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Comparative analysis of the prognostic value of CURB-65 and CRB-65 scores and their modifications in assessing in-hospital mortality in patients with community-acquired pneumonia

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ABSTRACT

Background. Mortality associated with community-acquired pneumonia (CAP) continues to be a crucial health problem worldwide. Correct assessment of CAP severity and the level of care is pivotal in the disease outcome.

Aim. To evaluate the prognostic value of the CURB-65 and CRB-65 scores and their modifications in determining the risk of in-hospital mortality in patients with CAP.

Materials and methods. The retrospective study included 1,412 patients with CAP aged over 18 years. In a population of 1,020 patients, which was subsequently split into test (n = 676) and training (n = 344) samples in the ratio 2 : 1, we compared the predictive value of the CURB-65 (confusion, urea > 7 mmol / l, respiratory rate ≥ 30 / min, low blood pressure (BP), and age ≥ 65 years) and CRB-65 (confusion, respiratory rate ≥ 30 / min, low blood pressure (BP), and age ≥ 65 years) scores in identifying patients at high risk of in-hospital death. The specified scoring systems were modified by changing the cut-offs for each criterion to increase their accuracy. For comparison, we used the ROC analysis with the calculation of the area under the curve (AUC).

Results. The modified CURB-65 score with new cut-off values (age > 72 years, respiratory rate > 21 / min, urea level > 9.5 mmol / l, systolic blood pressure ≤ 105 mm Hg, and diastolic blood pressure ≤ 65 mm Hg) was more accurate than the original one in predicting death and was named CURB-72. The AUC for CURB-72 and CURB-65 was 0.946 (95% confidence interval (CI): 0.916–0.967) and 0.905 (95% CI: 0.869–0.934), respectively (p = 0.0034). The modified CRB-65 (CRB-72) score also outperformed the original model, but showed no statistically significant difference. While comparing the modified scoring systems, the new CURB-72 score surpassed the CRB-72 score and demonstrated maximum accuracy in identifying CAP patients at risk of in-hospital mortality (p = 0.0347).

Conclusion. The modified CURB-65 (CURB-72) and CRB-65 (CRB-72) scores demonstrated potential for assessing the prognosis of CAP and are superior to classical scoring systems. CURB-72 showed the highest sensitivity and specificity.

Keywords: community-acquired pneumonia, pneumonia, CRB-65, CURB-65, mortality, prognosis, pneumonia, scores

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

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Сравнительный анализ прогностической значимости шкал CURB-65, CRB-65 и их модификаций в оценке госпитальной летальности у пациентов с внебольничной пневмонией

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РЕЗЮМЕ

Введение. Смертность от внебольничной пневмонии (ВП) остается серьезной проблемой систем здравоохранения разных стран. Правильная оценка тяжести и места лечения больного имеет решающее значение в исходе заболевания.

Цель. Оценить прогностическую значимости шкал CURB-65 и CRB-65 с их модификацией в определении риска смерти у госпитализированных больных с ВП.

Материалы и методы. В ретроспективное исследование включили 1 412 пациентов с ВП старше 18 лет. На популяции 1 020 больных, с последующим разделением на тестовую (n = 676) и обучающую (n = 344) выборки 2 : 1, выполнено сравнение прогностической ценности шкал CURB-65 (спутанность сознания, мочевина > 7 ммоль/л, частота дыхания ≥ 30/мин, низкое артериальное давление (АД) и возраст ≥ 65 лет) и CRB-65 (исключена мочевина) в идентификации пациентов с высоким риском госпитальной смерти. Проведена модификация указанных шкал с изменением точек разделения по каждому из критериев для повышения их точности. Для сравнения использовался анализ ROC-кривых с вычислением AUC (площади под кривой).

Результаты. Модифицированная шкала CURB-65 с новыми точками разделения (возраст > 72 лет, частота дыхания > 21/мин, уровень мочевины > 9,5 ммоль/л, систолическое АД ≤ 105 мм рт. ст. и диастолическое АД ≤ 65 мм рт. ст.) оказалась точнее исходной в прогнозировании смерти и названа CURB-72. Для CURB-72 и CURB-65 AUC составила 0,946 (95%-й доверительный интервал (95% ДИ) 0,916–0,967) и 0,905 (95% ДИ 0,869–0,934) соответственно (p = 0,0034). Измененная модель CRB-65 (CRB-72) также превзошла исходную, но статистически значимо они не различались. При сравнении модифицированных шкал между собой новая шкала CURB-72 продемонстрировала максимальную точность в выявлении пациентов с ВП с риском госпитальной летальности, превзойдя CRB-72 (p = 0,0347).

Заключение. Модифицированные CURB-65 (CURB-72) и CRB-65 (CRB-72) демонстрируют потенциал в оценке прогноза ВП и превосходят классические шкалы, при этом CURB-72 демонстрирует наибольшую чувствительность и специфичность.

Ключевые слова: внебольничная пневмония, CRB-65, CURB-65, смерть, прогноз, пневмония, шкалы

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии финансирования при проведении исследования.

Соответствие принципам этики. Все пациенты подписали информированное согласие на участие в исследовании и обработку персональных данных. Исследование одобрено этическим комитетом СибГМУ (заключение № 5789 от 26.02.2018).

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INTRODUCTION

Community-acquired pneumonia (CAP) remains one of the main causes of high morbidity, mortality, and high costs for healthcare systems in different countries [1, 2]. According to the 2016 Global Burden of Disease Study, more than 336 million episodes of lower respiratory tract infections (LRTIs) were reported worldwide, corresponding to 65.9 million hospitalizations and 2,377,697 deaths [3]. Despite modern advances in medicine, a deep understanding of the etiology and pathogenesis of the disease, and possibilities of antibacterial therapy, according to the World Health Organization, LRTIs ranked fourth among all causes of death in 2019 [4].

One of the key stages for a favorable outcome in CAP is an initial assessment of the severity and prognosis of the disease, allowing the doctor to determine the level of care, the volume of necessary research, and the intensity of therapy.

There are a number of systems for assessing the prognosis of CAP in the world. The most popular among them are the Pneumonia Severity Index (PSI) [5] and the CURB-65 score (confusion; urea > 7 mmol / l; respiratory rate ≥ 30 / min; systolic blood pressure (SBP) (< 90 mm Hg) or diastolic blood pressure (DBP) (< 60 mm Hg); and age ≥ 65 years) [6].

Both scoring systems were developed to facilitate decisions on the level of care based on the risk of a poor outcome in CAP. At the same time, PSI consists of 20 variables, including such laboratory tests as blood pH, which, in some cases, complicates its practical application. This scoring system classifies patients into five risk classes depending on the severity of the disease (based on the score) and assumes outpatient treatment for patients of risk classes I–II, short-term hospitalization for patients of risk class III, and full hospitalization for risk classes IV and V (with a high probability of resuscitation and intensive care (ICU) for the latter).

The CURB-65 score classifies patients into low-, intermediate-, and high-risk groups based on only five parameters, each of which is attributed one point. Patients with score 0–1 should be treated as outpatients, with score 2 are indicated short-term hospitalization, with score 3–5 – hospitalization with a high probability of transfer to the intensive care unit (ICU) with the maximum score [6]. The CRB-65 score, a simplified version of the CURB-65, does not include blood urea assessment and can be determined in just a few minutes at any stage of care. In this case, low-risk group is assigned to patients with score 0, intermediate-risk group – to patients with score 1–2, and high-risk group – to patients with score 3 and 4 [6].

There is no doubt that emergency room doctors with high work intensity and patient flow do not always resort to predictive models to make decisions on where to treat a patient. So, according to S.A. Rachina et al. (2016), doctors in Russian hospitals use both scores in routine practice only in isolated cases [7]. Foreign colleagues also come to disappointing conclusions. So, in the study by D.J. Serisier et al. (2013) involving practicing doctors, only 11.8% of pulmonologists and 21% of emergency room doctors were able to correctly determine severity classes on the PSI score. 20.4% of pulmonologists and 15% of emergency room doctors were able to perform the CURB-65 assessment successfully [8]. Thus, it is obvious that more complex scores, which include many parameters for assessment, are more likely to remain unclaimed in real clinical practice.

The aim of this study was to assess the prognostic value of the CURB-65 and CRB-65 scoring systems in hospitalized patients with CAP in determining the risk of an unfavorable outcome of the disease, followed by modification of these scoring systems to improve their accuracy.

MATERIALS AND METHODS

A retrospective study using a continuous sampling method included data obtained from 1,412 patients aged 18 years and older, hospitalized in emergency hospitals in Tomsk with a diagnosis of CAP in 2017. The study did not include patients with nosocomial pneumonia, pulmonary tuberculosis, malignant tumors of the lungs, and radiologically confirmed septic pneumonia. All patients signed an informed consent to participate in the study and for personal data processing. The study was approved by the Ethics Committee at Siberian State Medical University (Protocol No. 5789 of 26.02.2018).

Within this study, we assessed > 200 parameters, including features of the CAP development, data on the socio-demographic status, complaints, medical history, objective status, results of laboratory and instrumental studies, information about treatment at the pre-hospital and in-hospital stages, and information about the course of the disease during hospitalization and outcomes. The article provides a comparative assessment of the prognostic value of the CURB-65 and CRB-65 scores in identifying patients with an increased risk of in-hospital death. Modification of these scoring systems was also carried out with

changes in the cut-off value for each of the criteria to increase their accuracy. To evaluate parameters for each of the scoring systems, we included physical examination data, blood urea level (for CURB-65), and age determined at the time of patient admission to the emergency room.

The analysis of the obtained data was carried out using the statistical software package MedCalc, version 18.9.1. Quantitative variables were presented as the median and the interquartile range *Me* (Q_{25}; Q_{75}), qualitative variables – as absolute and relative frequencies *n* (%). To analyze the prognostic value of the CURB-65 and CRB-65 scores, the ROC analysis was used with calculating the area under the curve (AUC) and 95% confidence interval (CI) for AUC, determining the cut-off value using the Youden index and sensitivity and specificity for this point, as well as establishing the statistical significance of differences between AUCs for scoring systems and their modifications. The results were considered statistically significant at $p < 0.05$.

RESULTS

The study analyzed data obtained from 1,412 people (790 men (55.9%) and 622 women (44.1%)). The age of the patients was 61 (40; 76) years (from 18 to 103 years). In-hospital mortality was registered for 128 (9.1%) patients. A comparative assessment of the CURB-65 and CRB-65 scoring systems was carried out on the population of 1,020 patients with CAP.

The risk of death increased directly with an increase in scores for each scoring system (Table 1).

Table 1

Relationship between the number of unfavorable factors (score) and the risk of in-hospital death, *n* = 1,020

	Score	Discharged, *n* (%)	Died, *n* (%)
CURB-65	0	137 (100)	0 (0)
	1	98 (97.0)	3 (3)
	2	64 (87.7)	9 (12.3)
	3	13 (56.5)	10 (43.5)
	4	2 (25.0)	6 (75.0)
	5	0 (0)	2 (100)
CRB-65	0	170 (99.4)	1 (0.6)
	1	121 (93.8)	8 (6.2)
	2	21 (65.6)	11 (34.8)
	3	1 (11.1)	8 (88.9)
	4	1 (33.3)	2 (64.7)

Next, the general sample (*n* = 1,020) was split into test (*n* = 676) and training (*n* = 344) subsets in the ratio 2:1. No statistically significant differences were observed between them.

To compare the predictive value of the scoring systems, ROC curves were constructed for the general sample (Fig. 1) and for the test sample (Fig. 2). In both cases, AUC for the CURB-65 score was greater than for the CRB-65 score and was 0.870 (95% CI: 0.848–0.890) for CURB-65 and 0.839 (95% CI: 0.815–0.861) for CRB-65 ($p = 0$ .0036) in the general sample, and 0.905 (95% CI: 0.869–0.934) and 0.889 (95% CI: 0.851–0.920) in the test sample, respectively ($p = 0.3692$). In the test sample, the differences between the curves were subtle and not significant.

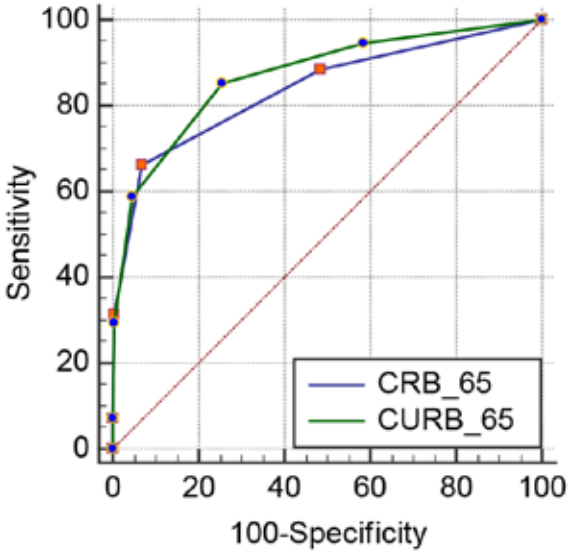

Fig. 1. Comparison of the ROC curves for the CURB-65 and CRB-65 scores in the general sample

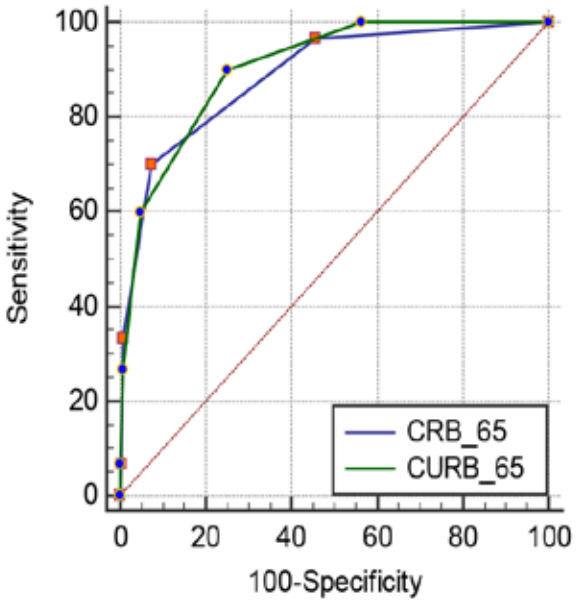

Fig. 2. Comparison of the ROC curves for the CURB-65 and CRB-65 scores in the test sample

The study hypothesized that modification of the scoring systems would increase their diagnostic value. To test this hypothesis on the test subset, the ROC analysis was performed for each of the factors, searching for the most accurate cut-offs. As a result, new cut-off values for each parameter were obtained in the study population (Table 2).

Table 2

Cut-off values in the classical and modified CURB-65 and CRB-65 scoring systems

Parameter	Classical CURB-65/ CRB-65 scores	Modified s CURB-72*/ CRB-72* scores
Age, years	> 65	> 72
Cognitive impairment	Yes	Yes
Blood urea, mmol / l	> 7	> 9.5
Respiratory rate, min	> 30	> 21
Systolic blood pressure, mm Hg	< 90	< 105
Diastolic blood pressure, mm Hg	< 60	< 65

*due to the new cut-off value based on age > 72 years, the modified scores were given the names CURB-72 and CRB-72.

ROC curves were constructed for each of the modified scoring systems in the test sample and compared with the ROC curves constructed for the classical scores (Fig. 3, 4)

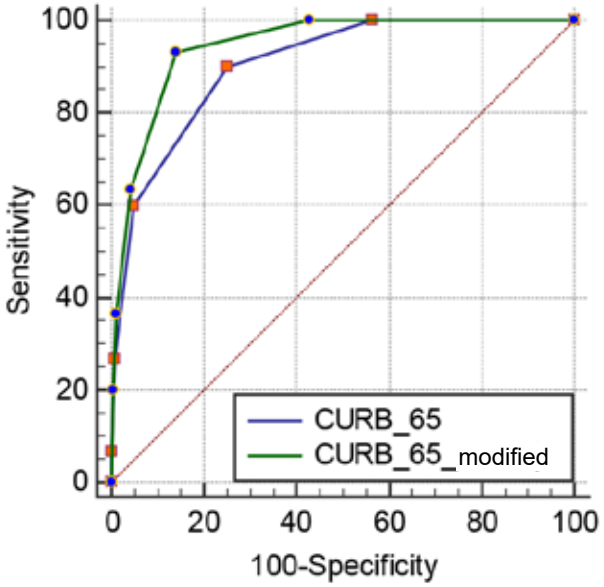

Fig. 3. Comparison of the ROC curves for the CURB-65 and modified CURB-65 (CURB-72) scores

AUC for the modified CURB-72 score surpassed the one for the classical CURB-65 model and was 0.946 (95% CI: 0.916–0.967) and 0.905 (95% CI: 0.869–0.934), respectively (p = 0.0034). When CRB-65 was modified to CRB-72, AUC increased from 0.889 (95% CI: 0.851–0.920) to 0.910 (95% CI: 0.874–0.938) but was not significantly different (p = 0.0724).

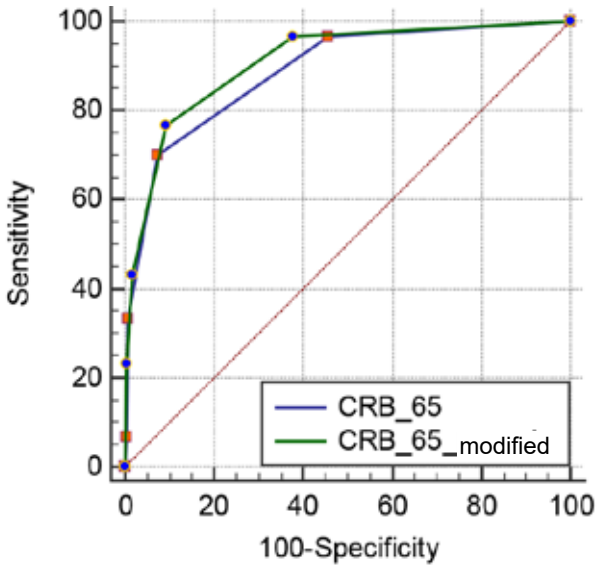

Fig. 4. Comparison of the ROC curves for the CRB-65 and modified CRB-65 (CURB-72) scores

The new CURB-72 score demonstrated maximum accuracy in identifying patients with CAP at risk of in-hospital mortality, surpassing CRB-72 (p = 0.0347) (Fig. 5).

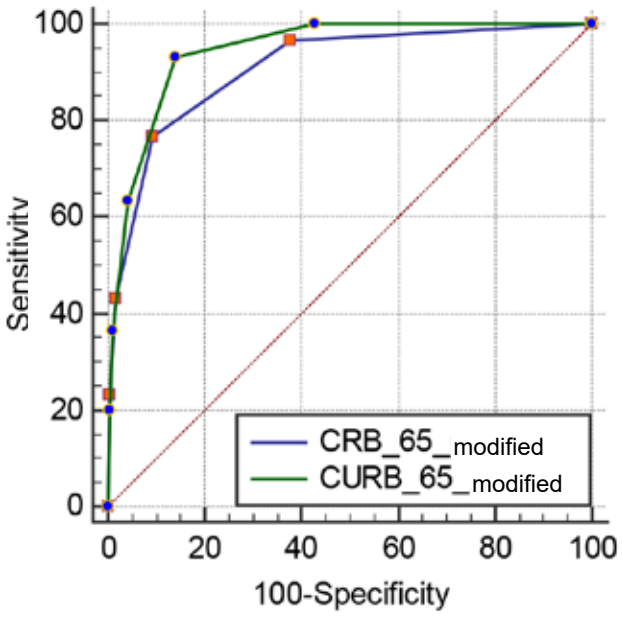

Fig. 5. ROC curves comparing the modified CURB-65 (CURB-72) and CRB-65 (CRB-72) scores

The cut-off value for both scoring systems (both modified and classical) was > 1 point. As a result, the modified CURB-65 score (CURB-72) with the

modified cut-off values showed the highest sensitivity and specificity (Table 3), which allowed for the most accurate identification of not only patients at high risk of death, but also patients with a favorable prognosis of the disease. Implementation of the proposed modified scoring system in routine clinical practice can reduce the burden on hospitals by redistributing low-risk patients to outpatient treatment.

Table 3

Characteristics of the ROC curves for the classical and modified CRB-65 and CURB-65 scores

Score	AUC, 95% CI	Sensitivity	Specificity
CRB-65	0.889 (0.851–0.920)	70.00	92.68
CURB-65	0.905 (0.869–0.934)	90.00	74.84
Modified scores			
CRB-72	0.910 (0.874–0.938)	76.67	90.76
CURB-72	0.946 (0.916–0.967)	93.33	85.99

DISCUSSION

W.S. Lim et al. (2003) developed and validated the CURB-65 and CRB-65 scoring systems for predicting 30-day mortality in patients with CAP. In the study population (n = 1,068), 9% of patients died [6].

The present study assessed outcomes only during hospitalization, which lasted 11 (9; 13.6) days, and did not track the health status of discharged individuals (n = 1,412). Among the patients included in the study, 9.1% died.

In the general sample in the present study, the mortality rate in patients with the CURB-65 score of ≥ 2 was slightly higher than in the study by W.S. Lim et al. [6]. Scientists demonstrated that among CAP patients with the CURB-65 score of 2, death occurred in 9.2% of cases (intermediate risk of death), with the score of ≥ 3 – in 22% (high risk of death). In our work, in patients with the score of 2, mortality was 12.3%, with the score of 3 – 43.5%. There were only two patients with the score of 5, and both of them died (Table 1).

In addition, W.S. Lim et al. concluded that low-risk patients (CURB-65 score of < 2 and CRB-65 score of < 1) can be provided with outpatient care. At the same time, according to our data, among patients with the CURB-65 score of 1, three (3%) died, and in the group with the CRB-65 score of 0, death was registered in one case, and, according to the decision-making strategy, these patients had to be treated in the outpatient setting [6]. Our results suggest that the predictive ability of the CURB-65 and CRB-65 scoring systems is not perfect. The opinions of other scientists on the significance of these scoring systems in identifying patients with mild CAP are ambiguous, and a number of studies question their accuracy [9, 10].

Thus, according to A. Ilg et al. (2019), among patients with the CURB-65 scores of 0 and 1, 15.6% were hospitalized in the intensive care unit, and 0.6% died [10]. At the same time, according to the meta-analysis by M.H. Ebell et al. (2019), the authors concluded that the CRB-65 score is effective in identifying patients at low risk of death and demonstrated that when this scoring system is applied to stratify patients, the risk of outpatient mortality in this group of patients is no more than 0.5% [11].

In the study, we came to the conclusion that the cut-off value for both scoring systems is > 1, and if at least one criterion in both the CURB-65 and CRB-65 scores is identified, the patient undoubtedly requires hospitalization. When comparing the CURB-65 and CRB-65 scores with each other, the former outperformed the latter in the general sample, but in the test sample, no differences were found.

The question of the significance of urea in the CURB-65 score remains open. According to various researchers, the CURB-65 and CRB-65 models demonstrate comparable value [12, 13]. So, in the meta-analysis by J.D. Chalmers et al. (2010), it was concluded that there are no significant differences between the scores in predicting death from CAP [14].

The present study demonstrated the maximum accuracy of the modified scales (CURB-72 and CRB-72) at higher blood pressure values and lower respiratory rates, which could result in an underestimated risk of death in classical scoring systems. In general, while the importance of assessing respiratory rate (as a sign of respiratory failure) is beyond doubt, the role of hypotension is the subject of debates and has been questioned by some scientists. So, H.Y. Li et al. (2015) demonstrated that CURB-65 can be simplified by excluding low blood pressure, which improves the prediction of mortality in patients with CAP [15]

In the population we studied, a decrease in SBP to a level of < 90 mm Hg was detected only in 34 (26.6%) of deceased patients. In turn, a decrease in DBP to a value of < 60 mm Hg was registered in 38 (29.7%) of the deceased. In addition, only 36 patients had a respiratory rate ≥ 30 / min. Moreover, out of 128 deceased patients, this criterion was identified only in 22 cases (17.2%). The data obtained were comparable to the results in the work by Q. Guo et al. (2023), where respiratory rate ≥ 22 / min and SBP ≤ 100 mm

Hg demonstrated higher odds ratio and greater reliability than generally accepted parameters of classical scoring systems (AUC 0.823 versus 0.519; 0.688 versus 0.622, respectively) [16].

Thus, respiratory rate ≥ 21 / min, SBP ≤ 105 mm Hg, and DBP ≤ 65 are more suitable for predicting mortality, as evidenced by significant improvements in AUC values for both scores. For urea, we concluded that the most accurate cut-off values should be higher than in the classical scores and amount to 9.5 mmol / l instead of 7 mmol / l.

The modified CURB-65 (CURB-72) score exhibited not only higher sensitivity in determining the risk of death, but also higher specificity, which allows to more accurately identify low-risk patients who can be treated in the outpatient setting, thus reducing the burden on hospitals. According to our data, the cut-off value for both modified scoring systems was > 1. That is, patients with the score of 1 or more should be hospitalized.

CONCLUSION

Given the high mortality associated with CAP, search for new ways to assess the risk of in-hospital death remains an important goal in modern science. The study proposed a new methodological approach to improve the predictive value of the CURB-65 and CRB-65 scores. We obtained results indicating that the modified CURB-65 (CURB-72) and CRB-65 (CRB-72) scores demonstrate potential in assessing the prognosis of CAP and surpass the classical scoring systems. At the same time, the CURB-72 score has maximum sensitivity and specificity. Further prospective studies with larger cohorts in different populations and settings are required.

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Authors' contribution

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