Derivation and validation of a novel severity scoring system for pneumonia at ICU admission.

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Summary: Severity scores are inaccurate in those admitted with pneumonia to the ICU, particularly elderly patients. Clinical trials may misclassify pneumonia severity leading to conflicting mortality outcomes. The Pneumonia SHOCK score is a simple tool that accurately predicts ICU pneumonia mortality.

Abstract

Background: Severity stratification scores developed in Intensive Care Units (ICUs) are used in interventional studies to identify the most critically ill. Studies that evaluate accuracy of these scores in ICU patients admitted with pneumonia are lacking. This study aims to determine performance of severity scores as predictors of mortality in critically ill patients admitted with pneumonia.

Methods: Prospective cohort study in a general ICU in Brazil. ICU severity scores (SAPS 3 and qSOFA), prognostic scores of pneumonia (CURB-65 and CRB-65), clinical and epidemiological variables in the first 6 hours of hospitalization were analyzed.

Results: A total of 200 patients were included between August 2015 and July 2018 with a median age of 81 years (IQR 67-90) and female predominance (52%) primarily admitted from the emergency department (65%) with community acquired pneumonia (80.5%). Poor discriminative performance in predicting mortality was found with SAPS 3, CURB-65, CRB-65 and qSOFA. Multivariate regression identified variables independently associated with mortality that were used to develop a novel pneumonia specific ICU severity score (Pneumonia SHOCK score) that outperformed SAPS3, CURB-65 and CRB-65 (AUC 0.80 vs 0.74, 0.65 and 0.63, respectively). Discriminate function of the Pneumonia SHOCK score was validated in an external multi-center cohort of critically ill patients admitted with community acquired pneumonia (AUC 0.81).

Conclusions: We created a parsimonious score system that accurately identifies elderly and non-elderly patients with pneumonia at highest risk of ICU death. These findings are critical to accurately stratify patients with severe pneumonia in therapeutic trials that aim to reduce pneumonia mortality.

Keywords: Pneumonia. Intensive Care Unit. Mortality. Severity Scores

Background

Pneumonia remains the principle infection leading to admission to Intensive Care Units (ICUs) throughout the world. Moreover, pneumonia persists as a significant cause of sepsis deaths with mortality rates consistently reaching 50%.[1-3] Mortality is highest in developing countries, and in the Brazilian public health system, pneumonia is the second most common ICU admission diagnosis and the third major cause of in-hospital mortality.[4]

Severity prediction scores have been refined and new ICU scores developed to create an ideal systematic model that performs well in a diverse, complex and increasingly aging ICU population. These tools, however, often include variables that are cumbersome to obtain within the first 24 hours after admission.[5,6]

Widely used scores such as the Simplified Acute Physiology Score (SAPS) 3 lack sufficient evidence for use in in patients with pneumonia admitted to the ICU.[5,7,8] Furthermore, severity of pneumonia by scores such as CURB-65, CRB-65 and the Pneumonia Severity Index have been used in recent trials to stratify patients by severity to evaluate the efficacy of corticosteroids, often with conflicting mortality outcomes. [9-13] Another trial of corticosteroids specifically excluded patients requiring immediate transfer to the ICU, a population that arguably is in dire need of adjuvant therapy for pneumonia.[14,15] Whether these mixed results accurately reflect the effect of corticosteroids in those with severe pneumonia and more broadly whether pneumonia specific severity scores are accurate in an ICU population admitted with pneumonia is unknown.

Given these research gaps, additional studies are required to determine whether pneumonia specific scores developed outside the ICU or severity scores specific to the ICU are accurate measures of mortality risk in an increasingly elderly population admitted to the

ICU with pneumonia. In this study, we evaluated whether ICU and non-ICU pneumonia severity scores accurately predict mortality in critically ill patients admitted with pneumonia.

Methods

This is an observational analytical cohort study conducted over a period of 3 years between August 2015 and July 2018 in a general ICU with 22 beds in a tertiary care hospital in Salvador, Bahia, Brazil. Over the study period, 2,401 patients were admitted to the ICU of which 200 met inclusion criteria with a diagnosis of pneumonia at time of admission. The external validation cohort was derived from the CAPO cohort of patients admitted to the ICU with pneumonia, yielding 362 patients with complete data (out of 405 patients total) with documented inspired oxygen % or assumed inspired fraction of oxygen ≥30% undergoing mechanical ventilation (Figure 1).

The primary outcome evaluated was ICU mortality. Data for our cohort was prospectively collected for all those admitted to the ICU with pneumonia from the emergency department (ED), hospital wards or inter-hospital transfers. Pneumonia was defined by clinical and radiographic data with infiltrate on chest imaging and compatible clinical syndrome for pneumonia. Nosocomial pneumonia, as defined by the Brazilian Consensus, is pneumonia acquired 48 hours or more after hospital admission, in contrast with community acquired pneumonia (CAP) which is present within the first 48 hours of admission.[16]

Clinical and laboratory data were prospectively collected daily and end of follow-up was determined by discharge from the ICU. Study variables included: age, weight, height, sex, comorbidities, functional capacity, admission diagnosis, origin, length of ICU and hospital stay, physiological and laboratory data within the first 6 hours of admission. Complications including need for mechanical ventilation, vasopressors and other supportive therapy in the ICU were noted. Calculated prognostic scores were recorded.

We analyzed the performance of SAPS 3 and quick Sepsis Related Organ Failure Assessment (qSOFA) as ICU specific severity scores, and the pneumonia specific scores CURB-65

and CRB-65. Other prognostic ICU scores that were evaluated included the *Modified Frailty Index* (MFI) and *Charlson Comorbidity Index* (CCI). Data was prospectively recorded in the Epimed Monitor system, which contained all variables of interest for this study. This study was approved by the Research Ethics Committee of Hospital Ana Nery under the number 2.571.265 and CAAE 52892315.1.0000.0045.

Statistical Analysis

Categorical variables were expressed as frequency and percentages, and continuous variables were expressed as medians with inter-quartile ranges (IQR).

The proportion of categorical variables between groups were compared using the Fisher's exact test or chi-squared test. The median of continuous variables were compared using the Mann-Whitney test when analyzing the outcome groups. All tests were two-tailed and considered statistically significant for $p \leq 0.05$.

To assess for potential confounders, variables that demonstrated possible statistical associations in univariate analysis ($p<0.1$) were transformed from continuous variables into categorical variables whose cutoff values were identified using ROC curve analysis for a specificity and sensitivity of 0.80 and the median (25-75) value of the variable in non-survivors. Clinically important variables that are routinely available in most resource settings, including creatinine and sodium, were also transformed to categorical variables using cutoffs determined by ROC curve analysis. Our step-wise multivariate logistic regression model yielded 8 variables associated with mortality ($p<0.2$) that were included in the composite Pneumonia SHOCK Score (Figure 2): age ≥75 years old, heart rate≥ 110 beats per minute, hematocrit ≤38%, white blood cells (WBC) $\geq 15x10^3$, Na ≥145mmol/L, FiO_2 ≥30%, use of vasopressors and presence of obtundation by glasgow coma scale less than 15.

The weight of each variable was determined based on variability in the *odds ratio* (OR) for a confidence interval (CI) of 95%. Given these parameters, age and vasopressor use were weighted two points while other variables were given 1 point in the score calculation, with total score values ranging from a minimum of 0 to a maximum of 10. Predictive performance of the Pneumonia SHOCK Score was evaluated by calculating the area under the receiver operating characteristics (ROC) curve, with area under curve AUC≥0.8 considered most predictive. Performance of the Pneumonia SHOCK Score with the pneumonia and ICU severity scores was compared using a two-tailed Z-test to evaluate the absolute AUC and difference in AUC derived from the empirical ROC curves produced by the NCSS Statistical Software. A Cox proportionate test analysis was performed to determine predictive performance adjusted for differences in baseline characteristics in survivors and non-survivors. External validation of the Pneumonia SHOCK Score was performed using data provided by the Community-Acquired Pneumonia Organization (CAPO) that was limited to patient with pneumonia admitted to the ICU.[17] The data were analyzed using Microsoft Excel suite Office 365, GraphPad Prism version 6.01 and Statistical Package for the Social Sciences (SPSS), version 25.0.

Results

The median age of this cohort was elderly with 81 (IQR 67-90) years and a predominance of women 104 (52%). Patients were primarily admitted from the ED (n=130, 65%) and the median ICU length of stay was 8 days (IQR 4-16). Majority of patients were admitted with a diagnosis of CAP (n=161, 80.5%), vital signs at time of admission were notable for a median systolic blood pressure of 130 mmHg (IQR 112-151), mean arterial pressure of 93.5 mmHg (IQR 79-108), heart rate of 91 bpm (IQR 77-109), respiratory rate of 22 breaths per minute (IQR 19-25) and axillary temperature of 36.2° C (IQR 35.5-36.7). Additional findings are detailed in Table 1.

ICU supportive care included use of vasopressors in 57 (28.5%) and mechanical ventilation in 27 (13.5%) patients. Other variables evaluated can be found in Table 1. Prognostic ICU scores determined by the Charlson Comorbidity Index (CCI), MFI and BRADEN demonstrated a median value of 1 (0-3), 2 (1-3) and 12 (10-14), respectively. Severity of disease was evaluated by pneumonia and ICU severity scores that included SAPS 3, CURB-65, CRB-65 and qSOFA with a median value of 55 (IQR 50-62), 2 (IQR 2-3), 2 (IQR 1-2), 1 (IQR 1-2), respectively (Table 2).

Comparison between non-survivors and survivors

Non-survivors were significantly older than survivors (median age 84 [IQR 75-91] vs 79 [IQR 64.5-88.5] years; p = 0.021). Initial heart rate was significantly higher in non-survivors compared with survivors (99 [IQR 85-114]. vs 87 [IQR 74-104] bpm, p ≦ 0.001), while respiratory rates did not differ (22 [IQR 19-26] vs 22 [IQR 19-25] bpm, p = 0.573). Fraction of inspired oxygen used was significantly higher in non-survivors (40% vs 25%, p<0.001). Laboratory results were notable for significant increases in leukocytes (13.4 vs 12.2, p=0.046) and BUN (31.8 vs 21.5, p<0.001) in non-survivors.

Mental confusion (n=26 (36.6%) vs n=17 (13.2%): p < 0.001) was significantly higher among non-survivors compared with survivors. CURB-65, CRB-65, qSOFA, SAPS 3 and BRADEN scores were significantly higher among non-survivors than survivors (p < 0.001) but no significant differences were noted in MFI and Charlson Comorbidity Index scores (p = 0.636 and p = 0.129) as shown in Table 2.

Existing Score Performance and the Pneumonia SHOCK Score

The Pneumonia SHOCK score performed significantly well in prediction of ICU mortality with an AUC of 0.80 (CI 0.73-0.86) (Figure 3). In those individuals with a score ≤ 2 the mortality rate was 9.3%, whereas those with a score >3 had a mortality rate >26% (Supplemental Figure 1).

Discriminate function of SAPS 3, qSOFA, CURB-65 and CRB-65 was limited, with no ICU or pneumonia severity score reaching an AUC threshold of 0.80 to accurately detect those at highest risk of death admitted to the ICU with pneumonia (AUC 0.74, 0.64, 0.63, 0.63, respectively). The Pneumonia SHOCK score did not differ significantly in performance in those admitted with community acquired or nosocomial pneumonia. Evaluation of the composite score by ROC analysis identified a cutoff score of 3.5 that was accurate and significantly outperformed all pneumonia severity scores in the discovery cohort ($p<0.0008$) (Figure 4A). To more fully determine differences in model performance beyond AUC comparisons, predictive performance by Cox proportionate test analysis demonstrated the superiority of the Pneumonia SHOCK score compared to SAPS3 in prediction of ICU mortality in those admitted with pneumonia (Supplemental Figure 2).

Patient characteristics, vital signs and mortality rate in the CAPO cohort were similar, albeit patients were younger than those included in our discovery cohort (Supplementary Table 1). Evaluation of pneumonia and ICU specific scores demonstrated poor performance similar to findings in our discovery cohort, with the Pneumonia SHOCK score significantly outperforming CURB-65, CRB-65 and qSOFA as determined by AUC comparisons ($p<0.006$). Furthermore, the Pneumonia SHOCK score performed well with continued excellent discriminate function in this external cohort with comparable performance to our discovery cohort ($p>0.80$) (Figure 4B).

Discussion

The findings presented here identify the shortcomings of both ICU and pneumonia specific severity scores in those patients admitted to the ICU with pneumonia, in both elderly and non-elderly populations. As ICU populations age around the world and are increasingly admitted with pneumonia, early identification and intervention is critical. [18-20] Validation of this score in ICU patients admitted with pneumonia from the CAPO cohort demonstrated that the Pneumonia SHOCK score also performs well in a younger ICU population distinct from our discovery cohort. Reliance on existing scores may fail to accurately identify those at highest risk of death in the ICU thereby resulting in delays in early interventions and robust monitoring. Moreover, it is apparent that elderly individuals may be misclassified at a higher risk of death by inaccurate scoring systems. Furthermore, poor score performance may confound clinical trial enrollment that aim to decrease mortality related to severe pneumonia, resulting in conflicting results. Our Pneumonia SHOCK score is a simple tool that leverages data gathered in routine ICU care within the first 6 hours of admission to determine the mortality risk of those admitted to the ICU with either community acquired or nosocomial pneumonia. Importantly, organisms identified in respiratory cultures in our discovery cohort were primarily health care associated gram negative pathogens, suggesting that the clinical definition of CAP based on duration of hospitalization may be inadequate to distinguish nosocomial from community acquired pneumonia. In this context, the Pneumonia SHOCK score was found to perform well in those admitted to the ICU with either nosocomial or community acquired pneumonias. Prior work that specifically evaluated pneumonia and ICU severity scores, such as the Pneumonia Severity Index, CURB-65, SAPS and acute physiology and chronic health evaluation (APACHE), have demonstrated poor performance in predicting pneumonia mortality in the ICU.[21-23] While other studies have evaluated pneumonia and ICU severity scores, most failed to include patients in the ICU and others focused exclusively on patients with community acquired pneumonia.[24-26] Furthermore, these studies have either excluded those patients directly

admitted to the ICU or focused narrowly on ventilator associated pneumonia.[21,23,27] Other scores designed for use in patients with pneumonia requiring ICU admission, such as the PIRO (predisposition, insult, response, and organ dysfunction) include variables not easily obtained within 24h after admission, compromising routine use for early prediction of mortality and clinical trial enrollment.[27,28] In contrast to findings in the DS-CRB-65 study, performance of our Pneumonia SHOCK score did not improve with inclusion of co-morbidities including heart failure, neoplasm, chronic renal or hepatic disease or neurologic dysfunction.[29] With the emergence of simple evidence-based interventions for those with hypoxic respiratory failure and severe pneumonia, including prone positioning, our score may identify those most likely to benefit from early implementation. Our study cautions intensivists' use of established pneumonia and ICU severity scores as they may inaccurately determine mortality risk, particularly in an elderly ICU population. As the ICU population worldwide comprises an increasingly elderly population, often admitted with pneumonia, accurate tools to predict mortality will be critical to target resources towards those at highest risk of death.

While our study has multiple strengths, including a well-characterized elderly discovery cohort with external validation and comparable mortality rate to other studies, there are certain limitations that should be acknowledged. First, as a single center study, there may be unknown patient and healthcare provider factors that were not readily apparent in this analysis. Given the robust prospective data collection utilized in this study, and heterogeneous cohort population, it is unlikely that our study participants differ from other populations that may confound the performance of the Pneumonia SHOCK score. Second, the relatively small but well-characterized study population in our hospital may have specific factors that independently improve score performance. While infection with resistant organisms in our Brazilian cohort may be distinct from other countries, the performance of the Pneumonia SHOCK score in the CAPO cohort from the United States suggests that this is unlikely to impact

score performance. The lack of available data on antibiotic resistance as well as on potential inappropriate use of antibiotics may have impacted the occurrence of shock and need of vasoactive drugs. Finally, delay in appropriate antibiotic therapy was not evaluated and may impact mortality rates in our cohort. While this may be a factor in determining variables associated with mortality, the performance of our score relies on simple, readily available data at the time of admission that accurately identifies those at highest risk of ICU death.

Conclusion

The Pneumonia SHOCK score is a novel parsimonious tool designed to aid intensivists and emergency physicians to accurately triage and intervene in those patients admitted to the ICU with pneumonia. The composite score developed here outperformed prior scores analyzed in our cohort, demonstrates excellent discriminate function in a distinct validation cohort and offers an alternative prognostic tool with robust performance to predict mortality in those with pneumonia.

Author contributions

K.M.A., N.M.F.F. and B.B.A. were responsible for study design, implementation, manuscript preparation and had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. T.A.C, I.B.B.F., R.C.M., G.P.T, M.L.O., L.P.N and S.A. contributed substantially to the study design, data analysis and interpretation, and writing and review of the manuscript. K.F.F and M.B.A. were responsible for advance statistical analysis, figure generation and manuscript review and preparation.

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Figure 1. Patient flowchart of discovery and validation cohort. 2,401 patients were initially admitted to the ICU in the discovery cohort between August 2015 to July 2018, of which 200 met inclusion criteria. In the validation cohort, 405 patients were initially included from CAPO dataset, of which 43 had incomplete data, resulting in 362 patients included in the final analysis.

Figure 2. Adjusted and Unadjusted Multivariate Regression Model for ICU Mortality.

Univariate analysis yielded unadjusted odds of death. Multivariate regression adjusted for differences in baseline characteristics (variables of $p<0.1$ identified in univariate analysis).

Figure 3. Performance of Pneumonia SHOCK score in the discovery cohort.

Receiver Operator Characteristics (ROC) curve analysis to determine accuracy of the Pneumonia SHOCK score in predicting ICU death. The Pneumonia SHOCK score performance was robust, with an AUC (95% CI) of 0.80 (0.73-0.86), sensitivity of 78.9 (68.0-86.8) and specificity of 65.1 (56.6-72.8).

Figure 4. Comparisons of Discriminate Function of Pneumonia scores, ICU scores and the Pneumonia SHOCK Score in the discovery and validation cohort. Receiver Operator Characteristics (ROC) curve analysis to determine score accuracy in prediction of ICU death.

A. The Pneumonia SHOCK score outperformed SAPS3, CURB-65, CRB-65 and qSOFA in prediction of mortality in the discovery cohort. P-values refer to comparisons of AUC of the Pneumonia SHOCK Score with the severity models analyzed in the discovery cohort.
B. In the validation cohort, the SHOCK score performed equally well with comparable discriminate function. The Pneumonia SHOCK Score was significantly superior to all severity models analyzed in the validation cohort, with p-values referring to AUC comparisons.

Table 1. Univariate Analysis of Baseline Cohort Characteristics.

Variables	All patients (n = 200)	Non-survivors (n = 71)	Survivors (n = 129)	p-value
Age, years	81 [67-90]	84 [75-91]	79 [65-89]	0.021
Female sex	104 (52.0)	32 (45.1)	72 (55.8)	0.183
BMI	23 [20-26.7]	22.2 [19.1-24.4]	23.4 [20.8-27.6]	0.014
ICU Length of Stay (Days)	8 [4-16]	13 [6-23]	6 [4-13.5]	0.001
ICU Diagnosis				0.001
Community acquired pneumonia	161 (80.5)	48 (67.6)	113 (87.6)	
Nosocomial Pneumonia	39 (19.5)	23 (32.4)	16 (12.4)	
Admission Source				0.409
Emergency	130 (65.0)	35 (49.3)	95 (73.6)	
Ward	22 (11.0)	13 (18.3)	9 (7.0)	
Home-care	12 (6.0)	6 (8.5)	6 (4.7)	
Transfer.	36 (18.0)	17 (23.9)	19 (14.7)	
Autonomy				0.104
Independent	131 (65.5)	42 (59.2)	89 (69.0)	
Need for Assistance	28 (14.0)	10 (14.1)	18 (14.0)	
Restricted / bedridden	41 (20.5)	19 (26.8)	22 (17.1)	
Vital Signs				
Systolic blood pressure,mmHg	130 [112-151]	127 [108-148]	133 [113-153]	0.159
Mean arterial pressure, mmHg	93.5 [79-108]	73 [61-83]	96 [81.67-110]	0.216
Heart rate, / min.	91 [77-109]	99 [85-114]	87 [74-104]	< 0.001
Respiratory rate, / min.	22 [19-25]	22 [19-26]	22 [19-25]	0.573
Temperature, °C	36.2 [35.5-36.7]	36.05 [35.2-36.5]	36.2 [35.8-36.7]	0.172
Laboratory results				
Leukocytes × 10^9/L	12.5 [9.1-17.5]	13.4 [10.2-18.7]	12.2 [8.8-16.1]	0.046
Platelets, x10^3/mm^3	217 [168-301]	214 [152-292]	221 [172-304]	0.656
Hematocrit, %	34.65 [29.5-38.7]	33.30 [27.4-37.5]	35.50 [30-39.3]	0.022
Creatinine, mg/dL	0.80 [0.6-1.3]	0.80 [0.5-1.5]	0.80 [0.6-1.2]	0.532
BUN, mg/dl	23.36 [16.4-40.4]	31.78 [19.4-47.8]	21.50 [15-32.7]	<0.001
PaO_2, mmHg	89 [71-127]	93 [77-135]	87 [69-115]	0.105
$FiO_{2,\%}$	26.5 [25-50]	40 [25-100]	25 [21-50]	<0.001
Na, mmol/L	140 [136-143]	140 [134-146]	140 [136.75-143]	0.411
Outcomes				
Confusion	43 (21.5)	26 (36.6)	17 (13.2)	<0.001
Mechanical Ventilation	57 (28.5)	30 (42.3)	27 (20.9)	0.002
Non-Invasive Ventilation	51 (25.5)	23 (32.4)	28 (21.7)	0.127
Use of Vasopressors	27 (13.5)	20 (28.2)	7 (5.4)	<0.001

Continuous variables are represented as median [25th - 75th percentile], values were compared using the Mann-Whitney U test. Qualitative variables are shown as frequency (%) and compared using the Fisher's exact test or Pearson's Chi-square test.

Table 2. Severity of illness scores in cohort stratified by mortality.

Severity Score	All patients (n = 200)	Non-survivors (n = 71)	Survivors (n = 129)	p-value
BRADEN	12 [10-14]	10 [9-12]	13 [11-15.75]	<0.001
MFI	2 [1-3]	2 [1-3]	2 [1-3]	0.636
Charlson Comorbidity Index	1 [0-3]	2 [1-3]	1 [0-3]	0.129
SAPS3	55 [50-61.75]	60 [55-71]	53 [47-58]	<0.001
qSOFA	1 [1-2]	1 [1-2]	1 [1-2]	0.001
CURB-65	2 [2-3]	3 [2-3]	2 [1-3]	<0.001
CRB-65	2 [1-2]	2 [1-2]	2 [1-2]	0.001

Data were expressed as a median [25th - 75th percentile]. Abbreviations: Multidimensional Fatigue Inventory (MFI); Simplified Acute Physiology Score (SAPS); quick Sequential Organ Failure Assessment (qSOFA); Confusion, Urea, Respiratory rate, Blood pressure and age (CURB-65); Confusion, Respiratory rate, Blood pressure and age (CRB-65). Increased BRADEN score reflects decreased risk of pressure ulcers. Increases in all other scores are associated with increased frailty, comorbidities and risk of death, respectively.

Figure 1

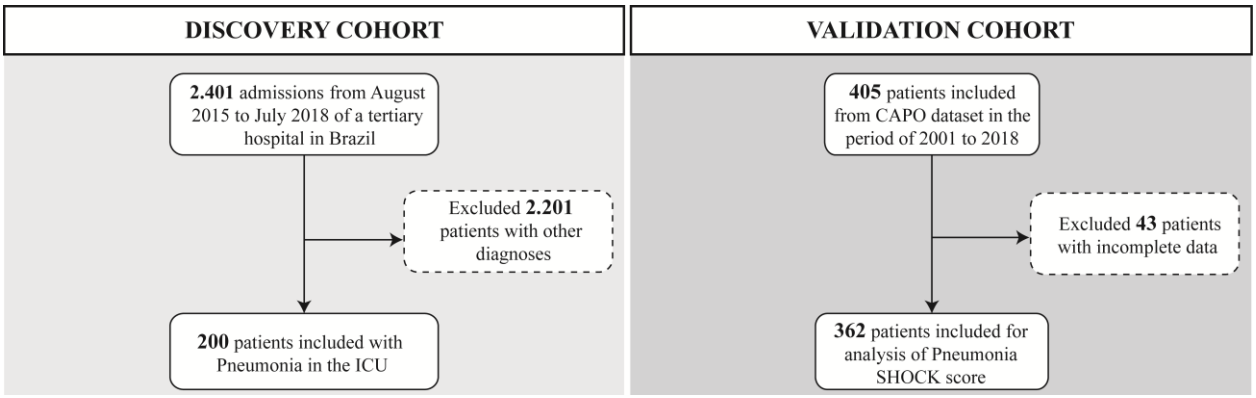


Figure 2

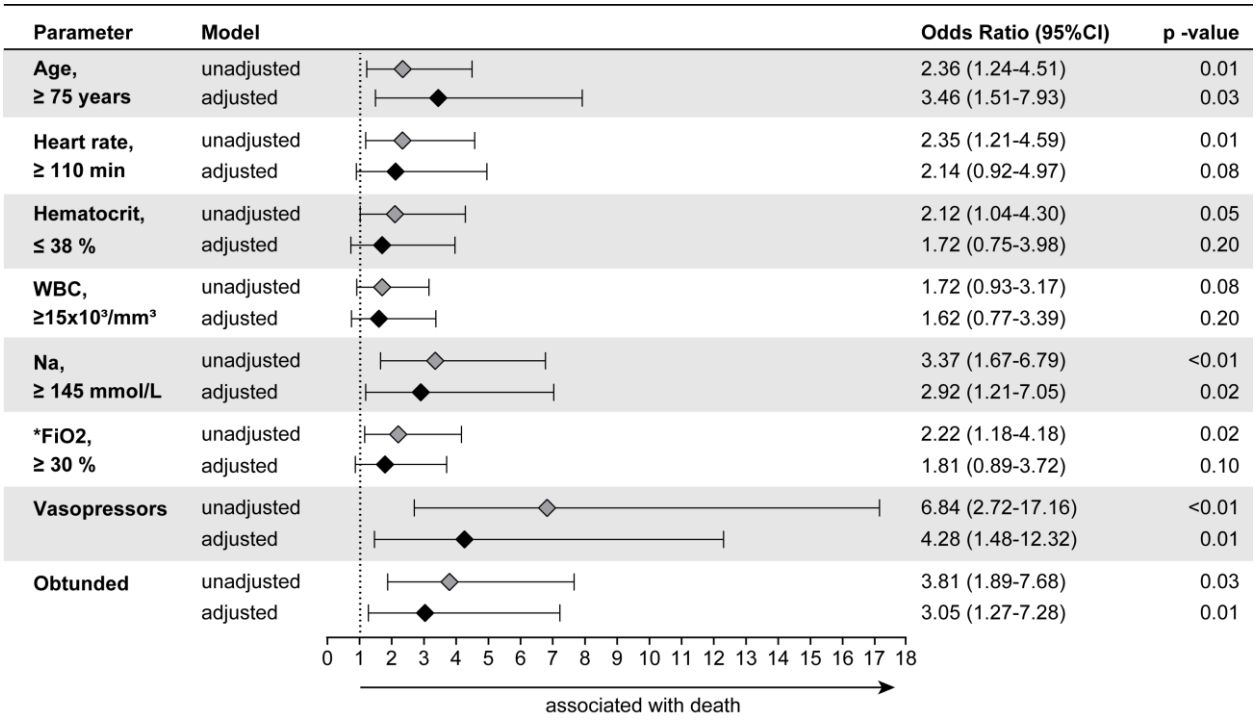


Figure 3

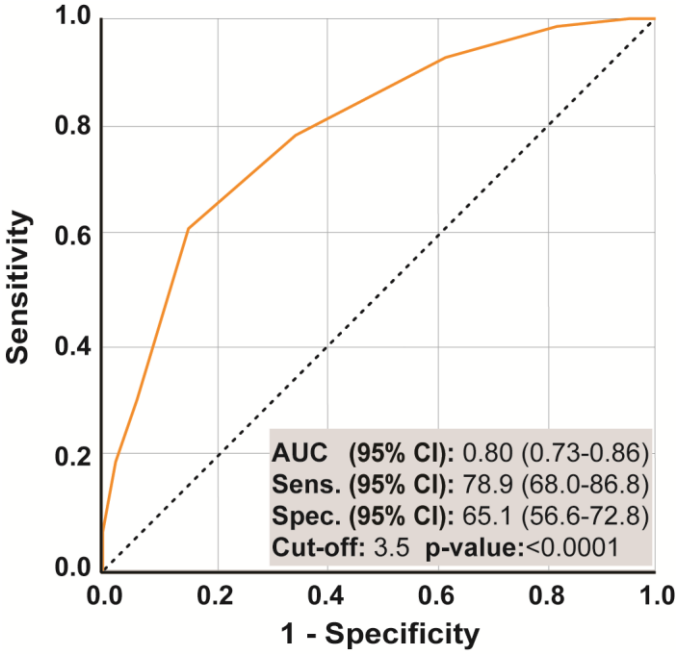
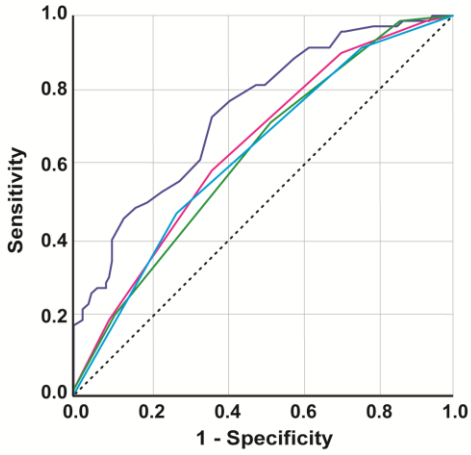


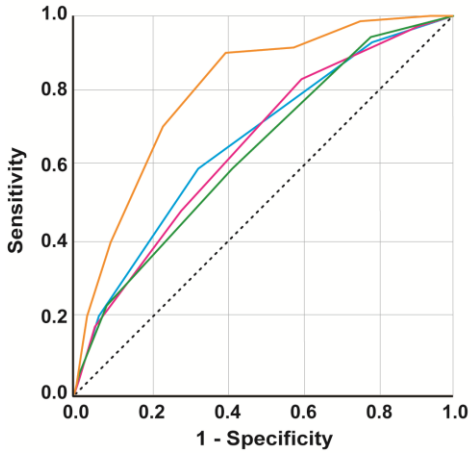
Figure 4

A



Scores	AUC (95% CI)	p-value	cut-off value	Sensitivity (95% CI)	Specificity (95% CI)
SAPS 3	0.74 (0.67-0.81)	0.1897	>58.5	53.5 (42.0-64.6)	76.7 (68.7-83.2)
CURB-65	0.65 (0.57-0.73)	0.0008	>2.5	59.1 (47.5-69.8)	63.5 (55.0-71.3)
CRB-65	0.63 (0.55-0.71)	0.0001	>1.5	71.8 (60.5-81.0)	48.1 (39.6-56.6)
qSOFA	0.64 (0.55-0.71)	0.0001	>1.5	47.9 (36.6-59.3)	72.8 (64.2-79.8)

B



Scores	AUC (95% CI)	p-value	cut-off value	Sensitivity (95% CI)	Specificity (95% CI)
SHOCK Validation	0.81 (0.75-0.86)	0.8071	>3.5	90.3 (81.3-95.2)	60.0 (54.3-65.5)
CURB-65	0.66 (0.59-0.73)	0.0033	>2.5	48.6 (37.4-59.9)	71.7 (66.3-76.6)
CRB-65	0.64 (0.57-0.71)	0.0009	>1.5	59.7 (48.2-70.3)	58.3 (52.5-63.8)
qSOFA	0.67 (0.60-0.74)	0.0062	>1.5	59.7 (48.2-70.3)	67.2 (61.6-72.4)