# Investigation of the predictive value of MuLBSTA score in predicting critical clinical outcomes in hospitalized patients with severe acute respiratory syndrome-coronavirus-2 pneumonia

## MuLBSTA skorunun şiddetli akut solunum sendromu koronavirüs 2019 pnömonili hospitalize hastalarda kritik klinik sonuçları öngörmedeki prediktif değerinin incelenmesi

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**Abstract**

**Aim:** Multilobar infiltration, lymphocytopenia, bacterial co-infection, smoking history, hypertension, and age>65 (MuLBSTA) score is a clinical prediction rule used to classify patients with viral pneumonia by expected mortality. We compared the predictive performance of MuLBSTA with PSI, CURB-65, and qSOFA for poor clinical outcomes in hospitalized severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) patients.

**Methods:** A retrospective study was conducted on patients with SARS-CoV-2 who were hospitalized in a tertiary medical center between March 11, 2020, and May 31, 2020. 271 out of 900 patients who tested positive for SARS-CoV-2 were included in the study. The MuLBSTA, PSI, CURB-65, and qSOFA scores were used to assess thirty-day mortality, need for intensive care unit (ICU), mechanical ventilation (MV) requirement, and development of acute respiratory distress syndrome (ARDS) in all patients. Prognostic factors were also analyzed for thirty-day mortality.

**Results:** Among all 271 hospitalized patients, 150 males (55.3%) were included. The mean age was 54.2±15.4 years. The 30-day mortality rate was 10.7%. Of the patients included in the study; 39 patients (14.3%) were admitted to the intensive care unit, 32 patients (11.8%) received mechanical ventilator support, and 23 patients (8.4%) were diagnosed with ARDS. In predicting mortality, the area under the curve (AUC) of the MuLBSTA, PSI, CURB-65 and qSOFA scores were 0.877 (95% CI 0,832 0,914), 0.853 (95% CI 0,806-0,893), 0.769 (95% CI 0,714-0,817) and 0.769 (95% CI 0,715-0,818), respectively. The MuLBSTA score showed a higher AUC value compared to other prediction scores. The MuLBSTA and PSI scores performed better than CURB-65 and qSOFA scores in determining patients' need for ICU, MV requirement, and ARDS development.

**Conclusion:** The MuLBSTA score is an efficient tool to predict poor clinical outcomes in hospitalized patients with SARS-CoV-2. Further studies are warranted to validate its use.

**Keywords:** COVID-19, early warning score, MuLBSTA score, qSOFA

**Öz**

**Amaç:** Multilobar infiltrasyon, lenfositopeni, bakteriyel koenfeksiyon, sigara öyküsü, hipertansiyon ve yaş>65 (MuLBSTA) skoru, viral pnömonisi olan hastaları beklenen mortaliteye göre sınıflandırmak için kullanılan bir klinik tahmin kuralıdır. Hastanede yatan SARS-CoV-2 hastalarında kötü klinik sonuçlar için MuLBSTA'nın prediktif performansını PSI, CURB-65 ve qSOFA ile karşılaştırdık.

**Yöntemler:** Bu çalışma 11 Mart 2020 ile 31 Mayıs 2020 tarihleri arasında üçüncü basamak bir üniversite hastanesinde yatan SARS-CoV-2'li hastalar üzerinde geriye dönük yapıldı. SARS-CoV-2 testi pozitif çıkan 900 hastadan 271'i çalışmaya dâhil edildi. Tüm hastalarda 30 günlük mortalite, Yoğun bakım ünitesi (YBÜ) ihtiyacı, mekanik ventilasyon gereksinimi ve akut respiratuar distress (ARDS) gelişimini değerlendirmek için MuLBSTA, PSI, CURB-65 ve qSOFA skoru kullanıldı. Otuz günlük mortalite için prognostik faktörler de analiz edildi.

**Bulgular:** Hastanede yatan 271 hastanın 150'si (%55.3) erkekti. Ortalama yaş 54.2±15.4 yıldı. Otuz günlük ölüm oranı %10,7 idi. Çalışmaya dâhil edilen hastalardan; 39 hasta (%14,3) YBÜ'ye yatırıldı, 32 hasta (%11,8) mekanik ventilatör desteği aldı ve 23 hasta (%8,4) ARDS tanısı aldı. Mortaliteyi tahmin etmede MuLBSTA, PSI, CURB-65 ve qSOFA skorlarının eğri altında kalan alan (AUC) değerleri sırasıyla 0.877 (%95 CI 0.832 0.914), 0.853 (%95 CI 0.806-0.893), 0.769 (95% CI 0,714-0,817) ve 0,769 (95% CI 0,715-0,818). MuLBSTA puanı, diğer tahmin puanlarına kıyasla daha yüksek bir AUC değeri gösterdi. MuLBSTA ve PSI skorları, YBÜ ihtiyacı, mekanik ventilasyon gereksinimive ARDS gelişimi olan hastaları belirlemede CURB-65 ve qSOFA skorlarından daha iyi performans gösterdi.

**Sonuç:** MuLBSTA skoru, hastanede yatan SARS-CoV-2 hastalarında kötü klinik sonuçları tahmin etmek için etkili bir araçtır. Kullanımını doğrulamak için daha fazla çalışmaya ihtiyaç vardır.

**Anahtar Sözcükler:** COVID-19, erken uyarı skorları, MuLBSTA skoru, qSOFA

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## INTRODUCTION

Clinical predictive scores such as pneumonia severity index (PSI) and confusion, BUN, respiratory rate, blood pressure, and age>65 (CURB-65) have been developed since the 2000s to assist physicians who are not experts in the field of respiratory tract infections. In such a global crisis, the use of clinical prediction scores, which is an early warning model, can guide to correctly placing patients admitted to the hospital into risk categories, making better clinical decisions, and encouraging the proper use of medical resources. Deciding on outpatient, service, or intensive care unit (ICU) follow-up at the time of admission to the emergency department in patients with pneumonia is critical in terms of disease management.

American Society for Infectious Diseases / American Thoracic Society and British Thoracic Society guidelines recommend incorporating clinical predictive scores into clinical decision-making in patients with pneumonia, along with physician evaluation. (1,2). PSI and CURB-65 are valid scores and have been widely used to estimate 30-day mortality in patients with community-acquired pneumonia. (1). The PSI and CURB-65 have been used previously in influenza virus infections and have produced conflicting results due to their low susceptibility (3-5). The Third International Consensus Definitions for Sepsis and Septic Shock guideline (Sepsis-3) recommends bedside quick Sequential Organ Failure Assessment (qSOFA) assessment, a new score for the early prediction of mortality or long-term need for ICU, in patients with suspected infection. (6). The qSOFA is derived from simple vital signs such as mental status, respiratory rate, and blood pressure, which are easily obtained in emergency departments, and includes similar parameters to CURB-65, although different cut-off values are based. Some studies show that qSOFA has a significant predictive ability for in-hospital mortality in patients with pneumonia (7-9). The Japanese Respiratory Society recommended the use of SOFA and qSOFA scoring systems in the assessment of pneumonia severity in the pneumonia prognostic guide updated in 2017 (10). In addition, it was stated that the MuLBSTA score, which Guo et al. (11) recently defined, has a strong predictive ability for mortality in cases of viral pneumonia. The MuLBSTA is derived from the parameters of multilobular infiltration, lymphopenia, bacterial coinfection, smoking history, hypertension, and age>65.

Despite the severity and fatal complications of the disease, there is no valid clinical predictive score to predict the outcome associated with the coronavirus disease 2019 (COVID-19). Our hypothesis in this study is that MuLBSTA will predict mortality and disease course better than other clinical prediction scores in hospitalized patients with COVID-19. The primary aim of this study was to evaluate the performance of MuLBSTA, PSI, CURB-65, and qSOFA in predicting 30-day mortality in patients hospitalized with COVID-19. Our secondary aim is to compare the ability of these clinical severity scores to predict ICU admission, mechanical ventilation (MV) requirement, and acute respiratory distress syndrome (ARDS) development.

## MATERIALS AND METHODS

This study was carried out retrospectively, observationally and in a single center between March and May 2020 in Bezmialem Vakıf University hospital, which provides tertiary intensive care services in northwest of Turkey. This study was approved by the Bezmialem Vakıf University Non-Interventional Research Ethics Committee (No: 08/155, date: 08.06.2020). All adult patients (≥18 years of age) who were positive for severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) and diagnosed with COVID-19 pneumonia were included in this study.

Patients under age 18 with end-stage renal and hepatic failure, hospitalization 72 hours before the onset of symptoms, lung cancer, cystic fibrosis, pulmonary tuberculosis, immunosuppressive therapy, transplantation history, and lack of data were excluded from the study. Informed consent was waived due to the retrospective nature of the study.

Patient data were obtained from the computerized database of the hospital. At the time of admission to the hospital, belonging to the patients; demographic data, comorbidities, clinical prediction scores of disease at the onset of infection (MuLBSTA, PSI, CURB-65, and qSOFA), routine laboratory tests, chest X-ray, thoracic computed tomography, microbiological culture results, ICU admission, MV requirement, and ARDS development were recorded.

**Table 1.** Descriptive data and comparison between survivors and non-survivors within 30 days of hospitalization.

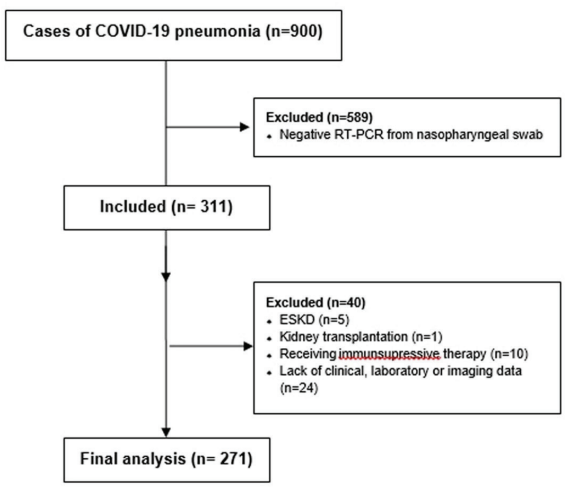
| | All patients (n=271) Mean±SD or n (%) | Survival (n=242) Mean±SD or n (%) | Nonsurvival (n=29) Mean±SD or n (%) | p value |
|---|---|---|---|---|
| Age (years) | 54.2±15.4 | 52.5±14.7 | 68.6±13.7 | **0.001** |
| Gender | | | | 0.708 |
| Female | 121 (44.6%) | 109 (45.0%) | 12 (41.3%) | |
| Male | 150 (55.3%) | 133 (54.9%) | 17 (58.6%) | |
| Comorbidity | | | | |
| CAD | 38 (14%) | 31 (12.8%) | 7 (24.1%) | 0.151 |
| CHF | 17 (%6.3%) | 9 (3.7%) | 8 (27.5%) | **0.001** |
| Diabetes mellitus | 66 (24.4%) | 57 (23.5%) | 9 (31.1%) | 0.375 |
| Hypertension | 114 (42.1%) | 95 (39.2%) | 19 (65.5%) | **0.007** |
| COPD | 17 (6.3%) | 14 (5.7%) | 3 (10.3%) | 0.406 |
| Asthma | 21 (7.7%) | 19 (7.8%) | 2 (6.8%) | 1.00 |
| Chronic kidney disease | 21 (7.7%) | 15 (6.1%) | 6 (20.6%) | 0.015 |
| Chronic liver disease | 1 (0.4%) | 1 (0.4%) | 0 | 1.00 |
| Cancer | 18 (6.6%) | 15 (6.1%) | 3 (10.3%) | 0.421 |
| CVA | 6 (2.2%) | 3 (1.2%) | 3 (10.3%) | **0.018** |
| Microbiological confirmed bacterial co-infection | 42 (15.5%) | 20 (8.2%) | 22 (75.8%) | **0.001** |
| Symptoms | | | | |
| Cough | 188 (69.4%) | 169 (69.8%) | 19 (65.5%) | 0.634 |
| Dyspnea | 99 (36.5%) | 80 (33%) | 19 (65.5%) | **0.001** |
| Myalgia | 49 (18.1%) | 47 (19.4%) | 2 (6.8%) | 0.098 |
| Fever>38.1$^0$C | 40 (14.7%) | 36 (14.8%) | 4 (13.7%) | **0.034** |
| Sore throat | 37 (13.7%) | 35 (14.4%) | 2 (6.8%) | 0.262 |
| Diarrhea | 23 (8.5%) | 21 (8.6%) | 2 (6.8%) | 0,745 |
| Nausea-vomiting | 49 (18.1%) | 45 (15.5%) | 4 (13.7%) | 0.525 |
| Anosmia | 13 (4.8%) | 12 (4.9%) | 1 (3.1%) | 0,719 |
| Abdominal pain | 9 (3.3%) | 7 (2.8%) | 2 (6.8%) | 0.255 |
| Fatigue | 100 (36.9%) | 92 (38.0%) | 8 (27.5%) | 0.271 |
| Altered mental status | 14 (5.2%) | 11 (4.5%) | 3 (10.3%) | 0.182 |
| Smoking history | | | | 0.320 |
| Current | 30 (11.1%) | 27 (11.1%) | 3 (10.3%) | |
| Ex | 40 (14.8%) | 33 (13.6%) | 7 (24.1%) | |
| Never | 201 (74.2%) | 182 (75.2%) | 19 (65.5%) | |

SD: Standart deviation, n: Numbers, CAD: Coronary artery disease, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, CVA: Cerebrovascular attack, ICU: Intensive care unit, MV: Mechanical ventilation, ARDS: Acute Respiratory Distress Syndrome.

Sensitivity and specificity were calculated by taking cut-off values ≥2 for CURB-65 score, ≥ 4 for PSI score, ≥ 2 for qSOFA, and ≥12 for MuLBSTA, as suggested in the literature (5, 9, 14). Calculated values were compared in terms of 30-day mortality, ICU admission, MV requirement and ARDS development. The date of nasopharyngeal swab collection was defined as the onset of infection. The length of hospital stay and outcome status of each patient were recorded. Patients hospitalized for less than 30-days were called to determine their survival if they were not seen in the outpatient clinic.

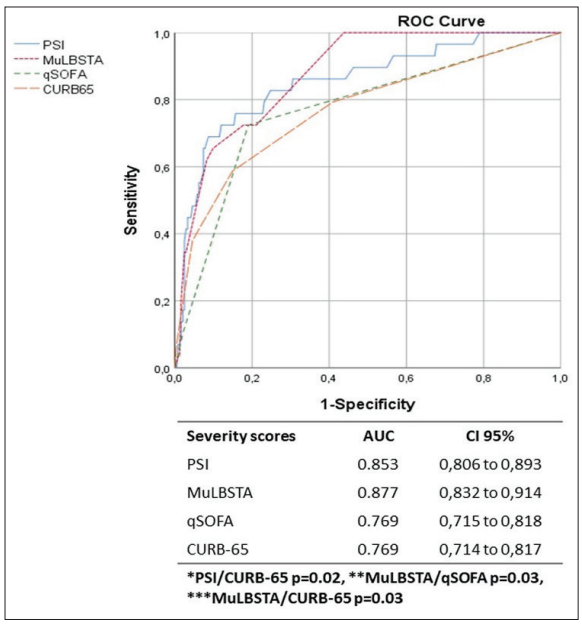
### Statistical analysis

Descriptive statistics of qualitative variables in the study are given as numbers and percentages, while descriptive statistics of numerical variables are given as mean, median, standard deviation, minimum and maximum. Pearson Chi-square and Fisher exact tests were used to comparing qualitative variables in terms of mortality status. The conformity of the numerical variables to the normal distribution was examined using the Shapiro-Wilk test. The Mann-Whitney U test was used for the mean comparison of the groups consisting of two categories. The statistical significance level was 0.05, and the SPSS Statistics for Windows (Statistical Package for the Social Sciences package program version 23.0, IBM Corp., Armonk, N.Y., USA) was used for calculations. Area under the curve (AUC) values were obtained by performing receiver operating characteristic (ROC) to evaluate risk estimation scores for critical clinical outcomes using the MedCalc statistical software.



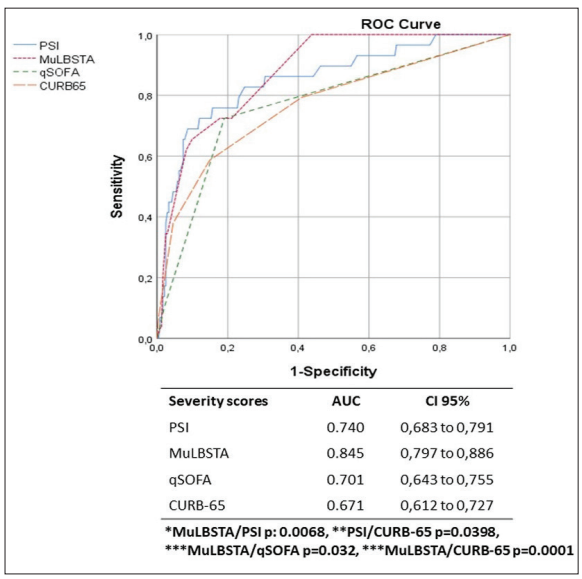

## RESULTS

Of the 900 patients with suspected COVID-19 hospitalized during the pandemic, 271 patients were included in the study, and 150 of them were male (Figure 1). The average age of the study population was 54.2±15.4 years (18-88). Among the participants, 39 (14,4%) were admitted to ICU, 32 patients (11,8%) needed MV support, ARDS developed in 23 (8,5%), and 29 patients (10,7%) died. While 30 patients (11%) were still smoking, 40 patients (14,7%) had quit smoking and




| Severity scores | AUC | CI 95% |
|---|---|---|
| PSI | 0.853 | 0,806 to 0,893 |
| MuLBSTA | 0.877 | 0,832 to 0,914 |
| qSOFA | 0.769 | 0,715 to 0,818 |
| CURB-65 | 0.769 | 0,714 to 0,817 |

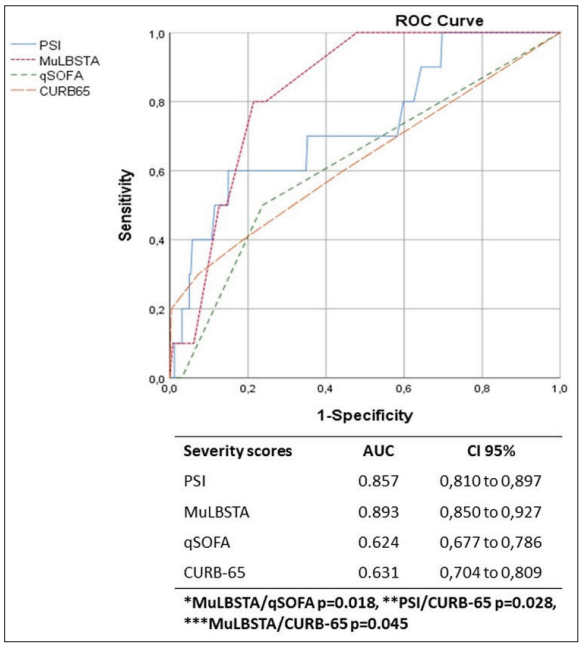
*PSI/CURB-65 p=0.02, **MuLBSTA/qSOFA p=0.03, ***MuLBSTA/CURB-65 p=0.03




| Severity scores | AUC | CI 95% |
|---|---|---|
| PSI | 0.740 | 0,683 to 0,791 |
| MuLBSTA | 0.845 | 0,797 to 0,886 |
| qSOFA | 0.701 | 0,643 to 0,755 |
| CURB-65 | 0.671 | 0,612 to 0,727 |

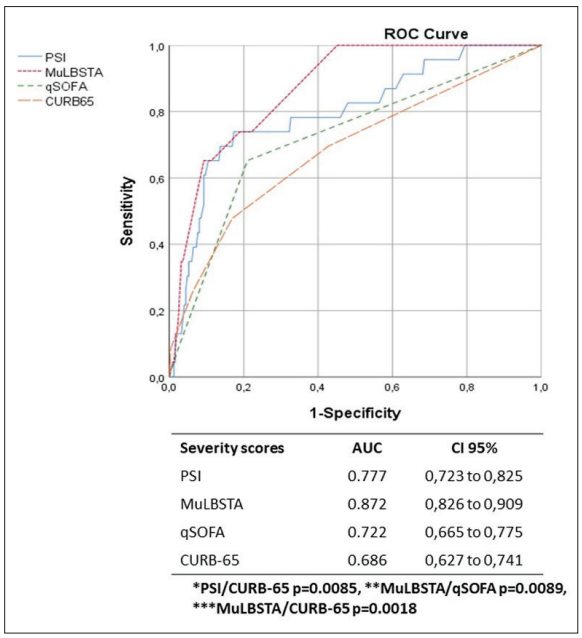
*MuLBSTA/PSI p: 0.0068, **PSI/CURB-65 p=0.0398, ***MuLBSTA/qSOFA p=0.032, ***MuLBSTA/CURB-65 p=0.0001

201 (74,1%) had never smoked. As a result of microbiological cultures, bacterial coinfection was detected in 42 patients. Demographic data, clinical characteristics, and severity scores of the patients were compared in Table 1 in terms of deceased and surviving cases. Univariate analysis among all patients defined congestive heart failure (p=0,01), hypertension (p=0,007), chronic renal failure (p=0,006), cerebrovascular event (p=0,002), pleural effusion (p=0,001), bacterial coinfection (p=0,001), and multilobar involvement in computed tomography (p=0,01) as risk factors for 30-day mortality associated with COVID-19.




| Severity scores | AUC | CI 95% |
|---|---|---|
| PSI | 0.857 | 0,810 to 0,897 |
| MuLBSTA | 0.893 | 0,850 to 0,927 |
| qSOFA | 0.624 | 0,677 to 0,786 |
| CURB-65 | 0.631 | 0,704 to 0,809 |

*MuLBSTA/qSOFA p=0.018, **PSI/CURB-65 p=0.028, ***MuLBSTA/CURB-65 p=0.045




| Severity scores | AUC | CI 95% |
|---|---|---|
| PSI | 0.777 | 0,723 to 0,825 |
| MuLBSTA | 0.872 | 0,826 to 0,909 |
| qSOFA | 0.722 | 0,665 to 0,775 |
| CURB-65 | 0.686 | 0,627 to 0,741 |

*PSI/CURB-65 p=0.0085, **MuLBSTA/qSOFA p=0.0089, ***MuLBSTA/CURB-65 p=0.0018

The MuLBSTA score had the highest accuracy in predicting 30-day mortality, followed by PSI, CURB-65, and qSOFA. The AUC values of MuLBSTA, PSI, CURB-65, and qSOFA for predicting 30-day mortality were 0.87, 0.85, 0.76, and 0.76, respectively. The best results for mortality were MuLBSTA with an AUC value of 0,877 and PSI with an AUC value of 0,853. Figure 2 shows the ROC curve of MuLBSTA, PSI, CURB-65, and qSOFA for 30-day mortality. For ICU admission, MuLBSTA with an AUC value of 0,845 was more efficient with statistically significant differences compared to other scores. Again, the most accurate scores for MV requirement (MuLBSTA AUC 0.836, PSI AUC 0.732) and ARDS development (MuLBSTA AUC 0.872, PSI AUC 0.799) were MuLBSTA and PSI, respectively. The AUC values and corresponding ROC curves for severity scores of ICU admission, MV requirement, and ARDS development are shown in Figures 3, 4, and 5.

## DISCUSSION AND CONCLUSION

In this study, we compared the predictive performance of the MuLBSTA score in 30-day mortality with PSI, CURB-65, and qSOFA. We observed that MuLBSTA and PSI scores are good predictors of prognosis in patients with SARS-CoV-2 pneumonia. In this study, SARS-CoV-2 patients with MuLBSTA score ≥12 were found to have higher 30-day mortality, ICU admission, MV requirement, and ARDS development than those with a score of <12. These findings suggest that for COVID-19 patients, the MuLBSTA score at first admission to the hospital may be useful for risk stratification. Calculation of MuLBSTA and PSI scores at hospital admission can predict critical clinical outcomes in patients with COVID-19, and their predictive value is superior to that of CURB65 and qSOFA.

The COVID-19 caused by SARS CoV-2 has caused significant mortality and has placed a significant burden on health systems all over the world. COVID-19 has a broad clinical spectrum, including asymptomatic infection, mild upper respiratory tract disease, pneumonia, respiratory failure, ARDS, multiorgan failure syndrome and, death (1). It has been shown that 26% to 33% of critically ill patients required ICU follow-up, and 4% to 15% died during the COVID-19 pandemic. (12-14).

ICU care and MV support are required to treat patients infected with SARS-CoV-2 at risk of adverse outcomes. Rapid and accurate clinical diagnosis of this patient group is the top priority for the effective use of limited resources. Initial assessment of disease severity at admission with early warning models will help physicians triage patients to the appropriate level of care and better communicate with family and caregivers about predictable outcomes.

The pathophysiology and risk factors of high mortality for COVID-19 are not yet fully understood. Male gender, advanced age, smoking, and comorbid diseases are well-known risk factors in COVID-19 patients (15, 16).

Chen et al (17) suggested the use of the MuLBSTA score, which is a new prognostic tool for viral pneumonia, in COVID-19 cases. Xu et al (18) reported that MuLBSTA was associated with better outcomes for both mortality (AUC: 0.956) and ICU admission (AUC: 0.875) compared to CURB-65, in their study of 117 patients with COVID-19 pneumonia. Similarly, in our study, MuLBSTA outperformed CURB-65 in all critical clinical outcomes.

In a prospective study conducted by Garcia Clemente et al. (19) in 249 patients with COVID-19 pneumonia, PSI and CURB-65 scores for mortality (AUC values of 0.874 and 0.852, respectively) and SMART-COP and MuLBSTA scores for ICU admission (AUC values of 0.749, 0.777, respectively) were reported better performance. In a recent retrospective multicenter study conducted in patients with COVID-19 pneumonia, the AUC values of PSI, CURB-65, qSOFA, and MuLBSTA scores in in-hospital mortality were reported as 0.835, 0.825, 0.728, and 0.715, respectively (20). Contrary to these studies, in our study, MuLBSTA showed the highest AUC value with 0.877. The reason for this may be the difference in the treatment protocols of the patients and an unusual mortality rate (15.4-20.9%) in the population of the relevant studies.

Although CURB-65 and qSOFA were good predictors of community-acquired pneumonia, they did not perform well in patients with COVID-19. One reason why CURB65 and qSOFA perform so poorly in patients with SARS-CoV-2 infection is that they do not attach sufficient importance to oxygenation assessment. Most severe cases of SARS-CoV-2 infection were young patients with respiratory failure; the risk factors identified during the pandemic seem to support this. The presence of oxygenation parameters in PSI, multilobar infiltration, lymphopenia, and smoking in MuLBSTA may have contributed to the high sensitivity and specificity.

Iijima Y et al (21), taking into account the difficulties in defining bacterial coinfection, which is one of the MuLBSTA parameters, stated that the modified MuLBSTA score, which is created by using C-reactive protein instead, gives better results than MuLBSTA, although it has not been validated yet.

During the pandemic, different researchers developed multiple prognostic scores. The COVID-19-Gram, the Critical Illness Risk Score, the Rapid COVID-19 Severity Index, and the COVID-19 Severity Index were created to early detect hospitalized patients at high risk of critical illness and transfer to the intensive care unit (22-24). In a study published recently by Ji et al (25), a new severity score (CALL) was proposed that evaluates comorbidity, age, lymphocyte count, and lactate dehydrogenase value. The authors observed that 96% of patients scoring 4-6 did not progress to severe disease and suggested that this clinical predictive score in Covid-19 patients would be simpler than the MuLBSTA suggested by Guo et al.

A mortality predictive score for hospitalized patients with COVID-19 was developed by the ISARIC4C consortium and named the Coronavirus Clinical Characterization Consortium Mortality Score (4C Mortality Score) (26). It was based on a prospective cohort study of 74,944 consecutive patients in 260 hospitals. However, the use of these scoring models was mostly for the hospitalized or critically ill, and none of them were aimed at patients before admission.

This study has limitations. First, some of the data may not have been fully collected due to the nature of the retrospective study design. Secondly, the results of this study may not be generalizable to other nations or other regions of Turkey, as it is a single-center study. Third, the SARS-CoV-2 pharyngeal or nasal swabs used in this study – although being the most practical option for most medical facilities - are not the gold standard method with confirmed false positive and false negative rates. Fourth, some other laboratory markers such as procalcitonin, D-dimer, and LDH, which are associated with mortality in patients with severe SARS-CoV-2 infection, were not included in this study. The reason we did not include these measurements in our study is that it is impractical to perform these tests or obtain these data for every emergency room patient with suspected COVID-19.

In this study, we found that MuLBSTA and PSI scores play a potential role in predicting 30-day mortality, ICU admission, MV requirement, and ARDS

development in hospitalized patients with COVID-19 infection. These scores can help any physician decide where a patient should be admitted (to the ward or ICU) or discharged. Our findings show that CURB-65 and qSOFA, which are widely used in pneumonia, underestimate the severity of the disease in patients hospitalized for COVID-19. We still need a fast and accurate tool to classify patients with SARS-CoV-2 pneumonia early in clinical practice.

In parallel with our results, studies in the literature show that the MuLBSTA score is a reliable scoring system to show the severity of COVID-19 infection, but further evaluation is needed. Researchers should work to develop new prognostic tools that can be used as an easily obtainable high sensitivity and a specificity screening test in COVID-19 patients.

### Conflict-of-interest and financial disclosure

The author declares that she has no conflict of interest to disclose. The author also declares that she did not receive any financial support for the study.

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