International Journal of Infectious Diseases and Therapy
2023; 8(3): 91-100
http://www.sciencepublishinggroup.com/j/ijidt
doi: 10.11648/j.ijidt.20230803.13
ISSN: 2578-9651 (Print); ISSN: 2578-966X (Online)

Novel Score for Prediction of Severity and Mortality in Hospitalized Patients with COVID-19

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To cite this article:
Skakun Oleksiy, Seredyuk Nestor. Novel Score for Prediction of Severity and Mortality in Hospitalized Patients with COVID-19. *International Journal of Infectious Diseases and Therapy*. Vol. 8, No. 3, 2023, pp. 91-100. doi: 10.11648/j.ijidt.20230803.13

Received: July 4, 2023; **Accepted**: July 18, 2023; **Published**: July 27, 2023

Abstract: Background: Despite the presence of many scores for the prediction of severity and mortality in COVID-19 patients, predictive accuracies of them are not high enough. Aim: Development of a scale for the prediction of severe condition and in-hospital mortality in hospitalized patients with COVID-19-associated pneumonia. Methods: The study included 135 adult patients hospitalized for COVID-19-associated pneumonia. Risk factors and optimal cut-off criteria for severe/critical condition and in-hospital mortality was established. Results: body mass index (BMI), scales CURB-65 and PSI, history of diabetes mellitus, SpO_2 level at admission, leukocyte count, lymphocyte percentage, levels of fasting glucose, alanine aminotransferase, ferritin, soluble IL-2 receptors, IL-6, and ferritin-hemoglobin ratio (FHR) were risk factors for disease progression to severe/critical condition. Logistic regression showed that only SpO_2, creatinine, and blood urea nitrogen were independent risk factors of severe/critical condition. Risk factors for in-hospital mortality included age, BMI, scales CURB-65 and PSI, SpO_2 level at admission, hemoglobin level, leukocyte count, levels of fasting glucose, creatinine, blood urea nitrogen, ferritin, IL-6, and FHR. However, logistic regression showed no relevant independent risk factor of in-hospital mortality. The novel score has been developed; it included the following parameters: blood pressure, BMI, ferritin level, SpO_2, creatinine level, history of arterial hypertension/ prior myocardial infarction / stroke, leukocyte count, elderly, history of diabetes mellitus (acronym "BIFOCALED"). There was good discriminative power of the novel score for severe/critical condition (AUC, 0.806, $p<0.001$) and in-hospital mortality (AUC, 0.804, $p<0.001$). The Youden index was 0.47 at the value of >2 points (sensitivity of 84.72%; specificity of 61.90%) for the prediction of severe/critical condition and 0.58 at the value of >5 points (sensitivity of 64.29%; specificity of 93.39%) for prediction of in-hospital mortality. Patients who scored >2 points had a far much higher risk of severe/critical condition (OR, 9.01; 95%CI, 3.97–20.44; $p<0.001$). In-hospital mortality was significantly higher in patients with >5 points according to the novel score (OR, 25.43; 95%CI, 6.88–93.99; $p<0.001$). Also, the probability of severe/critical condition and in-hospital mortality depending on the novel score was assessed. Conclusion: The BIFOCALED score may be used for predicting severe/critical condition and in-hospital mortality. The disease progression to severe/critical condition should be suspected in patients who scored >2 points; however, a score of >5 points is associated with high in-hospital mortality.

Keywords: COVID-19, Score, BIFOCALED, Severity, Mortality

1. Introduction

As of June 2023, WHO reported over 767 million confirmed cases of COVID-19 and almost 7 million death, globally [1]. However, the full impact of the pandemic on mortality seems to be much greater than reported deaths due to COVID-19 alone [2]. Also, the COVID-19 pandemic is related to health, social, and economic crises with an enormous impact on all spheres of human life [3].

According to the meta-analysis performed by Hu Y., the severe condition develops in 12.6–23.5% (with pooled estimates at 18.0%) of COVID-19 patients [4]. In-hospital mortality in patients with severe and critical COVID-19 is 19.4% [5].

It's important to recognize high-risk patients, as early treatment of such patients yields a favorable outcome [6-8]. There is a lot of research and meta-analysis studying risk

factors of unfavorable outcomes. Risk factors of severe condition and fatal outcomes include age [9, 10], male gender [11], smoking [12], obesity [13, 14], and comorbidities such as hypertension [15], heart failure [16], dyslipidemia [17], cyanotic heart diseases [18], dementia [19], diabetes mellitus [20], chronic kidney disease [21], liver diseases [22], cancer [23], chronic obstructive pulmonary disease [24]. Also, fever and shortness of breath are associated with the disease progression [25]. SpO_2 <95% at admission is found to be a risk factor for COVID-19 progression from non-severe to severe illness [26]. Following laboratory parameters may be used as predictors of unfavorable outcomes hemoglobin, leukocyte, lymphocyte, and platelet count, erythrocyte sedimentation rate, procalcitonin, lactate dehydrogenase, activated partial thromboplastin time, high-density lipoprotein cholesterol, D-dimer, ferritin, C-reactive protein, troponin, IL-1β, IL-2, IL-6, IL-8, TNF-α, sIL-2R, neutrophil-to-lymphocyte ratio [27-38]. Also, the ferritin-hemoglobin ratio is considered to be a predictor of fatal outcome [39]. CURB-65 and PSI scores were found to predict in-hospital mortality in COVID-19 patients [40].

Despite the presence of multiple scores, none have a good accuracy to predict 30-day in-hospital mortality alone, or the composite of 30-day in-hospital mortality or ICU admission [41]. Some scores are simple, whereas others are complex and there are somewhat difficulties in their use in real clinical practice. So, the development of novel scores with high accuracy that are easy to use in practice is important.

This study aimed to develop a scale for the prediction of severe condition and in-hospital mortality in hospitalized patients with COVID-19-associated pneumonia.

2. Materials and Methods

2.1. Study Design

This was a single-center prospective clinical study conducted between March and June 2021. The study included 135 adult patients hospitalized for pneumonia associated with COVID-19. All patients were unvaccinated for COVID-19.

2.2. Diagnostic Statements

Pneumonia was confirmed by either chest X-ray or chest computed tomography in each patient. Coronavirus SARS-CoV-2 as a causative agent of pneumonia was confirmed with either PCR or ELISA test. Pneumonia severity was assessed in accordance with the CURB65 and PSI scores.

The severity of COVID-19-associated pneumonia was established in accordance with the Protocol of Medical Care for Treatment of Coronavirus Disease (COVID-19) [42]. A severe condition was established in the presence of at least one of the following parameters: respiratory rate ≥ 30 breaths per minute, oxygen saturation ≤93%, and pulmonary infiltrates occupying > 50% of the lung area. The critical condition was diagnosed in the presence of at least one of the followings: acute respiratory distress syndrome, sepsis, altered consciousness, and multiple organ dysfunction syndrome.

Besides the conventional laboratory tests such as complete blood count, fasting glucose, biochemical profile, levels of ferritin, IL-6, and soluble interleukin-2 receptors were measured.

2.3. Patients Management

All patients were treated in accordance with the Protocol of Medical Care for Treatment of Coronavirus Disease (COVID-19) [42]. Each patient received systemic corticosteroids and either unfractionated or low-molecular-weight heparin.

2.4. Ethics Statement

Each prospective participant signed a consent form before enrolling in the study. All of the procedures in the study correspond to bioethical standards in accordance with the Helsinki Declaration.

2.5. Statistical Analysis

Statistical processing of the data was performed using MedCalc and MS Excel. The distribution of variables was assessed with the Shapiro-Wilk test. The median with interquartile range (Me [Q1–Q3]) was used for descriptive statistics for data with the abnormal distribution. Mann-Whitney U test, odds ratio (OR), and Spearman's rank correlation analysis were used. Logistic regression was used to calculate adjusted OR. ROC-curves were built and areas under the curve (AUC). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR). A p-value <0.05 was considered significant.

3. Results

3.1. General Characteristics of the Enrolled Patients

The median age of participants was 67.0 [61.0–74.0] years old. The median body mass index (BMI) was 27.0 [24.6-31.8] kg/m^2. Among enrolled patients, there were 53 (39.3%) men and 82 (60.7%) women with a male/female ratio of 1:1.5. The median time between the first symptom onset and hospital admission was 7.0 [5.3–10.0] days. According to the score CURB-65, patients had 1.0 [0.0–1.0] points. Participants got 67.0 [54.3–80.0] points according to PSI score at the moment of hospital admission. The most common comorbidities are shown in table 1. The median systolic and diastolic blood pressure at the moment of hospital admission was 130.0 [120.0–140.0] mm Hg and 80.0 [70.0–80.0] mm Hg respectively. The median SpO_2 at the moment of hospital admission was 95.0 [93.0–96.0]%. Laboratory parameters at the moment of hospital admission are shown in table 2.

Table 1. *The most common comorbidities.*

Comorbidity	Number of patients (%)
Arterial hypertension	106 (78.5%)
Diabetes mellitus	37 (27.4%)
Atrial fibrillation	16 (11.9%)
Prior myocardial infarction	13 (9.6%)
Prior stroke	10 (7.4%)
Hypothyroidism	8 (5.9%)
Severe valvular heart disease	6 (4.4%)

Table 2. *Laboratory parameters at the moment of hospital admission.*

Parameter	Value [IQR]
Hemoglobin, g/dL	13.1 [12.2–14.2]
Leukocytes $\times 10^9$/L	6.0 [4.7–8.4]
Lymphocytes, %	18.0 [12.0–24.5]
Fasting glucose, mmol/L	6.0 [5.3–8.4]
Total bilirubin, μmol/L	10.4 [8.4–13.9]
ASAT, IU/L	30.0 [21.3–40.0]
ALAT, IU/L	27.5 [20.1–41.4]
Creatinine, μmol/L	97.0 [86..4–110.9]
BUN, mmol/L	5.9 [4.9–7.6]
Ferritin, ng/mL	349.0 [183.0–595.8]
sIL-2R, ng/mL	5.6 [4.2–7.7]
IL-6, pg/mL	44.4 [13.0–91.8]
FHR	25.7 [13.3–45.8]

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; IQR, interquartile range; sIL-2R, soluble interleukin-2 receptors

3.2. Risk Factors for Severe/Crtitical Condition and In-Hospital Mortality

The severe/critical condition developed in 72 (53.3%) patients. 14 (10.4%) patients died during the in-patient stay. The most important risk factors are shown in table 3.

Table 3. *The most risk factors for severe/critical condition and in-hospital mortality with optimal cut-off values and unadjusted odds ratio for severe/critical condition and in-hospital mortality.*

Risk factor	Severe/critical condition			In-hospital mortality		
	Optimal cut-off value	Odds ratio (95% CI)	p	Optimal cut-off value	Odds ratio (95% CI)	p
Age, years old	63	1.94 (0.96–3.92)	0.066	71	6.67 (1.96–22.73)	0.002
BMI, kg/m^2	26.1	4.27 (2.05–8.88)	<0.001	29.1	6.41 (1.70–24.24)	0.006
Female gender	-	1.50 (0.75–3.01)	0.249	-	4.37 (0.94–20.39)	0.060
CURB-65, points	1	6.18 (1.72–22.25)	0.005	1	12.1 (3.59–40.81)	<0.001
PSI, points	91	5.71 (1.58–20.67)	0.008	81	8.10 (2.47–26.54)	<0.001
Arterial hypertension	-	1.55 (0.68–3.53)	0.302	-	1.72 (0.36–8.18)	0.493
Diabetes mellitus	-	2.26 (1.02–5.00)	0.044	-	3.03 (0.98–9.35)	0.053
Prior MI	-	0.73 (0.21–2.52)	0.620	-	0.70 (0.08–5.82)	0.740
Prior stroke	-	1.05 (0.31–3.64)	0.933	-	2.07 (0.40–10.73)	0.384
SpO_2 at admission	93	236.57 (14.04–3984.96)	<0.001	90	13.76 (4.03–46.92)	<0.001
Hemoglobin, mg/L	116	2.29 (0.82–6.39)	0.113	122	4.43 (1.42–13.84)	0.011
Leukocytes $\times 10^9$/L	7.1	3.88 (1.80–8.36)	<0.001	8.3	3.92 (1.25–12.24)	0.019
Lymphocytes, %	14	2.89 (1.35–6.17)	0.006	22	2.23 (0.47–10.68)	0.417
Fasting glucose, mmol/L	5.8	4.80 (2.29–10.05)	<0.001	7.8	4.67 (1.49–14.67)	0.008
Total bilirubin, μmol/L	8.68	1.71 (0.80–3.65)	0.166	11.10	6.67 (0.83–53.86)	0.075
ASAT, IU/L	20.5	1.87 (0.92–3.81)	0.086	14.3	4.20 (0.96–18.38)	0.057
ALAT, IU/L	24.5	3.15 (1.53–6.49)	0.002	25.3	1.66 (0.49–5.70)	0.419
Creatinine, μmol/L	105.6	2.37 (1.11–5.06)	0.026	105.7	6.80 (1.99–23.21)	0.002
BUN, mmol/L	6.1	2.36 (1.16–4.80)	0.018	10.3	15.98 (3.64–70.13)	<0.001
Ferritin, ng/mL	402	5.08 (2.32–11.13)	<0.001	396	6.48 (1.71–24.51)	0.006
sIL-2R, ng/mL	7.5	3.37 (1.48–7.70)	0.004	6.2	2.93 (0.93–9.30)	0.067
IL-6, pg/mL	62.5	2.78 (1.34–5.78)	0.006	91.0	3.32 (1.07–10.28)	0.037
FHR	33.98	5.09 (2.36–10.97)	<0.001	35.21	7.71 (2.03–29.22)	0.003

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CI, confidence interval; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; MI, myocardial infarction; sIL-2R, soluble interleukin-2 receptors

Logistic regression was performed with consideration of the most important risk factors according to table 3 excluding scales CURB-65, PSI, and FHR. Logistic regressions for risk factors of severe/critical condition and in-hospital mortality are shown in tables 4 and 5.

Table 4. *Logistic regression for risk factors of severe/critical condition.*

Variable	Coefficient	SE	Wald	p
Age	0.00010693	0.028075	0.00001451	0.9970
BMI	0.11188	0.060365	3.4350	0.0638
SpO_2	-1.45251	0.31363	21.4489	<0.0001
Leukocytes	0.064009	0.11044	0.3359	0.5622
Lymphocytes	0.00073431	0.033166	0.0004902	0.9823
Fasting glucose	0.13318	0.098958	1.8112	0.1784
Creatinine	-0.072483	0.029962	5.8523	0.0156
BUN	0.74374	0.34103	4.7561	0.0292
Ferritin	0.00091867	0.00088637	1.0742	0.3000
IL-6	-0.0040800	0.0038964	1.0965	0.2950
Constant	135.36432	30.28341	19.9802	<0.0001

Abbreviations: BMI, body mass index; BUN, blood urea nitrogen; IL-6, interleukin-6; SE, standard error

Table 5. *Logistic regression for risk factors of in-hospital mortality.*

Variable	Coefficient	SE	Wald	p
Age	0.11067	0.059403	3.4706	0.0625
BMI	0.13627	0.078989	2.9761	0.0845
SpO_2	-0.20451	0.14637	1.9522	0.1624
Leukocytes	0.12520	0.10650	1.3820	0.2398
Lymphocytes	0.026327	0.056534	0.2169	0.6414
Fasting glucose	0.099979	0.12569	0.6327	0.4264
Creatinine	0.020639	0.018752	1.2113	0.2711
BUN	-0.054169	0.17226	0.09888	0.7532
Ferritin	-0.00034613	0.0012050	0.08251	0.7739
IL-6	-0.00027411	0.0047983	0.003263	0.9544
Constant	0.86256	15.47824	0.003106	0.9556

Abbreviations: BMI, body mass index; BUN, blood urea nitrogen; IL-6, interleukin-6; SE, standard error

3.3. Novel Score

A scale for prediction of severe/critical condition and in-hospital mortality in hospitalized COVID-19 patients that is easy to use in real clinical practice was developed. It included the following factors: age, BMI, history of diabetes mellitus, history of hypertension, myocardial infarction, stroke, blood pressure, SpO_2, total leukocyte count, creatinine, ferritin, or FHR (table 6). The acronym "BIFOCALED" was chosen to alleviate use in real clinical practice. Each patient may be scored between 0 and 9.

Table 6. *BIFOCALED score.*

	Risk factor	Interpretation	Points
B	Blood pressure	SBP <90 mm Hg or DBP <60 mm Hg	1
I	Body mass index	BMI ≥25.0 kg/m^2	1
F	Ferritin	Ferritin ≥400 ng/mL or FHR ≥34	1
O	SpO_2	SpO_2 <95%	1
C	Creatinine	Creatinine ≥110 μmol/L	1
A	Arterial hypertension/ prior myocardial infarction/ stroke	Presence of ≥1 of the followings: hypertension, prior MI, stroke	1
L	Leukocytes	Leukocytes ≥10.0×10^9/L	1
E	Elderly	Age ≥65 years old	1
D	Diabetes mellitus	History of diabetes mellitus	1

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FHR, ferritin-hemoglobin ratio; MI, myocardial infarction; SBP, systolic blood pressure

Patients with severe/critical condition were higher scored according to the BIFOCALED score than patients with moderate condition (4.0 [4.0–5.0] points *vs* 2.0 [2.0–2.7] points, p<0.001). Non-survivors were higher scored compared to survivors (6.0 [3.0–7.0] points *vs* 3.0 [3.0–4.0] points, p<0.001).

There was good discriminative power of the BIFOCALED score for severe/critical condition (AUC, 0.806, p<0.001) and in-hospital mortality (AUC, 0.804, p<0.001) (figures 1 and 2).

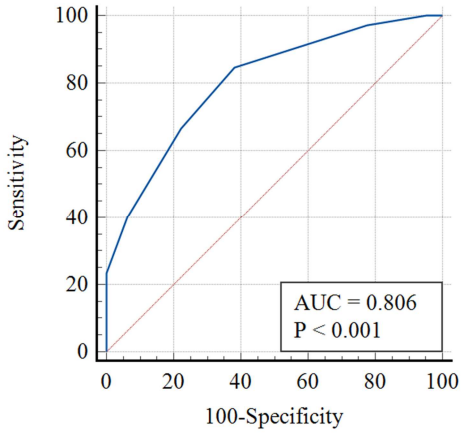

Figure 1. *ROC-curve showing discriminative power of the BIFOCALED score for severe/critical condition.*

The Youden index for the prediction of severe/critical condition was 0.47 at the value of >2 points (sensitivity of 84.72%; specificity of 61.90%) (table 7). The probability of severe/critical condition was 71.8% in patients with >2 points according to the BIFOCALED score and 22.0% in patients with ≤2 points (OR, 9.01; 95%CI, 3.97–20.44; p<0.001). The Youden index for the prediction of in-hospital mortality was 0.58 at the value of >5 points (sensitivity of 64.29%; specificity of 93.39%) (table 8). In-hospital mortality was 52.9% in patients with >5 points according to the BIFOCALED score and 4.2% in patients with ≤5 points (OR, 25.43; 95%CI, 6.88–93.99; p<0.001).

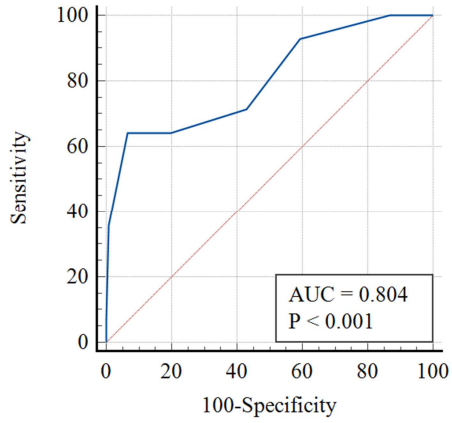

Figure 2. *ROC-curve showing discriminative power of the BIFOCALED score for in-patient mortality.*

Table 7. *Predictive ability of the BIFOCALED scale regarding severe/critical condition.*

Criterion	Sensitivity, %	Specificity, %	PLR	NLR	PPV, %	NPV, %
≥0	100.00	0.00	1.00		53.3	
>0	100.00	4.76	1.05	0.00	54.5	100.0
>1	97.22	22.22	1.25	0.13	58.8	87.5
>2	84.72	61.90	2.22	0.25	71.8	78.0
>3	66.67	77.78	3.00	0.43	77.4	67.1
>4	40.28	93.65	6.34	0.64	87.9	57.8
>5	23.61	100.00		0.76	100.0	53.4
>8	0.00	100.00		1.00		46.7

Table 8. *Predictive ability of the BIFOCALED scale regarding in-hospital mortality.*

Criterion	Sensitivity, %	Specificity, %	PLR	NLR	PPV, %	NPV, %
≥0	100.00	0.00	1.00		10.4	
>1	100.00	13.22	1.15	0.00	11.8	100.0
>2	92.86	40.50	1.56	0.18	15.3	98.0
>3	71.43	57.02	1.66	0.50	16.1	94.5
>4	64.29	80.17	3.24	0.45	27.3	95.1
>5	64.29	93.39	9.72	0.38	52.9	95.8
>6	35.71	99.17	43.21	0.65	83.3	93.0
>7	7.14	100.00		0.93	100.0	90.3
>8	0.00	100.00		1.00		89.6

The BIFOCALED score positively correlated with the CURB-65 score (r=0.47, p<0.001) and PSI (r=0.56, p<0.001).

Table 9 shows the distribution of scores in enrolled patients. Tables 10 and 11 show the probability of severe/critical condition and in-hospital mortality depending on the BIFOCALED score.

Table 9. *Distribution of scores in participants.*

Score	Number of patients
0	3
1	13
2	34
3	23
4	29
5	16

Score	Number of patients
6	11
7	5
8	1
9	0

Table 10. *Probability of severe/critical condition depending on BIFOCALED score.*

Score	Probability of severe/critical condition, %
0	0.0
1	15.4
2	26.5
3	56.5
4	65.5
5	75.0
6	100.0
7	100.0
8	100.0

Table 11. *In-hospital mortality depending on BIFOCALED score.*

Score	In-hospital mortality, %
0	0.0
1-2	2.1
3-4	7.7
5-6	14.8
7-8	83.3

4. Discussion

Our study showed that BMI, scales CURB-65 and PSI, history of diabetes mellitus, SpO_2 level at admission, leukocyte count, lymphocyte percentage, levels of fasting glucose, alanine aminotransferase, ferritin, sIL-2R, IL-6, and FHR were risk factors for disease progression to severe/critical condition. Logistic regression showed that only SpO_2, creatinine, and blood urea nitrogen were independent risk factors of severe/critical condition. Risk factors for in-hospital mortality included age, BMI, scales CURB-65 and PSI, SpO_2 level at admission, hemoglobin level, leukocyte count, levels of fasting glucose, creatinine, blood urea nitrogen, ferritin, IL-6, and FHR. However, logistic regression showed no relevant independent risk factor of in-hospital mortality.

The meta-analysis performed by Rahman A. et al. showed that male gender, hypertension, diabetes mellitus, fatigue/myalgia, and smoking history are risk factors for the severity of COVID-19 [43]. Ou M. et al. noted that age, platelet count, lymphocyte count, white blood cell count, levels of C-reactive protein, lactate dehydrogenase, procalcitonin, D-dimer, alanine aminotransferase, aspartate aminotransferase, and creatinine may be used for early identification and prediction of disease progression [44]. The meta-analysis performed by Booth A. et al. showed that risk factors of adverse outcomes include age, male gender, severe obesity, and active cancer [45]. Kaeuffer C. et al. concluded that overweightedness, obesity, advanced age, male sex, comorbidities, dyspnoea, and inflammation are risk factors for severe COVID-19 or death in hospitalized patients [46]. According to the meta-analysis performed by Li X. et al., patients who are male, with advanced age, obesity, a history of smoking, hypertension, diabetes, malignancy, coronary heart disease, hypertension, chronic liver disease, COPD, or CKD are more likely to develop severe COVID-19 symptoms [47]. Jiang N. et al. found that elderly, male gender, diabetes mellitus, cough, and diarrhea are associated with a higher risk of severe disease [48]. Zheng Z. et al. reported that males, aged over 65 years, smoking, hypertension, diabetes, cardiovascular and respiratory diseases, white blood cell count, aspartate aminotransferase, creatinine, procalcitonin, lactate dehydrogenase, high-sensitivity troponin I, D-dimer are associated with disease progression [25]. Utulu R et al. concluded that age ≥50 years, male gender, hypertension, and diabetes are risk factors of severe disease [49]. The research performed by Talebi S. S. et al. showed that heart disease history, neutrophil-to-lymphocyte ratio, and older age are associated with increased mortality in COVID-19 patients [50]. Ayon-Aguilar J. et al. concluded that age over 60 years, hypertension, diabetes mellitus, and obesity are associated with higher mortality [51]. According to the results of the study conducted by Sepandi M. et al., age, gender, and comorbidities such as diabetes mellitus, hypertension, kidney disorders, and heart diseases increased the risk of death in COVID-19 patients [52]. The results of these studies partially correspond to our findings. However, many studies showed that male gender is a risk factor for adverse outcomes, but our study didn't show a significant association between gender and clinical outcome.

The BIFOCALED score showed good discriminative ability for severe/critical condition (AUC, 0.806) and in-hospital mortality (AUC, 0.804). The Youden index was 0.47 for the prediction of severe/critical condition and 0.58 for the prediction of in-hospital mortality.

Multiple scores assessing COVID-19 severity have been developed. Philip C. et al. developed a predictive score for patients hospitalized for COVID-19 based on the absolute neutrophil count, partial pressure of oxygen, protein, and lactate dehydrogenase levels [53]. COVID-19 Severity Assessment Score (CoSAS) was developed by Subhani F. et al.; it has acceptable discriminative power (AUC, 0.78) and includes the following 10 components: age, gender, clinical frailty score, number of comorbidities, ferritin level, D-dimer level, neutrophil/lymphocyte ratio, C-reactive protein levels, systolic blood pressure, and oxygen saturation [54]. Sebastian A. et al. developed a COVID-GRAM score that includes ten independent predictive factors such as pathological changes typical of COVID-19 in chest radiographs, age, hemoptysis, dyspnea, loss of consciousness, number of comorbidities, history of malignancy, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, and bilirubin concentration [55]. Wang P. et al. showed that a combined NLR and D-dimer higher than 1 μg/mL index is a reliable predictor for severe illness in certain patients with COVID-19 with excellent discriminative power (AUC, 0.916) [56]. PAINT score developed by Wang M. et al. that includes 5 parameters such as pulmonary disease, age >75, immunoglobulin M levels, CD16+/CD56+ NK cells, and aspartate aminotransferase showed an excellent

discriminative power (C-index, 0.902 ± 0.021) for progression from mild/moderate to severe COVID-19 [57]. Martin-Rodriguez F. et al. reported that the qCSI score had an AUC of 0.749 for 90-day mortality and the NEWS score had an AUC of 0.777 for 90-day mortality [58]. Lombardi Y. et al. performing an analysis of the predictive ability of multiple scores found that AUC regarding in-hospital mortality for 4C Mortality Score was 0.793 [0.783–0.803], for ABCS score was 0.790 [0.780–0.801], for COVID-GRAM score was 0.771 [0.760–0.783], for RISE UP score was 0.770 [0.759–0.782], for CORONATION-TR score was 0.769 [0.757–0.780], for ANDC score was 0.759 [0.748–0.769] and for COVID-19 SEIMC score was 0.752 [0.743–0.762] [41]. Giamarellos-Bourboulis E. J. et al. developed a SCOPE score derived from circulating concentrations of C-reactive protein, D-dimers, IL-6, and ferritin that show an AUC of 0.81 [59] that is similar to BIFOCALED score. According to data from Pugazhvannan C. R. et al., the NEWS 2 score had an AUC of 0.88 for the prediction of in-hospital mortality [60] which is somewhat better compared to this parameter of the novel score. The BIFOCALED score compared to other scores include 9 parameters each of which is valued at 1 point, which is easy to remember and does not require complex calculations which is important in real clinical practice.

However, there are some limitations to our study. They include the followings: 1) absence of a validation group; 2) a small number of participants; 3) SARS-CoV-2 strain, vaccination status, and early use of antiviral drugs or specific monoclonal antibodies impact the probability of progression to severe/critical COVID-19 and in-hospital mortality. Considering these limitations, further studies of the predictive power of the BIFOCALED score are needed.

5. Conclusion

The BIFOCALED score may be used for predicting severe/critical condition and in-hospital mortality. The disease progression to severe/critical COVID-19 should be suspected in patients who scored >2 points; however, a score of >5 points is associated with high in-hospital mortality.

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