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Evaluation of risk scores as predictors of mortality and hospital length of stay for older COVID-19 patients

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Abstract

Objective: This study was intended to research the sensitivity of the Charlson Comorbidity Index (CCI), COVID-GRAM, and MuLBSTA risk scores for hospital length of stay (LOS) and mortality in older patients hospitalized with coronavirus disease 2019 (COVID-19).

Methods: A total of 217 patients (119 women) were included in the study. The first clinical signs, comorbidities, laboratory and radiology findings, and hospital LOS were recorded for each patient. The CCI, COVID-GRAM, and MuLBSTA risk scores were calculated, and their sensitivities for hospital LOS and mortality were evaluated using receiver operating characteristic (ROC) curve analysis.

Results: Of the hospitalized patients, 59 (27.2%) were followed in the intensive care unit, and mortality developed in 44 (20.3%). The CCI positively correlated with COVID-GRAM and MuLBSTA scores ($P<0.001$). COVID-GRAM and MuLBSTA results correlated with LOS and mortality ($P<0.001$). According to the ROC curve analysis, the cutoff points for mortality were 5 for CCI, 169 for COVID-GRAM, and 9 for MuLBSTA.

Conclusion: Older patients with comorbidities are the major risk group for severe COVID-19. COVID-GRAM and MuLBSTA scores appear to be sensitive and reliable mortality indicators for these patients.

KEYWORDS
Charlson comorbidity index, COVID-19, COVID-GRAM score, hospital length of stay, mortality, MuLBTSA score, older patients

1 | INTRODUCTION

Three years after the first case of coronavirus disease 2019 (COVID-19), more than 500 million confirmed cases and more than 6 million deaths have been reported worldwide.[1] Immunodeficiency syndromes, comorbidities, frailty, and advanced age are risk factors for severe disease and mortality.[2] The case fatality rate has been reported as 8% in patients aged 70–79 years and 15% in those ≥80 years.[3] Initial clinical symptoms and key biochemical parameters have been associated with disease severity. Lymphopenia, elevated aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), and D-dimer have been reported as useful mortality markers.[4]

The MuLBSTA risk score, which considers multilobular infiltration, hypo-lymphocytosis, bacterial co-infection, smoking history, hypertension, and age, was developed for patients with viral pneumonia in the pre-COVID period.[5] The sensitivity of this score has since been demonstrated for patients with COVID-19, with a cutoff score for severe disease reported as 11 points with 83.3% sensitivity and 71.4% specificity.[6,7]

Another method used to define risk involves the COVID-GRAM Critical Illness Risk Score.[8] The sensitivity of this score for intensive care and mortality has been reported as acceptable.[9] In a study involving 523 patients with a mean age of 65 years, the COVID-GRAM score showed 77% sensitivity and 85% specificity for 30-day mortality.[10]

In the elderly, comorbidities are one of the factors that increase the risk of serious disease. The Charlson Comorbidity Index (CCI) is a proven reliable method for evaluating morbidity.[11] In a longitudinal cohort study that included 88,747 patients with COVID-19, a CCI score with at least 1 point was associated with mortality along with age ≥ 50 years and male sex.[12]

Thus, this study was designed to determine the sensitivity and usefulness of MuLBSTA, COVID-GRAM, and CCI scores for predicting hospital length of stay (LOS) and COVID-19-related mortality in elderly patients with COVID-19.

2 | MATERIALS AND METHODS

2.1 | Study design and population

This study was performed using the database of Bezmialem Vakıf University and Istanbul Medeniyet University Faculty of Medicine, Istanbul, Turkey, and was approved by the Bezmialem Vakif University Ethics Committee 540,022,451–050.05.04.

Patients ≥65 years old with COVID-19 confirmed by ground-glass consolidation on computed tomography (CT) and/or positive nasal swab reverse transcription-polymerase chain reaction were included in the study. All of these patients were hospitalized in the pre-vaccine period.

Because LDH and direct bilirubin are included parameters for the COVID-GRAM risk score, to avoid conflict, patients with hematologic or hepatobiliary malignancies were excluded from the study, as well as patients transferred to another hospital during treatment and those with missing medical histories. Patients with oncologic disorders with no metastases were accepted, leaving 217 patients included in the analysis.

2.2 | Data analysis

Initial symptoms, comorbidities, and hospital LOS were verified. Pulmonary CT findings, serum creatinine (mg/dL), c-reactive protein (CRP; mg/L), D-dimer (ng/mL), LDH (U/L), troponin I (pg/mL), direct bilirubin (mg/dL), lymphocyte count (mm3), and neutrophil-lymphocyte ratio (NLR) were determined. The use of antibiotics was accepted as a sign of bacterial co-infection.

Comorbidities were identified, and the CCI was calculated for each patient, taking into account the following parameters: patient age, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident or transient ischemic attack, chronic obstructive pulmonary disease (COPD), dementia, connective tissue disease, peptic ulcer, liver disease, diabetes mellitus, hemiplegia, moderate to severe chronic kidney disease (moderate = creatinine > 3 mg/dL, severe = on dialysis or after kidney transplant), solid tumors, leukemia, lymphoma, and acquired immunodeficiency syndrome (AIDS).[11] An increasing score was associated with a gradual increase in cumulative mortality.

The MuLBSTA score calculated for each patient included the parameters of multilobe infiltrates (5 points), lymphocyte count ≤ 0.8 × 109/L (4 points), bacterial co-infection in sputum or blood culture (4 points), smoking history (previously smoked 2 points, and actively smoking 3 points), hypertension (2 points), and age ≥ 60 (2 points). The cutoff point was defined as 12, with a score of 0–11 at low risk for mortality and 12–20 at high-risk for mortality.[5] In this study, smoking history was unreliable, and all patients were scored as nonsmokers, making the upper limit of the MuLBSTA 17.

The COVID-GRAM risk score was calculated with the parameters of age, symptoms of hemoptysis, shortness of breath, loss of consciousness, and comorbidities of COPD, hypertension, diabetes, coronary artery disease, chronic heart failure, chronic kidney disease, cancer, cerebral vascular disease, hepatitis B, immunodeficiency, and malignancy. Laboratory markers were NLR, LDH, and direct bilirubin. The formula for calculating the COVID-GRAM risk score was as follows: (x-ray abnormality × 27.1464) + (age × 0.6139) + (hemoptysis × 33.6210) + (dyspnea × 14.0569) + (unconsciousness × 34.4617) + (number of comorbidities × 10.3826) + (cancer history × 31.2211) + (NLR × 1.25) + (LDH × 0.0534) + (direct bilirubin × 3.0605) – 6.6127.[8] The scores for critical illness, determined as the need for the intensive care unit (ICU), invasive ventilation, or death, were classified as < 1.7% low risk (0–56 points), 1.7%–40.4% intermediate risk (57–138 points), and ≥ 40.4% high-risk (> 139 points).

2.3 | Statistical analyses

The relevance of the variables to the normal distribution was analyzed with the Shapiro–Wilk and Kolmogorov–Smirnov tests. Because the data did not show normal distribution, the Mann–Whitney *U* test was used for comparisons between groups. Because the data were not normally distributed and nonparametric tests were used, descriptive statistics were provided as median values (minimum-maximum). Pearson's chi-square, Fisher's exact, and Fisher–Freeman–Halton tests were used to compare categorical variables expressed as n (%) between groups. The relationships between the variables were analyzed with the Spearman rank correlation coefficient. Receiver operating characteristic (ROC) analysis was applied to determine the ideal cutoff scores for the CCI, COVID-GRAM, and MuLBSTA to predict mortality. To determine the risk factors affecting the presence of mortality, backward binary logistic regression analysis was used. Statistical analyses were made with the SPSS version 22.0 program, and $P < 0.05$ was accepted as significant.

3 | RESULTS

Included in the study were 217 patients (119 women and 98 men) with a mean age of 72 years (65–95 years). Descriptive statistics of all variables are presented in Table 1. A total of 59 (27.2%) patients were cared for in the ICU, and mortality developed in 44 (20.3%) cases. The mean of the CCI was 4. The most common morbidities were hypertension and diabetes mellitus, and the most common symptoms were cough and dyspnea. A multilobar CT sign was observed in 88% of the patients. A positive correlation was observed between age and CCI (r = 0.427, $P<0.001$). Advanced age and mortality were observed for patients in the ICU ($P = 0.012$, $P = 0.001$). The CCI had a positive relationship with COVID-GRAM (r = 0.667, $P<0.001$) and MuLBSTA scores (r = 0.297, $P<0.001$), and COVID-GRAM and MuLBSTA scores correlated with each other (r = 0.477, $P<0.001$).

Hospital LOS had no relationship to patient age and CCI; however, for those with higher COVID-GRAM and MuLBSTA scores, hospital LOS was longer ($P<0.001$), particularly for lymphopenia, patients with higher LDH, CRP, D-dimer levels ($P = 0.007$, $P<0.001$, and $P = 0.029$), and mortality ($P = 0.027$). In addition, LOS was longer for patients that presented with dyspnea ($P = 0.016$). The differences in parameters and risk scores according to mortality are presented in Table 2. As initial symptoms, dyspnea and fever were associated with mortality, and bacterial co-infection was more common in this group ($P<0.001$).

For mortality, CCI, COVID-GRAM, and MuLBSTA variables were analyzed with the binary logistic regression backward method, and all variables were statistically significant. A 1 unit decrease in the CCI increased the risk of mortality 1.348 times ($P = 0.042$), a 1 unit increase in COVID-GRAM increased the mortality risk 1.036 times, and a 1 unit increase in MuLBSTA increased the mortality risk 1.352 times ($P<0.001$). These variables were analyzed using the ROC curve, and the ideal mortality cutoff for these scores was determined (Table 3). The sensitivity, specificity, and related interactive dot plots of the CCI, COVID-GRAM, and MuLBSTA scores are presented in Figures 1–6. In this study, new variables, COVID-GRAM, and MuLBSTA values were derived according to ideal cutoffs and analyzed with the binary logistic regression analysis backward method. The sensitivity of these variables for mortality was found to be statistically significant (Table 4).

4 | DISCUSSION

In elderly patients with COVID-19 and clinical signs of dyspnea and fever, increased LDH, CRP, D-dimer, creatinine, troponin, NLR, lymphopenia, and age are associated with disease severity.

The CCI was significantly higher in mortality cases. As a cutoff value, 5 (45.45% sensitivity, 78.61% specificity) appears useful for clinical practice ($P = 0.002$). New cutoffs were detected as 169 (54.76% sensitivity and 89.47% specificity) for COVID-GRAM and 9 (90.91% sensitivity and 57.80% specificity) for MuLBSTA ($P<0.001$). According to the new COVID-GRAM cutoff, those with a higher-than-ideal cutoff had a 7.483 times greater mortality risk than those with a lower-than-ideal cutoff. According to the new MuLBSTA cutoff, those with a higher-than-ideal cutoff had a 9.849 times greater risk for mortality than those with a lower-than-ideal cutoff (Table 4).

TABLE 1 Mean results of all variables with descriptive statistics.

Age, y	72 (65–95)	Creatinine (mg/dl)	1 (0.6–7.9)
LOS, d	8 (1–62)	LDH (U/L)	271.5 (124–1490)
Comorbidity count	2 (0–5)	Direct bilirubin (mg/dl)	0.3 (0.1–3.9)
CCI	4 (2–14)	Troponin (ng/ml)	13 (0.8–1412)
COVID-GRAM score	141.5 (71–322)	D-dimer (ng/ml)	330 (111–6422)
COVID-GRAM risk ratio	43.6 (3.2–100)	Lymphocyte (mm^3)	1200 (250–4290)
MuLBTSA score	11 (2–17)	NLR	4.2 (0.3–31.7)
ICU ratio	59 (27.2%)		
Mortality	44 (20.3%)		
Hypertension	130 (59.9%)	Cough	113 (52.1%)
Diabetes mellitus	78 (35.9%)	Dyspnea	97 (44.7%)
COPD	49 (22.6%)	Fever	70 (32.3%)
İschemic heart disease	46 (21.2%)	Myalgia	27 (12.4%)
Congestive heart failure	34 (15.7%)	Vomiting	22 (10.1%)
Cerebrovascular disease	10 (4.6%)	Diarrhea	15 (16.9%)
Malignancy	10 (4.6%)	Loss of consciousness	13 (6%)
Dementia	7 (3.2%)	Headache	12 (5.5%)
		Hemoptysis	4 (1.8%)

Abbreviations: CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; LDH, lactate dehydrogenase; LOS, length of stay; NLR, neutrophil-lymphocyte ratio.

TABLE 2 Variations in first symptoms, laboratory markers, and severity scores between survivors and nonsurvivors

	Survivors *n* = 173	Nonsurvivors *n* = 44	*P* value
Cough	94 (54.3)	19 (43.2)	0.186
Dyspnea	68 (39.3)	29 (65.9)	0.002
Fever	50 (28.9)	20 (45.5)	0.036
Myalgia	25 (14.5)	2 (4.5)	0.075
Vomiting	15 (8.7)	7 (15.9)	0.166
Diarrhea	9 (5.2)	6 (13.6)	0.087
Loss of consciousness	8 (4.6)	5 (11.4)	0.145
Headache	11 (6.4)	1 (2.3)	0.075
Hemoptysis	4 (2.3)	0 (0)	0.585
Creatinine (mg/dl)	1 (0.6–7.8)	1.4 (0.7–7.9)	0.001
LDH (U/L)	262 (124–1490)	375 (181–1471)	<0.001
Direct bilirubin (mg/dL)	0.3 (0.1–1.3)	0.4 (0.1–3.9)	0.001
Troponin (ng/ml)	11(1.3–1412)	22.2 (0.8–932)	0.002
D-dimer (ng/ml)	311(111–4291)	549 (140–6422)	<0.001
Lymphocyte (mm^3)	1300 (250–3500)	810 (290–4290)	<0.001
NLR	3.6 (0.3–29.8)	7.7 (1.1–31.7)	<0.001
Comorbidity count	2 (0–5)	2 (0–5)	0.076
CCI	4 (2–14)	5 (2–8)	0.004
COVID-GRAM score	136 (71–236)	171.5 (118–322)	<0.001
COVID-GRAM ratio	37.9 (3.2–98.2)	75.2 (21.5–100)	<0.001
MuLBTSA score	9 (2–17)	13 (7–17)	<0.001

Abbreviations: CCI, Charlson Comorbidity Index; COVID, coronavirus disease; LDH, lactate dehydrogenase; NLR, neutrophil-lymphocyte ratio.

Note: $P<0.05$ is accepted as significant.

TABLE 3 The ROC analysis with mortality cutoff points for CCI, COVID-GRAM, and MuLBSTA scores

	AUC	Standard error	AUC 95% CI	*P* value	Cutoff	Sens. (%)	Spec. (%)
CCI	0.638	0.045	0.570–0.702	0.002	>5	45.45	78.61
COVID-GRAM score	0.784	0.040	0.719–0.840	<0.001	>169	54.76	89.47
MuLBSTA score	0.795	0.036	0.735–0.847	<0.001	>9	90.91	57.80

Abbreviations: AUC, area under the curve; CCI, Charlson Comorbidity Index; CI, confidence interval; COVID, coronavirus disease; ROC, receiver operating characteristic.

Age and comorbidities are the factors that increase the risk of severe disease. In a study of 638 unvaccinated patients with COVID-19, more severe disease was observed in young adults with comorbidities according to elderly patients without comorbidities.[13] In a prospective cohort from Italy, age, male gender, a high CCI, and high white blood cell count and creatinine level were associated with mortality.[14] Independent of the index score, pulmonary involvement and a diagnosis of hypertension and diabetes influence disease severity.[15,16] The ability of the CCI to predict disease severity has been researched in several trials. In a meta-analysis, a per-point increase in the CCI score was associated with a 16% increase in mortality.[17] In that study, the CCI cut off score for mortality was ≥3. In another analysis of 1559 patients with COVID-19, a CCI score ≥4 was associated with mortality with 87.2% sensitivity and a 97.9% negative predictive value.[18] In our study, a cutoff score of 5 demonstrated 45.45% sensitivity and 78.61% specificity. Based on these results, the CCI is a sensitive method to define morbidity-related risk for patients with COVID-19.

The first clinical symptoms are other indicators of severe disease. In our patients, cough was the more prominent symptom, but dyspnea and fever were associated with mortality. Severe dyspnea and tachypnea were reported as poor clinical signs for the elderly.[19] Whatever the cause, hospital LOS is a negative prognostic indicator associated with elderly care. In our study, LOS was longer for patients with an elevated acute phase and eventual mortality.

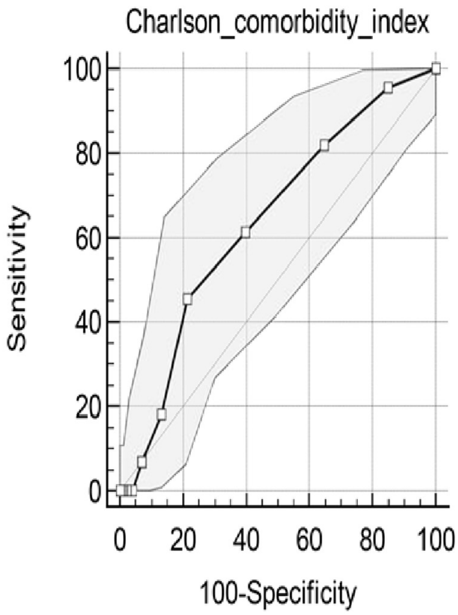

FIGURE 1 Charlson Comorbidity Index in predicting mortality.

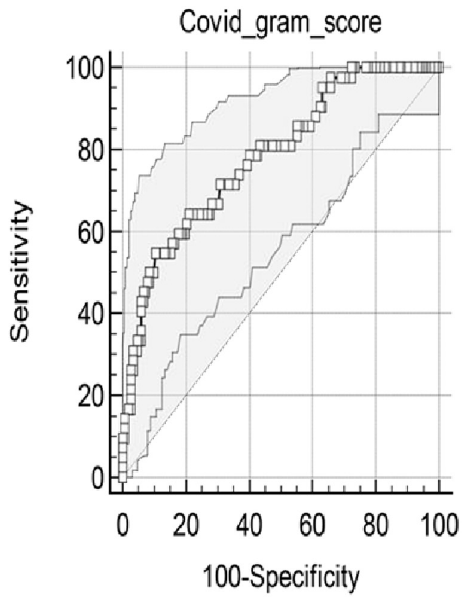

FIGURE 3 Coronavirus disease (COVID)-GRAM score in predicting mortality.

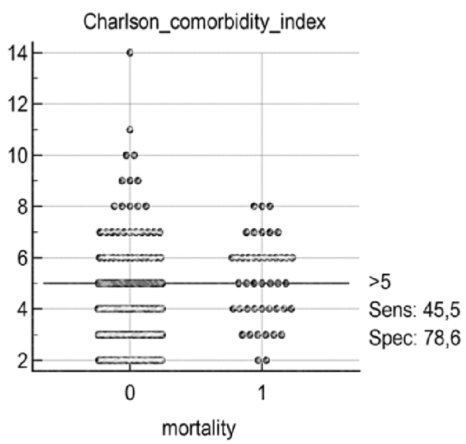

FIGURE 2 Interactive dot graph for Charlson Comorbidity Index in predicting mortality.

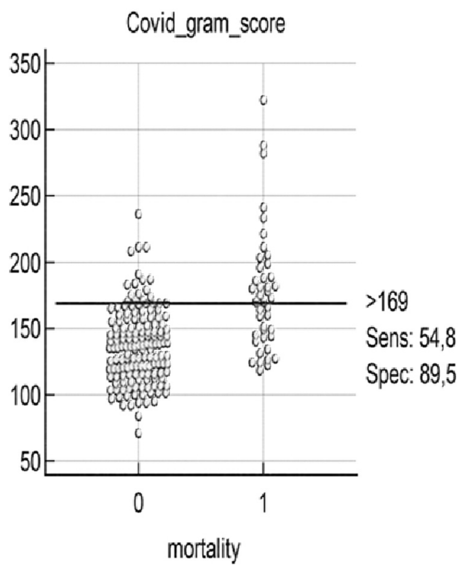

FIGURE 4 Interactive dot graph for coronavirus disease (COVID)-GRAM score in predicting mortality.

Ferritin, LDH, alanine aminotransferase, AST, CRP, procalcitonin, CK, troponin, D-dimer, serum amyloid A, N-terminal pro-B type natriuretic peptide, interleukin-4, interleukin-6, and interleukin-10 are additional markers of severe disease.[20,21] We found increased creatinine, LDH, troponin, D-dimer, NLR, and lymphopenia associated with mortality. Multilobular involvement was observed in 88% of our patients. Peripheral patchy or bilateral ground-glass opacities are the most common CT discoveries in COVID-19 cases, but CT findings alone are not associated with mortality.[22]

Practical methods that include laboratory and radiologic findings seem useful for disease management. For COVID-GRAM, a score of 139 (risk ratio ≥ 40.4%) was presented as a high-risk score for severe disease.[6] In our study, the ideal cutoff was a score of 169 with an odds ratio of 7.483. The sensitivity of this score was evaluated with the Pneumonia Severity Index, CURB-65 score, and MuLBSTA and determined to be superior to other scores for detecting high-risk patients.[23] In another study with 523 patients, the accuracy of this score was evaluated, and a sensitivity of 77% and specificity of 85% were determined for 30-day mortality.[10] For older patients, sensitivity was researched along with the International Severe Acute Respiratory Infection Consortium (ISARIC-4C) score and the quick COVID-19 Severity Index (qCSI), and the sensitivity of ISARIC-4C and COVID-GRAM had 88.1% sensitivity for mortality.[9]

The MuLBSTA score with a cutoff of 12 points was reported to have good predictivity for mortality in patients with COVID-19.[24] The sensitivity was compared with CURB-65 and APACHE II scores, and a cutoff value of 13.5 was determined for mortality. In that

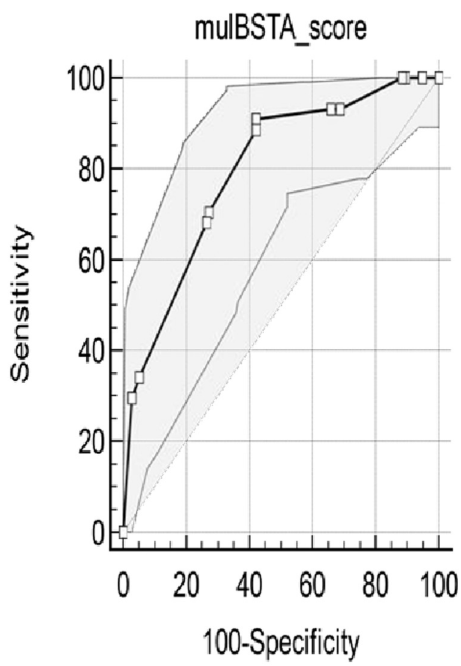

FIGURE 5 MuLBSTA score in predicting mortality.

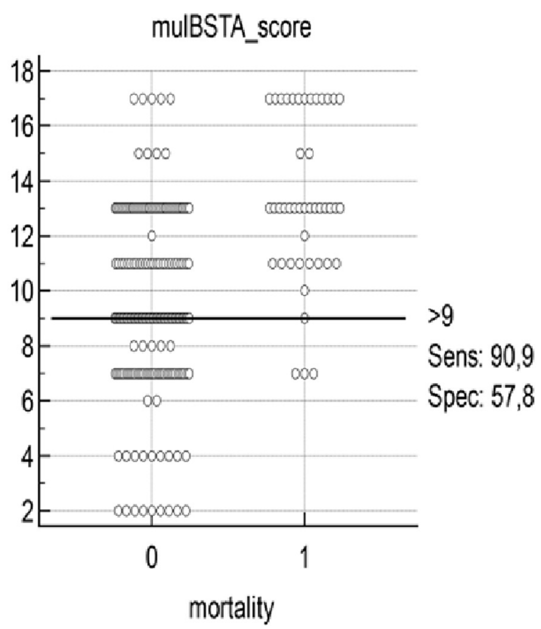

FIGURE 6 Interactive dot graph for MuLBSTA score in predicting mortality.

study, the sensitivity of MuLBSTA for mortality was better according to CURB-65.[25] In our study, a 9-point MuLBSTA score had 90.91% sensitivity and 57.80% specificity for mortality. The sensitivity of the MuLBSTA appears reliable for elderly patients with COVID-19. For older patients, the frailty scale and the Sequential Organ Failure Assessment (SOFA) score have been reported as other reliable methods for determining in-hospital mortality.[26]

The limitations of our study included its retrospective design, unreliable smoking history necessitating all patients being scored as nonsmokers, and acceptance of co-infections based on antibiotic use.

5 | CONCLUSION

For COVID-19, practical and sensitive disease severity scales enable more effective management of elderly patients with comorbidities. The CCI is a sensitive method to determine the burden of morbidity, and COVID-GRAM and MuLBSTA are reliable mortality indicators.

AUTHOR CONTRIBUTIONS

B.B. was responsible for data collection, data analysis, and manuscript preparation. K.T. was responsible for data collection. U.O. was responsible for data analysis.

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FUNDING INFORMATION

Not applicable.

CONFLICT OF INTEREST

There is no conflict of interest.

ETHICS STATEMENT

The project was reviewed by Bezmialem Vakif University Ethics Committee and approved number with 540,022,451–050.05.04.

INFORMED CONSENT

Not applicable.

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TABLE 4 The predictive value for mortality of new COVID-GRAM and MuLBSTA scores

	P value	OR	95% CI	
New COVID-GRAM (Reference value: 169)	<0.001	7.483	3.153	17.758
New MuLBSTA (*Reference value: 9*)	<0.001	9.849	3.215	30.170

Abbreviations: CI, confidence interval; COVID, coronavirus disease; OR, odds ratio.

Note: $P < 0.05$ is accepted as significant.

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