Evaluation of acute physiology and chronic health evaluation ii (apache-ii) vs. simplified acute physiology score ii (saps-ii) in an Iranian population: A multi-center prospective cross-sectional evaluation study.

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Abstract

Objectives: To evaluate APACHE-II and SAPS-II models in an Iranian population in order to support administrators in realistic planning and quality control process.
Design: A prospective cross-sectional evaluation study.
Setting: APACHE-II and SAPS-II were calculated for all consecutive admissions to four intensive care referral centers located in the top two most populated cities in Iran, from 2014 to 2017. The mortality rate in Iran and world standard rate were compared based on APACHE-II categories. Finally, the performance of models was assessed.
Main outcome measures: Area under the Receiver Operating Characteristics Curve (AUC), the Brier score and Hosmer-Lemeshow (H-L) goodness-of-fit test were employed.
Results: For 1946 patients, the overall observed mortality (23.7%) was more than international rates due to APACHE-II categories. The Brier score for APACHE-II and SAPS-II were 0.18 and 0.193, respectively. Although, none of prediction models were fitted to dataset (H-L ρ-value<0.01), both were associated with acceptable AUCs (APACHE-II=0.746 and SAPS-II=0.752).
Conclusion: In this study, despite poor performance measures of APACHE-II and SAPS-II as the most used models in Iran, finding recalibrated version of these prediction models in the country is necessary before applying it as a clinical prioritization or quality control tool.

Keywords: Intensive care unit, Risk assessment, Prediction models, Performance measures, Iran.

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Highlights

- APACHE-II and SAPS-II (esp. the first) are the most used risk model in Iran and due to limitation in resources, evaluating these prediction models is necessary for optimized resource allocation and evidence-based quality assessment. Also, we have lack of multi-center studies in this field.
- The observed ICU mortality rates were significantly higher than internationally published standards according to APACHE-II categories.
- With regards to poor performance measures of APACHE-II and SAPS-II in our sample, recalibration of current prediction models is considered as an obligatory research question before applying it.

Introduction

Nowadays, noticing Intensive Care Units (ICUs) as particular units aiming to provide specific health care services to a particular group of patients with common acute disorder, continuous time-limited decision making process remains as a significant challenging issue in this field. Regarding vulnerability and rapid fluctuations of vital organs esp. circulation, urinary and respiratory systems, clinical decision making should be supported by accurate prioritization [1]. It should be also noted that ICUs contribute to a growing proportion of health care expenditures which in turns include internal and external mechanical equipment.

In fact, accurate outcome prediction using available clinical related factors will support researchers and administrators in realistic planning, workload determination, optimized resource allocation, and evidence-based quality control process [2].Once the lack of continuous surveillance may result in organ malformation, higher length of hospital stay, increased payments or death, ICU admission is eligible [3]. However, an observational study in 2005 reported that 22% of ICU beds are occupied by patients who are just in need for continuous vital sign monitoring or advanced nursing services. A recent study confirmed that the clinical exigency of 35% (N=17440) of ICU admissions is lower than 10%.

Furthermore, available guidelines on ICU admission and discharge are not detailed enough to sift through the patients, aiming to optimize intensive care capacity or to estimate the number of ICU beds required for a specific center [4-7]. Employing prognostic scoring systems may help to provide a clinical appraisal of physiological instability and to make an estimation of patient specific probability of death [8]. Note that international reports reveal that ICU mortality rate may vary from 6.4% to 40% throughout the world [9].Utilizing scoring systems may help to provide a clinical standard for severity prioritization by the means of routine blood works.

Various contributing factors such as age, duration of acute disorder, special medical consideration (e.g. malignancy, immunosuppression or the need for kidney transplant) and emergency ICU admission increase the mortality rate in ICU. The first acute scoring system was introduced in 1980 which comprises two scores: first, a severity score where a higher value refers to more clinical deterioration and second, probability of death which in turn may be useful for benchmarking purposes among different institutions [10].

Acute Physiology and Chronic Health Evaluation II (APACHE-II) was developed in 1985 as a modified version of APACHE mainly to assess twelve physiological characteristics concentrating on organs' function quantification [11,12]. Simplicity of use and incorporation of routine laboratory variables have put it in a greater chance of acceptance in the intensive care setting.

The most deviated symptoms and laboratory results from normal definitions during the first 24-hour period post-admission will be included for further score calculation. This scoring system incorporates 14 variables, each of which is scored from 0 to 4 and results in an ordinal total score ranging from 0 to 71 in which higher score reflects more severity of acute disorder [13]. APACHE-II was first developed to predict an individual's mortality risk in ICU, however numerous studies evaluated this score as a patient triaging tool [14]. This may highlight the fact that APACHE-II score may be utilized as a quality control instrument [8, 15].

Similar existing scoring systems such as Simplified Acute Physiology Score II (SAPS-II) have been rarely evaluated within various countries around the world, but a few studies have confirmed the acceptable predictive power of SAPS-II in Europe and North America [16].Regarding the limited number of patients in previous studies around the country, a multi-center prospective study was conducted in the top two most populated cities in Iran to evaluate the predictive power and to provide performance-related statistics for APACHE-II and SAPS-II scoring systems.

Methods

This prospective cross-sectional study was conducted to collect a pre-specified set of variables in four referral centers in the top two most populated cities in Iran; Tehran, capital of Iran (ShohadayeTajrish and Emam Hussein hospitals) and Mashhad, northeast Iran (Emam Reza and Ghaem hospitals), from August 2014 to August 2017. More information about the participated hospitals and the distribution of the patients are presented in Table 1.

Patients who were admitted due to traumatic surgeries, burnt patients, patients underwent cardiac surgery or psychological disorders were excluded with regards to the nature of diagnoses [9]. In addition, any use of psychotropic agents in medication profile or symptoms of dysarthria or paramnesia due to a type of brain disorder were excluded in similarity with other studies in the field [9,13].

Hospital participated in the study	City	ICU bed number	Number of admissions	ICU type
ShohadayeTajrish H	Tehran	26	365 (18.8%)	General/ Surgical
Emam Hussein H	Tehran	44	981 (50.4%)	General/ Surgical
Emam Reza H	Mashhad	16	300 (15.4%)	General/ Surgical
Ghaem H	Mashhad	16	300 (15.4%)	General/ Surgical
Total		102	1946 (100%)	

Table 1. *Information about the participated hospitals and the distribution of the patients.*

A total of fourteen variables in APACHE-II in addition with remaining variables requested by SAPS-II were designed as a structured form to be filled out for consecutive 1946 adult (≤

16 yrs.) patients. The highest APACHE-II score for each particular patient during the first 24-hour period post-admission was considered as the final score. Regarding predetermined personnel cooperation framework, minimal missing values were included in these studies (less than 0.2%) which were excluded.

Using online valid calculators APACHE-II and SAPS-II scores were calculated for each particular patient by two of authors. In analysis process, to meet ethical principles, all names, identity codes were eliminated in the dataset.The Brier score (for overall performance assessment), Area under the Receiver Operating Characteristic Curve (AUC) (Discrimination: the ability of the model to distinguish between survivors and non-survivors) and Hosmer-Lemeshow (H-L) goodness-of-fit test (calibration: the degree of agreement between predicted mortality determined by the model and actual mortality) were considered as performance indicators for both models. Analyses were performed using medcalc-13.3.3.0 and R-3.3.1 (Resource Selection package) [17-19].

Results

A total of 1094 (56.2%) males and 852 (43.8%) females were included in this study (Table 2), 928 patients (47.7%) were post-surgical, N=230 (8.8%) of patients were diabetic and N=829 (42.6%) were supported by mechanical ventilation. The overall mortality rate was 23.7% (N=461) and the mean APACHE-II score for all patients was 10.8 (±6.128). About 67.4% (N=1311) of patients were associated with APACHE-II lower than 15.

Variable	**N (%)**	**APACHE-II**		**SAPS-II**	
		Mean ± SD	ρ value	Mean ± SD	ρ value
Gender					
Male	1094 (56.2%)	12.8 ± 6.13	0.288 a	20 ± 11.44	0.893 a
Female	852 (43.8%)	12.5 ± 6.12		20.1 ± 11.44	
Age Group					
16-25	291 (15%)	10.6 ± 6.16	0.000 b	12.5 ± 9.28	0.000 b
26-50	542 (27.8%)	10 ± 5.77		13.9 ± 9.74	
51-75	734 (37.7%)	13.6 ± 5.52		22.6 ± 9.6	
76-100	379 (19.5%)	16.4 ± 5.3		29.7 ± 9.41	
Addiction					
Yes	1738 (89.4%)	12.4 ± 4.85	0.445 a	18.2 ± 10.23	0.009 a
No	208 (10.6%)	12.7 ± 6.27		20.2 ± 11.56	
Diabetes Mellitus					
Yes	230 (8.8%)	13.9 ± 5.23	0.000 a	24.5 ± 10.01	0.000 a
No	1716 (91.2%)	15.5 ± 6.23		19.3 ± 11.48	
Post-Surgery					
Yes	928 (47.7%)	12.5 ± 5.91	0.248 a	19.1 ± 10.8	0.002 a
No	1018 (52.3%)	12.9 ± 6.3		20.8 ± 11.92	
Ventilation Support					
Yes	829 (42.6%)	15.6 ± 5.56	0.000 a	24.8 ± 10.86	0.000 a
No	1117 (57.3%)	10.2 ± 5.62		16.2 ± 10.8	
Outcome					
Alive	1485 (76.3%)	11.4 ± 5.65	0.000 a	17.5 ± 10.31	0.000 a
Dead	461 (23.7%)	16.7 ± 5.85		27.8 ± 11.28	

Table 2. *APACHE-II and SAPS-II scores by patients characteristics.*

a Analysis by independent T test.

b Analysis by one-way analysis of variance.

Mean APACHE-II score for living and dead outcomes were 11.4 and 16.7, respectively (ρ value<0.01).

APACHE-II score	**Total**	**Observed Mortality**	**International Standard (%)**	**ρ value a**
	N (%)	N (%)		
APACHE-II ≤ 15	1311 (67.4%)	69 (15%)	10%	ρ<0.01 b
16<APACHE-II<19	361 (18.6%)	161 (34.9%)	15%	ρ<0.01 b
20<APACHE-II<30	274 (14.0%)	231 (51.1%)	35%	ρ<0.01 b

Table 3. *Comparison of Observed Mortality Rates in ICUs with International Standards regarding APACHE-II Score.*

a Comparison was performed using chi square test.

b Observed mortality rate more than international standards.

As expected, mortality rate and APACHE-II score were increased similarly. Also, total population was associated with

20 (± 11.41) SAPS-II score. Further details about mortality rates in compared with international standards are reported in Table 3.

As shown in Table 4, while APACHE-II was associated with better overall performance (Brier score=0.17), SAPS-II performed a more acceptable discrimination of alive and dead cases (AUC=0.751). This is while, both scoring systems revealed unsuccessful calibration (H-L ρ value<0.01). AUCs of APACHE-II and SAPS-II are presented in Figure 1.

Scoring System	Overall Performance	Discrimination				Calibration	
	Brier Score	AUC	SE	95% CI	Difference a	ρ value a	H-L Test
	(min-max) (STD)						
APACHE-II	0.17 (0-0.94) (0.25)	0.746	0.0133	(0.726-0.766)	0.0061	0.4694	Chi2(8) =99.518, ρ<0.01
SAPS-II	0.196 (0-0.999) (0.35)	0.752	0.0132	(0.730-0.770)			Chi2(8) =1611.9, ρ<0.01

Table 4. *Performance measures calculated for APACHE-II and SAPS-II scoring systems.*

a Difference between AUCs.

AUC: Area Under the ROC Curve; SE: Standard Error; CI: Confidence Interval; H-L: Hosmer-Lemeshow.

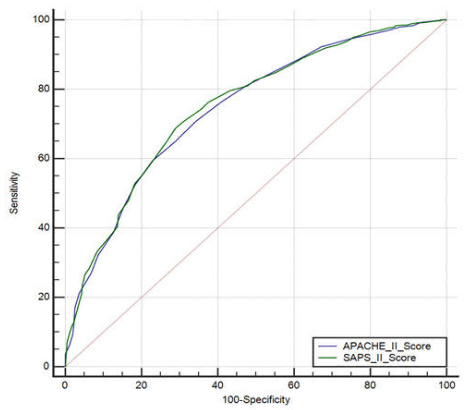

Figure 1. *Area under the ROC curve for APACHE-II and SAPS-II.*

Discussion

Main findings

Collecting patient's data from four tertiary care referral centers regarding the similar population distribution may increase the generalizability of results to a large subset of Iranian population.

While both of APACHE-II and SAPS-II scoring systems performed relatively admissible classifications of alive and dead cases (AUC=0.746, AUC=0.752, ρ value=0.4694), predicted probabilities estimated by APACHE-II were closer to observed events (Brier score=0.17) while, The H-L goodness-of-fit test revealed poor calibrations for both models (ρ value<0.01).

We also concluded that the observed ICU mortality rates were significantly higher than internationally published standards according to APACHE-II categories. This result is worth noting for Iranian ICU future policy making.

Comparison to similar studies

Correct outcome prediction in 75% of cases is similar to accuracy measures reported by Gupta et al. [12]. Gupta et al. assessed the prediction power of APACHE-II score among an Indian population with respiratory disorders.

The mean ± SD APACHE-II score for alive and dead cases were 11.34 ± 6.75 (N=287) and 23.09 ± 10 (N=43), respectively (ρ value<0.01). A subcategory of patients involved with Chronic Obstructive Pulmonary Disease (COPD) (N=81, mortality=14%) were associated with 17.83 ± 5.48 APACHE-II score [12].

In an observational study in RasoulAkram hospital, Tehran, Iran, observed mortality rate for low-risk patients (APACHE-II ≤ 15) was comparable to international standards. However, mortality rate for the rest of patients (APACHE-II>15) was significantly higher than reported standards (esp. 20 ≤ APACHE-II ≤ 30, mortality=39%) which may be due to variability of provided treatments in the center.

This may highlight the fact that APACHE-II score may be utilized as a quality control instrument [8,15]. Safavi et al. proved that APACHE-II was the most accurate prediction tool (with sensitivity=90%, specificity=32%, and accuracy=81%) in compare with Infection Probability Control (IPC) and APACHE-III to estimate the overall ICU mortality rate [14].

Only 7% difference in mortality rate for APACHE-II scores lower than 15 confirms the results provided by safavi et al. in 2007 [14]. Descriptive measures published in some similar national and international validation studies have been tabulated in Table 4.

A brief comparison of AUCs may indicate the fact that discriminative ability of APACHE-II in Iran is relatively lower than those published in similar studies around the world. The aforementioned issue may be addressed by model recalibration approach which may provide us more accurate outcome predictions in research, practice and policy making (esp. benchmarking) areas.

With regards to diversity of included patients requiring intensive care services, similar validation studies in Thailand, Germany, southern Korea, and Saudi Arabia acknowledged that prediction power of SAPS-II is comparable to APACHE-II. However, APACHE-II represented more acceptable discriminative ability in some critical care settings (Table 5) [11, 20-31].

Study	Publication Year	Number of Patients	Gender (%)		Age	APACHE-II	Major Diagnosis	AUC (%)
		N	Female	Male	(Mean)	(Mean ± SD)		
Amini et al. [20]	2008	56	12.5	87.5	24.4	44.7 ± 5.13	Concussion	81
Khwannimit et al. [21]	2007	1316	42.7	57.3	55.6	-	Case-mix	91
Safavi et al. [14]	2007	360	42	58	39.4	15.5 ± 4.1	Respiratory failure	74
Gupta et al. [12]	2004	393	30.6	69.4	43.32	12.87 ± 8.25	Respiratory failure	63
Ho et al. [22]	2007	1311	38	62	53.9	17±7.7	Respiratory failure	85
Khwannimit et al. [23]	2009	2022	40	60	62	10.1 ± 10.9	Case-mix	90.6
Sakr et al. [24]	2008	1851	37	63	61.6	22	Post-surgery	78
Park et al. [25]	2009	705	54.2	45.8	56.12	-	Neurosurgery	79
Arabi et al. [26]	2002	969	37.46	63.63	40.09	18.85 ± 9.13	Case-mix	83
Gursel et al. [27]	2005	63	46	54	64	19 ± 6	Pneumonia	81
Markgraf et al. [28]	2001	3583	-	-	62.5	-	Case-mix	82
Arabi et al. [29]	2003	250	45	55	58.4	-	Septic shock	78
Chiavone et al. [30]	2000	600	39	61	50	16.7 ± 7.3	Case-mix	380
Yasami et al. [31]	2013	150	31.3	68.7	47.56	13.54	Multiple trauma	70
Current study	2016	1800	41.5	58.5	53.8	10.8	Case-mix	74.5

Table 5. *Similar validation studies on APACHE-II scoring system.*

APACHE-II: Acute Physiology and Chronic Health Evaluation II; AUC: Area Under the ROC Curve; COPD: Chronic Obstructive Pulmonary Disorders.

Significant deviation of mortality rate from international standards among patients who have been screened as high risk cases by APACHE-II (APACHE-II>16) may be the consequence of unacceptable provided treatments which are poorly adapted to international guidelines or published intensive care frameworks.

Integration of different clinical prediction models for benchmarking purposes will support researchers and administrators to step forward in severity prioritization, ICU bed allocation scheme, and evidence-based distribution of intensive care capacities.

Strengths and limitations

Prospective data collection approach, minimal missing values, recruiting acceptable number of patients for evaluation purposes, and representativeness of our sample due to geographic situation and annual number of ICU admissions in four included hospitals may be noted as strengths for this study.

Regardless of the diagnosis at the time of admission, all patients were included aiming to assess the performance of APACHE-II within patients involving with various organ malfunctions.

Although, a 4-year sampling duration will adjust the effect of time-related confounders and may guarantee the inclusion of probable seasonal disorders, but time and sample-related limitations remains as an inevitable issue.

Future studies

Further evaluation of recalibrated version of APACHE-II and SAPS-II prediction models on large samples of target population rather than development of various, incomparable, and clinically impractical models in acute prioritization area is suggested by authors.

Also, using data mining techniques may help finding more hidden patterns/ accurate models for risk or length of stay prediction in ICUs.

Conclusion

With regards to poor performance measures of APACHE-II and SAPS-II in our included sample, recalibration of current prediction models is considered as an obligatory research question before applying it as a clinical prioritization or quality control instrument.

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