

The Predictive Value of CURB-65 and Pneumonia Severity Index in Patient with COVID-19 Pneumonia and Correlation with Laboratory Parameters

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Abstract

Objective: Coronavirus disease-2019 (COVID-19) pneumonia is a disease with a high mortality rate caused by the severe acute respiratory syndrome-coronavirus-2 virus. Therefore, it is essential to identify patients at risk for mortality. This study aims to determine the ability of pneumonia scores to predict mortality and correlation with laboratory parameters.

Materials and Methods: A total of 312 pneumonia patients with positive polymerase chain reaction results were included in this single-center retrospective study conducted between 10.03.2020 and 10.06.2020. All data obtained from the hospital database, confusion, urea, respiratory, blood pressure, 65 or older (CURB-65) and Pneumonia Severity Index (PSI), scores were calculated. Receiver operator characteristics (ROC) curve analysis was performed for the prognostic value.

Results: The demographic data followed as; 175 (56.1%) of 312 patients were male and 137 (43.9%) were female; mean age was 58.2±16.1 years. The mortality rate was 16% (n=50). The length of hospital stay was 10.6±6.4 day. CURB-65, PSI, and PSI risk class was found to be higher in cases that resulted in mortality compared to those without mortality (p<0.001). CURB-65, PSI, PSI risk classification were positively correlated with, D-dimer, ferritin, and neutrophil lymphocyte ratio. The area under the ROC curve was 0.851 [95% confidence interval (CI): 0.803-0.899] for PSI, 0.833 (95% CI: 0.779-0.888) for PSI risk class score and 0.795 (95% CI: 0.725-0.865) for CURB-65. In determining mortality; optimal cut-off values were ≥1 for CURB-65 (sensitivity 86.0% specificity 61.1%), ≥6.5 for PSI (sensitivity 82%, specificity 70.6%), and ≥4 for PSI risk classification (sensitivity 76.0%, specificity 72.9%).

Conclusion: CURB-65, PSI, and PSI risk classifications were found eligible for use in COVID-19 and combining these scores with laboratory parameters can be useful to determine the prognosis.

Keywords: CURB-65, ferritin, D-dimer, NLR, COVID-19 pneumonia, PSI

Introduction

Coronavirus disease-2019 (COVID-19) is an infectious respiratory disease caused by the severe acute respiratory syndrome-coronavirus-2. It was first discovered in 2019 in Wuhan, China, and has since spread worldwide, leading to the 2019-2020 coronavirus pandemic [1]. Since the pandemic began, there have been approximately 400 million cases of COVID-19 and more than 5 million deaths worldwide [2]. The clinical manifestations of the disease range from asymptomatic to acute respiratory failure. The symptoms are dry cough, fever,

chills, malaise, myalgia, pleuritic chest pain and shortness of breath [3]. The mortality of the disease is associated with older age and comorbidities [4-6].

It is important for healthcare providers to diagnose COVID-19 pneumonia, identify patients with a high risk of mortality and to decide whether to treat patients as outpatients or inpatients under pandemic conditions. In particular, some objective criteria have been defined to help the physician decide on hospitalization. Many treatment guidelines, updated recently, recommend confusion, urea, respiratory, blood pressure, 65 or



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older (CURB-65) and Pneumonia Severity Index (PSI) scoring in this regard [7]. CURB-65 was defined by the British Thoracic Society in 2002 and is useful in classifying patients at high risk of mortality. Variables of CURB-65 are confusion, blood urea nitrogen, systolic blood pressure, respiratory rate, and age. Patients with a score of 3 and above have high mortality rates. Due to the small number of variables, it can be easily used in emergency and primary care, as it allows us to quickly predict the requirements and duration of hospitalization, discharge, or intensive care hospitalization of the patients [8,9]. PSI has 19 parameters and classifies patients into 5 different groups in terms of risk factors. The primary purpose of this score is more closely related to the question of which patients should be hospitalized rather than mortality. The main parameters in this scoring are; age, comorbidity, and abnormalities in vital signs. Additionally, laboratory tests, blood gas, chest X-ray are also needed for PSI. PSI class of I-III was reported to represent a low risk of death. Patients who had a PSI class of \geq IV were defined as being at a high risk of death [10]. Details of these scores are in the Supplemental File.

In addition to these scoring systems, some laboratory parameters are considered to be associated with mortality. These are D-dimer, ferritin, neutrophil lymphocyte ratio (NLR) and lactate [11-13]. Tools for predicting mortality in patients with COVID-19 pneumonia still remain unclear. This study aims to determine the prognostic values of CURB-65, PSI scores and laboratory parameters in patients hospitalized for COVID-19 pneumonia.

Materials and Methods

Patients

This single-centered and retrospective study was conducted out between 10.03.2020-10.06.2020 at Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency, which is a pandemic hospital. Patients who were admitted to the emergency department with positive COVID-19 real time-polymerase chain reaction (RT-PCR) test, clinical and radiological pneumonia findings were included in the study. All pneumonia patients with RT-PCR positive hospitalized. A total of 312 patients with complete data were enrolled in the study.

Data Collection and Processing

During the study period, age, gender, date of admission to the clinic of emergency, hospitalization (service or intensive care unit), Glasgow Coma scale at the time of admission, comorbidities, laboratory findings (NLR, D-dimer, ferritin, lactate), vital signs, COVID-19 PCR results, radiological imaging and mortality status was obtained from the hospital database system. CURB-65 and PSI scores were calculated, and the results were recorded in the study form. Details of the scores are shown in the Supplemental File.

Ethical Approval

This study was approved by the Local Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital and was conducted in accordance with the Helsinki Declaration (decision no: 1527, date: 02.06.2020).

Statistical Analysis

For statistical analyses, the SPSS 22.0 Windows program was used. Number and percentage were used as categorical variables. Mean, standard deviation, minimum, maximum and median were used as numerical variables. Rates in independent groups were compared with the chi-square test. Since the numerical variables did not meet the normal distribution, comparisons of two independent groups were performed using the Mann-Whitney U test. Relations between numerical variables were performed with Spearman correlation analysis since parametric test condition was not met. Cut-off analysis were performed using receiver operating characteristic (ROC) curve analysis. The statistical alpha significance level was accepted as $p < 0.05$.

Results

A total of 312 patients participated in the study and 175 (56.1%) of the patients were male, 137 (43.9%) were female. While 185 (59.3%) patients did not have any comorbidities, 127 (40.7%) patients had various comorbidities. The most common comorbidity was hypertension 72 (23.1%). Demographic characteristics of the patients, laboratory results, CURB-65, PSI scores and clinical outcomes are shown in Table 1.

A positive correlation was found between CURB-65, PSI score, PSI risk classification, and age, D-dimer, ferritin, NLR, and hospitalization time. CURB-65, PSI score was found to be negatively correlated with the day of mortality Table 2. CURB-65, PSI score, PSI risk classification level were statistically significantly higher in those with comorbidity than in those without comorbidity (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$). CURB-65, PSI score, PSI risk classification level was higher in those with hypertension (HT) than in those without HT (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$). Likewise, CURB-65, PSI score, and PSI risk classification level was higher in patients with coronary artery disease (CAD) compared with those without CAD (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$). In those with diabetes mellitus (DM) and congestive heart failure (CHF), the PSI score and PSI risk classification level were higher than those without DM and CHF. In terms of mortality, there was a statistical difference between the CURB-65, PSI, PSI risk classes of patients with and without mortality (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$) Table 3.

ROC analysis of CURB-65, PSI, and PSI classifications is shown in Figure 1. Area under the curve (AUC) was 0.795 [95% confidence interval (CI): 0.725-0.865], 0.851 (95% CI: 0.803-0.899), 0.833 (95% CI: 0.779-0.888), respectively.

Youden's index was used to determine the optimal cut-off point in determining mortality. Accordingly, CURB-65 ≥ 1 has 86.0% sensitivity, 61.1% specificity, PSI score ≥ 86.5 has 82.0%

sensitivity, 70.6% specificity, PSI risk classification ≥ 4 has 76.0% sensitivity, 72% specificity Table 4.

Table 1. Demographic, clinical and laboratory characteristics			
Age mean \pm SD (min-max)		58.2 \pm 16.1 (22-97)	
Sex n (%)	Male	175 (56.1)	
	Female	137 (43.9)	
Comorbidities n (%)	No	185 (59.3)	
	Yes	127 (40.7)	
	DM	50 (16.0)	
	HT	72 (23.1)	
	CAD	27 (8.7)	
	COPD	21 (6.7)	
		CKD	18 (5.8)
		CHF	6 (1.9)
		CvD	4 (1.3)
		Malignancy	4 (1.3)
		Others	34 (10.9)
CURB-65 mean \pm SD (min-max)		0.79 \pm 1.01 (0-5)	
PSI score mean \pm SD (min-max)		79.6 \pm 39.9 (16-204)	
PSI risk class mean \pm SD (min-max)		2.65 \pm 1.44 (1-5)	
PSI risk class n (%)	1	101 (32.4)	
	2	55 (17.6)	
	3	47 (15.1)	
	4	70 (22.4)	
	5	39 (12.5)	
D-dimer mean \pm SD (min-max)		955.4 \pm 1.779.7 (2.2-21.200)	
Ferritin mean \pm SD (min-max)		329.9 \pm 475.7 (4-5.032)	
Lactate mean \pm SD (min-max)		1.97 \pm 5.35 (0.62-93)	
NLR mean \pm SD (min-max)		4.71 \pm 4.77 (0.55-32.64)	
Mortality n (%)	No	262 (84.0)	
	Yes	50 (16.0)	

Results are expressed as count (%) for categorical variables and as mean (standard deviation minimum-maximum) for quantitative variables. DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CKD: Chronic kidney disease, CHF: Congestive heart failure, CvD: Cerebrovascular disease, NLR: Neutrophil lymphocyte ratio, PSI: Pneumonia Severity Index, COPD: Chronic obstructive pulmonary disease, SD: Sstandard deviation, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older

Table 2. Correlation of CURB-65, PSI score and PSI risk class with age, D-dimer, ferritin, NLR, lactate, hospital stay and mortality in patients with COVID-19 pneumonia						
	CURB-65		PSI score		PSI risk class	
	r	p	r	p	r	p
Age	0.710	<0.001	0.793	<0.001	0.687	<0.001
D-dimer	0.410	<0.001	0.430	<0.001	0.419	<0.001
Ferritin	0.317	<0.001	0.376	<0.001	0.324	<0.001
Lactate	0.071	0.218	0.103	0.075	0.101	0.082
NLR	0.322	<0.001	0.333	<0.001	0.310	<0.001
Hospital stay	0.221	0.001	0.295	<0.001	0.269	<0.001
Mortality day	-0.464	0.004	-0.333	0.044	-0.298	0.073

NLR: Neutrophil lymphocyte ratio, PSI: Pneumonia Severity Index, COVID-19: Coronavirus disease-2019, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older

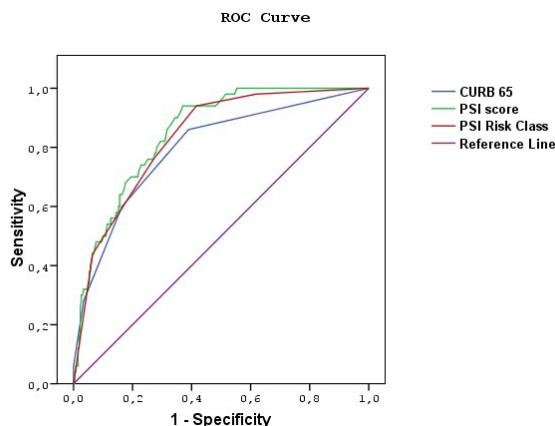


Figure 1. ROC analysis of CURB-65, PSI and PSI risk class
 ROC: Receiver operator characteristics, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, PSI: Pneumonia Severity Index

Discussion

This infection, which affects the whole world, causes many deaths as well as many economic, social and psychological effects. Therefore, it is important to determine the course of the infection well managing for the disease. The analysis of demographic, epidemiological and clinical data is important to develop right strategies against COVID-19.

Table 4. Prognostic accuracy of CURB-65, PSI, PSI risk class with optimal cut-off values

	Sensitivity	Specificity	PPV	NPV
CURB-65 ≥ 1	86.0%	61.1%	29.7%	95.8%
PSI score ≥ 86.5	82.0%	70.6%	34.7%	95.4%
PSI risk class ≥ 4	76.0%	72.9%	34.9%	94.%

CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, PSI: Pneumonia Severity Index, PPV: Positive predictive value, NPV: Negative predictive value

Table 3. Relationship between comorbidities and scores

Comorbidity	Minimum Mean \pm SD (min-max)	Maximum Mean \pm SD (min-max)	p
CURB-65	0.65 \pm 0.98 (0-5)	0.98 \pm 1.02 (0-4)	0.001
PSI	70.0 \pm 38.1 (16-194)	93.5 \pm 38.4 (22-204)	<0.001
PSI risk class	2.3 \pm 1.4 (1-5)	3.2 \pm 1.3 (1-5)	<0.001
DM			
CURB-65	0.76 \pm 1.04 (0-5)	0.90 \pm 0.84 (0-3)	0.078
PSI	76.8 \pm 40.1 (16-204)	94.3 \pm 35.2 (42-188)	0.001
PSI risk class	2.5 \pm 1.5 (1-5)	3.3 \pm 1.1 (1-5)	<0.001
HT			
CURB-65	0.69 \pm 1.00 (0-5)	1.11 \pm 0.97 (0-3)	<0.001
PSI	73.3 \pm 38.8 (16-194)	100.6 \pm 36.0 (40-204)	<0.001
PSI risk class	2.4 \pm 1.4 (1-5)	3.5 \pm 1.1 (2-5)	<0.001
CAD			
CURB-65	0.73 \pm 0.99 (0-5)	1.37 \pm 1.01 (0-3)	<0.001
PSI	76.5 \pm 38.8 (16-204)	112.2 \pm 37.1 (57-188)	<0.001
PSI risk class	2.5 \pm 1.4 (1-5)	3.9 \pm 0.9 (2-5)	<0.001
COPD			
CURB-65	0.80 \pm 1.01 (0-5)	0.62 \pm 0.97 (0-3)	0.389
PSI	79.6 \pm 39.9 (16-204)	79.1 \pm 40.8 (22-165)	0.899
PSI risk class	2.6 \pm 1.4 (1-5)	2.8 \pm 1.4 (1-5)	0.654
CHF			
CURB-65	0.78 \pm 1.01 (0-5)	0.83 \pm 0.75 (0-2)	0.602
PSI	79.1 \pm 40.0 (16-204)	105.3 \pm 24.5 (66-132)	0.047
PSI risk class	2.6 \pm 1.4 (1-5)	3.8 \pm 1.0 (2-5)	0.040
Mortality			
CURB-65	0.59 \pm 0.84 (0-3)	1.82 \pm 1.17 (0-2)	<0.001
PSI	71.4 \pm 35.1 (16-204)	122.7 \pm 35.7 (60-194)	<0.001
PSI risk class	2.4 \pm 1.3 (1-5)	4.1 \pm 1.0 (1-5)	<0.001

Results are expressed as mean (standard deviation minimum-maximum) for quantitative variables.
 DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, PSI: Pneumonia Severity Index, SD: Standard deviation, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older

The mean age and gender distribution of the patients participating in the study are similar those the studies in the literature [14,15]. As it is known, studies have shown that additional diseases such as HT, DM, CAD and older age are risk factors for mortality in COVID-19 pneumonia. In our study, mortality rates were found to be higher, especially in patients with HT and DM [16]. The Chinese Center for Disease Control and Prevention reported that the overall mortality rate was 2.3% in 44,672 cases. When only severe and critical illness groups were included in the evaluation, the mortality rate was 12.4% [17]. In our study mortality rate was 16%. The reason for this high rate is that our study was conducted in a tertiary hospital. Sharifpour et al. [18] showed that elevated C-reactive protein and procalcitonin are potential predictors of COVID-19 disease severity. There are also studies showing that high D-dimer levels, high ferritin levels, lymphopenia and hypoalbuminemia are risk factors for the severe COVID-19 disease and mortality [19,20]. Liu et al. [21] showed that NLR is an independent risk factor for determining the severity of the disease and mortality in hospitalized patients, and its height is effective in predicting critical illness. In our study, there was a significant positive correlation with laboratory parameters (D-dimer, ferritin, and NLR) and CURB-65, PSI score, PSI risk classification ($p < 0.001$, in all). The use of scoring systems together with these parameters may be effective in demonstrating the severity of COVID-19.

Bradley et al. [22] showed that the CURB-65 score was not a guide for discharge, but patients with a high CURB-65 score were at risk of mortality. PSI is also a well-known scoring system for assessing the severity of community-acquired pneumonia, and its efficacy has also been confirmed in viral pneumonia and there is a significant association between PSI and mortality [23,24]. Satici et al. [25] showed that the PSI score was a better predictor than CURB-65 with a higher AUC. In the same study, the optimal cut-off value is ≥ 2 for CURB-65, while it is ≥ 4 for PSI. Likewise, in our study, the PSI score was found to be better than CURB-65 with an AUC of 0.851 (95% CI: 0.803-0.899). In the study by Fan et al. [24], the optimal cut-off value for CURB-65 was found to be ≥ 1 , the optimal cut-off for PSI risk class was ≥ 3 and the sensitivity of the PSI score was found to be higher than CURB-65. In our study, it was determined as the optimal cut-off for PSI risk classification ≥ 4 for mortality. On the other hand, CURB-65 ≥ 1 was found to be a good predictor with 86% sensitivity. Although there are differences between the scores, both scores appear to be good predictors, especially in identifying high-risk patients in terms of mortality.

Study Limitations

The main limitations were the study was; single-centered and retrospective, the sample size was limited, the scores and laboratory parameters were calculated only at the admission,

repeated measurements of patients during follow-up were not calculated.

Conclusion

In conclusion, addition to older age and comorbidities in COVID-19 patients, D-dimer, ferritin and NLR that can be used to predict the severity of the COVID-19 pneumonia. Additionally, it has been demonstrated that high CURB-65, PSI score, and PSI risk classification values are useful for determining the severity of the disease and mortality at the admission. It is thought that the creation of new scoring systems by adding biomarkers may better guide clinicians.

Ethics

Ethics Committee Approval: This study was approved by the Local Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital and was conducted in accordance with the Helsinki Declaration (decision no: 1527, date: 02.06.2020).

Informed Consent: Prospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.A., E.A., Design: H.A., E.A., Data Collection or Processing: H.A., Y.E.A., Analysis or Interpretation: H.A., Y.E.A., Literature Search: E.A., Writing: H.A., Y.E.A.

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Supplemental File. CURB-65	
Parameters	Score
Confusion	1
BUN >20 mg/dL (7 mmol/L) or urea > 42.8 mg/dL	1
Respiratory rate ≥30/min	1
Systolic blood pressure <90 mm/Hg or diastolic blood pressure <60 mm/Hg	1
Age ≥65 year	1

CURB-65 score [8]. CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, BUN: Blood urea nitrogen

Pneumonia severity index	
Demographic factors	Point
Age- male	Age in years
Age- female	Age in years-10
Nursing home resident	10
Comorbidities	
Neoplastic disease	30
Liver disease	20
CHF	10
Cerebrovascular disease	10
Renal disease	10
Physical examination findings	
Altered mental status	20
Respiratory rate ≥30/min	20
Systolic blood pressure <90 mmHg	20
Temperature <35 °C or ≥40 °C	15
Heart rate ≥125/min	10
Laboratory and radiological findings	
Arterial pH <7.35	30
BUN ≥30 mg/dL	20
Sodium <130 mEq/L	20
Glucose >250 mg/dL	10
Hematocrit <%30	10
PaO2 <60 mm/Hg or SaO2 <%90	10
Pleural Effusion	10

CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, BUN: Blood urea nitrogen

PSI risk classification	
Class	Point
1	<50 years no comorbidity
2	<70
3	71-90
4	91-130
5	>130

PSI and PSI risk classification [9,10]. PSI: Pneumonia Severity Index

Optimal cut-off points of scores			
Test	Results	Sensitivity	Specificity
CURB-65	-1.0	1.000	0.000
	0.5	0.860	0.611
	1.5	0.600	0.836
	2.5	0.280	0.966
	3.5	0.060	1.000
	4.5	0.020	1.000
	6.0	0.000	1.000
PSI score	81.5	0.880	0.668
	82.5	0.860	0.683
	83.5	0.840	0.687
	84.5	0.820	0.691
	85.5	0.820	0.695
	86.5	0.820	0.706
	87.5	0.800	0.718
	88.5	0.780	0.721
	89.5	0.780	0.725
	90.5	0.760	0.729
	92.0	0.760	0.740
	93.5	0.760	0.748
	94.5	0.740	0.760
95.5	0.740	0.763	
96.5	0.740	0.771	
97.5	0.720	0.779	
PSI risk class	0.0	1.000	0.000
	1.5	0.980	0.382
	2.5	0.940	0.584
	3.5	0.760	0.729
	4.5	0.440	0.935
	6.0	0.000	1.000

CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, PSI: Pneumonia Severity Index