






Mortality prognostic factors associated with SAPS 3 and APACHE II in elderly patients admitted in intensive care unit

Fatores prognósticos associados ao SAPS 3 e APACHE II em pacientes idosos admitidos em unidade de terapia intensiva

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ABSTRACT

Study design: a descriptive, prospective cohort study. **Objectives:** identify the risk factors associated with SAPS 3 and APACHE II score to improve mortality prediction in elderly admitted in the intensive care unit (ICU). **Methodology:** a cohort study with 174 elderly patients admitted in ICU from July 2016 to June 2017. The primary independent variables analyzed were: presence of stress hyperglycemia, the need for invasive mechanical ventilation (IMV), acute renal failure, level of consciousness and use of vasopressors. The outcomes studied were death and hospital discharge. **Results:** ICU and hospital mortality were 17.8% and 29.8%, respectively. The multivariate analysis of factors associated with hospital death not contemplated in the obtaining of SAPS 3 demonstrated that IMV, Chronic Obstructive Pulmonary Disease (COPD) and Mean Arterial Pressure (MAP) <70 mmHg improved the prediction of mortality. The Hosmer-Lemeshow test ($p=0.472$) and area under ROC curve=0.80 (CI95%:0.731-0.872) confirmed, respectively, an appropriate calibration and acceptable-to-excellent discriminatory power for this model. IMV and COPD were also factors associated with the APACHE II score in prediction of mortality with appropriated calibration ($p=0.471$) and acceptable-to-excellent discriminatory power (area under ROC curve=0.80 [CI95%:0.730-0.868]). **Conclusion:** IMV, COPD, and MAP <70 mmHg were associated with SAPS3 and APACHE II to predict mortality in elderly admitted to ICU.


Keywords: Prognostic Factors; Mortality; Elderly; Intensive Care Unit; SAPS 3; APACHE II.

RESUMO

Modelo de estudo: estudo descritivo, coorte prospectiva. **Objetivos:** identificar os fatores de risco associados ao escore SAPS 3 e APACHE II para melhorar a predição de mortalidade em idosos internados em unidade de terapia intensiva (UTI). **Metodologia:** estudo de coorte com 174 idosos internados em UTI no período de julho de 2016 a junho de 2017. As principais variáveis independentes analisadas foram: presença de hiperglicemia de estresse, necessidade de ventilação mecânica invasiva (VMI), insuficiência renal aguda, nível de consciência e uso de vasopressores. Os desfechos estudados foram morte e alta hospitalar. **Resultados:** A mortalidade na UTI e hospitalar foi de 17,8% e 29,8%, respectivamente. A análise multivariada de fatores associados à morte hospitalar não contemplada na obtenção do SAPS 3 demonstrou que a VMI, Doença Pulmonar Obstrutiva Crônica (DPOC) e Pressão Arterial Média (PAM) <70 mmHg melhoraram a predição de mortalidade. O teste de Hosmer-Lemeshow ($p = 0,472$) e a área sob curva ROC = 0,80 (IC95%: 0,731-0,872) confirmaram, respectivamente, calibração adequada e poder discriminatório aceitável a excelente para este modelo. VMI e DPOC também foram fatores associados ao escore APACHE II na predição de mortalidade com calibração adequada ($p = 0,471$) e poder discriminatório aceitável-a-excelente (área sob curva ROC = 0,80 [IC95%: 0,730-0,868]). **Conclusão:** VMI, DPOC e PAM <70 mmHg foram associados ao SAPS3 e ao APACHE II para prever mortalidade em idosos internados em UTI.

Palavras-chave: Fatores Prognósticos; Mortalidade; Idosos; Unidade de Terapia Intensiva; SAPS 3; APACHE II.

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BACKGROUND

Admission to the Intensive Care Unit (ICU) is associated with high mortality and contributes to higher one-year mortality rates after discharge¹. Elderly patients are responsible for approximately 42-50% of the admissions and about 60% of ICU stays². Clinical outcomes in intensive care are measured using scores that frequently consider the severity of baseline comorbidities³. The Acute Physiology and Chronic Health Evaluation II (APACHE II)⁴ and the Simplified Acute Physiology Score 3 (SAPS 3)⁵ scores are widely used in clinical practice to calculate the individual's prognosis as well as to guide therapeutic decisions in ICU patients.

Some independent predictors of death in elderly patients admitted in ICU were previously described in literature: stress hyperglycemia, need for invasive mechanical ventilation (IMV), multiple organs dysfunctions, altered level of consciousness, septic shock, need for vasoactive agents, chronic obstructive pulmonary disease (COPD), and mean arterial pressure (MAP) below 70mmHg⁶⁻¹¹. However, the SAPS 3 and APACHE II scores do not consider some of the risk factors already described to affect independently the mortality rates, which might underestimate their predictive values.

This study aimed to recognize risk factors that might be associated with the SAPS 3 and APACHE II to improve the prediction of hospital mortality of elderly patients admitted to ICU.

MATERIALS AND METHODS

The present study was a prospective cohort study conducted between July 2016 and June 2017 on patients admitted to a public regional ICU in Recife, Pernambuco.

Population

Patients of both sexes aged 60 or more years admitted and stayed in the ICU for more than 24 hours were eligible for inclusion.

Patients were excluded if diagnosed with terminal cancer under palliative care. Multiple ICU readmissions within a single hospital stay were considered as one single admission.

All patients received standard medical treatment under the direction of the consultant physician.

The primary outcome measures were death or hospital discharge.

Data acquisition

All data were collected concurrently for consecutive ICU admissions. A structured questionnaire was used to extract data from medical records and guide the history taking of a patient or the family.

Data included sociodemographic information, age, sex, past medical conditions (such as hypertension, diabetes, COPD, chronic kidney or hepatic disease) and lifestyle habits (such as alcohol intake and smoking). The APACHE II and SAPS 3 scores were calculated following the original methodology, using the worst physiologic values in the first ICU day and the first two hours after admission, respectively.

Regarding the Glasgow Coma Scale (GCS), the best results were adopted to define the level of consciousness. Multiple organs failure was defined according to the criteria of Knaus et al⁴.

All patients were followed until discharge from the hospital or death.

Operational definitions

Stress hyperglycemia was defined as capillary blood glucose > 180 mg/dL¹⁵. Capillary blood glucose was performed using the first drop of blood obtained through finger puncture with disposable lancets. A measurement was performed every four hours and the higher value in the first 24 hours was chosen.

Acute Kidney Injury (AKI) was defined following the Acute Kidney Injury Network (AKIN) classification: absolute increase within 48 hours in serum creatinine \geq 0.3 mg/dL; a percentage increase in serum creatinine \geq 50% or 1.4-fold

from the baseline; or documented oliguria of < 0.5 ml/kg/h for at least 6 hours¹⁶. Creatinine blood samples were processed using the Beckman Coulter AU automated method.

Altered level of consciousness was defined as 8 points or less in the GCS¹⁷ in absence of sedative drugs and orotracheal tube.

COPD was defined as the presence of a post-bronchodilator forced expiratory volume in one second (FEV1) $< 80\%$ of the predicted value in combination with a FEV1/forced vital capacity (FVC) $< 70\%$ in a spirometry test or self-reported physician's diagnosis of chronic bronchitis, emphysema, or COPD, associated within use of long-acting muscarinic antagonist (LAMA) and long-acting beta-agonist (LABA) or inhaled corticosteroids¹⁸.

Intermittent non-invasive blood pressure monitoring was used to acquire diastolic blood pressure (DBP) and systolic blood pressure (SBP). Mean arterial pressure (MAP) was calculated by the formula $(2 \times \text{DBP} + \text{SBP})/3$.

Statistical analysis

The sample size was calculated based on the purpose of identifying at least five predictors of death. For multiple regression models of dichotomous variables, at least ten outcomes for each predictor might be needed to compound the model with statistical precision¹². In a model with five dichotomous predictors, as planned for this study, at least 50 outcomes are needed. Expecting a mortality rate of 30% ^{13,14}, the minimum sample size is 167 individuals.

We considered for the statistical analyses that the SAPS 3 and APACHE II scores are correlated (Pearson test: $r = 0.83$; $p < 0.001$). Independent analyses were performed to determine which factors might be associated with the scores to improve the prediction of hospital death. The relationship between hospital death and each potential factor associated with the SAPS 3 and APACHE II was determined and adjusted using simple logistic regression models. According to

the recommendations of Hosmer-Lemeshow¹⁹, the factors with a significance level of $p < 0.25$ were selected and included in a multivariate logistic regression model. The results were adjusted for two models: one to investigate factors associated with the SAPS 3 and another to examine factors associated with the APACHE II. The selection of factors for each model was performed employing the backward stepwise method, adopting a significance level of 5% . For each adjusted model, the goodness of fit was evaluated using the Hosmer-Lemeshow and the discriminatory power was evaluated using the area under the ROC curve. The Stata 12.1SE software (StataCorp, 4905 Lakeway Drive, College Station, Texas 77845 USA) was used to process the statistical analyses.

Ethical standards

The study protocol was previously approved by the Institutional Ethics Committee (CAAE: 31993814.6.0000.5208) and respected the Resolution 196/96 of the Brazilian National Health Council, which deals with the guidelines and standards for research involving humans. The investigation was also carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients prior to the inclusion in this study.

RESULTS

A total of 174 patients was eligible for the study (Figure 1). Mean age was 71.5 years. The ICU and hospital mortality rates were 17.8% and 29.8% , respectively. The mean of the APACHE II and SAPS 3 scores were 19.1 (16.7 among discharged patients and 24.9 among those in which the outcome was death) and 43.6 (38.7 among discharged patients and 55.0 among those in which the outcome was death), respectively. The mean length of ICU and hospital stay were 7.2 and 32 days, respectively. Population characteristics and prevalence of outcomes are shown in Table 1.

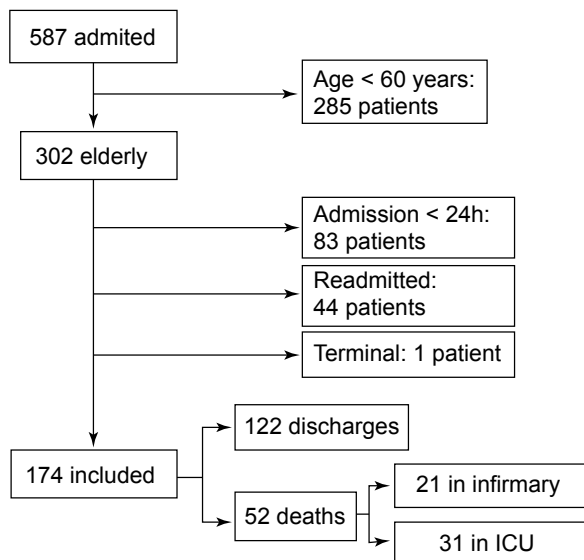


Figure 1: Diagram of inclusion and follow up of the population studied.

Table 1 Summary of sociodemographic, clinical, and laboratorial data of the study population.

Variable	Sample	Outcome: death
	N	N (%)
Gender		
Male	79	25 (31.6%)
Female	95	30 (31.5%)
Ethnicity		
White	85	23 (27.1%)
Non-White	89	32 (35.9%)
Marital Status		
Single	22	5 (22.7%)
Married	87	24 (27.5%)
Widowed	52	7 (13.4%)
Divorced	13	6 (46.1%)
Years of study		
0	36	12 (50.0%)
1-4	79	27 (34.1%)
5-8	34	10 (29.4%)
9-11	18	4 (22.3%)
12-16	1	0 (0.0%)
≥ 17	6	1 (16.7%)
Organic system affected		
Neuro	13	6 (46.1%)
Cardio	82	16 (19.5%)

(continue...)

Table 1 (Continuation)

Variable	Sample	Outcome: death
	N	N (%)
Pneumo	32	13 (40.6%)
Gastro	25	11 (44%)
Nefro/Metab	20	9 (45%)
Reason of admission		
High-risk post-op	62	11 (17.7%)
ARF	25	9 (36%)
ALC	13	7 (53.8%)
Shock	15	9 (60%)
ACS	16	1 (6.2%)
Arrhythmias	4	2 (50%)
Other	23	8 (34.7%)
IMV	74	41 (55.4%)
Length of IMV (days)	5.9 ± 5.5	8.1 ± 8.5
TQT	15	9 (60%)
Length of TQT (days)	47 ± 50.3	31.2 ± 22.5
Hypertension	139	40 (28.7%)
DM	87	25 (28.7%)
COPD	7	4 (57.1%)
Smoking	36	10 (27.7%)
Alcoholism	19	6 (31.5%)
Chronic Hepatic Disease	8	5 (62.5%)
Kidney Injury		
Acute	45	25 (55.5%)
Chronic	31	13 (41.9%)
Cancer	25	8 (32%)
Infection	77	34 (44.1%)
Vasoactive agent	79	35 (44.3%)
MAP (mmHg)		
< 70	31	23 (74.1%)
70-109	66	14 (21.2%)
≥ 110	77	18 (23.3%)
Respiratory rate		
< 12	1	0 (0%)
12-24	110	30 (27.2%)
≥ 25	63	25 (39.6%)
Cardiac rate		
< 120	146	43 (29.4%)
120-159	27	12 (44.4%)
≥ 160	1	0 (0%)

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Table 1 (Continuation)

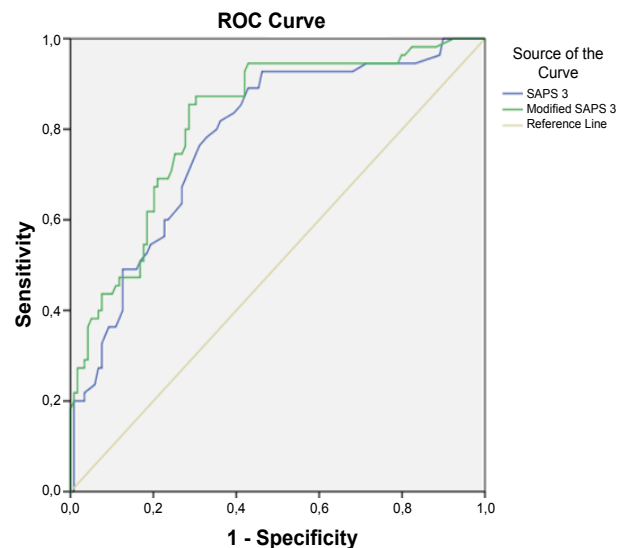
Variable	Sample	Outcome: death
	N	N (%)
Temperature (° C)		
< 34,5	50	19 (38%)
≥ 34,5	124	36 (29.1%)
Hematocrit (%)		
< 30	87	34 (39.1%)
30-45	84	19 (22.6%)
≥ 46	3	2 (66.6%)
Platelets (in thousands)		
< 20	2	2 (100%)
20-49	3	1 (33.3%)
50-99	17	8 (47.1%)
Total Bilirubin (md/dL)		
≥ 100	152	44 (28.9%)
< 2	159	45 (28.3%)
2-5.9	10	7 (70%)
≥ 6	5	3 (60%)
Leucocytes		
< 15,000	112	31 (27.6%)
≥ 15,000	62	24 (38.7%)
pH		
≤ 7,25	29	16 (55.1%)
> 7,25	145	39 (26.8%)

ARF = acute respiratory failure; ALC = altered level of consciousness; ACS = acute coronary syndrome. IMV = invasive mechanical ventilation; TQT = tracheostomy; DM = diabetes mellitus; COPD = chronic obstructive pulmonary disease; MAP = mean arterial pressure.

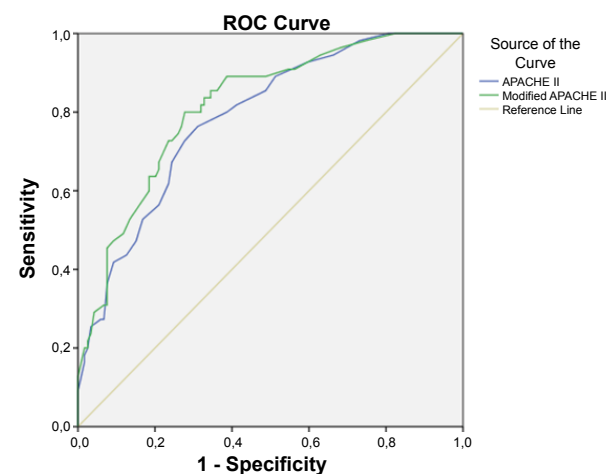
According to the multivariate analyses (Table 2), IMV, OCPD and MAP < 70 mmHg were associated with the SAPS 3 to predict hospital mortality. The Hosmer-Lemeshow test ($p = 0.472$) and the area under ROC curve (0.80 [CI95%:0.731-0.872]). Figure 2 confirms appropriate calibration and acceptable discriminatory power for the model composed of those four variables.

The results of the univariate and multivariate analyses of factors associated with hospital death not included in the APACHE II score are shown in Table 2. According to the multivariate analyses IMV and OCPD were associated with the APACHE II to predict hospital mortality. The Hosmer-Lemeshow test ($p = 0.471$) and the area under ROC curve (0.80 [CI95%:0.730-0.868]).

Figure 3 confirms appropriate calibration and acceptable discriminatory power for the model composed of those three variables.

**Figure 2:** Receiver Operating Characteristics (ROC) curve for SAPS3.

Blue line - ROC curve for isolated SAPS 3 score (AUC 0.77 [CI95%: 0.706-0.852]). Green line – ROC curve for the modified SAPS 3 score including COPD, IMV, and MAP < 70 mmHg (AUC 0.80 [CI95%:0.731-0.872]).

**Figure 3:** Receiver Operating Characteristics (ROC) curve for APACHE II.

Blue line - ROC curve for isolated APACHE II score (AUC 0.78 [CI95%: 0.718-0.857]). Green line – ROC curve for the modified APACHE II score including COPD, and IMV (AUC 0.80 [CI95%:0.730-0.868]).

Table 2

Univariate analyses and final model of factors associated with hospital death not included in the SAPS 3 and APACHE II.

Variable	Univariate model		Multivariate model	
	OR (CI 95%)	p-value	OR (CI 95%)	p-value
IMV	6.48 (3.14-13.40)	<0.001	3.83 (1.49-9.83)	0.005
Length of IMV	1.13 (1.06-1.21)	<0.001	-	-
TQT	2.99 (1.02-8.73)	0.047	-	-
Length of TQT	1.01 (0.99-1.03)	0.570	-	-
COPD	3.31 (0.71-15.33)	0.126	6.82 (1.22-38.18)	0.029
Hypertension	0.48 (0.22-1.04)	0.067	-	-
DM	0.80 (0.42-1.54)	0.508	-	-
Smoking	0.88 (0.39-1.99)	0.755	-	-
Alcoholism	0.82 (0.28-2.41)	0.716	-	-
Hepatic Failure	4.22 (0.97-18.36)	0.051	-	-
AKI	3.16 (1.55-6.44)	0.002	-	-
Hyperglycemia	0.77 (0.40-1.49)	0.439	-	-
Vasoactive agents	2.55 (1.31-4.98)	0.005	-	-
MAP < 70 mmHg	3.45 (1.66-7.19)	<0.001	2.78 (1.15-6.74)	0.023
RF < 25	0.55 (0.28-1.07)	0.077		
Na				
<130 mEq/l	1.26 (0.50-3.17)			
130-149 mEq/l	1.0 (reference)	0.057	-	-
≥150 mEq/l	5.37 (1.28-22.55)			
K				
<3.5 mEq/l	1.00 (0.42-2.39)			
3.5-5.4 mEq/l	1.0 (reference)	0.999	-	-
≥ 5.5 mEq/l	0.98 (0.32-2.96)			
Ht < 30%	1.95 (1.00-2.78)	0.046	-	-
Platelets < 100 000	2.18 (0.88 - 5.43)	0.098		
Total Bilirubin < 2 mg/dL	0.25 (0.08 - 0.74)	0.011	-	-
GCS ≤ 8	2.77 (1.33-5.77)	0.007	-	-
ICU stay length	1.06 (1.01-1.10)	0.008	-	-
SAPS 3	-	-	1.03 (1.00-1.06)	0.027
APACHE II	-	-	1.08 (1.02-1.14)	0.027

IMV = invasive mechanical ventilation; TQT = tracheostomy; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; MAP = mean arterial pressure; AKI = acute kidney injury; GCS = Glasgow coma scale; RF = respiratory frequency; Na = serum sodium; K = serum potassium; Ht = hematocrit. † stress hyperglycemia.

DISCUSSION

Our findings suggest that the need for IMV, history of COPD and MAP below 70 mmHg are important prognostic factors associated with hospital death in elderly patients admitted to ICU.

The SAPS 3 was associated with the need for IMV, history of COPD and MAP below 70 mmHg

demonstrated an improved predictive power in comparison with the data originally described in this score. This tendency was also verified for the association between APACHE II, the need for IMV and a history of COPD. There were no differences in the predictive power of these two models.

The need for IMV was independently associated with hospital mortality. These results are in

accordance with previous findings^{13,20}. Farfel et al. did not consider age as a factor associated with hospital mortality in the elderly with no need for IMV²¹. Silva et al. found that patients older than 65 years in the use of IMV presented a poor prognosis and reported a mortality rate three times higher in ICU, higher length of need for IMV and lower rates of extubating compared to younger patients with similar clinical conditions²². Mortality rates two years after ICU discharge in subjects aged 80 or more years with a history of need for IMV were higher in those with acute illness (78%), admitted because of surgical urgencies (46%) and elective admissions (35%)²².

According to our results, COPD is also associated with hospital death in elderly individuals. This finding is in accordance with those reported by Teixeira et al. They observed that patients with history of COPD had a high mortality rate in ICU (27%) and two years after hospital discharge (68%)²⁴. Ongel et al. recommend that cases with severe COPD and cardiac comorbidities might be carefully monitored in intensive care settings because of the elevated risk of mortality²⁵.

Some recent studies reported that stress hyperglycemia was associated with worse outcomes in adults²⁶ and elderly^{13,27} patients admitted to ICU. Despite that, our study did not assure this association. Gale et al.²⁸ described that the aggressive glycemetic control in patients with stress hyperglycemia is associated with increased mortality. In our study, the correction of glycemetic levels was not evaluated which might partially justify the absence of the association described in literature.

The association between AKI and ICU mortality is controversial. Some studies recognized a relationship between increased length of stay in ICU, mortality and AKI²⁹. It also seems to predict hospital readmission in individuals discharged of ICU and is associated with a higher probability of death 30 days after discharge³⁰. Nevertheless, other studies demonstrated that AKI is not associated with mortality in subjects admitted in ICU and higher creatinine levels are associated with lower mortality rates in hemodialytic patients^{31,32}. This study did not observe any associations between mortality and AKI. It is plausible that the wide variability of criteria adopted to define

AKI is responsible for those divergences among the studies.

We were also unsuccessful to establish any relationship between need for vasoactive agents, level of consciousness, and mortality. According to the literature, vasoactive agents might predict mortality in patients aged 90 years or more²⁷.

Limitations

Our study presented some limitations: It was performed just in one center, based on a convenience sample, standard treatment was defined according to the on-call physician's discretion. Also, some important variables were not possible to be included in the final model, such as oxygenation index (PaO₂/FiO₂ ratio) and drugs in use.

The study included high-risk post-op patients, which corresponded to 35.5% of the sample. Surgical patients tend to present higher rates of unfavorable outcomes, which may have played some influence in our results.

In the ICU where this study was performed, the mortality rate is under the regional mean, in some cases up to 50% lower.

CONCLUSION

The past of COPD, need for IMV during the admission and MAP < 70mmHg are associated with the APACHE II and SAPS3 scores to predict mortality in the elderly patients admitted in ICU.

Disclosure

The authors declare no conflict of interest. This study obtained no financial support. Partial results of this study were present at the VII Congresso Luso Brasileiro de Medicina Intensiva.

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