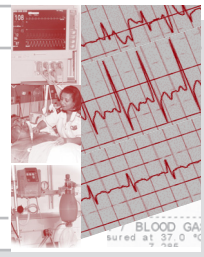
ARTICLE

Validating the use of the APACHE II score in a tertiary South African ICU



[1]Lung Unit, Department of Medicine, Tygerberg Hospital and Stellenbosch University, Cape Town
[2]Centre for Statistical Consultation, Stellenbosch University, W Cape
E van der Merwe[1]
M Kidd[2]
S Metzker[1]
C T Bolliger[1]
E M Irusen[1]

Background. In order to evaluate both outcome of intensive care unit (ICU) patients and ICU care, the risk-adjusted mortality can be calculated using the APACHE II equation. Our aim was to: (*i*) describe the case mix of admissions to our ICU; (*ii*) investigate the impact of such variation on outcome; and (*iii*) validate the use of the APACHE II risk prediction model in a developing country.

Methods. Prospective data collection of consecutive adult admissions over 13 months in a tertiary, predominantly medical, ICU. Survivors and non-survivors were compared for age, sex and diagnoses. ICU mortality was calculated for diagnostic categories and for the whole group. Risk of death was calculated according to the APACHE II method. The goodness of fit of the APACHE II equation was assessed with a calibration curve. The discrimination of the model was assessed with a receiver operator characteristic (ROC) curve.

Results. There were 304 admissions with an average APACHE II score of 17.4 and 37% ICU mortality. Diagnostic groups with high ICU mortalities included medical patients (42%), severe sepsis (59.4%), community-acquired pneumonia (CAP) (53%), pulmonary tuberculosis (45%) and immunocompromised patients (62%). A calibration curve for the APACHE II equation, applied to our data, shows that the predicted ICU mortality was within the 95% confidence interval (CI) of the actual mortality. The only exception was the group with a 70% predicted risk of ICU death. The area under the ROC curve was 0.83 (95% CI: 0.78 - 0.88). The standardised mortality ratio was 0.98 (95% CI: 0.79 - 1.17).

Conclusions. This study validates the use of the APACHE II model to accurately describe the risk of ICU death of the patient population in a tertiary ICU in a developing country. Patients with severe sepsis and/or CAP had a significantly higher mortality. The main reason for this appeared to be a high risk of death at ICU admission. The principles of appropriate management of early sepsis should be taught to all doctors through continuing medical education.

The worldwide pressure on intensive care unit (ICU) beds, especially in low-income countries, often forces doctors to admit patients who will benefit most. Furthermore, in order to provide a quality service, constant self-evaluation is required. ICU mortality does not depend on the standard of care only, but also on the case mix of the patients and the discharge policies of the unit. **Risk-adjusted mortality** is a frequently used quality indicator to evaluate ICU care — this method adjusts for case mix. **Predicted risk of ICU death** can be calculated using a scoring system. This predicted risk of ICU death can then be compared with the **actual mortality** rate. A number of ICU severity scoring systems have been developed. A large Scottish study compared the performance of five scoring systems (Acute Physiology and Chronic Health Evaluation (APACHE) II, APACHE III, APACHE UK and Simplified Acute Physiology Score (SAPS) II and Mortality Probability Model) in terms of discrimination and calibration.[1] Although SAPS II demonstrated the best overall performance, the APACHE II was the most appropriate model for comparison between different ICUs. For this reason we used the APACHE II system to evaluate severity of illness and outcome in our ICU.[2] The severity scoring systems that are currently in use were all developed in First-World settings. Our aims with this study were: (*i*) to describe the case mix of adult admissions to our ICU; (*ii*) to investigate the impact of such variation on outcome; and (*iii*) to validate the APACHE II risk prediction model for use in our setting.

Methods

The setting was a largely medical, adult 8-bed ICU in a tertiary hospital. Non-medical cases are also frequently admitted. Data were collected prospectively for consecutive admissions over 13 months from 1 March 2002 to 31 March 2003.

ICU survivors and non-survivors were compared for age, sex and diagnoses using the chi-square test for categorical and Student's *t*-test for continuous variables. The ICU mortality was calculated for the whole study group and individually for certain sub-groups: medical admissions, non-medical admissions, gender, patients with severe sepsis (as defined in the 1992 American College of Chest Physicians and Society of Critical Care Medicine consensus statement[3]), community-acquired pneumonia (CAP), hospital-acquired pneumonia, pulmonary tuberculosis, drug overdose, asthma, immunocompromised patients, trauma and post emergency surgery.

The main outcome measure was death or survival at discharge from the ICU after adjustment for case mix using the APACHE II method.[2] Risk of ICU death was calculated according to the original APACHE II method. Patients who died in the first hour after admission to ICU or who were in full cardiorespiratory arrest and then died in the first 4 hours after admission were excluded from the APACHE II method of risk prediction. The criteria for these exclusions were determined by similar exclusions used in the development of the original models.[4] These cases were, however, included in all other statistics in this study. The goodness of fit of the APACHE II equation for the analysed data was assessed with a calibration curve. The discrimination of the model was assessed with a receiver operator characteristic curve (ROC curve). Classification tree analysis was used to determine significant cut-off points for both the 'raw' APACHE II score and for the APACHE II method calculated risk of ICU death. The standardised mortality ratio was calculated.

Results

There were 304 admissions in total. The mean age (± standard deviation (SD)) was 40.7 ± 17 years (Table I). Only 16.4% were aged 60 years or older (Table II). Medical admissions accounted for 65.1% of the total admissions. Non-medical admissions included orthopaedic, gynaecological, neurosurgical, obstetric, abdominal and vascular surgical admissions, as well as trauma patients. Only 23 patients (7.6%) were admitted for observation after elective surgery.

The ICU mortality for all admissions was 37%. The ICU mortality of the various diagnostic groups is given in Table I. Medical and non-medical admissions had ICU mortalities of 40.2% and 31.1% respectively. Two patients died after elective surgery — both were found to have malignant tumours and subsequent medical management was conservative. The mean age for ICU survivors and non-survivors was similar (Table I). The ICU mortality of the older patients (60 years and older) was not higher than that of younger patients (Table II). The mortality of patients with severe sepsis and/or CAP was significantly higher than that for patients without these diagnoses (59.4% v. 25%, $p < 0.01$ and 53% v. 32%, $p < 0.01$, respectively). Other groups with high ICU mortalities were patients with pulmonary tuberculosis (45%) and patients who were known to be

Table I. Characteristics of the group

Diagnosis	No. of cases	% of total admissions*	Survivors	Non-survivors	Mortality (%)
Age (yrs) (mean ± SD)	–	–	41 ± 17	40 ± 17	–
Male sex	167	54.9	112	55	32.9
Female sex	137	45.1	79	58	42.3
Medical admissions	198	65.1	118	80	40.2
Non-medical admissions	106	34.9	73	33	31.1
Bacterial sepsis at admission to ICU	106	35	43	63	59.4
Community-acquired pneumonia	66	21.7	31	35	53
Hospital-acquired pneumonia	16	5.3	11	5	31
Pulmonary tuberculosis	20	6.8	11	9	45
Drug overdose	24	7.8	20	4	16.7
Asthma	25	8.3	23	2	8
Immunocompromised patients	13	4.3	5	8	62
Trauma	22	7.2	17	5	23
Post emergency surgery	52	17.1	32	20	38.5

* Please note that patients could be included in more than one diagnostic group.

Table II. ICU mortality rates (%) according to age

	Age group (yrs)							
	11 - 19	**20 - 29**	**30 - 39**	**40 - 49**	**50 - 59**	**60 - 69**	**70 - 79**	**80 - 89**
Mortality rate (%)	21.7	36.1	38.5	29.2	52.3	28.6	38.9	25.0
No. of patients	23	61	78	48	44	28	18	4
% of total admissions	7.6	20.1	25.7	15.8	14.5	9.2	5.9	1.3

Table III. Outcomes and diagnoses of known immunocompromised patients

Case No.	Diagnoses	Outcome
1	Acute lymphocytic leukaemia/post chemotherapy/neutropenic sepsis	Died
2	Aplastic anaemia/neutropenic sepsis	Died
3	Renal transplant/lung abscess	Died
4	Renal transplant/sepsis	Died
5	Rheumatoid arthritis, SLE /interstitial lung disease/pulse dose steroids	Died
6	Vasculitis/pulse dose steroids/sepsis	Died
7	Vasculitis/pulse dose steroids/sepsis	Died
8	HIV/CAP	Died
9	HIV/lung abscess	Died
10	HIV/*Rickettsia*	Died
11	HIV/ hydrocephephalus/TBM/ VP shunt	Survived
12	HIV/malignant hypertension	Survived
13	HIV/*Varicella* pneumonia	Survived

SLE = systemic lupus erythematosus; CAP = community-acquired pneumonia; TBM = tuberculous meningits; VP = ventricular peritoneal.

immunocompromised (62%). The specific diagnoses and outcomes of known immunocompromised patients are given in Table III.

The average APACHE II score was 17.4 (SD ± 0.6). Eleven patients were excluded according to the APACHE II method as described above. The distribution of APACHE II scores is shown in Fig. 1. The average APACHE II scores of patients with sepsis and CAP were 22.2 and 20.1, respectively, which were both higher than the average APACHE II score for the whole group. Nine patients with sepsis and 6 with pneumonia were excluded according to the APACHE II method because they died soon after admission.

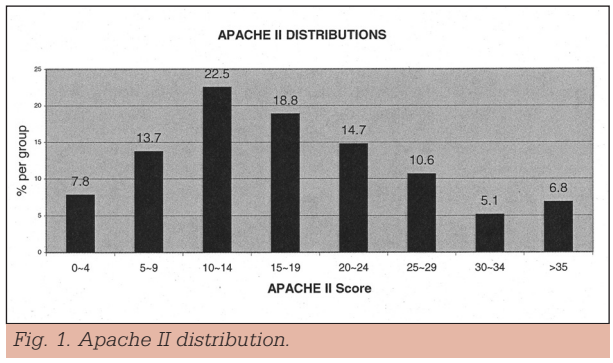


Fig. 1. Apache II distribution.

A calibration curve for the APACHE II equation applied to our data is shown in Fig. 2. It demonstrates that the predicted hospital mortality was within the 95% confidence interval (CI) of the actual mortality. The only exception was the group with a 70% predicted risk of ICU death: the upper error bar was at 0.69, which was just below the predicted 0.7. Fig. 3 shows a ROC curve for the APACHE II method of risk prediction — the area under the curve was 0.83 (95% CI: 0.78 - 0.88).

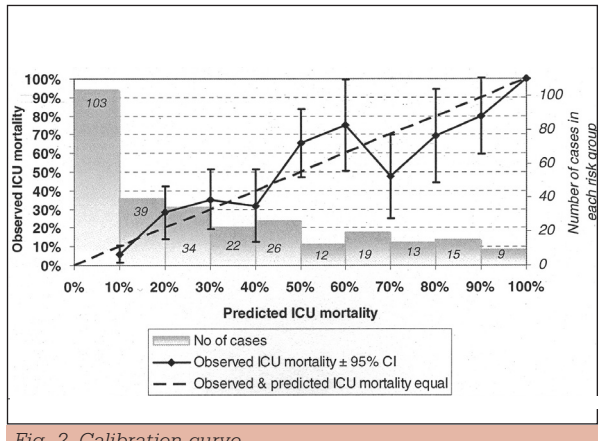


Fig. 2. Calibration curve.

Classification tree analysis shows that patients with an APACHE II score of ≥ 28 had an ICU mortality of 80% (specificity 95%, sensitivity 34%). An APACHE II method predicted risk of ≥ 45% was associated with an ICU mortality of 71% (specificity 86%, sensitivity 62%).

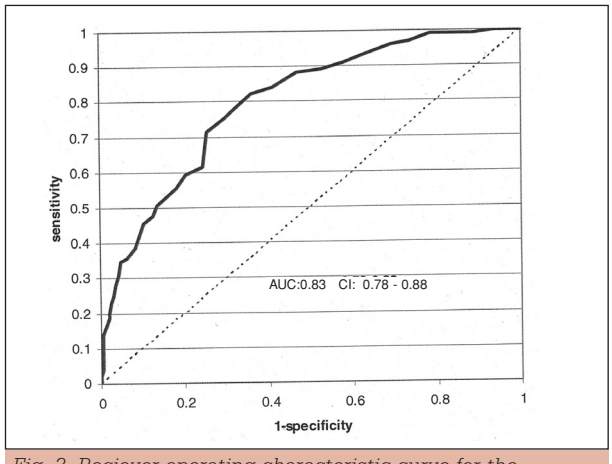


Fig. 3. Reciever operating characteristic curve for the APACHE II method.

The standardised mortality ratio for the whole group was 0.98 (95% CI: 0.79 - 1.17).

Discussion

This study had two main findings. Firstly it validated the use of the APACHE II model to accurately describe the risk of ICU death of the patient population in our ICU. Secondly, patients with severe sepsis and/or CAP had a higher mortality than that generally described in the literature. There may be several reasons for this, which we discuss further on.

Validation of APACHE II

In order to validate the use of a scoring system, both the **discrimination** and the **calibration** of the model have to be assessed. Discrimination is the model's ability to accurately label any given individual as a survivor or non-survivor. This can be assessed with the area under the ROC curve where 0.5 represents random chance and 1 perfect discrimination. The calibration, or fit, describes a model's ability to describe a group of patients accurately. Fit can be captured quantitatively by using tests such as the Hosmer-Lemshow C statistic and graphically by plotting the distribution of the observed and expected mortality rates (a calibration curve).[5]

The area under the ROC curve in this study indicates a good discrimination of the model when applied to our patient population (Fig. 3). We used the calibration curve (Fig. 2) to assess fit: in all but one risk group, the predicted mortality was within the 95% CI of the actual mortality. This indicates an overall good fit of the APACHE II model for the analysed data. The higher risk groups (≥ 60% risk) contained much smaller numbers of patients than the lower risk groups and mislabelling one or two patients in these groups could have accounted for the one outlier.

The standardised mortality ratio is the ratio of actual number of ICU deaths to the predicted number of ICU deaths. It allows for comparisons between ICUs. A ratio of < 1 shows better than predicted outcome and > 1 indicates worse than predicted outcome. The standardised mortality ratio of 0.98 indicates a good comparison with the original model.

Classification tree analysis was used to determine cut-off points with high specificity for predicting a poor outcome for both the 'raw' APACHE II score and the APACHE II predicted risk of death. The sensitivity of these cut-off points, however, was low. This information could be used to exclude certain patients with high APACHE scores from ICU admission because of a high likelihood of ICU death. However, scoring systems provide only probabilities and do not accurately predict whether an individual will survive. They therefore should not be used alone to determine decisions about admission to intensive care.[6]

ICU mortality in various diagnostic groups

Patients with severe sepsis had a significantly higher ICU mortality (59%) than those without (25%). Mortality rates reported in the literature for this condition in developed countries range from 31% to 56%.[7-10] It should be noted that 9 patients (17.6%) in this group were extremely ill on ICU admission – they either died in the first hour after admission to the ICU or were in full cardiorespiratory arrest and then died in the first 4 hours after admission. (According to the APACHE II method, these patients were not included in the APACHE II risk prediction model.) The rest of this group of patients had a higher average APACHE score (and therefore risk of death) than the average for all admissions. We might have to review our ICU admission strategy when it comes to cases in which further medical treatment is almost certainly futile. The problem remains that it is difficult to predict accurately which patients will fall into this category. There appears to be a general feeling among ICU doctors that young patients with the diagnosis of septic shock – even though they might have very high APACHE II scores – should at least be 'given a chance' in the ICU because the condition is potentially reversible.

It is the impression of the authors that there is often considerable delay in patients with severe sepsis receiving appropriate resuscitation and treatment before ICU admission. This might be due to a variety of factors, e.g. the availability of tertiary ICU beds, delays in the transport of critically ill patients to referral centres, and the workload and level of expertise in some primary and secondary health care facilities. Given the current evidence of the impact of early goal-directed resuscitation and early adequate antibiotics on the outcome of patients with sepsis, these factors might well have contributed to the high mortality in these patients.[7,11] Medical staff involved in the care of septic patients should be educated in the management principles as set out in the Surviving Sepsis Campaign.

Patients with CAP also had a high ICU mortality (53%). Although similar mortality rates for severe CAP requiring ICU have been reported,[12] most centres report mortalities between 23% and 36%.[13-15] The reasons for this poor outcome are probably similar to those in the group with severe sepsis. Firstly, 6 patients (9%) in this group either died during the first hour after admission or had cardiopulmonary resuscitation before ICU admission and then died within 4 hours after admission. The average APACHE II score for the remaining 60 patients was 20.1, which was also well above the average for the whole group.

As expected, the group of immunocompromised patients also had a high ICU mortality. Known HIV-positive patients are not necessarily excluded from admission to our ICU — numerous factors are taken into consideration, e.g. the stage of disease and last available CD4 count. We do not perform routine HIV testing on all cases referred for admission, only when it is thought to contribute to the differential diagnosis or management. Despite isolation facilities, patients who have received chemotherapy and then develop severe sepsis continue to have a very poor outcome in our ICU even though the prognosis for the underlying condition might be relatively good.

The mortality of patients with pulmonary tuberculosis (PTB) and respiratory failure requiring mechanical ventilation is reported to be in the range of 29 - 69%.[16-18] We admitted 20 patients with active pulmonary tuberculosis of whom 45% died. Only 1 patient had multidrug-resistant PTB. Owing to the fact that PTB is a slowly responding disease these patients tend to stay in the ICU for longer periods of time, putting further pressure on the availability of ICU beds. With the current TB epidemic in the Western Cape, this might become an even bigger problem in the future. There have been calls for a guideline statement on the admission of these patients to the ICU.[19]

The original APACHE II score was developed using hospital as opposed to ICU mortality.[2] A point of criticism of our study is that we only investigated ICU mortality and not hospital mortality as outcome. We specifically wanted to evaluate care in our ICU and we felt that once patients are discharged there are too many other variables over which we have no influence. As a discharge policy, when medical support is withdrawn in cases where further medical treatment is deemed futile, patients are generally not discharged to die in other wards. One exception is patients with hypoxic encephalopathy, signs predictive of a poor neurological outcome and who are already weaned from the ventilator.

In conclusion, this was the first time that data of severity scoring and outcomes of consecutive adult ICU admissions were prospectively collected and analysed in our hospital. We constantly need to reassess our standard of care. There is now a baseline outcome (the standardised mortality ratio) in place against which we can measure future outcomes. The principles of appropriate management of early sepsis should be taught to all doctors through continuing medical education.

Although we validated the use of the APACHE II model in our unit, it might not be the most appropriate system for South Africa, and more research is needed to establish which score should be implemented.

1. Livingston BM, Mackirdy FN, Howie JC, Jones R, Norrie JD. Assessment of the performance of five intensive care scoring models within a large Scottish database. *Crit Care Med* 2000; **28:** 1820-1827.
2. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. *Crit Care Med* 1985; **13:** 818-829.
3. Bone RC, Balk RA, Cerra FB, *et al.* Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992; **101:** 1644-1655.
4. Knaus WA, Zimmerman JE, Wagner DP, *et al.* APACHE — acute physiology and chronic health evaluation: A physiologically based classification system. *Crit Care Med* 1981; **9:** 591-597.
5. Angus DC. Scoring system fatigue … and the search for a way forward. *Crit Care Med* 2000; **28:** 2145-2146.
6. Gunning K, Rowan K. ABC of intensive care: Outcome data and scoring systems. *BMJ* 1999; **319:** 241-244.
7. Rivers E, Nguyen B, Havstad S, *et al.* Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; **345:** 1368-1377.
8. Rangel-Frausto MS, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel RP. The natural history of the systemic inflammatory response syndrome (SIRS): a prospective study. *JAMA* 1995; **273:** 117-123.
9. Brun-Buisson C, Doyon F, Carlet J, *et al.* Incidence, risk factors, and outcome of severe sepsis and septic shock in adults. A multicenter prospective study in intensive care units. French ICU Group for Severe Sepsis. *JAMA* 1995; **274:** 968-974.
10. Bernard GR, Vincent J-L, Laterre P-F, *et al.* Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 2001; **344:** 699-709.
11. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. *Chest* 2000; **118:** 9-11.
12. Ewig S, Torres A. Severe community-acquired pneumonia. *Clin Chest Med* 1999; **20:** 575-587.
13. Gowardman J, Trent L. Severe community acquired pneumonia: a one-year analysis in a tertiary referral intensive care unit. *N Z Med J* 2000; **113:** 161-164.
14. Ewig S, Ruiz M, Mensa J, *et al.* Severe community-acquired pneumonia. Assessment of severity criteria. *Am J Respir Crit Care Med* 1998; **158:** 1102-1108.
15. Brown PD, Lerner SA. Community-acquired pneumonia. *Lancet* 1998; **352:** 1295-1302.
16. Lee PL, Jerng JS, Chang YL, *et al.* Patient mortality of active pulmonary tuberculosis requiring mechanical ventilation. *Eur Respir J* 2003; **22:** 141-147.
17. Penner C, Roberts D, Kunimoto D, Manfreda J, Long R. Tuberculosis as a primary cause of respiratory failure requiring mechanical ventilation. *Am J Respir Crit Care Med* 1995; **151:** 867-872.
18. Potgieter PD. The influence of the tuberculosis epidemic on ICU resources. *S Afr Med J* 1995; **85:** 1196.
19. Bateman ED. ICU care for tuberculosis patients — fielding on the boundary. *S Afr Med J* 1997; **87:** 635-634.