RESEARCH ARTICLE

# Use of the APACHE II Score for the Assessment of Outcome and Mortality Prediction in an Iranian Medical-Surgical Intensive Care Unit

Mehrzad Bahtouee[1], Seyed Sajjad Eghbali[2], Nasrollah Maleki[3]*, Vahid Rastgou[1], Niloufar Motamed[4]

**Background:** The Acute Physiology and Chronic Health Evaluation (APACHE) II is still commonly used as an index of illness severity in patients admitted to intensive care unit (ICU) and has been validated in many research and clinical audit purposes.
The aim of this study is to investigate the diagnostic value of APACHE II score for predicting mortality rate of critically ill patients.
**Methods:** This was a retrospective cross-sectional study of 200 patients admitted in the medical-surgical adult ICU. Demographic data, pre-existing comorbidities, and required variables for calculating APACHE II score were recorded. Receiver operating characteristic (ROC) curves were constructed and the area under the ROC curves was calculated to assess the predictive value of the APACHE II score of in-hospital mortality.
**Results:** Of the 200 patients with mean age of 55.27 ± 21.59 years enrolled in the study, 112 (54%) were admitted in the medical ICU, and 88 (46%) in the surgical ICU. Finally, 116 patients (58%) died and 84 patients (42%) survived. The overall actual and predicted hospital mortality were 58% and 25.16%, respectively. The mean APACHE II score was 16.31 in total patients, 17.78 in medical ICU, and 14.45 in surgical ICU, and the difference was statistically significant between the two groups (P= 0.003). Overall, the area under ROC curve was 0.88. APACHE II with a score of 15 gave the best diagnostic accuracy to predict mortality of patients with a sensitivity, specificity, positive and negative predictive values of 85.3%, 77.4%, 83.9%, and 73.9%, respectively.
**Conclusion:** Despite significant progress has been made in recent decades in terms of technology and equipment, therapeutics and process of care and identifies in the ICU setting, these scientific efforts have not directly led to a further reduction in mortality for patients hospitalized in the ICU.
**Keywords:** APACHE; Intensive Care Units; Mortality; ROC Curve

Predictive scoring systems are measures of disease severity that are used to predict outcomes, typically mortality, of patients in the intensive care unit (ICU). There is no specific agreed classification of the predictive scoring system that are used in patients of multidisciplinary ICU [1]. The commonly used ICU scoring systems for the adult population are: acute physiology and chronic health evaluation (APACHE), simplified acute physiology score (SAPS), mortality prediction model (MPM), organ dysfunction and infection system (ODIN), sequential organ failure assessment (SOFA), multiple organs dysfunction score (MODS), logistic organ dysfunction (LOD) model and three-day recalibrating ICU outcomes (TRIOS) [2].

The APACHE score is probably the most common and best-known validated predictive scoring system in the ICU. The APACHE II is still commonly used as an index of illness severity in critically ill patients admitted to ICU, and has been validated in many research and clinical audit purposes [3]. Accurate use of the APACHE II scoring system requires adherence to strict guidelines and regular training of medical staff using the system [4]. A prospective study by Del Bufalo et al. [5] showed that the APACHE II score was a good predictor of hospital outcome and better than SAPS II, with the ratio between the actual and predicted hospital mortality being 86% for APACHE II and 83% for SAPS II.

However, the APACHE II score is neither very sensitive nor specific in terms of mortality prediction. The major limitation of this scoring system is that many patients have several comorbid conditions and selecting only one principal diagnostic category may be very difficult. In addition, the physiological variables are all dynamic and can be influenced by multiple factors. All these factors can lead to a risk of overestimation of predicted mortality [6-7].

[1]Department of Internal Medicine, Shohadaye Khalije Fars Hospital, Bushehr University of Medical Sciences, Bushehr, Iran.
[2]Department of Pathology, The Persian Gulf Biotechnology Research Center, Bushehr University of Medical Sciences, Bushehr, Iran.
[3]Department of Hematology- Oncology and Bone Marrow Transplant, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran.
[4]Department of Community Medicine, School of Medicine, Bushehr University of Medical Sciences, Bushehr, Iran
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*Corresponding author: Nasrollah Maleki, MD. Department of Hematology- Oncology and Bone Marrow Transplant, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. E-mail: malekinasrollah@gmail.com

Differences in the ratio of actual to predicted hospital mortality detected by using the APACHE II system not only may reside in operational factors within the ICU organization but also may be related to weaknesses in the APACHE II model to measure factors intrinsic to the disease process in some patients. It was suggested that case-mix must be examined in detail before concluding that differences in the ratio of actual to predicted hospital mortality are caused by differences in quality of care [8].

A prospective study by Meyer et al. [9] showed that among the 578 surgical ICU patients who were predicted by clinical judgment and APACHE II score to die, more than 40% of actually survived. The overall accuracy was 95.2% for clinical assessment and 90.9% for APACHE II. This study demonstrated that clinical assessment is superior to APACHE II in predicting outcome in this group of surgical patients, although the difference is small. In addition, this study suggested that neither clinical assessment nor the APACHE II score is very reliable at predicting which surgical ICU patients will die.

The aim of this study is to determine the difference between actual death and predicted death calculated by APACHE II score and to investigate the diagnostic value of APACHE II score for predicting mortality.

# Methods

### Design and population

This study was approved by the Ethics Committee of the Bushehr University of Medical Sciences. This was a retrospective cross-sectional study. Patients older than 16 years who were hospitalized for more than 24 hours in the medical-surgical adult ICU in Persian Gulf Martyrs Hospital, a tertiary care teaching hospital in Bushehr, Iran, between June 2012 and May 2013 were recruited for the study. A total of 200 patients were included. Exclusion criteria were as follows: age less than 16 years, ICU stay less than 24 h, patients who had undergone CABG surgery, burn patients, absence of all 19 physiological parameters, mental health problems, and patients who were transferred from another ICU to our ICU.

### Data collection

A data collection sheet was prepared to summarize the information obtained from each patient record, including the demographic features (age and gender), pre-existing comorbidities, Glasgow Coma Scale (GCS), physiological variables and laboratory results. The GCS is comprised three subscales i.e. verbal response (5 items), eye opening response (4 items) and motor response (6 items) ranged between 3 and 15 [10].

APACHE II scores were calculated for each patient from data collected during the first 24 hours of ICU admission. APACHE II included of 12 physiologic variables (temperature, mean arterial pressure, heart rate, respiratory rate, A-a PO2 (FiO2>50%) or PaO2 (FiO2<50%), arterial pH or HCO3, serum sodium, potassium and creatinine, hematocrit, white blood cell count and GCS), a chronic health evaluation and age adjustment score. Each variable is weighted from 0 to 4 score. The range of APACHE II score is from 0 to 71 points. Points of 25 or less denote less than 50% mortality, while points of 35 or more denote more than 80% mortality [11].

### Statistical Analysis

The statistical analysis of the data was done using the SPSS software for Windows, version 21 (SPSS Inc., Chicago, IL, United States). A P-value of < 0.05 was considered statistically significant. The results were expressed as means ± standard deviations. The comparison of the continuous variables was accomplished with Student's t-test, and, for the comparison of the categorical variables, the Pearson chi-squared test ($\chi 2$ test) and Fisher exact test were used. The Mann-Whitney U test was used to compare differences between two independent groups when the dependent variable was either ordinal or continuous, but not normally distributed. The Kolmogorov-Smirnov test was used for assessing the normal distribution of quantitative variables, and Levene's test was used to assess the equality of variances. Receiver operating characteristic (ROC) curves were constructed and the area under the ROC curves was calculated to assess the predictive value of the APACHE II score of in-hospital mortality. Sensitivity, specificity, positive and negative predictive value were also calculated.

# Results

### Characteristic data

Of the 200 patients enrolled in the study, 116 (58%) were men, and 84 (42%) were women. One hundred and twelve (54%) were admitted in the medical ICU, and 88 (46%) in the surgical ICU. Overall, 116 (58%) of the patients had at least one comorbidity. Relevant comorbidities included hypertension (29.5%), cerebrovascular accident (12.5%), diabetes mellitus (10.5%), cancer (9.5%), ischemic heart disease (9.5%), congestive heart failure (8%), chronic renal failure (6.5%), chronic obstructive pulmonary disease (5%), asthma (2%), hyperlipidemia (2%), Alzheimer (1.5%), cirrhosis (1.5%), HIV/AIDS (1%), sickle cell anemia (0.5%), peptic ulcer disease (0.5%), and epilepsy (0.5%). Finally, we assessed the long-term outcome of patients. Of the total 200 patients were admitted, 116 patients (58%) died and 84 patients (42%) survived.

There was significant difference in the presence of comorbidity between patients admitted to the medical ICU (74.1%) in comparison to surgical ICU (37.5%) (X2=27.11, p=0.0001). In addition, a significant difference was observed in the male-to-female ratio in patients admitted to the surgical ICU (male: 67%, female: 33%) in comparison to medical ICU (male: 50.9%, female: 49.1%) (X2=5.27, p=0.03).

In this study, we calculated the average age, length of ICU stay, APACHE II score, actual death and predicted death. Since the variables were not normally distributed, the Mann-Whitney test was used to data analysis. As shown in (Table 1), there was statistically significant difference between patients admitted to the medical and surgical ICU in terms of average age, length of ICU stay, APACHE score, actual death and predicted death.

### Average age and length of ICU stay

Average age of patients was 55.27 ± 21.59 years (ranging from 17-96). There was significant difference in the average age between patients admitted to the medical ICU (58.88 ± 19.83 years) and surgical ICU (50.68 ± 22.95 years) (P-value= 0.009).

The mean length of ICU stay was 7.43 ± 6.56 days (ranging from 1-34). A significant difference was observed in mean ICU stay between patients admitted to the medical

ICU (7.79 ± 6.80 days) and surgical ICU (6.98 ± 7.00 days) (P-value= 0.04).

**APACHE II score, actual death and predicted death**

The mean APACHE II score was 16.31 ± 7.96 in total patients, 17.78 ± 7.95 in patients admitted to the medical ICU, and 14.45 ± 7.62 in patients admitted to the surgical ICU, and the difference was statistically significant between the two groups (P-value= 0.003).

The overall actual hospital mortality was 58 %. Significant differences in actual death were detected between patients admitted to the medical ICU (65.17%) and surgical ICU (48.86%) (P-value= 0.0001). Furthermore, the overall predicted hospital mortality was 25.16 %. A significant difference was observed in the predicted death between patients admitted to the medical ICU (30.81%) and surgical ICU (17.98%) (P-value= 0.0001).

**The predictive value of mortality of the APACHE II score**

To determine the optimal discriminatory threshold values of the APACHE II score, ROC curves were constructed and the area under the ROC curves was calculated. Overall, the area under ROC curve was 0.88 (95% CI: 0.83-0.93, P = 0.0001). The area under ROC curve was 0.87 (95% CI: 0.80-0.95, P = 0.0001) for patients admitted to the medical ICU and 0.86 (95% CI: 0.77-0.94, P = 0.0001) for patients admitted to the surgical ICU.

APACHE II with a score of 15 gave the best diagnostic accuracy to predict mortality of patients with a sensitivity, specificity, positive and negative predictive values of 85.3%, 77.4%, 83.9%, and 73.9%, respectively. There was significant difference in the actual mortality rate between patients with APACHE score of 15 and higher (83.89 ± 36.91) and patients with APACHE score less than 15 (20.73 ± 40.78) (P-value= 0.0001, Z= -8.88).

**The difference between the actual and predicted mortality**

As shown in (Table 2), the difference between the actual and predicted death was higher in patients admitted to the medical ICU in comparison to surgical ICU, and there was no statistically significant difference (P-value= 0.734).

As shown in (Table 3), the difference between the actual and predicted death in both levels APACHE II score (<15 and ≥ 15) was lower in patients admitted to the medical ICU in comparison to surgical ICU. This difference was significant at the APACHE II score <15 (P value= 0.018), but not significant in the APACHE II score ≥ 15 (P value=0.146).

**Outcome of patients in different levels of APACHE II score**

The relationship between frequency and outcome of patients with different levels of APACHE II score is shown in (Table 4). In this study, there was a significant relationship between different levels of APACHE II score and outcome of patients, so that approximately 80% of patients with APACHE II score less than 15 survived, while more than 80% of patients with APACHE II score ≥ 15 died (Table 5).

There was significant difference in outcome between patients admitted to the medical ICU (Survivors: 34.8%, Non-survivors:65.2%) in comparison to surgical ICU (Survivors: 51.1%, Non-survivors:48.9%) (X2=5.38, p=0.022). The outcome of death in both levels APACHE II score (<15 and ≥ 15) was higher in patients admitted to the medical ICU in comparison to surgical ICU, but there was no statistically significant difference (Table 6).

**Table 1- The average age, length of ICU stay, APACHE II score, actual death and predicted death in patients admitted to the medical and surgical ICU.**

| Variable | Medical ICU (Mean ± SD) | Surgical ICU (Mean ± SD) | t* or z* | P-value |
|---|---|---|---|---|
| Average age (years) | 58.88 ± 19.83 | 50.68 ± 22.95 | 2.65 | 0.009 |
| Length of ICU stay (days) | 7.79 ± 6.80 | 6.98 ± 7.00 | - 2.05 | 0.04* |
| APACHE II score | 17.78 ± 7.95 | 14.45 ± 7.62 | 2.98 | 0.003 |
| Actual death (%) | 65.17 | 48.86 | - 8.88 | 0.0001* |
| Predicted death (%) | 30.81 | 17.98 | - 5.26 | 0.0001* |

* The Mann-Whitney test was used.

**Table 2- The difference between the actual and predicted death in patients admitted to the medical ICU in comparison to surgical ICU.**

| ICU ward | The difference between the actual and predicted mortality | Average rank | z | p value* |
|---|---|---|---|---|
| Medical ICU | 34.36 ± 40.36 | 99.30 | | |
| Surgical ICU | 30.88 ± 42.81 | 102 | -0.334 | 0.734 |

*The Mann-Whitney test was used.

**Table 3- The difference between the actual and predicted death in both levels APACHE II score in patients admitted to the medical ICU in comparison to surgical ICU.**

| APACHE II score levels | ICU ward | The difference between the actual and predicted mortality | Average rank | z | p value* |
|---|---|---|---|---|---|
| | Medical ICU | 11.37 ± 40.48 | 34.73 | | |
| <15 | Surgical ICU | 13.20 ± 40.22 | 47.07 | -2.37 | 0.018 |
| | Medical ICU | 45.70 ± 35.53 | 56.08 | | |
| ≥ 15 | | | | -1.45 | 0.146 |
| | Surgical ICU | 49.40 ± 37.32 | 65.47 | | |

*The Mann-Whitney test was used.

**Table 4- Frequency and outcome of patients in different levels of APACHE II score.**

| APACHE II score | No. of patients (%) | Outcome of patients<br>Survivors<br>No. (%) | Non-survivors<br>No. (%) |
|---|---|---|---|
| 0 – 4 | 14 (7%) | 12 (14.3%) | 2 (1.7%) |
| 5 – 9 | 36 (18%) | 31 (36.9%) | 5 (4.3%) |
| 10 – 14 | 32 (16%) | 22 (26.2%) | 10 (8.6%) |
| 15 – 19 | 46 (23%) | 14 (16.6%) | 32 (27.6%) |
| 20 – 24 | 35 (17.5%) | 2 (2.4%) | 33 (28.5%) |
| ≥ 25 | 37 (18.5%) | 3 (3.6%) | 34 (29.3%) |
| Overall | 200 (100%) | 84 (42%) | 116 (58%) |

**Table 5- Relationship between different levels of APACHE II score and outcome of patients.**

| APACHE II score | Outcome of patients<br>Survivors<br>No. (%) | Non-survivors<br>No. (%) | X2 | r | p value |
|---|---|---|---|---|---|
| < 15 | 65 (79.3%) | 17 (20.3%) | | | |
| ≥ 15 | 19 (16.1%) | 99 (83.9%) | 79.24 | 0.64 | 0.0001 |

**Table 6- The outcome of death in levels APACHE II score in patients admitted to the medical ICU in comparison to surgical ICU.**

| APACHE II score levels | ICU ward | Outcome of patients<br>Survivors<br>No. (%) | Non-survivors<br>No. (%) | X2 | P value |
|---|---|---|---|---|---|
| | Medical ICU | 29 (78.4%) | 8 (21.6%) | | |
| < 15 | Surgical ICU | 36 (80%) | 9 (20%) | 0.032 | 1.000 |
| | Medical ICU | 10 (13.3%) | 65 (86.7%) | | |
| ≥ 15 | Surgical ICU | 9 (20.1%) | 34 (79.1%) | 1.17 | 0.306 |

## Discussion

In 2006, we carried out a study to determine the actual and predicted mortality rate by using the APACHE II scoring system in 100 critically ill patients in Fatemeh Zahra Hospital of Bushehr, Iran [12]. This old hospital was propagated and then a newly constructed hospital with new and more advanced ventilators and monitoring systems was opened, the Persian Gulf martyrs hospital. More skillful staffs and physicians with a subset of specialties such as anesthesiology, pulmonology, internal medicine, infectious diseases and neurology were employed. In addition, an anesthesiologist was defined as a resident doctor 24 hours. This changes caused us to have anticipation of less mortality and more favorable outcome but this was not the case as is shown here. A comparison of these two studies is shown in (Table 7). In the present study, APACHE II with a score of 15 gave the best diagnostic accuracy to predict mortality of patients with a sensitivity, specificity, positive and negative predictive values of 85.3%, 77.4%, 83.9%, and 73.9%, respectively. However, in our previous study, APACHE II with a score of 11.5 gave the best diagnostic accuracy to predict mortality with a sensitivity and specificity of 83.9% and 56%, respectively. This shows that the Apache II score in the present study is more accurate than our previous study. The difference between the actual and predicted death in the present study was higher in comparison to our previous study, which is unacceptable to the other prestigious centers in the world. This can happen for four reasons. First, we may offer poor quality care to our ICU patients. Second, the APACHE II scoring system may need to be modified for use in our patients. Third, the APACHE II score may not be suitable for predicting mortality rate of our patients, and we should use other predictive systems. Forth, the increased sophistication and managing by more doctor groups may have led to this unfavourable outcome via high and unnecessary procedures and instrumentations and overlaps between the managing groups originating from a managing discrepancy.

In a study by Hosseini et al. [13] using a cut-off score 13.5, The APACHE II score predicted hospital mortality with a sensitivity of 96.6%, a specificity of 62.8% and accuracy of 79.7%, with an area under the ROC curve of 0.857. In another study by Fadaizadeh et al. [14], a total of 415 records of patients admitted during a 1-year period were retrospectively reviewed. For APACHE score, the best cutoff point chosen was 13.5, with 90% sensitivity and 75% specificity, and a Youden value of 0.65. In a similar study which was conducted by Haq et al. [15] with a cut-off score of 13, the APACHE II score predicted hospital mortality with a sensitivity of 69% and specificity of 66%, with an area under the ROC curve of 0.74. As can be seen, in our study, the diagnostic power of Apache II score is desirable compared with foreign and domestic studies and in some cases even better.

In the present study, there was a significant relationship between the APACHE II score and rate of mortality (p=0.0001), so that about 80% of patients with a score less than 15 survived, whereas only about 16% of patients with a score ≥ 15 survived. There was also a significant relationship in other parts of the world. Naved et al. [16] investigated the relationship between the APACHE-II score system with mortality and length of stay in ICU. In the scores range from 3 to 10, 90% of patients were discharged and only 10% of patients died, while in the scores range of 31 to 40, 84.6% of patients died. This revealed that there might be more chances of death in case of high APACHE-II score. Insignificant but an inverse correlation was observed between APACHE-II score and length of ICU stay.

The present study showed that there was significant difference in the mean APACHE II score and actual mortality rate between patients admitted to the medical ICU in comparison to surgical ICU. This difference represents the fact that prognosis of patients admitted to the medical ICU is worse than patients admitted to the surgical ICU, that this would be due to higher average age and underlying chronic disease in patients admitted to the medical ICU. Other studies have shown remarkably similar results [17].

**Limitations of the study**

The present study has several limitations. First, this study was a single-center with a limited sample size and these results may not be generalizable to other ICUs. Sample size is a relevant limiting factor on the measured calibration when using the Hosmer-Lemeshow goodness-of-fit test. Second, as a single-center study, there may be bias due to case mix, quality of ICU care, ICU policy, and admission criteria. Third, this study did not directly compare the admission APACHE II score with other scoring systems that assess the risk of hospital mortality at ICU admission such as the SAPS, SOFA, and MPM models.

**Table 7- A comparison of ICU patients in the Persian Gulf Martyrs Hospital in 2014 with the Fatemeh Zahra Hospital in 2006.**

| Variable | Persian Gulf Martyrs Hospital | Fatemeh Zahra Hospital | 95% CI | P value |
|---|---|---|---|---|
| Mean age of patients (Years) | 55.27 ± 21.59 | 40.18 ± 21.04 | 1.1-8.6 | 0.02 |
| Actual hospital mortality (%) | 58% | 31% | 18.2-39.5 | 0.0001 |
| Eventual hospital mortality (%) | 25.16% | 19.73% | 7.2-20.9 | 0.03 |
| Mean APACHE II score | 16.31 | 12.84 | 2.4-4.6 | 0.0001 |
| Area under ROC curve | 0.88 | 0.76 | 0.74-0.84 | 0.0001 |

CI: Confidence Interval
ICU: Intensive Care Unit
APACHE: Acute Physiology and Chronic Health Evaluation
ROC: Receiver-Operating Characteristic

## Conclusion

The APACHE II score is a reliable method for predicting mortality in our ICU. Our observed mortality rate was greater than the predicted death rate, in comparison to the other prestigious centers in the world. Therefore, it seems that we must improve our intensive cares to reduce mortality. Despite significant progress has been made in recent decades in terms of technology and equipment, therapeutics and process of care and identifies in the ICU setting, these scientific efforts have not directly led to a further reduction in mortality for patients hospitalized in the ICU.

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**Ethical approval:** Ethics approval was obtained for this study from the Ethics Committee of the Bushehr University of Medical Sciences. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments.

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