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Original Research Article

A Study of Apache Index and Its Relationship with Oxidative Stress in Cardiac Patients in Hospital Located in Mangalore, Karnataka

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Abstract

Objective: This preliminary study aims (1) at validating the use of Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system in cardiac patients admitted to the intensive cardiac care unit (ICCU) for prediction of the risk for mortality, (2) to evaluate the use of a modified APACHE II (mAPACHE II) with addition of the scores related to urinary levels of oxidative stress parameters in prediction of the risk for mortality. ***Design:*** Hospital based prospective study. ***Setting:*** Tertiary care hospital in South India. ***Methods:*** Cardiac patients (n=100) admitted to the intensive cardiac care unit between the age of 18-77 years were enrolled. APACHE II score was calculated. The predicted mortality was calculated on the basis of this score. Urinary malondialdehyde (MDA) and ceruloplasmin (Cp) levels were analyzed and mAPACHE II was calculated. ***Results:*** The mean APACHE score was 11 ± 4.14. The ICCU mortality rate within 24 hours after admission was 8%. The area under the receiver operating curve (ROC) for APACHE II score was found to be 0.8 indicating good discrimination and for mAPACHE II score was 0.7 indicating moderate discrimination. ***Conclusion:*** APACHE II scoring system has a good discrimination when applied to cardiac patients. However, mAPACHE II also shows moderate discrimination when applied to these patients.

Keywords: APACHE II, ICCU, mAPACHE II, Mortality, Oxidative stress.

Key Messages: Our study shows that by applying APACHE II and mAPACHE II scores we can predict mortality in ICCU patients and that these scores can be used in developing country like India for predicting outcome in cardiac patients.

INTRODUCTION

Multiple severity systems have been developed over the years for assessing overall ICCU performance which includes quality care, resource allocation, cost effectiveness and improving decision making for therapeutic intervention. In this study, the widely used APACHE II score has been applied along with mAPACHE II to determine the outcome in the ICCU.

APACHE II scoring system is based on severity of disease, introduced by Knaus WA *et al*., [1]. The APACHE II score is in the range of 0-70. Higher scores indicate that the condition of the patient is critical and the prognosis is poor.

Oxidative stress can result from increased production of free radicals which can damage the cells by lipid peroxidation or by oxidizing DNA or proteins. MDA and Cp are used as indicators of oxidative stress. Studies have reported increased plasma levels of MDA and Cp in cardiac patients.

The purpose of this preliminary study is to (i) validate APACHE II scoring system in cardiac patients admitted to the ICCU - as there is a paucity of literature on this subject in the Indian context and (2) to evaluate the use of a modified APACHE II (mAPACHE II) with addition of the scores related to urinary levels of oxidative stress parameters in prediction of mortality risk.

MATERIALS AND METHODS

After obtaining the approval of the ethical committee clearance of Yenepoya deemed to be University, informed consent was obtained from either the patients or their family/caregivers. This study was conducted on patients (n=100) admitted in the ICCU. The inclusion criteria were patients between the age of

18 -77 years of both genders and those admitted to the ICCU for the first time. The patients (n=100) were further sub-classified into groups of 10 years age intervals.

Parameters for calculating APACHE II were obtained within 24 hours of their admission to ICCU as in the study conducted in Brazil [2] and documented as per the guidelines mentioned by Knaus *et al*., [1]. Then APACHE II score was calculated as follows :

APACHE II = (acute physiology score) + (age points) + (chronic health points) as per the study conducted by Knaus *et al*., [3, 1].

Mortality Rate

Predicted mortality was calculated by using the equation formulated by Knaus et al in 1981[2] and standardized mortality ratio (SMR) was calculated.

Urine Analysis

The urine samples were collected from all these cardiac patients and from 58 normal healthy, age, sex matched adult volunteers, who were non alcoholic, non-smokers for control data of the urinary oxidative stress parameters. MDA and Cp concentrations were determined.

Scoring of urinary MDA (M- score) and ceruloplasmin (C- score)

Scores were applied for different concentrations of urinary MDA and Cp ranging from +4 to -4 as applied for APACHE II in the original study by Knaus *et al*., [1]. The mAPACHE II score was calculated by adding the M score and C score to APACHE II score (APACHE II ± M score ± C score).

STATISTICAL ANALYSIS

Student's t test was used for comparing the mean of continuous variables. Chi square test was used for comparing the proportions of categorized measurements. Discrimination between survivor and non-survivor was assessed by plotting the ROC (Receiver Operating Characteristic) curve for the APACE II score and mAPACHE II score.

Data was analyzed using SPSS software version 17 (SPSS Inc, Chicago IL).

All statistical tests were 2 – tailed and $p<0.05$ was considered to be statistically significant.

RESULTS

The total number of patients in the MICU considered for the current study were 350, ranging from the age of 18-57 years.

Table-1: Demographic details of the study groups and the scores evaluated in this study

			Study groups	
Sl. No	Variable		Patient group (n=100)	Control group (n=58)
1.	Age (years) mean ± SD		56.3 ± 14.2	27.9 ± 7.6
2.	Gender			
	Male		76 (76%)	38(65.5%)
	Female		24 (24%)	20 (34.5%)
3.	Score evaluated (mean ± SD			
	a) APACHE II score		11.0 ± 4.1	-
	b) mAPACHE II		16.2 ± 4.7	-
4.	ICU outcome in terms of mortality			
	a) Survivors		92 (92%)	-
	b) Non-survivors		8 (8%)	-
5.	Mean age (years)			
	a) Survivors (n=92)		56.2 ± 14.2	-
	b) Non-survivors (n=8)		67.5 ± 8.6	-
6.	Gender			
	a)Survivors (n=92)	Male	71(77.2%)	-
		Female	21(22.8%)	
	b)Non-survivors (n=8)	Male	6 (75%)	-
		Female	2 (25%)	

The data expressed is mean ± SD of various scores (APACHE II score and mAPACHE II in 100 patients.The maximum score for APACHE II is 71. Higher the score greater is the chanc

The mean age of the patient group was 56.3 ± 14.2 years. Among the patients, 76 were male and 24 were female. The mean APACHE II score of the patient group was 11.0 ± 4.1 and mAPACHE II was 16.2 ± 4.7 (Table-1).

Table-2: Frequency of survivors and non survivors in various age groups of the patients

Sl. No	Age groups		Mortality	
		Survivor (%)	Non survivors (%)	Total (%)
1.	18-27	03 (100)	0 (0)	03 (100)
2.	28-37	07 (100)	0 (0)	07 (100)
3.	38-47	10 (100)	0 (0)	10 (100)
4.	48-57	35 (97.2)	1 (2.8)	36 (100)
5.	58-67	14 (78.6)	4 (21.4)	18 (100)
6.	68-77	15 (85.0)	2 (15)	17 (100)
7.	>77	08 (88.9)	1 (11.1)	09 (100)
	Total	92 (92)	8(8)	100 (100)

The data represented in the survivors and non survivors is the frequency with percentage in parenthesis. The number of survivors gives an indication of survival and number of non survivors indicates the mortality.

MORTALITY

The ICCU mortality rate observed in this study (n = 100) was 8% (Table-2) whereas the predicted mortality was 48% and the overall SMR was 0.16.

Table-3: Comparison of Scores of survivors and non-survivors

Sl. No	Score	Mortality	Mean ± SD	t	p
1	APACHE II	Non-Survivors	14.9 ± 3.8	2.8	p<0.01**
		Survivors	10.7 ± 4.0		
2	mAPACHE II	Non-Survivors	20.9 ± 4.5	3.014	p<0.01**
		Survivors	15.8 ± 4.5		

*Survivors n= 92; Non survivors n = 8. The scores include 1. APACHE II, 2 and mApache II. The mean scores of the two groups, survivors and non survivors, was compared by Student t test. Level of significance was as follows: p<0.01 as highly significant **; p>0.05 was considered non significant (ns).*

Table-4: Comparison of the frequencies of patients and controls in the M score categories

Sl. No	M score categories	Study groups		p value
		Patient (n=100) n (%)	Control (n=58) n (%)	
1.	0.00	4 (4)	48 (82.8)	p<0.001
2.	1.00	6 (6)	5 (8.6)	
3.	2.00	13 (13)	2 (3.4)	
4.	3.00	13 (13)	1 (1.8)	
5.	4.00	64 (64)	2 (3.4)	
C Score categories				
1.	0.00	31 (31)	49 (84.5)	p<0.001
2.	1.00	8 (8)	3 (5.2)	
3.	2.00	21 (21)	6 (10.3)	
4.	3.00	15 (15)	0 (0.0)	
5.	4.00	25 (25)	0 (0.0)	

The participants in the two study groups were categorized into 0,1,2,3,4 based on their urinary MDA levels and Cp levels, i.e., M score and C score. The frequencies of patients and controls in each category for M score and C score were compared. Statistical test used: chi square; level of significance p<0.05.

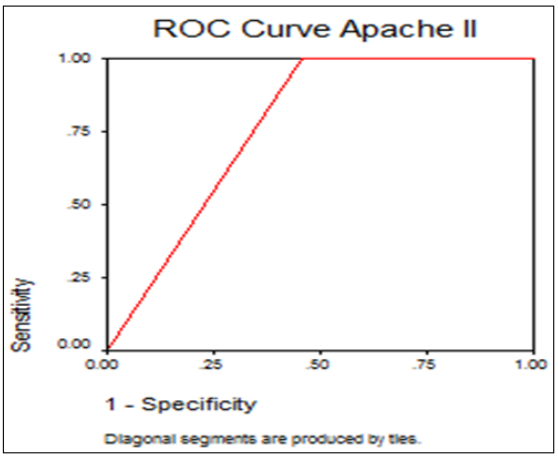

Fig-1: ROC curve for APACHE II

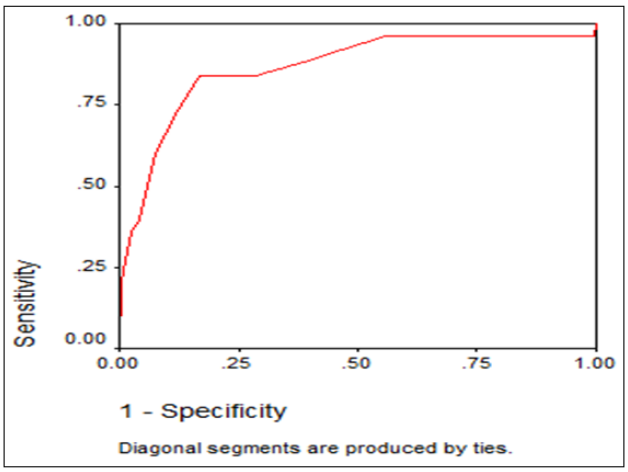

Fig-2: ROC curve for mAPACHE II

The mortality prediction ability of APACHE II was determined by plotting sensitivity against 1-specificity and thus recording the area under the ROC curve.

The area under the ROC curve for APACHE II was 0.8 (Figure-2) - Negative predictive value =85.3%, positive predictive value = 4.5%, sensitivity = 62.5% specificity = 68.5% and accuracy rate =68%.

The area under the ROC curve for mAPACHE II was 0.7 (Figure-2) - Negative predictive value = 98.15%, positive predictive value = 14.9%, sensitivity = 87.5% specificity = 56.5% and accuracy rate =59%.

DISCUSSION

This preliminary study is done to validate the relevance of APACHE II and mAPACHE II in predicting the mortality of patients admitted to the ICCU in the Indian context since there is a paucity of data in the Indian scenario.

As per Knaus *et al.,* the data of the patients was collected within 24 hours of admission and mortality was considered within this period [3, 1].

The mean APACHE II score of this study was 11 ± 4. This indicates that lower the APACHE II score, better is the outcome of the patients. Earlier, lower APACHE II scores have been reported from U.S.A and Sweden [4, 5]. The average APACHE II scores of several studies were higher than that reported in this study, such as, Australia [6], four studies from India [7, 2], West Indies [8], Iran [9], Germany [10] and Pakistan [11].

The lower APACHE II scores in this study maybe due to the fact that the APACHE II score was calculated based on the parameters collected for the initial 24 hours following the admission of the patient to the ICCU. The length of stay of patient beyond 24 hours in the hospital was not taken into account because the 24 hours follow up after admission of the patient reflected the greatest degree of derangement of some of the parameters considered to calculate acute physiologic score [1].

Ushashree *et al*., [12] and Khalid Al-Fartosi *et al*., [13], have reported an increase in the levels of oxidative stress parameters, MDA and Cp, in plasma of cardiac patients. Considering this fact, this study was a preliminary attempt to evaluate whether addition of urinary levels of oxidative stress parameters would increase the discrimination power of the APACHE II score. Hence, mAPACHE II was determined by adding M score and C score to APACHE II.

The observed mortality (non-survivors was 8% (Table-2), while the predicted mortality was 48% in this study. Earlier studies have not reported such a difference between the observed and predicted mortality [12] probably because this study has taken into account the mortality rate within 24 hours after admission. The duration of stay of the patient in the ICCU/ in the wards of the hospital beyond 24 hours was not taken into account unlike some of the earlier reports. A study based in Hong Kong showed an observed mortality rate of 36% having considered the total stay in the hospital and they report that the observed mortality was concordant with the predicted mortality [14].

With a low APACHE II the actual mortality was 8% in this study, while in other studies, with higher APACHE II the actual mortality was higher. Hence this study validates the fact that lesser the APACHE II, lesser is the mortality [1].

Mean APACHE II score among the survivors was lower (10.7 ± 4.0) than in the non-survivors (14.9 ± 3.8) ($p<0.01$) (Table-4) in this study. These findings are similar to the findings observed in the studies conducted in India [7], West Indies [8], Germany [10], Pakistan [11] and Iran [15]. This also reinforces the fact

that mortality increases with increase in APACHE II. In addition, the mean of mAPACHE II score was higher in the non-survivors than in the survivors (Table-3). This indicates that the APACHE II can be associated with the urinary parameters for oxidative stress to determine the outcome in ICCU patients.

The actual mortality rate in the ICCU recorded was 8% in the current study and the APACHE II score was 11 ± 4.1, which is comparatively lesser than that recorded in Sweden [5] and Canada [16]. This may be attributed to the fact that these studies have considered the in hospital mortality than ICU mortality whereas in the current study only mortality in the ICU within 24 hours after admission was considered and no follow up information was documented after transfer from ICU to the wards. In addition, since this was a preliminary investigation, the sample size was low (n=100).

In this study, SMR is 0.16 indicating that less mortality has occurred than expected as SMR is slightly lower than 1. It also indicates that that the observed mortality is less than the predicted mortality, within 24 hours of admission into the ICCU as followed in this study. When compared with other studies the SMR in this study is lower than in the studies conducted in India [7], Iran [9], Pakistan [11] and Hong Kong [14] and Canada [16].

The area under the ROC curve was 0.8 for APACHE II in this study which showed good prediction capability (Figure-1). It was similar to that reported as in Brazil [17] and Hong Kong [14]. This indicates that APACHE II score is a good prognostic tool that can be used for patients admitted to the ICCU within 24 hours after admission. However, the area under the ROC curve for mAPACHE II (Figure-2) was slightly lower (0.7), but indicated a moderately good outcome. This again consolidated the fact that oxidative stress can be analyzed with APACHE II to predict the outcome in the ICCU.

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CONCLUSION

There are valid cardiac markers in the 21st century for diagnosis of cardiac disorders. However, there is no particular national cardiac surgical database and particular risk stratification model in a developing country like India for predicting outcome in cardiac patients. Hence, an attempt has been made for this purpose by applying APACHE II and mAPACHE II in this study which shows that both can be used to predict mortality in ICCU patients. Further comprehensive studies are needed to confirm the findings in this study.

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