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Research article

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Evaluation of the effectiveness of quick COVID-19 Severity Index and COVID-GRAM Critical Illness Risk Score in determining mortality and severity in COVID-19

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Ethics Committee Approval
Ethics Committee approval was taken from the İzmir Katip Çelebi University Local Ethics committee, 25/05/202, Decision number: 0288. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: With the COVID-19 pandemic, the increase in the number of patients admitted to the emergency department has led to an increase in the need for intensive care and mechanical ventilation. Methods that can predict the development of serious disease will allow for a more accurate use of resources. This study was conducted to test the ability of the Quick COVID-19 Severity Index and the COVID-GRAM Critical Illness Risk Score to predict serious disease development and mortality.
Methods: This is a prospective cohort study. Among the patients admitted to the emergency department, those hospitalized due to COVID-19 were included in the study. The Quick COVID-19 Severity Index and COVID-GRAM Critical Illness Risk Scores of the patients were calculated, and the ability of these scores to predict serious illness and mortality was investigated.
Results: A total of 556 patients were included in this study. Development of critical illness, described as the need for non-invasive / invasive ventilation or the need for intensive care unit admission, was found significant when the Quick COVID-19 Severity Index was above 5 and the COVID-GRAM Critical Illness Risk Score showed high risk (AUC: 0.927; $P < 0.001$, AUC: 0.986; $P < 0.001$, respectively). A Quick COVID-19 Severity Index over 6 and COVID-GRAM Critical Illness Risk Score indicating high risk were found to be associated with mortality (AUC: 0.918, $P < 0.001$, AUC: 0.982, $P < 0.001$, respectively).
Conclusion: Both the Quick COVID-19 Severity Index and the COVID-GRAM Critical Illness Risk Score can be used to assess severity in COVID-19 patients in the emergency room. However, the COVID-GRAM Critical Illness Risk Score was more successful in differentiating low- and high-risk patients.

Keywords: COVID-19, Severity, Mortality, Emergency department

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Introduction

COVID-19 is a serious health problem that may cause critical illness and even death. In COVID-19, critical illness is generally associated with multi-organ failure and pneumonia that can progress to acute respiratory distress syndrome ARDS [1]. With the onset of the pandemic, hospitals around the world have faced an influx of COVID-19 patients, and a serious workload and resource shortage has developed. Therefore, early recognition of COVID-19 patients at high risk of critical illness and death, as well as the prevention of unnecessary hospitalization of low-risk patients to the intensive care unit (ICU) and unnecessary resource consumption has become a serious necessity [2]. Some early warning scores, such as the quick sepsis-related organ failure assessment (qSOFA), the Rapid Emergency Medicine Score (REMS), the Modified Early Warning Scores (MEWS), the National Early Warning Score (NEWS) and the National Early Warning Score-2 (NEWS-2) were evaluated for use in patients with COVID-19 and found to be beneficial [3, 4]. However, these scorings are not specific for COVID-19 and are suitable for the general patient population.

Recently, Quick COVID-19 Severity Index (qCSI), and COVID-GRAM Critical Illness Risk Score (COVID-GRAM), specific to COVID-19, were developed to assess disease severity. Developed by Haimovich et al. [5], qCSI is a simple scoring that assesses the probability of severe shortness of breath in a COVID-19 patient at 24 hours. The COVID-GRAM, developed by Liang et al. [6], evaluates the risk of developing critical illness and mortality. Few studies have been conducted that evaluate the efficacy of both scorings.

The aim of this study is to assess the effectiveness of qCSI and COVID-GRAM to evaluate the risk of critical illness and mortality in subjects diagnosed with COVID-19 in the emergency department (ED).

Materials and methods

Study design

This is a prospective observational cohort study. Approval was obtained from the Izmir Katip Celebi University non-interventional clinical studies ethics committee with the application number 2021- GOKAE - 0346 and the decision number 0288. Written consent was obtained from all subjects to participate in the study.

Setting

The study was carried out in the ED of a tertiary hospital receiving 400,000 admissions annually, from Jan. 6, 2021 to Dec. 31, 2021. In the ED, there are two main sections, the isolated area where patients with a diagnosis of COVID-19 are treated, and the clean area where patients other than COVID-19 are treated. In the isolated area, one nurse, one emergency medicine specialist, and one emergency medicine resident doctor work in each shift. This study was conducted in an Celebi University non-interventional clinical studies ethics committee isolated area.

Participants

Patients over the age of 18 presented to the ED with a confirmed diagnosis of COVID-19 or whose diagnosis of COVID-19 was confirmed by RT-PCR after applying to the ED were included in the study. Pregnanacy, trauma, presence of intubation and/or cardiopulmonary arrest at the time of admission were determined as exclusion criteria.

Variables

The primary outcome of the study was the development of critical illness, which was defined as presence at least one of the following [7];

1. The need for non-invasive ventilation
2. The need for invasive ventilation
3. The need for ICU admission.

Mortality was the secondary outcome of the study.

Data sources

Age, gender, comorbid diseases, history of hemoptysis, cancer history, presence of dyspnea, Glascow coma scale, respiratory rate, SO2, O2 flow rate, neutrophil/lymphocyte ratio, lactate dehydrogenase, and direct bilirubin level were recorded for the subjects who met the inclusion criteria. Using the recorded data, qCSI and COVID-GRAM were calculated for each one of the subjects. The qCSI is a scale calculated using respiratory rate, SO2, and O2 flow rate and scored between 0 and 12 points [5]. The qCSI is also available as a web-based risk calculator (https://www.mdcalc.com/calc/10304/quick-covid-19-severity-index-qcsi#evidence. Access date: Sept. 13, 2022). The COVID-GRAM is calculated by using the data of abnormal radiological findings, age, hemoptysis, dyspnea, altered consciousness, number of comorbid diseases, presence of cancer, neutrophil/lymphocyte ratio, lactate dehydrogenase level, and direct bilirubin level It is a scoring that categorizes the risk as low, moderate and high [6]. COVID-GRAM is also available as a web-based risk calculator (https://www.mdcalc.com/covid-gram-critical-illness-risk-score#next-steps. Access date: Jan. 13, 2022).

Bias

Study data were collected by a nurse working outside the ED who was blinded to the study to avoid potential bias, as it may influence the decisions of the patient's primary physician.

Study size

The sample size was calculated using the computer program G*Power 3.1.9.2. When calculating the sample size, according to the data obtained from a previous similar study, H1: 15%, H0: 56%, and the odds ratio was 9.4 [8]. The calculated sample size was 402, with an alpha value of 0.05 and a power of 0.95.

Statistical analysis

Data obtained in the study were analyzed using IBM SPSS Statistics for macOS, Version 26.0. Armonk, NY: IBM Corp. Categorical variables were expressed as numbers and percentages, while numerical variables were expressed as mean and standard deviation when presenting the descriptive statistics. ROC analysis was used to evaluate the power of the scales to predict the risk of critical illness and mortality and to determine the appropriate cut-off values. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were used to evaluate the success of the tests in predicting critical illness and mortality. The Chi-square test was used for the comparison of two categorical variables. The results were expressed at a 95% confidence interval. *P* value, and less than 0.05 was considered statistically significant.

Results

A total of 556 patients diagnosed with COVID-19 were included in the study. The mean age of the patients, of whom 286 (51.4%) were male, was 48 (19) years. Other socio-demographic data of the subjects are presented in Table 1.

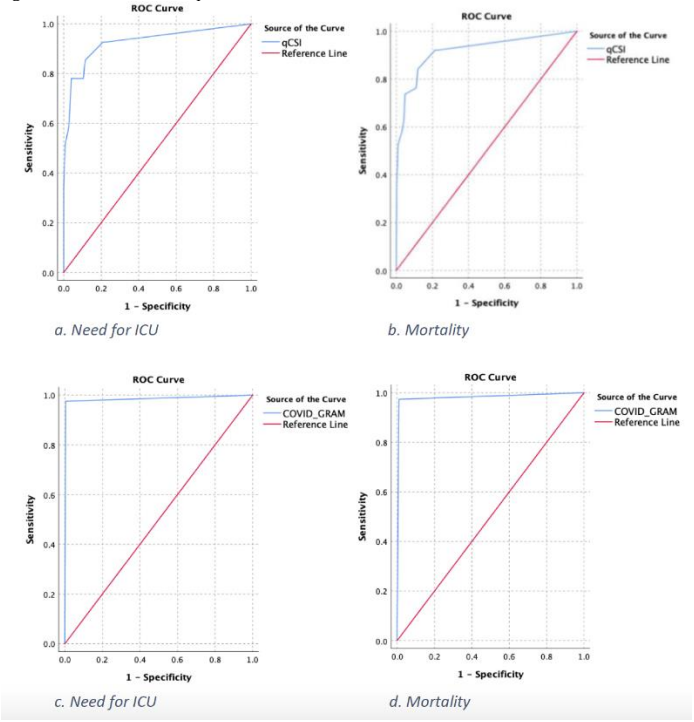
Table 1: Socio-demographic characteristics of subjects

		Mean	SD
Age		48	19
Respiratory rate		16	4
Oxygen saturation (%)		93	13
		Number	%
Gender	Female	270	51.4
	Male	286	48.6
Admission	Discharged	380	68.3
	Admitted to ward	140	25.2
	Admitted to ICU	36	6.5
Mortality	No	518	93.2
	Yes	38	6.8

SD: standard deviation, ICU: Intensive care unit

In the ROC analysis to evaluate the power of the COVID-GRAM and qCSI to predict critical illness and mortality, the area under the curve (AUC) of qCSI in predicting the development of critical illness was 0.927% (0.874-0.979). T and the cut-off value was 5. The AUC of qCSI to predict mortality was found to be 0.918% (0.861-0.975) with a cut-off value of 6 ($P < 0.001$, $P < 0.001$, respectively). In the ROC analysis for the COVID-GRAM, the AUC of the risk for development of critical illness was 0.986% (0.958-1.013), and the AUC for the risk of mortality was 0.982% (0.952-1.012). The score indicates high risk ($P < 0.001$, $P < 0.001$, respectively). The ROC curves of COVID-GRAM and qCSI scores for estimating mortality and critical illness risk are given in Figure 1.

Figure 1: ROC curves for qCSI



It has been observed that the COVID-GRAM is associated with the development of critical illness and mortality, and this relationship is due to the high rate of critical illness and high mortality in the high-risk group. In low and medium risk groups, critical illness and mortality rates were found to be similarly low ($P < 0.001$, $P < 0.001$, respectively). Considering the relationship of qCSI with critical illness and mortality, it was seen that a score above 5 was significant in terms of the development of critical illness, and a score above 6 was significant in terms of mortality ($P < 0.001$, $P < 0.001$ respectively) (Table 2).

Table 2: Association of COVID-GRAM critical illness risk score and qCSI with mortality

		Mortality			
		No	Yes	Total	*P*-value
COVID-GRAM	Low risk	375 (100.0%)	0 (0.0%)	375	<0.001
	Medium risk	138 (99.3%)	1 (0.7%)	139	
	High risk	5 (11.9%)	37 (88.1%)	42	
Total		518 (93.2%)	38 (6.8%)	556	
qCSI	≤6	<0.001	10 (2%)	503	<0.001
	>6	<0.001	28(52.8%)	53	
Total		518 (93.2%)	<0.001	556	
		Development of critical illness			
		No	Yes	Total	*P*-value
COVID-GRAM	Low risk	375 (100.0%)	0 (0.0%)	375 (100.0%)	<0.001
	Medium risk	138 (99.3%)	1 (0.7%)	139 (100.0%)	
	High risk	2 (4.8%)	40 (95.2%)	42 (100.0%)	
Total		515 (92.6%)	41 (7.4%)	556 (100%)	
qCSI	≤5	461 (98.1%)	9 (1.9%)	470 (100%)	<0.001
	>5	54 (62.8%)	32(37.2%)	86 (100%)	
Total		515 (92.6%)	41 (7.4%)	556 (100%)	

COVID-GRAM: COVID-GRAM Critical Illness Risk Score, qCSI: quick COVID-19 severity index

It was observed that qCSI, with a cut-off value of 5 could predict the development of critical illness with a sensitivity of 78% and a specificity of 90% (PPV: 37, NPV: 98). Since the low- and medium-risk scores were similar according to the COVID-GRAM, both were considered low risk for Intensive Care Unit (ICU) admission. Thus, two risk categories were obtained as low/medium risk and high risk. According to these two categories, this scoring can predict the development of critical illness with 98% sensitivity and 99% specificity (PPV: 95, NPV: 99) (Table 3).

Considering the diagnostic value of the tests in terms of mortality, it was seen that qCSI with a cut-off value of 6 could predict mortality with 74% sensitivity and 95% specificity (PPV:53, NPV:98). Since the low- and medium-risk scores were similar according to the COVID-GRAM, both were accepted as low risk in terms of mortality. Thus, two risk categories were obtained as low/medium risk and high risk. According to these two categories, this scoring can predict mortality with 97% sensitivity and 99% specificity (PPV: 88, NPV: 100) (Table 4).

Table 3: Predictive value of qCSI and COVID-GRAM critical illness risk score regarding critical illness development

Test	Risk category	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
qCSI	≤5 (low)	78	90	37	98
	>5 (high)	(62.3-89.4)	(86.54-92.02)	(30.5-44.4)	(96.64-98.92)
COVID-GRAM	Low/medium	97.6	99.6	95	99.8
	High	(87.1-99.9)	(98.6-99.9)	(83.4-98.8)	(98.7-99.9)

COVID-GRAM: COVID-GRAM Critical Illness Risk Score, qCSI: quick COVID-19 severity index, PPV: Positive predictive value, NPV: Negative predictive value

Table 4: Predictive value of qCSI and COVID-GRAM critical illness risk score regarding mortality

Test	Risk category	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
qCSI	≤6 (low)	74	95	53	98
	>6 (high)	(56.9-86.6)	(92.9-96.85)	(42.2-63.2)	(96.7- 98.8)
COVID-GRAM	Low/medium	97	99	88	99.8
	High	(86.2-99.9)	(97.8-99.7)	(75.5-94.7)	(98.7- 99.9)

COVID-GRAM: COVID-GRAM Critical Illness Risk Score, qCSI: quick COVID-19 severity index, PPV: Positive predictive value, NPV: Negative predictive value

Discussion

In this study, which was conducted to evaluate the success of COVID-GRAM and qCSI in determining the severity of COVID-19 patients admitted to the ED, both scores were found to be successful in predicting both need for ICU and mortality.

According to Armiñanzas et al. [8], COVID-GRAM was more successful than the CURB-65 score in estimating the severity of COVID-19 disease, but both scorings can be used for

risk classification. In the study conducted by Doğanay et al. [9], the CURB-65 score was found to be more successful than the COVID-GRAM. Rodriguez-Nava et al. [10] found that qCSI was successful in predicting ICU hospitalization in COVID-19 patients. However, to our knowledge, this study is the first to compare the COVID-GRAM and qCSI in predicting the development of critical illness in COVID-19 patients. In the present study, we found that a high COVID-GRAM and a qCSI above 5 were significant in predicting the risk of developing critical illness in patients with COVID-19. However, the COVID-GRAM Critical Illness Risk Score was found to be more successful than qCSI in both identifying and ruling out critical illness (Sensitivity: 97.56 vs. 78, Specificity: 99.61 vs. 90, PPV: 95 vs. 37, NPV: 99.81 vs. 98).

In a study by Martin-Rodriguez et al. [11], CURB-65 and qCSI were compared to predict mortality in COVID-19 patients, and CURB-65 was found to be more successful. Armiñanzas et al.'s [8] results indicated that the COVID-GRAM was effective in showing 30-day mortality and was more successful than CURB-65 in this regard. A study by Covino et al. [12] found that the ISARIC-4C score, COVID-GRAM, NEWS, and qCSI had similar success in predicting in-hospital mortality in COVID-19 patients. In the present study, we found that the COVID-GRAM indicating high risk and qCSI above 6 were significant in predicting the risk of mortality in patients with COVID-19. However, the COVID-GRAM was found to be more successful than qCSI in both identifying and ruling out risk of the development of critical illness (Sensitivity: 97 vs. 74, Specificity: 99 vs. 95, PPV: 88 vs. 53, NPV: 99.81 vs. 98).

This study has some limitations. Vaccination information of patients for COVID-19 was not questioned. Therefore, the possible effects of the vaccine on the development of critical illness or mortality may have affected our results.

Conclusion

COVID-GRAM and qCSI appear to be promising tools for predicting critical illness development and mortality in patients with COVID-19. However, this still needs to be confirmed by further studies.

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