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APACHE II SCORING TO PREDICT OUTCOME IN POST-CARDIAC ARREST

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Abstract

Introduction—Despite advancements in management of cardiac arrest, mortality remains high and few severity of illness scoring systems have been calibrated in this population. The goal of the current investigation was to assess the Acute Physiology and Chronic Health Evaluation II score in post-cardiac arrest.

Measurements—This is a prospective observational study of adult post-cardiac arrest patients at a tertiary-care center. The primary outcome variable was in-hospital mortality and secondary outcome variable was neurologic outcome. APACHE II scores were used to predict outcomes using logistic modeling.

Main Results—A total of 228 subjects were included in the analysis. The median age of the cohort was 70 (IQR: 64 – 71) and 32% (72/228) of the patients were female. The median downtime was 15 minutes (IQR: 7 – 27) and initial lactate 5.9 mmol/L (IQR: 3.5 – 8.4). 71 (57%) of deaths occurred prior to the 72-hour follow-up and overall in-hospital mortality was 55% (125/228). Discrimination of APACHE II score in all cardiac arrest patients increased in stepwise fashion from 0-hr to 72-hr follow-up (AUC: 0-hr: 0.62; 24-hr: 0.75; 48-hr: 0.82; 72-hr: 0.86).

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None of the authors have any conflicts to declare.

COMPETING INTERESTS

The authors state that they have no competing interests.

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Conclusions—APACHE II score is a poor predictor of outcome at time zero for out-of-hospital cardiac arrest (OHCA) post-arrest patients consistent with the original development of the score in the critically ill. For in-hospital cardiac arrest (IHCA) at time zero and for both IHCA and OHCA at 24 hours and beyond, the APACHE II score was a modest indicator of illness severity and predictor of mortality/neurologic morbidity.

Keywords

cardiac arrest; severity of illness; mortality prediction; resuscitation; risk score

Introduction

Cardiac arrest occurs in over 400,000 patients per year in the United States.¹ Mortality rates remain high with recent estimates of greater than 90% in some locations.² Furthermore, the majority of patients who survive initial resuscitation efforts often succumb during the post-arrest period due to neurologic injury, refractory shock, or recurrent arrest.^{3,4} Previous reports in cardiac arrest have demonstrated that survival following cardiac arrest is dependent on characteristics specific to the event itself including location, presence or absence of bystander cardiopulmonary resuscitation (CPR), access to Advanced Life Support (ALS), initial cardiac rhythm, no-flow and low-flow intervals.⁵ Severity of illness scoring systems designed for the general critically ill population do not take these arrest-specific factors into account and therefore the application of these scoring systems in post-cardiac arrest patients remains less clear. While several of these scores are utilized when describing post-arrest populations in the literature, the majority of severity indices have not been validated specifically in the post-arrest population.

Severity of illness prediction models in the post-arrest population can serve several purposes including risk prediction of death to help with family coping and expectations, risk adjustment for comparing patient populations for quality assessment and research, and stratification of patients entering into clinical investigation. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score, a severity of illness score that was derived and validated in a critically ill population, is a composite measure of 12 variables including chronic co-morbid conditions as well as acute pathophysiologic parameters.⁶ The score has been validated in general critical illness as well as in specific patient populations including the surgical⁷ and trauma patients.^{8,9} Though first derived in 1985, the APACHE II score remains relevant in 2012 as illustrated by over 50 publications this year alone based on this scoring system.^{10–13} The post-arrest condition is heavily dependent on pre-arrest and intra-arrest conditions and APACHE was not designed to capture this data. Therefore, validation of the general severity scores in the post-arrest population is required before widespread use can be applied confidently.

Like many illness severity scores designed for the general critically ill population, the APACHE II score has not been adequately tested in the post-cardiac arrest population. One previous investigation was performed in a Finnish population, however several limitations were present in that investigation including whether included subjects were from the out-of-hospital or in-hospital population or both, exclusion of patients in the coronary care units, and limited report of area under the curve (of the Receiver Operator Characteristic Curve) (AUC) for the APACHE II at serial time points.¹⁴ Regardless of limitations, the study has also yet to be validated in another population.

The purpose of the current investigation was to determine whether the APACHE II score accurately predicts hospital outcomes for patients following out-of-hospital cardiac arrest. We hypothesized that APACHE II would successfully predict outcome in post-cardiac arrest

patients despite the absence of cardiac arrest event-specific criteria. Given the significant differences in post-arrest out-of-hospital and in-hospital arrest patients, we further set out to evaluate differences in severity of illness score prediction in both of these distinct groups. In order to test our hypothesis, we evaluated the APACHE II score in both the OHCA and IHCA population.

Methods

Design

A prospective, observational cohort study of cardiac arrest patients during the period from 11/2007 to 1/2011.

Setting

An urban tertiary care academic teaching hospital with 650 inpatient beds and approximately 50,000 Emergency Department (ED) visits per year. The hospital is also a regional cardiac arrest referral center that receives post-cardiac arrest patient transfers from outside hospitals.

Population

The study population included all adult (age >18 years) patients who had suffered either an out-of-hospital cardiac arrest (OHCA) or an in-hospital cardiac arrest (IHCA) with successful return of spontaneous circulation (ROSC) as defined by the presence of palpable pulses. Excluded from the study population were patients who had suffered cardiac arrest with primary traumatic etiology.

Data Collection and Definitions

Data collection included patient demographic information (including age, sex and race), comorbid conditions, all variables necessary for computing severity scores, in-hospital mortality and neurologic status at hospital discharge. APACHE II score was calculated at serial intervals (0-hr, 24-hr, 48-hr, 72-hr) based on the worst vitals and laboratory values in each 24-hr interval. Initial laboratory values were used to calculate the 0-hr APACHE II score but were not included in the 24-hr calculations. The worst value was defined as the value that would be assigned the greatest number of severity points as previously described.⁶ Subjects receiving vasopressor therapy were automatically assigned the worst value for mean arterial blood pressure in each score. Cardiac arrest event data was recorded in the Utstein style which includes information on time course of resuscitation, initial cardiac rhythm, presence of cardiac arrest after advanced life support (ALS) arrival, witnessed cardiac arrest, presence of bystander CPR, intra-arrest medications, and time of return of spontaneous circulation (ROSC).^{15,16} Neurologic outcome was determined based on neurologic assessments at the time of hospital discharge and the Cerebral Performance Category (CPC) score was used to categorize neurologic outcomes.¹⁷ CPC 1 indicates full recovery; CPC 2 indicates moderate disability (able to work at least part-time, and independent for activities of daily living, with or without neurological manifestations such as hemiplegia, seizures, ataxia, dysarthria, dysphasia, or permanent memory or mental changes); CPC 3 indicates severe disability (conscious, but fully dependent for daily support because of severely impaired cognitive function); CPC 4 is comatose or in a persistent vegetative state, and those with CPC 5 have died. Good neurological recovery was defined as CPC 1 and 2. CPC scores were dichotomized into good (CPC 1 or 2) outcome and poor (CPC 3, 4, or 5) outcome, which is an accepted categorization for investigations in post-cardiac arrest patients.^{18,19} We defined downtime as the total “low-flow” time (CPR only) plus the total “no-flow” time (without a pulse and without CPR). Data were recorded

initially on a standardized data collection form and then transferred to the electronic database (Microsoft Access, Microsoft, Redmond, WA, USA). The study was approved by the Institutional Review Board at Beth Israel Deaconess Medical Center.

Intervention

None

Outcome Measures

The primary outcome for this investigation was in-hospital mortality.

Statistical Analysis

Simple descriptive statistics were used to summarize the study population. Data for continuous variables are presented as means with standard deviations or median with inter-quartile ranges (IQR) depending on distribution of the variable. Categorical data are presented as frequencies with percentages. Logistic regression was used to assess the association between APACHE II with outcomes for which APACHE II was considered an independent continuous predictor variable. A logistic regression was performed to determine the ability of APACHE II score to predict in-hospital mortality. Discrimination of the models was assessed using the Area Under the Curve (AUC) of the Receiver Operator Characteristic (ROC) Curve. Calibration was assessed using the Hosmer-Lemeshow Goodness-of-Fit test and $P > 0.05$ was considered well calibrated. We calculated sensitivity, specificity, positive and negative predictive value for different cutoff points for the scores at the serial intervals. A pre-planned comparison between OHCA and IHCA of the performance of APACHE II was also performed. Except where otherwise indicated an alpha of 0.05 was used as the cut point for statistical significance and all analyses were performed in SAS v9.2 (SAS Institute Inc., Cary, NC, USA).

Results

A total of 228 subjects were included in the analysis. The median age of the cohort was 70 (IQR: 64 – 71) and 32% (72/228) of the patients were female. Baseline characteristics and cardiac arrest event data as well as a comparison of data between OHCA and IHCA cohorts are in Table 1. The overall mortality for all subjects was 55% (125/228) with a mortality rate of 61% (69/114) in the OHCA group and 49% (56/114) in the IHCA group. The percent of good neurological outcome (CPC 1–2) overall was 40% (91/228) with 34% (39/114) in the OHCA group and 46% (52/114) in the IHCA group. Of the patients who died during their hospital stay 57% (71/125) died prior to the 72 hour follow up. The median ICU length of stay was 4 days (IQR: 2 – 8) and the median hospital length of stay was 6 days (3 – 11). The median downtime was 15 minutes (IQR: 7 – 27) and initial lactate 5.9 mmol/L (IQR: 3.5 – 8.4).

Vitals and laboratory data to calculate 0-hour APACHE II scores are in Table 2. Mean APACHE II score at baseline was 28 ± 8 and at 72-hrs was 22 ± 8 . APACHE II score characteristics at each time point are shown in Table 3. APACHE II was a significant predictor of mortality at baseline (0-hr OR per point increase in APACHE II score: 1.09, 95%CI: 1.05 – 1.13), such that a 1-point increase in APACHE II score at 0-hr is associated with a 9% increase in the probability for death. The predicted probability for death per point increase in APACHE II score increased over time: 24-hr OR: 1.10, 95%CI: 1.06 – 1.15; 48-hr OR: 1.20, 95%CI: 1.12 – 1.28; 72-hr OR: 1.22, 95%CI: 1.13 – 1.31. Discrimination of the APACHE II score, as represented by the AUC (Figure 1), increased in a stepwise fashion from 0 hours to 72 hours (Table 3). Table 3 includes data on the increases in the risk for death at 5-point and 10-point increases of APACHE II score. APACHE II prediction was

sufficiently calibrated to the data at 0-hr, 24-hrs, and 48-hrs (all Hosmer-Lemeshow Chi-Square $P > 0.05$). However, at 72-hrs the model was not sufficiently calibrated to predict either in-hospital mortality or poor neurologic outcome (both H-L $P = 0.002$). We evaluated the sensitivity, specificity, positive and negative predictive values of different cutoff values for APACHE II score (Table 4). By 72-hrs, a score of 35, which was present in 13/127 (10%) of subjects available, had specificity of 99% and positive predictive value 92%.

While the strong majority of enrolled patients were comatose, there were 10% of subjects (22/228) with an initial glasgow coma score ≥ 8 . Removing these patients from the analysis did not change the overall results. In addition, we did not make adjustments to temperature in the APACHE II score for the initial analysis, however in order to ensure this did not affect the findings we performed a second analysis after “normalizing” temperatures during induced hypothermia such that a patient would be assigned a score of “0” even if hypothermic. With this adjustment, the overall results during the hypothermic time periods were identical (24 hour OR 1.10 [95% 1.06–1.15] versus normalized OR 1.10 [95% 1.06–1.15] and 48 hours OR 1.20 [95% CI 1.12–1.28] versus 48 hours normalized OR 1.20 [95% CI 1.12–1.28]).

Discussion

We evaluated the APACHE II score in a population of post-arrest patients comprising both OHCA and IHCA. We had pre-determined that the two populations would be analyzed separately given the heterogeneity of these two groups of patients. Overall (both groups combined), the APACHE II score was a modest predictor of mortality at 24-, 48-, and 72-hour time points, but somewhat poor at time zero. The performance of the APACHE II score increased incrementally over the next 24, 48, and 72 hours however the percent of patients dying (and therefore dropping out of the analysis) at those time points was substantial. When examining only OCHA the APACHE II score was a very poor predictor of outcome at time zero though discrimination improved at 24, 48, and 72 hours. In contrast, the APACHE II score performed modestly in predicting outcome in the IHCA cohort at time zero and also continued to improve over time.

The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was first published in 1985 by Knaus, et. al, as a convenient method for providing a general measure of severity of disease.⁶ The original authors of this tool found that an increasing score closely correlates with risk of death in intensive care unit patients, and it has since been used to predict outcome in a wide range of disease states. Its utility in predicting mortality has been validated in critically ill trauma patients²⁰, transplant patients²¹, and septic patients²², among others. The use of the APACHE II score specifically in post-arrest populations has been employed previously though has not been validated.¹⁴ In this one single previous investigation, authors utilized a national database of critically ill patients and evaluated the cardiac arrest population specifically. Limitations of this study included the lack of clarity around inclusion criteria and failure to provide exact AUC information for the data points when the APACHE II score was measured. Another possible limitation of this investigation is that withdrawal of care by providers could affect mortality rates and/or timing of death. Another study recently published in *Resuscitation* examined APACHE III in survival to discharge in OHCA and IHCA populations finding a similar results and AUC as our analysis (all patients at ICU admission had 0.75 AUC, OHCA 0.72, and IHCA 0.72).²³ Previous investigators have noted that the APACHE II performed as well as or better than the APACHE III in certain populations.²⁴ Though the APACHE II score was based on a publication from 1985, common usage in critically ill populations illustrates the continued relevance in 2012. The fact that the score has similar characteristics to the recently published data on APACHE III in the post-arrest population further accentuates this point.

In our study, we found that APACHE II score does not perform well at time zero in the OHCA population and the use of the score in this population may be invalid. That stated, the APACHE II score was not originally designed or validated for time zero measurements, but instead was designed for characterization of a population after 24 hours of admission (used worst values over 24-hour period). Thus, our findings that the APACHE II score is not helpful at time zero is not unexpected and is consistent with the intent of the score in the critically ill general population and further emphasizes the influence of event specific characteristics such as downtime, presence or absence of a witness or bystander CPR on the initial post-cardiac arrest syndrome. While the APACHE II score performed fairly well at subsequent time points of 24, 48, and 72 hours, the majority of deaths occurred prior to that period. Despite this concern, for patients alive at the 24, 48, and 72-hour mark, the APACHE II score is a modest predictor illness severity and is a good predictor at the 72-hour mark. This was true for both the IHCA and OHCA populations.

In reference to other severity of illness scoring systems specifically evaluating post-cardiac arrest patients, the OHCA score was originally described by Adrie et al and validated by Hunziker et al. This score utilized creatinine, lactate, initial cardiac rhythm, and no-flow and low-flow intervals. It was found that these variables (on hospital presentation) were associated with mortality with AUC of 0.82⁵. This score was validated by Hunziker et al. in the United States and found a similar AUC of 0.85.²⁵ The advantage of this scoring system is that the required variables are all present upon hospital admission and calculation of the score does not require 24 hours of observation. The disadvantage is the complicated calculations that are required to determine the score from the variable set, as well as some potential difficulty with accurate descriptions of no-flow and low-flow times. Another scoring system, the “lactate-hypotension index”, requires only two variables upon entry into the hospital and has an AUC = 0.82 for prediction of outcome.²⁶ The advantages of this scoring system is the ease of use, however the current disadvantage is that the score has yet to be prospectively validated though studies remain ongoing.

Conclusions

The APACHE II score is not a good predictor of outcome at time zero after out-of-hospital cardiac arrest consistent with the original development of the score in the critically ill. For in-hospital cardiac arrest at time zero and for both IHCA and OHCA at 24 hours and beyond, the APACHE II score was a modest indicator of illness severity and predictor of mortality and neurologic morbidity. The discrimination was best at the 72 hour mark after cardiac arrest.

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Figure 1.
Comparison of ROC curves for APACHE II to predict in-hospital mortality at serial time points

Table 1

Baseline and event characteristics of the study cohort.

Characteristic	All CA	OHCA	IHCA
Total number (N)	228	114	114
Age – yr. (+/- SD)	67 (16)	66 (17)	68 (59)
Female – no. (%)	72 (32)	32 (28)	40 (35)
Race – no. (%)			
White	188 (82)	98 (86)	90 (79)
Black	23 (10)	6 (5)	17 (15)
Asian	9 (4)	3 (3)	6 (5)
Other/Unknown	8 (4)	6 (5)	2 (2)
Co-Morbid Conditions – no. (%)			
Coronary artery disease (CAD)	78 (34)	38 (33)	40 (35)
Congestive heart failure (CHF)	55 (24)	20 (17)	35 (31)
Chronic obstructive pulmonary disease (COPD)	21 (9)	10 (9)	11 (10)
Diabetes	35 (15)	17 (15)	18 (16)
Hypertension	127 (56)	60 (52)	67 (59)
Witnessed Arrest – no. (%)	189 (83)	83 (73)	106 (93)
Bystander CPR – no. (%)	172 (75)	70(61)	102 (90)
Initial arrest rhythm – no. (%)			
Ventricular fibrillation/tachycardia	86 (38)	52 (44)	34 (30)
Pulseless Electrical Activity	99 (43)	33 (29)	66 (58)
Asystole	32 (14)	21 (18)	11(10)
Unknown	11 (5)	7 (6)	4 (4)
Intravenous Medication Administered – mg. (IQR)			
Epinephrine	2.0 (1.0 – 3.0)	1.0 (1.0 – 3.0)	2.0 (1.0 – 3.0)
Atropine	1.0 (1.0 – 2.0)	2.0 (1.0 – 3.0)	1.0 (1.0 – 2.0)
Downtime – min			
Median (IQR)	15 (7 – 27)	20 (10 – 35)	11 (5 – 20)
Mean (+/- SD)	20.3 (19.5)	25.6 (21.1)	15.5 (16.8)
Initial lactate – mmol/L (+/- SD)			
Median (IQR)	5.9 (3.5 – 8.4)	5.5 (3.7 – 8.1)	6.1 (3.1 – 8.6)
Mean (+/- SD)	6.3 (3.5)	6.1 (3.2)	6.5 (3.7)
Vasopressor use – no. (%)	143 (63)	66 (57)	77 (68)
Therapeutic hypothermia no. (%)	80 (35)	53 (46)	27 (24)
In-hospital mortality – no. (%)	125 (55)	68 (60)	56 (49)
Good neurological outcome defined by CPC score 1–2: no. (%)	91 (40)	39 (34)	53 (46)

Table 2

Baseline APACHE II score variables.

Variable	All CA (n = 228)	OHCA (n = 114)	IHCA (n = 114)
Age – years (+/- SD)	67 (16)	66 (17)	68 (16)
Temperature – C (+/- SD)	36.2 (1.2)	35.9 (1.3)	36.4 (1.1)
MAP (+/- SD) *	84 (25)	84 (27)	84 (23)
HR – bpm (+/- SD)	102 (30)	98 (28)	107 (32)
RR – bpm (+/- SD)	19 (6)	17 (5)	20 (6)
pH (+/- SD)	7.2 (0.2)	7.2 (0.2)	7.2 (0.2)
Na – mEq/L (+/- SD)	139 (11)	139 (4)	139 (14)
K – mEq/L (+/- SD)	4.7 (3.1)	4.4 (1.1)	5.0 (4.2)
HCO ₃ – mEq/L (+/- SD)	19 (5.7)	18 (4.5)	20 (6.5)
Creatinine – mg/dL (+/- SD)	1.8 (1.4)	1.7 (1.4)	1.9 (1.5)
Hematocrit – % (+/- SD)	36 (19)	37 (7)	35 (27)
WBC – 10 ³ /μL (+/- SD)	13.7 (7.4)	13.2 (6.4)	14.3 (8.5)
GCS – median (IQR)	3 (3 – 3)	3 (3 – 3)	3 (3 – 7)
Chronic Organ Insufficiency/Immunocompromised – no. (%)	39 (17)	10 (9)	29 (25)
APACHE II Score – mean (+/- SD)	28 (8)	27 (8)	28 (8)

* patients on vasopressors were automatically assigned the worst MAP score.

Table 3

Association of APACHE II score with mortality and neurologic outcome.

	0-hr	24-hr	48-hr	72-hr
Number	228	187	175	158
Mean APACHE II (+/- SD)	28 (8)	29 (9)	26 (9)	22 (8)
In-Hospital Mortality				
OR (95% CI)	1.09 (1.05 – 1.13)	1.10 (1.06 – 1.15)	1.20 (1.12 – 1.28)	1.22 (1.13 – 1.31)
5 Point Increase	1.53 (1.26 – 1.86)	1.63 (1.32 – 2.00)	2.46 (1.78 – 3.40)	2.67 (1.85 – 3.86)
10 Point Increase	2.35 (1.59 – 3.47)	2.64 (1.75 – 4.00)	6.03 (3.15 – 11.5)	7.12 (3.41 – 14.9)
All Patients AUC	0.62	0.75	0.82	0.86
OHCA AUC	0.58	0.71	0.79	0.89
IHCA AUC	0.72	0.79	0.84	0.83
Poor Neurologic Outcome				
OR (95% CI)	1.08 (1.03 – 1.12)	1.10 (1.06 – 1.15)	1.18 (1.11 – 1.25)	1.21 (1.23 – 1.29)
5 Point Increase	1.46 (1.20 – 1.78)	1.63 (1.33 – 2.01)	2.52 (1.67 – 3.03)	2.55 (1.79 – 3.63)
10 Point Increase	2.14 (1.46 – 3.15)	2.66 (1.76 – 4.03)	5.07 (2.80 – 9.19)	6.49 (3.19 – 13.2)
All Patients AUC	0.59	0.73	0.78	0.85
OHCA AUC	0.58	0.74	0.79	0.90
IHCA AUC	0.65	0.71	0.77	0.79

AUC = Area Under the Curve of the Receiver Operator Characteristic (ROC) Curve

CI = Confidence Interval

IHCA = In-hospital Cardiac Arrest

OHCA = Out-of-Hospital Cardiac Arrest

OR = Odds Ratio

Table 4

Sensitivity, Specificity, Positive and Negative Predictive values at cutoff values of APACHE II score.

APACHE II Cutoff	N	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
In-Hospital Mortality					
0-hr					
25	143	75	43	62	59
35	39	26	92	79	50
24-hr					
25	142	86	36	57	73
35	53	38	81	67	57
48-hr					
25	86	88	63	66	86
35	23	28	94	78	61
72-hr					
25	48	65	80	69	77
35	13	24	99	92	66
Poor Neurologic Outcome					
0-hr					
25	143	73	42	66	50
35	39	25	92	82	44
24-hr					
25	142	84	37	64	65
35	53	37	83	74	50
48-hr					
25	86	82	63	70	78
35	23	25	93	78	55
72-hr					
25	48	62	84	77	71
35	13	20	99	92	58