Original Article

Comparison of APACHE II and APACHE IV score as predictors of mortality in patients with septic shock in intensive care unit: A prospective observational study

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Abstract

Background and Aims: Prediction of outcome in intensive care unit (ICU) patients is of imperative importance. Our aim was to assess and compare the performance of Acute Physiology and Chronic Health Evaluation (APACHE) II and APACHE IV scores in predicting mortality in adult patients suffering from septic shock admitted to our ICU.

Material and Methods: This was a prospective observational study conducted in a 14-bedded medical ICU of a tertiary care center from January 2019 to March 2020; 128 patients suffering from septic shock were included and APACHE II and IV scores were calculated. We also calculated the predicted and actual mortality rates and standardized mortality ratios. The receiver operating characteristic curves were used to assess discrimination.

Results: Out of the 128 patients, 63 patients (49.21%) died. The mean (± standard deviation) admission APACHE II score was 16.7 ± 5.53, while the mean APACHE IV score was 67.25 ± 25.99. The non-survivors had significantly higher APACHE II and IV scores when compared to those who survived ($P < 0.001$). APACHE II had a slightly better discriminative power (with the area under the Receiver operating characteristic (ROC) curve of 0.78) than APACHE IV (with the area under the ROC curve of 0.74). The mean predicted mortality rate (PMR) of the patient population calculated on the basis of the APACHE II scoring system was 22.46 ± 15.76, and the mean PMR calculated as per the APACHE IV scoring system was 11.64 ± 15.59.

Conclusion: Both APACHE II and APACHE IV underestimated mortality in septic shock patients. Both APACHE II and APACHE IV were comparable in differentiating survivors from non-survivors. However, there was a good correlation between the two models.

Keywords: APACHE, ICU, mortality, septic shock

Introduction

Sepsis is said to be a major cause of in-patient mortality as well as morbidity among intensive care unit (ICU)-admitted patients.[1] Despite the availability of better care, the advancement of medical therapy, and the introduction of newer antibiotics, the outcome of septic shock patients continues to be extremely poor.[2]

Various predictive scoring systems which measure the severity of the disease are used to predict the outcomes, typically mortality, of patients in the ICU. Among the best-known and most widely used score is the Acute Physiology and Chronic Health Evaluation (APACHE) score.

APACHE uses the worst physiologic values measured within 24 h of admission to the ICU to calculate the final APACHE score.[3] Knaus simplified it to develop APACHE II, where

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12 routine physiological measurements, age, and the presence or absence of emergency/elective surgery are used to derive the final score. APACHE II is one of the most reliable prognostic scoring systems and has been validated for both surgical and non–surgical ICU patients. It is simple, clinically more useful, accurate, and valid.[4]

Later APACHE III system was introduced. It had five new variables to the existing APACHE II scoring system. In 2006, APACHE III was remodeled to introduce APACHE IV. New variables were added to APACHE III for the calculation of APACHE IV score and were mechanical ventilation, the impact of sedation on the Glasgow Coma Scale (GCS), PaO_2/FiO_2 ratio, thrombolysis, and disease-specific subgroups.

In 2009, Bhattacharyya M conducted a study on 2,919 patients and evaluated the performance of the APACHE IV scoring system in Indian ICU. His study concluded that APACHE IV is a relevant tool for the estimation of ICU performance.[5]

To date, most of the studies comparing the two scoring systems are from western literature and there is a paucity of data on the comparison of APACHE II and APACHE IV in predicting mortality in patients with sepsis and septic shock in Indian ICU scenario. Hence, we undertook this study to evaluate the ability of APACHE II and APACHE IV in predicting mortality in ICU patients suffering from septic shock.

Material and Methods

This was a prospective observational study that was carried out in the 14-bedded ICU of a tertiary care hospital from January 2019 to March 2020. The Institutional Ethics Committee (IEC/2018/140 dated 28/11/2018) approval was taken before the study and it was registered prospectively with the Clinical Trials Registry of India (CTRI/2019/01/017025). The study adhered to the principles of the 2013 Declaration of Helsinki.

After taking written informed consent from the patients' attendants, 128 patients (>18 years) admitted to the ICU with a diagnosis of septic shock were included in the study. Patients aged less than 18 years, burns, head injury, patients on chemotherapy, or known cases of malignancy, were excluded from the trial. The diagnosis of septic shock was based on the Third International Consensus definition for sepsis, i.e., the inability to maintain the mean arterial blood pressure of 65 mmHg without vasopressor support after adequate fluid resuscitation and serum lactate levels of >2 mmol/L.

Demographic variables like name, age, gender, and address were noted. All these patients were assessed in the first 24 h by using the APACHE II and APACHE IV scoring systems. For measurement of the APACHE scores, during the first 24 h of ICU admission, the highest and the lowest values of parameters like pulse, blood pressure, temperature, respiratory rate, serum sodium, glucose, creatinine, Blood Urea Nitrogen (BUN), hematocrit, and white cell count were recorded. A single reading of the parameters including blood pH, PCO_2, PO_2, FiO_2, serum albumin, bilirubin, and the GCS was noted at the same time. Also, a 24-h urine output during the first 24-h after admission and the presence of any chronic health condition, like chronic liver disease, was recorded. The predicted mortality and estimated length of stay in the ICU based upon the sum of categorical variables were calculated from the computer-generated algorithm. Each patient was followed up during the course of admission in the ICU and the outcome was compared with the initial score given to the patient to determine the predictive accuracy of the scoring system.

Statistics

The statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 25.0 for Windows). The demographics and health characteristics of the study population that were continuous variables were summarized using means and standard deviations (SD). All the categorical variables were expressed as percentages. The correlation between the models was calculated by Spearman's rho coefficient. The Student's paired *t*-test was used to compare the scores. The area under the curve (AUC) was used to measure the discrimination for hospital mortality. Wilcoxon's signed-rank test was used for the paired comparisons of abnormal distribution variables into the groups. Kruskal–Wallis test was performed to compare the mortality rate predicted by the APACHE II and APACHE IV scores.

Results

Out of the 128 patients, there were 93 males and 35 females; 63 patients expired while 65 were discharged from the ICU. The mean age of these patients was 41 years. Around 73% of the patients were males while 27% were females. About 87% of the patients were ventilated during their stay in the ICU. The demographic parameters of the patients are shown in Table 1.

The APACHE II score of the patients ranged from 3 to 32 with a mean of 16.7 ± 5.53. The patient distribution according to the APACHE II scores is shown in Figure 1. The mean APACHE II score of the survivors was 14.10 ± 5.09 and that of the non-survivors was 19.21 ± 4.84 ($P < 0.001$).

On the other hand, the APACHE IV score of the patients varied from 13 to 156 with an average of 67.25 ± 25.99. The

mean APACHE IV score of the survivors was 56.6 ± 20.29 and that of the non-survivors was 77.9 ± 26.83 ($P < 0.001$). Patient distribution according to the APACHE II score is shown in Figure 2.

Both APACHE II and IV scores were significantly higher among the non-survivors when compared to those who survived [Table 2]. The APACHE II and IV scores showed a fair correlation with each other with the Spearman's rho correlation coefficient of 0.797 ($P < 0.001$). A higher APACHE II score was associated with a higher APACHE IV score [Figure 3].

Discrimination for APACHE II and APACHE IV models was fair with the area under the ROC curve of 0.78 and 0.74, respectively [Figure 4]. The cutoff point with the best Youden index for APACHE II was 16 and for APACHE IV was 65. Among the patients with APACHE II score ≥16, there were 77% non-survivors and among patients with APACHE II score <17, there were 23% non-survivors ($P = 0.001$) [Figure 3]. Similarly, among the patients with APACHE IV score ≥65, there were 71% non-survivors and among the patients with APACHE IV score <65, there were 29% non-survivors ($P < 0.001$).

The mean predicted mortality rate (PMR) of the study population on the basis of the APACHE II scoring system was 22.46 ± 15.76, and the mean PMR by the APACHE IV scoring system was 11.64 ± 15.59. The observed mortality rate was 49.21%. Thus, the standardized mortality ratio (SMR) for the APACHE II score was 0.46 and for the APACHE IV score was 0.23.

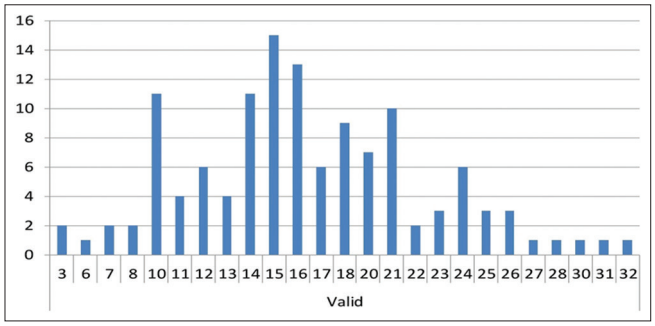

Figure 1: APACHE II scores of the patients (X-axis—APACHE II scores, Y-axis—number of patients)

Discussion

Both the APACHE II and APACHE IV scores are considered robust scoring systems in the ICU setting for prognostication and prediction of mortality. However, the application of both these systems is strongly context-specific. Both the APACHE II and IV scoring models were developed for the North American population. While of late, there have been some attempts to validate these scores in the Indian patients, the validation of these scores in the Indian patients suffering from septic shock has rarely been reported.

Compared with APACHE II, the APACHE IV is more complex, has more variables, and is time-consuming. These two scoring systems have been compared by various authors in various patient populations with conflicting results. While

Table 1: Demographic parameters of the patients

Variables	Data
Males	93 (72.66%)
Females	35 (27.34%)
Age (years – mean±SD)	41.49±16.80
Mechanical ventilation	112 (87.5%)
Mean duration of ventilation (days)	9.33±9.34
Mortality (%)	49.21
ICU stay in days (mean±SD)	9.33±9.335

Table 2: Average APACHE II and APACHE IV scores of survivors and non-survivors

	Average Mean±SD	Survivors Mean±SD	Non-survivors Mean±SD	*P*
APACHE II	16.7±5.53	14.10±5.09	19.21±4.84	<0.001
APACHE IV	67.25±25.99	56.6±20.29	77.9±26.83	<0.001

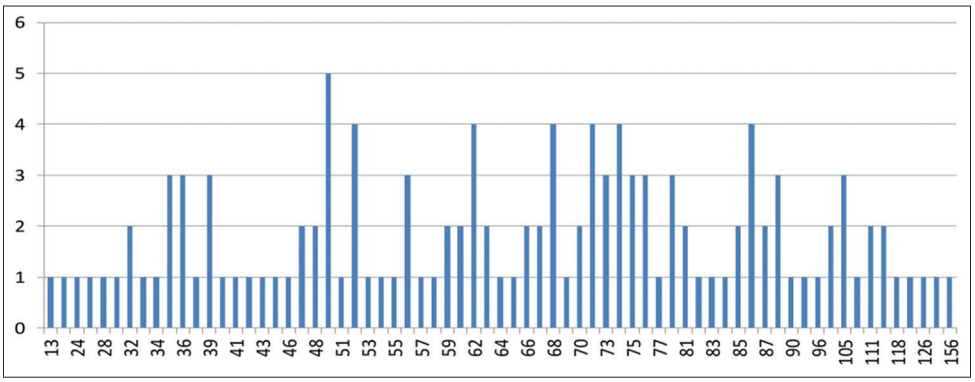

Figure 2: APACHE IV scores of the patients (X-axis—APACHE IV scores, Y-axis—number of patients)

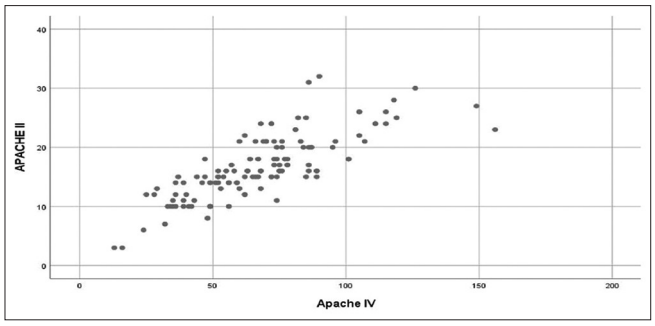

Figure 3: Association between APACHE II and APACHE IV scores

some studies have demonstrated APACHE IV as a better predictor of mortality than APACHE II in ICU patients, others have shown that both the scoring systems work equally well.[6-8]

The APACHE II score observed in our study ranged from 3 to 32 with a mean score of 16.7 ± 5.53 which was comparable to that reported earlier.[6,8,9] The survivors had a lower mean APACHE II score compared with the non-survivors, which was statistically significant ($P < 0.001$). The mortality increased with the increasing APACHE II score, which was also statistically significant ($P < 0.001$). Similar results were found in other studies.[7-10]

The APACHE IV score ranged from 13 to 156 in our study with a mean of 67.25 ± 25.99, which were comparable to that reported earlier.[11-13] The survivors had a lower mean APACHE IV score compared to the non-survivors, which was statistically significant ($P < 0.001$) as found in other studies. The mortality increased with the increasing APACHE IV score, which was also statistically significant ($P < 0.001$) as observed in the other studies.[12,13]

The APACHE II scoring system has a comparable AUC of the ROC curves to the APACHE IV score in predicting mortality in the ICU. The area under the ROC curve observed for the APACHE II model was 0.78 which was similar as reported in various other studies.[6,9,10] The area under the ROC curve observed in our study for APACHE IV was 0.73 which was 0.93 in the Ayazoglu study, 0.861 in the Keegan *et al.*[7] study, and 0.884 in the Kramer *et al.*[14] study.[6] The AUC of the ROC curve of the mortality prediction scores indicates the capacity of the model to differentiate between those who will die and those who will survive the ICU admission, also known as the model Discrimination. The discrimination of the APACHE II model was marginally better than the APACHE IV model in our study and the finding was not consistent with the Brinkman *et al.* study but was consistent with the Ayazoglu study, Kamal *et al.*[13] study, and Lee *et al.*[15] study.[6,8,12]

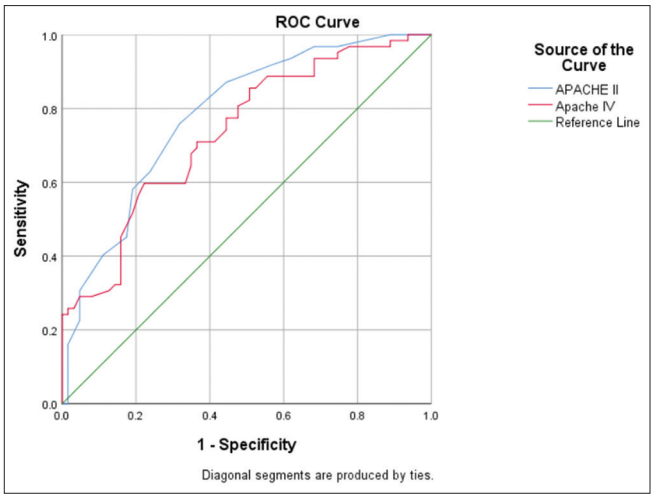

Figure 4: ROC curve to determine the area under the curve for APACHE II and APACHE IV

Calibration refers to the degree of concordance between the estimated probability of mortality and the observed probability. If a model has good calibration, it means that the model can predict mortality well. The ability of both APACHE II and APACHE IV in predicting death was poor in our study. Both of these scores grossly underestimated mortality. On comparing the two scales, the APACHE II had better calibration than APACHE IV. Poor calibration of the two scales raises a serious question on the applicability of these models in this subset of patients. Venkataraman *et al.*[16] had also suggested the need to recalibrate these scales while applying them to the Indian scenario.

One limitation of our study is that it was performed at a single center. Hence, our results cannot be generalized to other ICUs because of differing admission diagnoses, dissimilar patient characteristics, and other causes.

Conclusion

Both APACHE II and APACHE IV have comparable discrimination, while both the scales have poor calibration while estimating mortality in the ICU patients suffering from septic shock. There is a need to perform further research to evaluate the ability of these scores to predict outcomes in Indian patients suffering from septic shock.

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Conflicts of interest
There are no conflicts of interest.

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