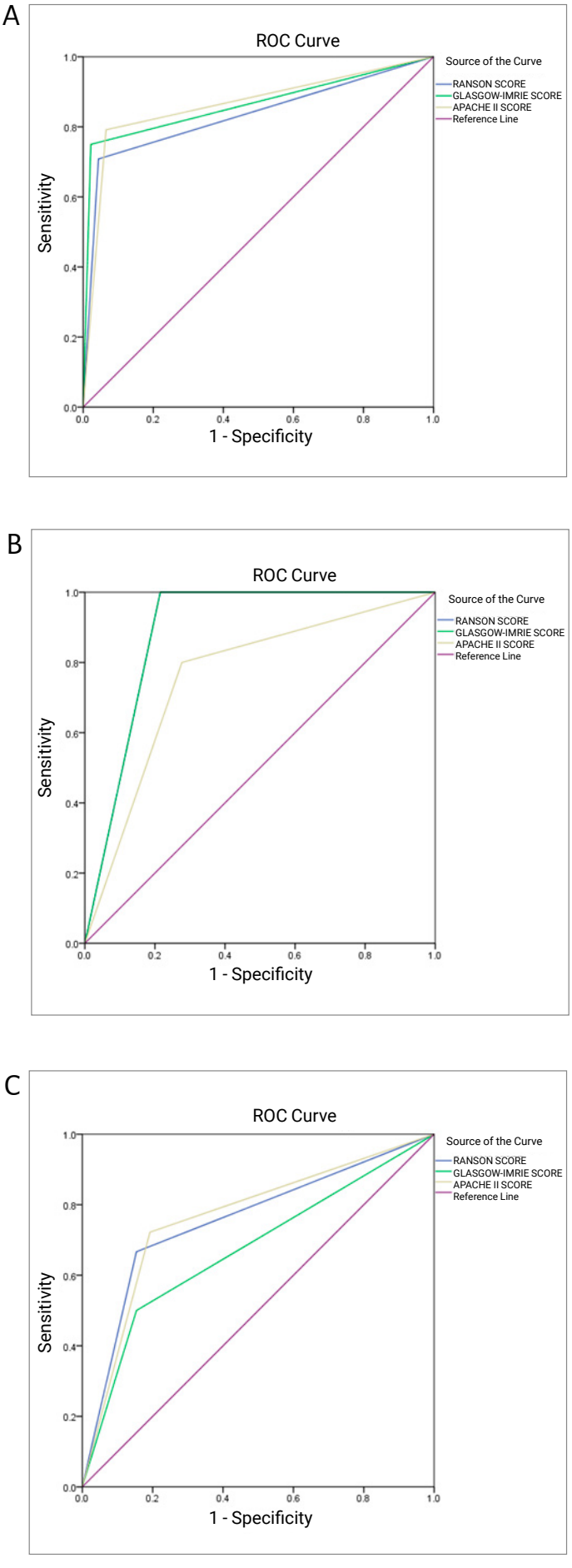

Fig. 2. ROC curves for predicting (A) incidence of severe AP, (B) mortality, and (C) complications.

In predicting mortality, APACHE II score had a significantly high odds ratio of 10.44 predicting a higher odd of mortality in patients with a score above the cut-off value. The odds ratio could not be calculated for Ranson and Glasgow-Imrie scores as there was no mortality in patients with a score less than the cut-off value. Ranson and Glasgow-Imrie score had an equal AUC which was more than the AUC of APACHE II. An equal AUC for both the scores suggested that both scores were equally capable of predicting mortality in AP. Ajay Khanna reported a similar AUC for Glasgow-Imrie and Ranson score in predicting mortality, however the author found that APACHE II had a greater AUC than the other 2 scores [20]. The modest difference in this finding could be due to the small sample size in both studies.

Complications such as APFC and ANC were seen in 28% of patients. The odds ratio for predicting complications was 9.21, 6.42, and 8.46 for the Ranson, Glasgow-Imrie, and APACHE II scoring systems respectively. All values were significant with a $P < 0.05$ denoting a higher chance of having complications in patients with a score above the cut-off value. The difference in AUC of the three scores was also not substantial. This finding related to predicting complications concurs with the finding of Ajay Khanna [20]. The AUC for the three scores regarding complications in the same order was found to be 0.70, 0.64, 0.68 by Ajay Khanna in his study. Thus, each score was at par with each other in predicting complications. In the study by Marco Simoes et al., the author found no significant correlation between the prognostic scores and incidence of complications [18]. The difference in the etiological factors leading to the difference in the occurrence of complications could be the cause for this digression.

The mean length of hospital stay in patients with AP was found to be shorter as compared to studies by Marco Simoes et al. [18] and Ajay Khanna [20]. Both authors found a mean length of stay of 10 days. In patients with severe AP, the values for the length of hospital stay were falsely low in our study. The data was skewed towards the lower value as all the deaths in severe AP took place within 4 to 6 days of admission. Also, most patients in our study with severe AP had a single organ failure in the form of acute kidney injury which responded well within a week to adequate resuscitation. However, this outcome could vary in different studies depending upon the level of care, monitoring, as well as the management conducted by the health-care staff of the hospital. The length of hospital stay was significantly prolonged for all the three systems when the score was above their cut-off values. This result was congruous with the studies of Marco Simoes et al. [18] and Ajay Khanna [20].

There has been a significant advancement in imaging techniques such as CECT and endoscopic ultrasound which can help in the assessment of disease accurately. However, the availability of such methods of imaging is limited to tertiary care centres in metropolitan areas only. The scoring systems can prove to be helpful in planning the management of acute pancreatitis in a country like ours where the majority of the population resides in rural areas with limited access to affordable healthcare. The data from our study exhibit that the Glasgow-Imrie and APACHE II scoring systems are comparable to each other in predicting the severity of AP. Ranson score lags behind the other two scores in predicting the severity of the disease. However, regarding mortality, Glasgow-Imrie and Ranson scores were equally capable of, and better than APACHE II score in predicting the outcome. All the three scores were similar to each other in predicting complications in patients with AP. A score above the cut-off values in each scoring system was predictive of a significantly prolonged length of hospital stay.

CONCLUSION

AP can prove to be a critical and life-threatening disease which requires careful consideration in its management. For the prediction of severe disease, mortality, and complications in patients, various scores such as the Ranson, Glasgow-Imrie, and APACHE II were used. All the scores had a positive correlation with the outcomes in our study. Both Glasgow-Imrie and APACHE II scores were comparable to each other in predicting the incidence of severe disease. Ranson score was less sensitive and accurate compared to the other two scores. The calculation of APACHE II score is based on a large number of parameters and is in itself cumbersome to calculate. Also, APACHE II score was initially designed to prognosticate any patient admitted to the intensive care unit and not for AP specifically, in contrast to Glasgow-Imrie score which was specifically fashioned for AP.

Glasgow-Imrie score is, therefore, recommended for predicting severe AP. The score is sensitive and specific enough to use it as an indicator of a severe form of the disease. A simple and accurate prediction of severity will help in proper management of patients with acute pancreatitis, prevent adverse events such as mortality and make satisfactory use of hospital resources such as HDU and ICU.

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