

# Can We Improve Confusion, Uremia, Respiratory Rate, Blood Pressure, Age >65 with Lactate and Procalcitonin to Predict Mortality in Pneumonia?

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## Keywords

CURB-65 · Lactate · Procalcitonin · Pneumonia · Emergency

## Abstract

**Introduction:** Pneumonia is a common diagnosis in the emergency department (ED). Some scoring systems such as Confusion, Uremia, Respiratory Rate, Blood Pressure, Age>65 (CURB-65) are used to determine the severity of this disease. We aimed to determine the best scoring system (CURB-65, serum lactate+CURB-65, serum procalcitonin+CURB-65) to predict the severity and 30-day mortality of pneumonia patients admitted to our ED. **Methods:** This study was planned as a prospective study. 480 community-acquired pneumonia patients admitted to our ED between February 1, 2020, and January 31, 2021, were included. CURB-65 score, CURB-65+lactate levels, and CURB-65+procalcitonin levels were evaluated to predict disease severity. **Results:** A total of 480 pneumonia patients, 281 (58.5%) men and 199 (41.5%) women, with a mean age of 61.7 ± 19.06 years, were included in the study. The sensitivity/specificity pair and cut-off value of CURB-65 for 30-day mortality was 71.9/74.8%. These values were 68.5% and 61.9% for CURB-65+lactate (cut-off = 17.50) and 78.1% and 90.7% for CURB-65+procalcitonin (cut-off = 2.095). **Discussion:** Infectious

diseases such as pneumonia, urinary tract infection, and sepsis are common reasons for ED presentations and may be fatal, especially in the elderly population. In such infectious diseases, it is difficult to predict the prognosis of the patients including discharge, hospitalization service, mortality probability in the EDs those are becoming much more crowded each day and several scoring systems have been improved. In this study, the highest sensitivity and specificity were determined in CURB-65+procalcitonin. **Conclusion:** CURB-65 is superior to CURB-65+lactate; however, CURB-65+procalcitonin is superior to both in predicting 30-day mortality.

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## Introduction

Pneumonia is a common infectious disease with high mortality and morbidity. This diagnosis is one of the most important reasons for hospitalization from the emergency department (ED). Mortality ratio of hospitalized patients is around 12% and 40% for intensive care unit (ICU) patients [1].

Although pneumonia diagnosis looks easy in the ED, variety in the etiology, and clinic make the management much more difficult [2]. In these patients, it is important to predict or recognize the patients who are under risk for acute respiratory failure [3]. Several scoring systems have been improved such as confusion, uremia, respiratory rate, blood pressure, age > 65 (CURB-65), and pneumonia severity index (PSI) to evaluate the clinical status and predict the mortality of these patients [4, 5]. PSI predicts 30-day mortality but includes 20 variables, so its use is complicated and difficult in the ED. CURB-65 score has been used as a safe predictor of 30-day mortality among patients with pneumonia for many years. It also helps clinicians in making the decision to admit or discharge such patients. CURB-65 is easy and practical, but it is not much effective for young patients [6].

Serum lactate levels have become a valuable marker for predicting severity of infectious diseases, especially sepsis [7]. Similarly, procalcitonin is known as a powerful serum marker for infections and has been shown in pneumonia studies [8]. In the literature, there is a lack of data on serum lactate and CURB-65 combination to predict the severity and prognosis of pneumonia [9]. In this study, we aimed to determine the best scoring system (CURB-65, serum lactate+CURB-65, serum procalcitonin+CURB-65) to predict severity and 30-day mortality of pneumonia patients presented to our ED.

## Material and Methods

### Study Design

After the ethics committee approval (Date: November 6, 2019, Decision number: 598), in this prospective study, we included 480 community acquired pneumonia-diagnosed patients between 1 February 2020 and 31 January 2021 who were presented to our ED. Written informed consent was obtained from all patients to participate in this study. Demographic data, presentation complaint, vital signs, laboratory results (serum lactate levels, blood urea nitrogen (BUN), procalcitonin, C-reactive protein, white blood cell, initial CURB-65 score of the patients were noted on the study form. The patients we included in this study met one major of the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) pneumonia criteria, such as septic shock, mechanical ventilation support requirement, or met three minor criteria of respiratory rate  $\geq 30$  breaths/min, partial pressure of oxygen in the arterial blood/fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) ratio  $\leq 250$ , multilobular infiltration, confusion, uremia, leukopenia, thrombocytopenia, hypothermia, hypotension requiring aggressive fluid replacement. Pneumonia diagnosis of this patient group was clarified with these criteria. Follow-up of these patients was maintained from the hospital automation

system and government death system. It is recorded that patients were hospitalized (ICU or clinics). Whether the patients were alive after 1 month, 3 months, and 1 year was called by phone. The learned information was recorded. The causes of death of deceased patients were recorded by learning from both patient relatives and death notification systems (official state records). Patients who refused to participate in the study, patients under 18 years old, pregnant patients, immunosuppressed patients, and hospital-acquired pneumonia patients were excluded from the study. In addition, patients with positive COVID-19 polymerase chain reaction test and/or lung involvement compatible with COVID-19 pneumonia were excluded from the study.

### CURB-65 Lactate and Procalcitonin Analysis

CURB-65+lactate value was calculated by adding lactate level to CURB-65. In addition, CURB-65+procalcitonin value was calculated by adding procalcitonin value to CURB-65. Then, the power of CURB-65, CURB-65+lactate, and CURB-65+procalcitonin values to predict 30-day mortality was analyzed. Lactate and procalcitonin values added to CURB-65 were added as values obtained from laboratory results.

### Statistical Analyses

SPSS 23.0 (IBM Corp., Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) was used for statistical analyses of the patients' data. Homogeneity of each parameter was evaluated with Kolmogorov-Smirnov and Shapiro-Wilks tests. Mean, median, and standard deviation were calculated for definitive data. Mann-Whitney U test was used for quantitative variables, and  $\chi^2$  test was used for qualitative variables. Spearman's correlation test was used for correlations. In the first step, categorical variables providing  $p < 0.05$  in univariate analysis were selected. Then, possible continuous variables with  $p < 0.05$ , which could be important clinical determinants in univariate analyses, were selected. Receiver operating characteristics (ROC) analysis was used for determining the cut-off levels. Sensitivity and specificity were calculated. Definitive statistics were expressed as mean  $\pm$  standard deviation and median (interquartile range). The significance level for the  $p$  was 0.05 with 95% confidence interval.

## Results

We included 281 (58.5%) males and 199 (41.5%) females, a total of 480 pneumonia patients with the mean age of  $61.7 \pm 19.1$ . According to the presentation symptoms; 224 patients had dyspnea (46.7%), 179 patients had cough (37.3%), 96 patients had (20.6%) unconsciousness, 31 patients had feeding problems (6.5%), 26 patients had chest pain (5.4%), 17 patients had phlegm (3.5%), 10 patients had fatigue (2.1%), 9 patients had sore throat (1.9%), 8 patients had enteritis (1.7%), 6 patients had (1.3%) flank pain (1.3%), 6 patients had nausea/vomiting (1.3%), 4 patients had headache (0.6%), and 3 patients had hemoptysis (0.6%).

Some of the patients had more than one symptom at the same time (for example, dyspnea, and cough were seen together).

When we considered the initial CURB-65 scores of the patients, 160 (33.3%) patients' scores were 0, 116 (24.2%) patients' scores were 1, 96 (20%) patients' scores were 2, 63 (13.1%) patients' scores were 3, 38 (7.9%) patients' scores were 4, and 7 (1.5%) patients' scores were 5. Three hundred and thirty-two (69%) of the patients were hospitalized. Ninety-seven (20%) of these patients were hospitalized in the ICU. Besides, 31 (6.5%) patients were discharged from the ED, and 117 (24.4%) patients were referred to other hospitals for ICU bed insufficiency.

According to 30-day mortality, three hundred and two (62.92%) patients survived and 178 (37.08%) patients died, and mean ages of these patient groups were  $56.4 \pm 19.01$  and  $70.6 \pm 15.54$ , respectively. When 1-year mortality was evaluated, 302 (62.9%) patients survived at the end of 1 year. Three-month mortality ratio was 28.1%.

Age was related with mortality in our study. Other parameters of our study according to presence of mortality are given in Table 1.

We used ROC curve to analyze the 30-day mortality prediction levels of CURB-65, CURB-65+lactate, CURB-65+procalcitonin (Fig. 1; Table 2). AUC of CURB-65+procalcitonin was the highest when compared with others.

CURB-65 score values over 1.5 (cut-off) were 71.9% sensitivity and 74.8% specificity for 30-day mortality. These values were 68.5% and 61.9% for CURB-65+lactate (cut-off = 17.50) and 78.1% and 90.7% for CURB-65+procalcitonin (cut-off = 2.095).

## Discussion

Infectious diseases such as pneumonia, urinary tract infection, and sepsis are common reasons for ED presentations and may be fatal, especially in the elderly population. In such infectious diseases, it is difficult to predict the prognosis of the patients including discharge, hospitalization service, mortality probability in the EDs; those are becoming much more crowded each day, and several scoring systems have been improved. CURB-65 is the most reliable scoring system with the highest sensitivity for pneumonia and usually used by emergency clinicians. Similarly, PSI is also an effective scoring system for pneumonia [10].

In this study, we added lactate and procalcitonin values to the CURB-65 value, respectively. We

compared these values with the CURB-65 value. The highest sensitivity and specificity were determined in CURB-65+procalcitonin. Increase in procalcitonin seems to be a predictor of mortality in pneumonia patients. It was determined in the results of our study that the specificity and sensitivity of this predictor reached higher values with the CURB-65 score. Considering the value of procalcitonin together with CURB-65 in pneumonia patients may help clinicians more effectively in predicting the prognosis of patients.

CURB-65 is a simple and widely used scoring system in clinical practice [11]. Patients with a CURB-65 score  $>3$  require ICU hospitalization [12].

According to the data we obtained in our study, we found that when lactate value is added to the CURB-65 value, it predicts mortality less effectively than the CURB-65 value. Serum lactate level is an important marker, especially in sepsis patients, and it also helps to determine the treatment goals of sepsis patients. It identifies tissue hypoperfusion and is used as a guide to normalize lactate level via fluid resuscitation [13]. Increment in serum lactate level helps to predict tissue hypoperfusion, aerobic glycolyse, and other reasons (liver failure, etc.). Increased serum lactate levels are associated with worse poor prognosis regardless of the source [14]. It is also stated that the sensitivity and specificity of lactate alone are low [15]. The blood samples of the patients included in the study were performed during the first admission to the ED. Although our patients were diagnosed with pneumonia, the fact that the lactate value did not increase yet may be considered the reason for the less effective CURB-65+lactate value.

In a 90-day mortality study of 2,099 community-acquired pneumonia patients (mean age: 60) study, CURB-65 and procalcitonin were evaluated. Mean hospitalization length was 10 days and 90-day mortality ratio was 2.19%. Procalcitonin was an independent predictor in that study and combined with CURB-65 to predict 90-day mortality. They suggested that procalcitonin was a good predictor for determining 90-day mortality and prognosis of community-acquired pneumonia when compared with other prognostic models (AUC = 0.900 and Youden index = 0.706) [8]. In our study, mean age was 61.7 years, and 90-day mortality ratio was 28.1%. Mortality ratio is around 1–5%, community acquired pneumonia out-patients, and this ratio is 12% in hospitalized patients [16]. In a prospective cohort study, 90-day mortality ratio was 12.99% [17]. This ratio is higher in developing countries [18]. But the condition of the hospital may be a determinant factor for this ratio because third degree hospitals such

**Table 1.** Parameters of our study according to presence of mortality

|  | Mortality | N   | Median | IQR   | U*       | p value |
|--|-----------|-----|--------|-------|----------|---------|
| Age, years                               | –         | 302 | 59     | 32    | 15,401   | <0.001  |
|  | +         | 178 | 72     | 20    |          |         |
| Fever, °C                                | –         | 302 | 36.5   | 0.2   | 24,569.5 | 0.089   |
|  | +         | 178 | 36.5   | 0.5   |          |         |
| Pulse, bpm                               | –         | 302 | 90     | 20    | 20,791   | <0.001  |
|  | +         | 178 | 98     | 32    |          |         |
| Systolic blood pressure, mm Hg           | –         | 302 | 120    | 30    | 23,417   | 0.687   |
|  | +         | 178 | 120    | 40    |          |         |
| Diastolic blood pressure, mm Hg          | –         | 302 | 80     | 10    | 21,060   | <0.001  |
|  | +         | 178 | 70     | 20    |          |         |
| Oxygen saturation (SpO <sub>2</sub> ), % | –         | 302 | 97     | 4     | 15,496.5 | <0.001  |
|  | +         | 178 | 91.5   | 13    |          |         |
| Respiratory rate, breaths/min            | –         | 302 | 19     | 8     | 20,546   | <0.001  |
|  | +         | 178 | 20     | 9     |          |         |
| CURB-65                                  | –         | 302 | 1      | 2     | 11,577   | <0.001  |
|  | +         | 178 | 2      | 2     |          |         |
| Blood urea nitrogen, mg/dL               | –         | 302 | 31     | 19    | 12,132   | <0.001  |
|  | +         | 178 | 58.5   | 67    |          |         |
| Lactate, mg/dL                           | –         | 302 | 14.5   | 9     | 17,737.5 | <0.001  |
|  | +         | 178 | 19.5   | 18    |          |         |
| Procalcitonin, µg/L                      | –         | 97  | 0.05   | 0.07  | 620      | <0.001  |
|  | +         | 32  | 0.305  | 1.67  |          |         |
| C-reactive protein, mg/dL                | –         | 302 | 26.1   | 76.2  | 16,493.5 | <0.001  |
|  | +         | 178 | 97.45  | 174.8 |          |         |
| White blood cell, 10 <sup>3</sup> /µL    | –         | 300 | 9.5    | 6.3   | 19,435   | <0.001  |
|  | +         | 175 | 12.2   | 8.3   |          |         |
| Neutrophil                               | –         | 300 | 6.6    | 5.8   | 18,222.5 | <0.001  |
|  | +         | 175 | 9.5    | 7.2   |          |         |
| Lymphocyte                               | –         | 300 | 1.45   | 1.4   | 21,692   | 0.001   |
|  | +         | 176 | 1.0    | 1.2   |          |         |
| Eosinophil                               | –         | 302 | 0      | 0     | 26,461   | 0.637   |
|  | +         | 178 | 0      | 0     |          |         |

\*Mann-Whitney U. IQR, interquartile range.

as ours hospitalizes patients with much poorer clinical status. Similarly, ICU hospitalization may be almost dependent on the hospital's condition. This decision may vary between second- and third-degree hospitals similar to difference between developed and developing countries. In our study, 20.2% of our patients were hospitalized in the ICU.

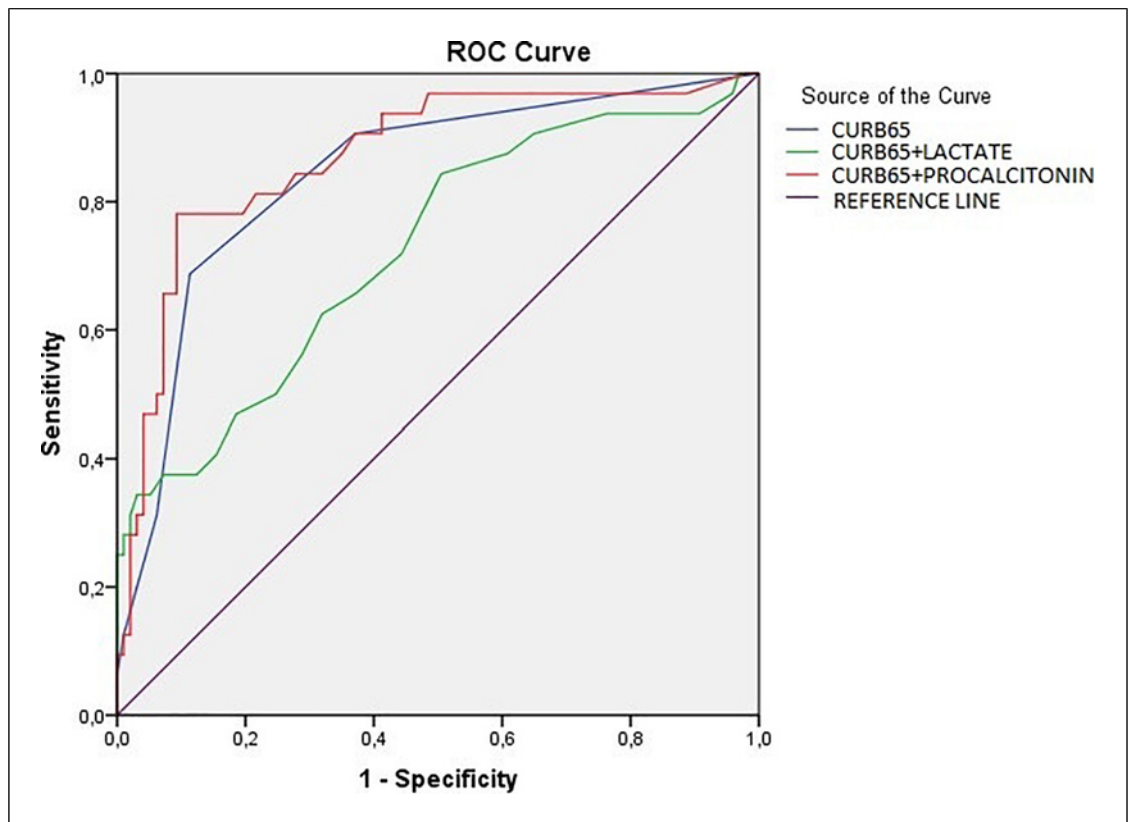
Similar to Song's study, we can say that CURB-65 and procalcitonin combination predicts mortality effectively [8]. In our study, 160 patients' scores were 0, 116 patients' scores were 1, 96 patients' scores were 2, 63 patients' scores were 3, 38 patients' scores were 4 and, 7 patients' scores were 5. In Song's study, just 2 of non-fatal patients' CURB-65 scores were >3.

When we considered our and Song's study according to sensitivity and specificity, CURB-65 score values over

1.5 were 71.9% sensitive and 74.8% specific for 30-day mortality. These values were 68.5% and 61.9% for CURB-65+lactate (cut-off = 17.50) and 78.1% and 90.7% for CURB-65+procalcitonin (cut-off = 2.095). Song suggested that neutrophil to lymphocyte ratio and procalcitonin have similar sensitivity for 90-day mortality prediction, but procalcitonin was more specific than neu/lymph ratio, but CURB-65 was the most specific score [8].

## Conclusion

We believe that clinicians can use CURB-65-procalcitonin combination more effectively than CURB-65 as a predictor of mortality in patients with community-acquired pneumonia.



**Fig. 1.** CURB-65 and Lactate/Procalcitonin mortality prediction graph.

**Table 2.** Mortality prediction ratios for \*CURB-65, CURB-65+lactate, and CURB-65+procalcitonin

|                      | AUC (95% CI)        | Cut-off | Specificity (%) | Sensitivity (%) | p value |
|----------------------|---------------------|---------|-----------------|-----------------|---------|
| CURB-65              | 0.871 (0.795–0.946) | 1.5     | 74.8            | 71.9            | <0.001  |
| CURB65+lactate       | 0.705 (0.656–0.753) | 17.50   | 61.9            | 68.5            | <0.001  |
| CURB65+procalcitonin | 0.871 (0.795–0.946) | 2.095   | 90.7            | 78.1            | <0.001  |

\*CURB-65: Confusion, Uremia, Respiratory Rate, Blood Pressure, Age>65. CI, confidence interval.

### Limitation of the Study

There are some limitations to our study. The first of these is that this study is a single center experience. Second, only patients with community-acquired pneumonia were included in the study. Results from multi-center studies with more patients will be more important.

### Statement of Ethics

This manuscript was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The Ethics Committee of the Adana City Training and Research

Hospital approved the study (date: November 6, 2019, decision number: 598). Written informed consent was obtained from all patients to participate in the study.

### Conflict of Interest Statement

The authors have no conflicts of interests to declare.

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## Author Contributions

Dr. Ahmet Burak Urfalioglu, Dr. Kemal Sener, Dr. Adem Kaya, Dr. Akkan Avci, and Dr. Sadiye Yolcu: conceptualization, methodology, investigation, and writing – original draft. Dr. Ahmet Burak Urfalioglu, Dr. Dervis Yildiz, Dr. Adem Kaya, Dr. Durdu Mehmet Uzucek, and Dr. Satuk Bugra Yapici: resources, formal analysis, and writing – review and editing. Dr. Ahmet Burak Urfalioglu, Dr. Akkan Avci, Dr. Sadiye Yolcu: conceptualization, methodology,

and writing – review and editing. All authors read and approved the final version of the manuscript.

## Data Availability Statement

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

## References

- 1 Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/ American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44 Suppl 2(Suppl 2):S27–72.
- 2 Ananda-Rajah MR, Charles PG, Melvani S, Burrell LL, Johnson PD, Grayson ML. Comparing the pneumonia severity index with CURB-65 in patients admitted with community acquired pneumonia. *Scand J Infect Dis*. 2008;40(4):293–300.
- 3 Khokhar SR, Stern Y, Bell K, Anderson K, Noe E, Mayeux R, et al. Persistent mobility deficit in the absence of deficits in activities of daily living: a risk factor for mortality. *J Am Geriatr Soc*. 2001;49(11):1539–43.
- 4 Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003;58(5):377–82.
- 5 Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med*. 1997;336(4):243–50.
- 6 Buising KL, Thursky KA, Black JF, MacGregor L, Street AC, Kennedy MP, et al. A prospective comparison of severity scores for identifying patients with severe community acquired pneumonia: reconsidering what is meant by severe pneumonia. *Thorax*. 2006;61(5):419–24.
- 7 Nguyen HB, Rivers EP, Knoblich BP, Jacobsen G, Muzzin A, Ressler JA, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med*. 2004;32(8):1637–42.
- 8 Song Y, Sun W, Dai D, Liu Y, Li Z, Tian Z, et al. Prediction value of procalcitonin combining CURB-65 for 90-day mortality in community-acquired pneumonia. *Expert Rev Respir Med*. 2021;15(5):689–96.
- 9 Arnold RC, Shapiro NI, Jones AE, Schorr C, Pope J, Casner E, et al. Multicenter study of early lactate clearance as a determinant of survival in patients with presumed sepsis. *Shock*. 2009;32(1):35–9.
- 10 Falcone M, Corrao S, Venditti M, Serra P, Licata G. Performance of PSI, CURB-65, and SCAP scores in predicting the outcome of patients with community-acquired and healthcare-associated pneumonia. *Intern Emerg Med*. 2011;6(5):431–6.
- 11 Hunton R. Updated concepts in the diagnosis and management of community-acquired pneumonia. *JAAPA*. 2019;32(10):18–23.
- 12 Baez AA, Cochon L, Nicolas JM. A Bayesian decision support sequential model for severity of illness predictors and intensive care admissions in pneumonia. *BMC Med Inform Decis Mak*. 2019;19(1):284. Published 2019 Dec 30.
- 13 Levy MM, Evans LE, Rhodes A. The surviving sepsis campaign bundle: 2018 update. *Intensive Care Med*. 2018;44(6):925–8.
- 14 Casserly B, Phillips GS, Schorr C, Dellinger RP, Townsend SR, Osborn TM, et al. Lactate measurements in sepsis-induced tissue hypoperfusion: results from the Surviving Sepsis Campaign database. *Crit Care Med*. 2015;43(3):567–73.
- 15 Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*. 2021;47(11):1181–247.
- 16 Kim MA, Park JS, Lee CW, Choi WI. Pneumonia severity index in viral community acquired pneumonia in adults. *PLoS One*. 2019;14(3):e0210102.
- 17 Curbelo J, Luquero Bueno S, Galván-Román JM, Ortega-Gómez M, Rajas O, Fernández-Jiménez G, et al. Inflammation biomarkers in blood as mortality predictors in community-acquired pneumonia admitted patients: importance of comparison with neutrophil count percentage or neutrophil-lymphocyte ratio. *PLoS One*. 2017;12(3):e0173947. Published 2017 Mar 16.
- 18 Bahlis LF, Diogo LP, Kuchenbecker Rd S, Fuchs SC. Clinical, epidemiological, and etiological profile of inpatients with community-acquired pneumonia in a public hospital in the interior of Brazil. *J Bras Pneumol*. 2018;44(4):261–6.