Evaluation of prognostic indicators for elderly patients admitted in intensive care units

Avaliação de índices prognósticos para pacientes idosos admitidos em unidades de terapia intensiva

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ABSTRACT

Objective: The elderly constitute a population with their own features and frequent admissions in intensive care units. This study has the objective to evaluate the ability to predict the survival of these patients through the APACHE II, UNICAMP II, SAPS II and SAPS 3 indexes, global and Central America/ South equations.

Methods: Elderly patients admitted from 01/01/2006 to 12/3/2006, defined as age ≥ 60 years, were included in this study. Those who were readmitted were excluded. The rate of lethality standardized, calibration and discrimination for each index in the remaining patients were analysed. The outcome were death or hospital discharge.

Results: Three hundred eighty six elderly patients were included in this study, being 36 excluded by readmission, remaining 350 for analysis. The rate of lethality standardized came near to the unit in all indexes, except the SAPS II (TLP=1.5455) which underestimated the lethality. The calibration, via Hosmer-Lemeshow tests was inadequate ($p \leq 0.05$), except for the UNICAMP II ($p > 0.5$). On the calibration curve, the models have distanced themselves from the pattern line. All of them presented an excellent discrimination via receiver operating characteristics curves (≥ 0.8).

Conclusions: In the studied population, the models presented an excellent discrimination and inadequate calibration. SAPS II underestimated the lethality.

Keywords: Intensive care; Intensive care units; Severity of ilness index; Prognosis; Aged

INTRODUCTION

The World Health Organization defines as elderly a person with 65 years old and over. For developing countries, such as Brazil, this definition is applied from 60 years old. The number of elderly persons is growing throughout the world and also in our country. According to the last census, held in 2000, the elderly population in Brazil was 14.536,029, 8.6%. Estimates show that this percentage shall achieve 14% in 2025, in other words, 32 million of elderly[1]. They constitute a population with characteristics and special features, with expressive use of health services, especially in intensive care units (ICU), which may correspond to more than 50% of the hospital admissions.[2,3]

The performance of a generic prognostic index may differ when they are applied in different populations, morbid entities and seasons. The age factor is considered in these indexes. There are different categories of age groups, each one receiving a distinct score. The growing number of elderly in intensive care units leads us to speculate about two points: 1 – Can the prognostic indicators adequately evaluate these patients? There is an index which is more appropriate for this population?

The Acute Physiology and Chronic Health Evaluation II (APACHE II), published by Knaus et al. in 1985, is the most widespread prognostic indexes. It was developed based on data collected from 5,815 patients over 13 hospitals in the United States from 1979 to 1982.[4] The University of Campinas II (UNICAMP II) model is an adaptation of prognostic indicators to the Brazilian reality, developed by Terzi et al. in 2002, with data from 862 patients admitted at the ICU from Hospital das Clinicas da UNICAMP from April, 1988 to October 1989.[5] The Simplified Acute Physiology Score II (SAPS II) was developed by Le Gall et al. in 1993. Although it is not diffused in Brazil as the APACHE II, it is often used in Europe. Data collected between September 1991 and February 1992, of 13,152 patients from 12 European and north-Americans countries were used in its elaboration.[6] Published in 2005 by Moreno et al., the SAPS 3 was developed from a database of 16,784 patients from 35 countries from October to December 2002. Between the innovations that this new index brings there is the presence of seven personalized equation – in addition to a standard global equation - for different parts of the world, amongst Central and South-America.[7]

This study has the objective to evaluate the ability to predict the survival of ICU elderly inpatients through the APACHE II, UNICAMP II, SAPS II and SAPS 3 (global equations and Central America/South) indexes,.

METHODS

This study was carried out in an ICU with 14 beds of a *t*ertiary-level private general hospital, with capacity for 150 beds, in the city of Cuiabá, Mato Grosso. This is a mixed ICU with both clinical, surgical and coronary patient's admission. The horizontal alignment of patients is made by two boarded certified physicians by Brazilian Intensive Care Medicine Association – AMIB, one of them with training in general surgery and the other in clinical medicine, together with their medical assistants. The ten physicians on call were boarded certified (four) and/or carried out AMIB post-graduation in intensive medicine (seven). Beyond that, physicians with various specialties were involved in patient's alignment when called. The nursing team is composed of a nurse and nine nursing technicians, by swing shift. There is at least one physiotherapist in 24 hours a day. The service has microprocessed ventilate orthoses (in the proportion of one per bed), invasive and non-invasive hemodynamic monitoring (including Swan-Ganz catheter), hemodialysis, respiratory and digestive endoscopy, enteral and parenteral nutrition support. It carries out the systematic collection of prognostic indicators and other data relating to the patient in all admissions, since the beginning of its operation in 1997. It also presented an annual average of 628.91 ±184.64 admissions by year in the last 11 years of operation, summarizing 7,011 patients admitted until 12/31/2008. It receives, in an optional stage, anesthesiology, general surgery, infectology and internal medicine residents from two schools of medicine of the city, beyond the undergraduate students from the local Liga Acadêmica de Medicina Intensiva (LIGAMI). The hospital still offers the clinical laboratory services, image with computed tomography and hemodynamic 24 hours per day.

Eligibility criteria, data collection and definitions of terms and variables

The data were prospectively collected from January 1st to December 31, 2006, through a standardized datasheet, by a team previously trained and subsequently inserted into Access 2003 data bank (Microsoft Corporation). All patients admitted with age ≥ 60 years old, excluding those whose admissions were readmission were admitted. The data analyzed were the demographic, clinical variables and laboratorial of the remaining patients for calculation of scores, as recommended by its authors.

The APACHE II is calculated through the sum of the three parts score: physiological variables, age and chronic disease. In the first, 12 clinical and laboratorial variables, receive points from zero to four, in accordance with the degree of normality deviation presented. They are evaluated within the first 24 hours of admission, using the value that presented the biggest change in that period. It includes the following parameters: temperature, mean arterial pressure, heart rate (HR), respiratory frequency, *Glasgow Coma Scale* (GCS), oxygenation, arterial pH; sodium, potassium and serum creatinine, besides the hematocrit and total leukocyte count (TLC). In the second, there are a score for age from 45 years old. Covering the elderly population, there are an age group from 55 to 64, 65 to 74 and ≥ 75 years old. Finally, there is a score for patients immunocompromised or carriers of serious organ dysfunction. In computing the calculated risk of death (CRD), an equation of logistic regression that takes into account the situation or not of the postoperatory of urgency and 50 potential categories of diagnosis is used.

The model UNICAMP II is similar to APACHE II. It differs by replacing the 50 categories of diagnosis by the presence or not of three other variables: 1- renal insufficiency (creatinine ≥ 1,6mg/dL); 2- mechanical ventilation and 3 – character of urgency or emergency of admission.

SAPS II includes the following variables: age, type of admission (clinical, programmed surgery or not), chronic

diseases (metastatic neoplasm, hematological or acquired immunodeficiency syndrome), GCS, systolic blood pressure (SBP), HR, temperature, oxygenation, urinary output and serum urea dosage, potassium, sodium, bicarbonate, bilirubins and TLC. The degree of normality deviation and the character description of the condition bestow a score for each variable. For the elderly, there is a distinct score for the following age groups: 60 to 69, 70 to 74, 75 to 79 and ≥ 80 years old.

SAPS 3 comprises three parts. In the first one, the computed data are those which comprises the preconditions for the patient admission in the ICU, as well as the characteristics of this admission. Thus, age, co-morbidities, time previous to admission, place of the hospital from where comes the patient and previous use of vasoactive drugs are evaluated. In the second part the cause and electivity or not of the admission, presence and type of infection, besides the anatomical location of the surgical procedure are analyzed. Finally, in the third part, the normality deviations of the variables GCS, bilirubin, temperature, creatinine, HR, TLC, pH, platelets, SBP and oxygenation receive a specific score. In a different way of prognostic indicators previously described in SAPS 3 the data are collected at the time of admission. Includes the same age group of SAPS II.

All variables were evaluated in most patients. Even so, some were absent. Patients who were discharged after a period within less than 24 hours may have presented some normality deviation in variables after the discharge from the ICU, reflecting in the measurement of the indexes APACHE II, UNICAMP II and SAPS II. Arterial blood gas analysis and determination of serum bilirubin were only carried out on a clinical judgment basis. The unsolicited laboratory exams based on the patient clinical evaluation were accepted as normal. Patients transferred to other services were followed until its final outcome. In sedated patients it was used the GCS prior to sedation. This study was approved by the local research ethics committee. This study did not interfere with the care of patients. The evaluated event was hospital discharge or death.

Statistical analysis

The ability to predict the prognostic indicators was evaluated through three properties: 1- Rate of standardized lethality (RSL); 2- calibration and 3 - discrimination.

The RSL is obtained by dividing the observed lethality by the predicted one for a particular model. Thus, the RSL equal to the unit indicates that the observed lethality corresponds to the estimated one. If it was higher or lower it respectively indicates the observed lethality, higher or lower than the predicted one.

For calibration, we evaluated the degree of correspondence between the observed lethality and that expected on the zones of CRD. This study is performed via goodness-of-fit (GOF) Hosmer–Lemeshow[8] and the calibration curve.

In the GOF, the frequency of deaths and discharges are compared, observed and predicted, for ten zones of CRD. It is performed the sum of the x^2 from frequencies and it is estimated the p for a distribution with eight degrees of loose. A p-value higher than 0.05 indicates a test which described well the observed lethality, in other words, the appropriate calibration. A p-value lower than or equal to 0.05 shows discrepancy between the predicted and observed ones, therefore an inadequate calibration. The difference between the $\hat{C}$ and $\hat{H}$ tests is expressed in the way individuals grouping is done in each zone of risk. In the $\hat{H}$ test the patients are placed in defined zones by the predicted risk of death, regardless the number of individuals in each zone. In the evaluation of the calibration curve we compared the curve of observed lethality with a diagonal line which represents the appropriate calibration. A higher or lower curve respectively indicates the observed lethality, higher or lower than the predicted one.

In the discrimination study the sensitivity and specificity of a method are evaluated. This analysis is carried out via the area under the receiver operating characteristics (AUROC) curve, which allows evaluating the correlation between sensitivity (true positives) and complementary specificity (1-specificity) or false negative e results. The greater the true positive and lower the false negative, the more the curve is closer to the upper left angle and the greater the area under the curve shall be. Thus, in general, a ROC = 0.5 shows that discrimination is not better than at random chance; equal or higher than 0.7 and lower than 0.8, a acceptable discrimination; equal or higher than 0.8 and lower than 0.9, excellent discrimination; higher or equal to 0.9, exceptional discrimination.[9]

Calculations were performed through the programs EXCEL 2003 Microsoft Corporation and MedCalc Version 7.0.0.4 Frank Schoonjans. The confidence intervals (CI) presented are of 95%.

RESULTS

Three hundred eighty six elderly patients were evaluated, being 36 excluded by readmission, remaining 350 for analysis. The arterial blood gas analysis in 74 patients (21.14%) and dosage of serum bilirubin (52 patients, 14.86%) were only carried out on a clinical judgment basis. The unsolicited laboratory examination based on the patient clinical evaluation was accepted as normal. Three patients (0.86%) transfer-

red to other services, were followed until its final outcome.

The demographic and clinical characteristics, the main causes of admissions and the results of RSL, GOF and AUROC are shown, respectively, in tables 1, 2 and 3. The unit is within the confidence intervals of RSL of the tested models, with the exception of SAPS II, that underestimates the lethality of the studied patients. In the Hosmer-Lemeshow tests, the calibration was inadequate for the studied models (p = 0,05), except for the UNICAMP II (p > p=0,1649). At visual analysis of the calibration curves, presented in figures 1 to 5, we note that the models have distanced themselves from the pattern line. This fact is a remarkable one for the APACHE II, SAPS II and SAPS 3 global equation. In the SAPS 3 Central/South America Equation, the model overestimates the lethality in risk zones from 0 to 40%. There is underestimation in the zones from 40 to 60%. After this point, there is concordance between the predicted and observed lethality, however, these zones had a smaller number of patients. In the UNICAMP II model, the distortions between predicted and observed occurs in the zones from 30 to 40% and 60 to 70%, in which there is lethality underestimation, and in the zones from 10 to 20% and 80 to 90%, in which occurs lethality overestimation. All indices presented an excellent discrimination (ROC ≥ 0,8).

Table 1 - Demographic and clinical characteristics

Variables	Result
Mean age (years)	73.4 ± 8.29
Gender	
Male	182 (52.00%)
Female	168 (48.00%)
Average time of stay in ICU (days)	5.56 (±9.68)
Vasoactive drugs	125 (37.71%)
Mechanical ventilation	119 (34.00%)
Enteral nutrition support	107(30.57%)
Parenteral nutrition support	8 (2.29%)
Hemodialysis	54(15.43%)
Mean APACHE II	16.15 ±8.85
Mean SAPS II	33.33 ±16.34
Mean SAPS 3	54.21 ±15.38
ICU lethality	98 (28.00%)
Hospital lethality	107 (30.57%)

ICU – intensive care unit; APACHE – Acute Physiologic Chronic Health Evaluation; SAPS - Simplified Acute Physiology Score result in number (%) or mean ± standard deviation.

Table 2 – Main causes of admission and associated conditions

Variables	Number	%
Main causes of admission		
Coronary failure	64	18.29
Sepse	60	17.14
Postoperatory of gastroenterological	57	16.28
Peripheral vascular disease	27	7.71
Urological postoperatory	14	4.00
Orthopedic postoperatory	13	3.71
Metabolic turbulence	12	3.43
Respiratory failure	12	3.43
Neurological postoperatory	12	3.43
Congestive heart failure	11	3.14
Consciousness level degradation	10	2.86
Vascular postoperatory	8	2.29
Trauma	7	2.00
Shock	7	2.00
Irregular heartbeat	6	1.71
Pulmonary embolism	5	1.43
Cardiopulmonary arrest	5	1.43
Other postoperatories	5	1.43
Other	15	4.29
Associated conditions		
Renal dysfunction (creatinine ≥ 1,6mg/dL)	82	23.43
Cancer	49	14.00

Table 3 – Evaluation of the prediction ability of the analyzed prognostic indicators

	APACHE II	UNICAMP II	SAPS II	SAPS 3 Global equation	SAPS 3 Central/South America equation
RSL	1.2197 (0.9995-1.4742)	0.9335 (0.7650-1.1283)	1.5455 (1.2665-1.8680)	1.0982 (0.8999-1.3273)	0.8574 (0.7026-1.0363)
GOF $\hat{C}$	19.70 p=0.0115	11.70 p=0.1649	46.79 p<0.0001	Cg=17.57 p=0.0246	Cg=15.95 p=0.0431
GOF $\hat{H}$	23.46 p= 0.0028	Hg=13.33 p=0.1009	43.39 p<0.0001	Hg=16.42 p=0.0368	Hg=16.66 p=0.0339
AUROC	0.813 (0.768 - 0.852)	0.844 (0.801 - 0.880)	0.835 (0.792 - 0.873)	0.881 (0.843 - 0.913)	0.886 (0.848 - 0.917)

RSL - lethality standardized rate; GOF - goodness-of-fit Hosmer–Lemeshow; AUROC - area under *receiver* operating characteristic. The numbers between brackets correspond to confidence intervals of 95%

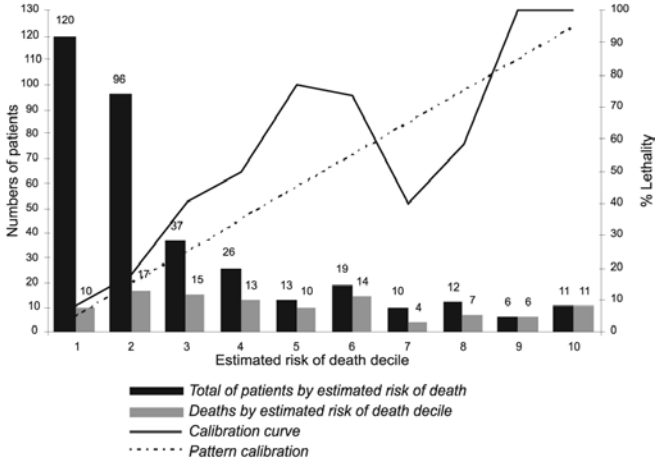

Figure 1 – Calibration curve APACHE II

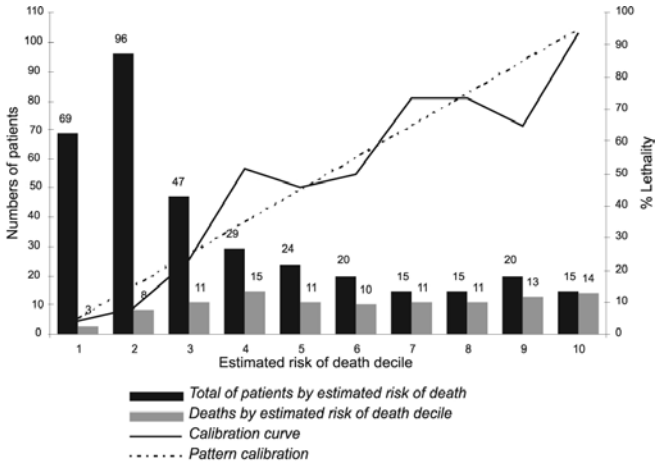

Figure 2 – Calibration curve UNICAMP II

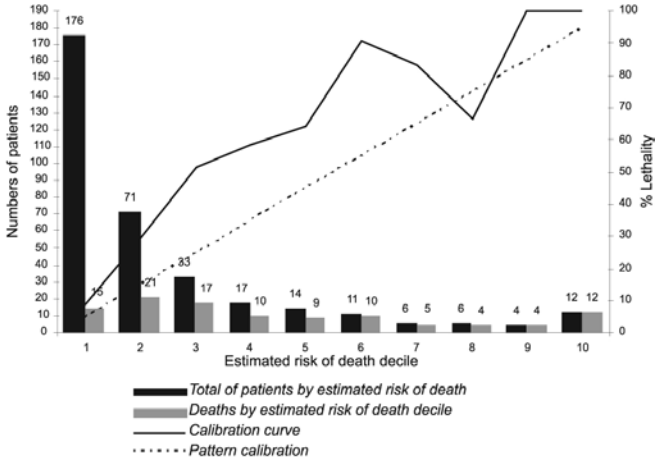

Figure 3 – Calibration curve SAPS II

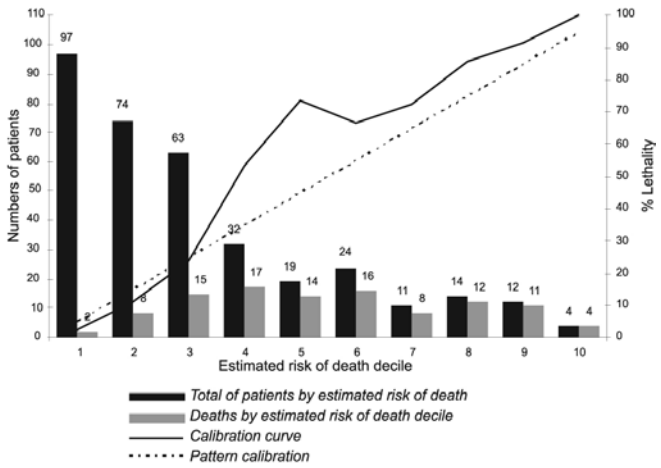

Figure 4 – Calibration curve SAPS 3 – Global equation

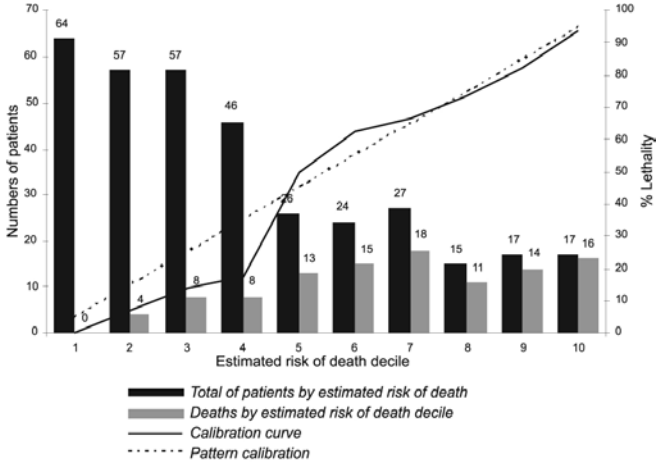

Figure 5 – Calibration curve SAPS 3 – Central/South equation

DISCUSSION

Prognostic indicators are created from data collected from a given population, with its own profile pathologies and age brackets which, after examination, are extrapolated to another one. There are substantial differences between the populations which served as a basis for these used scores and for this study. The APACHE II and SAPS II used data banks of the European and North-American population. The UNICAMP II model and the SAPS 3, especially the equation drawn up for Central and South America involved Brazilian patients. The population of our study was composed only by private patients, supposedly with better conditions of access to health and nutrition services. The UNICAMP II model was created based on the public and academic hospital population, with approximately one

third of patient's owners of health *care*. The Brazilian sample already included in the SAPS 3 database is more comprehensive, it involves various hospitals in different states of the country, with public, academic and private institutions. Thus, it was expected that the UNICAMP II model and the SAPS 3 and mainly the equation drawn up for Central/South America, would present a better performance, which do not occurred. This fact can be explained by possible differences in the pathologies distribution and age brackets in those populations. The great part of the studies showed an inadequate calibration and good discrimination when prognostic indicators are applied in a population different from the original. Beyond the geographical, cultural and social differences between populations, there are differences of decades between the population of this study and those which were used as basis for some of the evaluated scores.

The scores evaluated in this work had already been applied in Brazil. The largest Brazilian study on prognostic indicators, which examined eight prognoses models in 3,378 patients, found an inadequate calibration, good discrimination and mortality underestimation for the various indexes, among them APACHE II and SAPS II.[10] SAPS 3, on the other hand, was evaluated in oncologic patients, most of them with an advanced age. The global and Central/South America equations presented discrimination and appropriate calibration. The RLS was the closest one to the unit for the Central/South America equation. In the same study SAPS II underestimated mortality, did not adequately calibrated and presented an excellent discrimination.[11] Another study with oncology patients found similar performance for APACHE II.[12] The advanced age was identified as a factor related to the worst prognosis in severely ill patients with hematological neoplasias admitted in the ICU.[13] The oncology patients are representative in our sample, filling up 14% of admissions.

The evaluated prognostic indicators in this study had already been applied in our population. In our service, the UNICAMP model and SAPS II 3, global and Central/South America equations, had shown adequate performance, while SAPS II underestimated mortality and presented a deficient calibration and adequate discrimination.[14,15]

Another aspect to be considered is the application of generic indexes to a specific group of patients. Changes in clinical and laboratory variables may be masked in the elderly prognostic index evaluation such as not heart rate increasing due to a conduction disorder, non-fever symptoms and leukocytosis. Beyond that, cognitive changes, common in these patients, may preclude the evaluation of the GCS. The patient's local origin, in other words, the community, domicile internment or nosocomial, may interfere in the variables measurement used in the calculation of prognostic indicators.[16]

Despite all these factors about the preparation of prognostic indicators, several studies showed their inadequate performance when applied in the elderly. A study evaluating the performance of APACHE II in ICU general patients found RSL close to the unit, calibration and discrimination appropriate. When the elderly patients were analyzed separately, the lethality observed was higher than predicted one, the calibration was lost, but it maintained the discrimination.[17] Cultural, religious and ethical factors may influence the decision of an elderly patient ICU admission.[18] This quota of critical patients, not admitted in the ICU, is not taken into account in these studies which evaluates the lethality and the prognostic indexes performance in the elderly population. In the face of a lack of ICU surge capacity, elderly patients may be left behind due to the admission of a younger one. The age over 70 years old was identified as the third cause for not admission in the ICU. These patients whose admission was denied presented greater lethality.[19]

Coronary failure diagnosis is the most frequent in the studied population. This condition was included in the development of SAPS 3 but not in the other indexes which we have studied in this population. Thus, it is expected that it may not be properly evaluated by APACHE II, UNICAMP II and SAPS II, impacting their performance in the elderly population of this sample. However, a study analyzing the performance of APACHE II in coronary patients, mainly with acute myocardial infarction, in a population whose mean age was 72 ±10 years found adequate performance of this score, except in the subgroup which presented death in the first eight hours of admission.[20]

There is still a significant proportion of patients with acute or chronic renal dysfunction, a condition with higher prevalence among the elderly. Many of these patients required hemodialysis, situation in which the generic prognostic indicators, among them APACHE II and SAPS II, do not presented an adequate performance.[21]

Our study presents limitations. It was performed in a single center, then subject to the biases related to the type of patient and received treatment. The number of patients is small which may hide failures in calibration. A study evaluating the Mortality Probability Models (MPM) II through various simulations made in computer showed that the smaller the number of patients involved, the better is the calibration by goodness-of-fit of Hosmer-Lemeshow test. However, discrimination tends to remain despite the number of patients.[22] Studies with few hundreds of patients, such as ours, may present this limitation. It can be noticed that the UNICAMP II model did not provide adequate

performance of the calibration curve despite the p > 0.05 in GOF.

Finally, it is important to emphasize that despite all improvement developed in the area of prognostic indicators its use presents limitations. They are useful tools in risk stratification of patients, but insufficient to predict individual risk, and therefore should not be used to guide the treatment or suspension in a given patient.

CONCLUSION

This study emphasizes the importance of elderly patients in the scenario of intensive medicine. It shows that the generic prognostic indexes may present failures when applied in a group so peculiar as the elderly ones. It is concluded that the prognostic indicators evaluated in this population presents an appropriate discrimination and deficient calibration. There was lethality underestimation by SAPS II.

RESUMO

Objetivo : Os idosos constituem uma população com características próprias e freqüentes admissões em unidades de terapia intensiva. O presente estudo teve por objetivo avaliar a capacidade de predizer a sobrevida desses pacientes através dos índices APACHE II, UNICAMP II, SAPS II e SAPS 3 equações global e América Central/Sul.

Métodos: Foram incluídos pacientes idosos admitidos no período de 01/01/2006 a 31/12/2006, definidos como idade ≥ 60 anos. Foram excluídos aqueles reinternados. Nos pacientes restantes, analisou-se a taxa de letalidade padronizada, a calibração e a discriminação para cada índice. O evento avaliado foi óbito ou alta hospitalar.

Resultados: Foram admitidos na UTI 386 pacientes idosos, sendo 36 excluidos por reinternações, restando 350 para análise. A taxa de letalidade padronizada aproximou-se da unidade em todos os índices, exceto no SAPS II (TLP=1,5455) que subestimou a letalidade. A calibração, por meio dos testes de Hosmer-Lemeshow, foi inadequada (p ≤ 0,05), exceto para o UNICAMP II (p > 0,5). Na curva de calibração, os modelos se afastaram da linha ideal. Todos mostraram excelente discriminação por meio da área sob curva recebedora das características dos operadores (≥ 0,8).

Conclusões: Na população estudada, os modelos apresentaram excelente discriminação e calibração inadequada. O SAPS II subestimou a letalidade.

Descritores: Cuidados intensivos; Unidades de terapia intensiva; Índice de gravidade de doença; Prognóstico; Idoso

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