



Usefulness of the COVID-GRAM and CURB-65 scores for predicting severity in patients with COVID-19



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ABSTRACT

Aim: The aim of this study was to determine the usefulness of COVID-GRAM and CURB-65 scores as predictors of the severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Caucasian patients.

Methods: This was a retrospective observational study including all adults with SARS-CoV-2 infection admitted to Hospital Universitario Marqués de Valdecilla from February to May 2020. Patients were stratified according to COVID-GRAM and CURB-65 scores as being at low–medium or high risk of critical illness. Univariate analysis, multivariate logistic regression models, receiver operating characteristic curve, and area under the curve (AUC) were calculated.

Results: A total of 523 patients were included (51.8% male, 48.2% female; mean age 65.63 years (standard deviation 17.89 years)), of whom 110 (21%) presented a critical illness (intensive care unit admission 10.3%, 30-day mortality 13.8%). According to the COVID-GRAM score, 122 (23.33%) patients were classified as high risk; 197 (37.7%) presented a CURB-65 score ≥ 2 . A significantly greater proportion of patients with critical illness had a high COVID-GRAM score (64.5% vs 30.5%; $P < 0.001$). The COVID-GRAM score emerged as an independent predictor of critical illness (odds ratio 9.40, 95% confidence interval 5.51–16.04; $P < 0.001$), with an AUC of 0.779. A high COVID-GRAM score showed an AUC of 0.88 for the prediction of 30-day mortality, while a CURB-65 ≥ 2 showed an AUC of 0.83.

Conclusions: The COVID-GRAM score may be a useful tool for evaluating the risk of critical illness in Caucasian patients with SARS-CoV-2 infection. The CURB-65 score could be considered as an alternative.

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Introduction

In December 2019, the novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in the city of Wuhan, China (Sohrabi et al., 2020). Spreading around the world in the early part of 2020, this disease outbreak is now considered a pandemic, with more than 45 million cases worldwide and more than 1 100 000 deaths by the end of October 2020, according to the World Health Organization (who.int/emergencies, 2020).

The clinical presentation of COVID-19 typically includes fever and pulmonary involvement (Shi et al., 2020; Lai et al., 2020), although almost any organ can be affected (Stokes et al., 2020). In

some patients, the disease progresses quickly to respiratory failure and even death (García-Alamino, 2020). The proportion of patients who become critically ill reaches almost 25% (Ye et al., 2020; Petrilli et al., 2020), and the case fatality rate has been shown to range between <0.1% and >25% (Li et al., 2020). Different risk factors have been associated with severe disease and mortality, including age and male sex (Hur et al., 2020; Michelozzi et al., 2020), various comorbidities (Alqahtani et al., 2020; Zhao et al., 2020), and some clinical laboratory and radiological findings (Zhang et al., 2020; Cappabianca et al., 2020).

Although only a small percentage of patients require admission to the intensive care unit (ICU) or mechanical ventilation, the COVID-19 population overwhelmed healthcare systems all over the world during the first wave of the pandemic and threatens to continue to do so. Some tools have been proposed to evaluate the risk of severe infection, in order to provide the most appropriate care and optimize limited resources (Yee et al., 2020; Zhou et al., 2020; Sprung et al., 2020; Ryan et al., 2020; Altschul et al., 2020). The COVID-GRAM score, validated to predict the risk of critical illness or death in the Chinese population, was one of the first published (Liang et al., 2020). The CURB-65 score (Lim et al., 2003) has been proposed for use in Spain as the reference prognostic tool for SARS-CoV-2 pneumonia (mscbs.gob.es, 2020).

The aim of this study was to determine whether the COVID-GRAM score could also be used as a prognostic score at the time of hospital admission in Caucasian patients with SARS-CoV-2 infection, and to compare its accuracy with that of the CURB-65 score.

Methods

Design and inclusion

This retrospective observational cohort study was conducted from February 27 to May 25, 2020. All adults with a laboratory-confirmed SARS-CoV-2 infection admitted to a tertiary university hospital were included. The following exclusion criteria were applied: age <18 years; patients who had been included previously in the study. All patients received standard-of-care treatment according to the local protocol.

Data collection

The following patient characteristics at hospital admission were collected: age, sex, body temperature, respiratory rate, heart rate,

arterial systolic and diastolic blood pressure, oxygen saturation (SaO₂), and mental status. For the assessment of comorbidity, obesity and all other conditions included in the original study (Liang et al., 2020) were examined: number of comorbidities, chronic obstructive pulmonary disease (COPD), diabetes, hypertension, coronary artery disease, cerebrovascular disease, hepatitis B virus (HBV), cancer, chronic renal disease, and immunodeficiency disease. Laboratory parameters were recorded: haemoglobin, white blood cell, neutrophil, lymphocyte, and platelet counts, neutrophil to lymphocyte ratio, serum creatinine and urea, sodium, potassium, blood glucose, and levels of C-reactive protein (CRP), procalcitonin (PCT), lactate dehydrogenase (LDH), direct bilirubin, and total bilirubin. Chest radiography abnormalities were recorded. When direct bilirubin was unknown, total bilirubin was included if available. Unknown variables at admission were included as normal values. Admission to the ICU, length of hospital and ICU stay, and 30-day mortality were also included.

Altered mental status was defined as disorientation with respect to person, place, or time, stupor, or coma. Coronary artery disease was defined as the presence of a current or past history of angina or myocardial infarction. HBV infection was defined when serum surface antigen (HBsAg) and/or HBV viral load were detected, or when the patient had previously been diagnosed with HBV and hepatitis core antibody (anti-HBc) and hepatitis surface antibody (anti-HBs) were detected. Cancer history was defined as a current or past history of solid tumours or haematological malignancies.

The main outcome measure was 'critical illness', a composite endpoint that combines ICU admission and 30-day mortality. This endpoint has been adopted previously in other studies to assess the severity of infectious diseases (Liang et al., 2020).

The COVID-GRAM score was obtained after entering these variables into a calculation tool designed by Liang et al. (2020) (accessible at <http://118.126.104.170/>), which stratifies the patient according to the risk of critical illness as low, medium, or high. The CURB-65 score (Lim et al., 2003) was also calculated, with a CURB-65 score ≥ 2 being considered as a high risk of critical illness. Severe illness was defined as a qSOFA score ≥ 2 (Singer et al., 2016) and a World Health Organization (WHO) score ≥ 5 (who.int/blueprint, 2020).

Statistical analysis

All data were analysed and processed using SPSS software (IBM SPSS Statistics version 19.0 (IBM Corp., Armonk, NY, USA)).

Table 1

Demographic characteristics of patients hospitalized with COVID-19 who did or did not develop critical illness.

	Total (n = 523)	Critical illness		P-value ^a
		No (n = 413)	Yes (n = 110)	
Age, mean (SD), years	65.63 (17.89)	63.58 (17.52)	73.31 (17.25)	<0.001
Sex, n (%)				0.032
Male	271 (51.8)	204 (49.4)	67 (60.9)	
Female	252 (48.2)	209 (50.6)	43 (39.1)	
Obesity, n (%)	123 (23.5)	91 (22)	32 (29.1)	0.121
COPD, n (%)	44 (8.4)	28 (6.8)	16 (14.5)	0.009
Diabetes, n (%)	114 (21.8)	83 (20.1)	31 (28.2)	0.068
Hypertension, n (%)	225 (43)	157 (38)	68 (61.8)	<0.001
Coronary artery disease, n (%)	53 (10.1)	37 (9)	16 (14.5)	0.084
Cerebrovascular disease, n (%)	53 (10.1)	33 (8)	20 (18.2)	0.002
HBV infection, n (%)	4 (0.8)	3 (0.7)	1 (0.9)	0.180
Unknown, n (%)	162 (31)			
Malignancy, n (%)	56 (10.7)	39 (9.4)	17 (15.5)	0.07
Chronic kidney disease, n (%)	51 (9.8)	27 (6.5)	24 (21.8)	<0.001
Immunodeficiency, n (%)	25 (4.8)	16 (3.9)	9 (8.2)	0.06
≥ 1 comorbidities, n (%)	312 (59.7)	221 (53.5)	91 (82.7)	0.009

COPD, chronic obstructive pulmonary disease; HBV, hepatitis B virus; SD, standard deviation.

^a T-test or Chi-square test (as appropriate in each case).

Qualitative variables were expressed as absolute frequencies and percentages, while quantitative variables were summarized as the mean and standard deviation (SD). Univariate methods were first used to test the differences between study subgroups, with the *t*-test for continuous variables and the Chi-square test for categorical variables. The independent variables significantly associated with critical illness or mortality in the univariate analysis and/or with clinical relevance according to the literature were entered into multivariate logistic regression models. The adjusted odds ratio (OR), relative risk (RR), and 95% confidence interval (CI) were calculated. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the COVID-GRAM score and CURB-65 score were calculated, and receiver operating characteristic (ROC) curves and the area under the curve (AUC) for predicting critical illness and 30-day mortality were calculated. Survival curves were generated by the Kaplan–Meier method, and the log-rank test was used to compare survival between groups. For all analyses, the significance level was set at 5%.

Results

Patient characteristics

A total of 523 patients (51.8% male, 48.2% female) were included during the study period. Mean age was 65.63 years (SD 17.89 years, range 19–105 years). Fifty-four (10.3%) patients required ICU admission, and 30-day mortality was 13.8%. Globally, 110 (21%) patients presented a critical illness. Twenty-eight (5.8%) patients had a WHO score ≥ 5 and 13 (2.8%) had a qSOFA score ≥ 2 .

The main epidemiological and clinical characteristics of the patients, laboratory and chest radiography findings, and comparisons between patients with and without critical illness are shown in Tables 1–3.

COVID-GRAM score and CURB-65 score for predicting critical illness

One hundred and twenty-two (23.33%) patients were classified as high risk according to their COVID-GRAM score, while 197 (37.7%) patients presented a CURB-65 score ≥ 2 .

The proportion of patients with a high COVID-GRAM score was significantly greater in the group of patients with a critical illness compared to those without a critical illness (64.5% vs 30.5%, respectively; $P < 0.001$) (Table 1). A high COVID-GRAM score showed a sensitivity of 53%, specificity of 84%, PPV of 48%, and NPV of 87% for critical illness (Table 4). The ROC curve showed an AUC of 0.779 for predicting critical illness (Figure 1A).

Logistic regression analysis was applied, adjusting by sex, obesity, and severity of illness at admission. A high COVID-GRAM score emerged as an independent predictor of critical illness (OR 9.40, 95% CI 5.51–16.04; $P < 0.001$) (Table 5).

Since 162 patients (30.97%) had missing data, patients with complete data ($n = 361$, 69.03%) were analysed separately ($n = 361$). The proportion of patients with a high COVID-GRAM score was significantly greater in the group of patients with a critical illness than in the group without a critical illness (74.1% vs 14.7%; $P < 0.001$). When logistic regression analysis was applied in this group of patients, a high COVID-GRAM score was also shown to be an independent predictor of critical illness (OR 17.67, 95% CI 6.79–45.97; $P < 0.001$).

The sensitivity, specificity, PPV, and NPV of a CURB-65 score ≥ 2 for critical illness are shown in Table 4. The ROC curve showed an AUC of 0.727 for predicting critical illness (Figure 1B).

COVID-GRAM score and CURB-65 score for predicting 30-day mortality

The accuracy of the COVID-GRAM score for predicting 30-day mortality was evaluated. Among the patients with a high COVID-GRAM score, mortality was 10.7% (56 patients). A high COVID-GRAM score showed a sensitivity of 77%, specificity of 85%, PPV of 46%, and NPV of 96% (Table 4), and an AUC of 0.88 for 30-day mortality (Figure 1C). A high COVID-GRAM score emerged as an independent predictor of mortality when logistic regression analysis was applied (OR 20.42, 95% CI 10.72–38.90; $P < 0.001$).

When the group of patients with complete data was analysed separately, a high COVID-GRAM score also emerged as an independent predictor of mortality (OR 24.52, 95% CI 8.41–71.54; $P < 0.001$).

Table 2

Clinical characteristics at admission and treatment of patients hospitalized with COVID-19 who did or did not develop critical illness.

	Total (n = 523)	Critical illness		P-value ^a
		No (n = 413)	Yes (n = 110)	
Unconsciousness, n (%)	88 (16.8)	53 (12.8)	35 (31.8)	<0.001
Dyspnoea, n (%)	238 (45.5)	163 (39.5)	75 (68.2)	<0.001
Haemoptysis, n (%)	5 (1)	3 (0.7)	2 (1.8)	0.296
Chest pain, n (%)	81 (15.5)	68 (16.5)	13 (11.8)	0.231
Fever, n (%)	378 (72.3)	289 (70)	89 (80.9)	0.23
Dry cough, n (%)	338 (64.6)	267 (63.9)	74 (67.3)	0.514
Headache, n (%)	53 (10.1)	48 (11.6)	5 (4.5)	0.029
Rash, n (%)	3 (0.6)	3 (3.7)	0	0.37
Anosmia, n (%)	31 (5.9)	28 (6.8)	3 (2.7)	0.11
Temperature >38 °C or <36 °C, n (%)	138 (26.4)	78 (18.9)	60 (54.5)	<0.001
Heart rate >90 beats/min, n (%)	123 (23.5)	80 (19.4)	43 (39.1)	<0.001
Respiratory rate, n (%)				<0.001
<20 breaths/min	271 (51.8)	234 (56.7)	37 (33.6)	
20–30 breaths/min	105 (20.1)	60 (14.5)	45 (40.9)	
>30 breaths/min	22 (4.2)	5 (1.2)	17 (15.5)	
Unknown	123 (23.5)	112 (27.1)	11 (10)	
Systolic blood pressure <100 mmHg, n (%)	36 (6.9)	27 (6.5)	9 (8.2)	0.645
SaO ₂ <90 %, n (%)	105 (20.1)	63 (15.3)	42 (38.2)	<0.001
High COVID-GRAM, n (%)	122 (23.3)	63 (15.3)	59 (53.6)	<0.001
CURB-65 score ≥ 2 , n (%)	197 (37.7)	126 (30.5)	71 (64.5)	<0.001
qSOFA score ≥ 2 , n (%)	13 (2.48)	7 (1.7)	6 (5.5)	0.002

SaO₂, oxygen saturation.

^a Chi-square test.

Table 3
Laboratory and chest radiography findings at admission among patients hospitalized with COVID-19 who did or did not develop critical illness.

	Total (n = 523)	Critical illness		P-value ^a
		No (n = 413)	Yes (n = 110)	
Neutrophil count, ×10 ⁹ /l, mean (SD)	4.8 (2.7)	4.5 (2.5)	5.8 (3.2)	<0.001
Lymphocyte count, ×10 ⁹ /l, mean (SD)	1.2 (1.4)	1.2 (1.1)	1.2 (2.4)	0.896
Neutrophil to lymphocyte ratio, mean (SD)	5.85 (5.91)	5.00 (4.59)	9.01 (8.63)	<0.001
Platelet count, ×10 ⁹ /l, mean (SD)	203.33 (92.28)	207.71 (93.92)	186.89 (84.22)	0.035
Haemoglobin, g/l, mean (SD)	13.58 (1.69)	13.67 (1.56)	13.24 (2.10)	0.049
CRP, mg/l, mean (SD)	8.35 (7.33)	6.94 (6.07)	12.94 (9.06)	<0.001
Procalcitonin, ng/mL, mean (SD)	0.3 (2.09)	0.21 (1.85)	0.61 (2.80)	0.303
Lactate dehydrogenase, U/l, mean (SD)	223.98 (222.29)	203.35 (140.70)	301.16 (392.31)	0.013
Total bilirubin, mmol/l, mean (SD)	0.43 (0.96)	0.50 (1.06)	0.17 (0.40)	0.089
Creatinine, μmol/l, mean (SD)	1.32 (0.58)	0.89 (0.47)	1.34 (1.21)	<0.001
Abnormal chest radiography, n (%)	397 (75.9)	299 (72.4)	98 (89.1)	<0.001

CRP, C-reactive protein, SD, standard deviation.

^a T-test or Chi-square test (as appropriate in each case).**Table 4**

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of high COVID-GRAM scores and CURB-65 scores ≥2 in predicting critical illness and 30-day mortality in 523 patients hospitalized with COVID-19.

	(TP)/total positives)	(TN)/total negatives)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
Critical illness						
High COVID-GRAM score	59/122	51/401	0.53 (0.44–0.62)	0.84 (0.81–0.88)	0.48 (0.39–0.57)	0.87 (0.84–0.91)
CURB-65 score ≥2	71/197	39/326	0.64 (0.55–0.73)	0.69 (0.65–0.73)	0.36 (0.29–0.43)	0.88 (0.85–0.92)
30-day mortality						
High COVID-GRAM score	56/122	385/401	0.77 (0.68–0.87)	0.85 (0.82–0.88)	0.46 (0.37–0.55)	0.96 (0.94–0.98)
CURB-65 score ≥2	62/197	10/316	0.86 (0.78–0.94)	0.70 (0.64–0.75)	0.31 (0.25–0.38)	0.97 (0.95–0.99)

CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; TN, true negative; TP, true positive.

Table 5

Multivariable logistic regression model for predicting the development of critical illness in 523 patients hospitalized with COVID-19.

Variables	OR (95% CI)	P-value
Male sex	1.65 (1.03–2.64)	0.038
Obesity	2.25 (1.30–3.89)	0.004
qSOFA ≥2	0.658 (0.46–0.95)	0.024
High COVID-GRAM score	9.40 (5.51–16.04)	<0.001

CI, confidence interval; LDH, lactate dehydrogenase; OR, odds ratio.

Among the patients with a high CURB-65 score, mortality was 11.85% (62 patients). A CURB-65 score ≥2 showed a sensitivity of 86%, specificity of 70%, PPV of 31%, and NPV of 97% (Table 4), and an AUC of 0.83 (Figure 1D) for 30-day mortality.

Kaplan–Meier curves for high COVID-GRAM score and CURB-65 score ≥2 for 30-day mortality are shown in Figure 2.

There was no significant difference in ICU admission according to the COVID-GRAM score (16.7% for high-risk patients vs 83.3% for low–intermediate-risk patients; $P = 0.222$) or the CURB-65 score (31.5% for CURB-65 score ≥2 vs 68.5% for CURB-65 score <2; $P = 0.322$).

Discussion

This appears to be the first study to analyse the usefulness of the COVID-GRAM score in a non-Chinese population. The strength of this study lies in the fact that it included all adults admitted with a diagnosis of COVID-19 to a tertiary-level European hospital during the beginning of the COVID-19 pandemic.

The mean age of the study patients was higher (65.63 vs 48.9 years) and the proportion of comorbidities was also higher (59.7% vs 25.1%) when compared to the study of Liang et al. (Liang et al.,

2020). This could explain why critical illness and mortality were also higher among the present study patients compared to the original study (Liang et al., 2020) (21% vs 8.2%, and 13.8% vs 3.2%, respectively).

The results of this study are more similar in terms of mean age and comorbidities to those published in European and North American populations with SARS-CoV-2 infection (Richardson et al., 2020; Suleyman et al., 2020; Giacomelli et al., 2020; Guisado-Vasco et al., 2020), in which the reported mortality was even higher than among the present study patients (about 20% in most reports).

Univariate analysis identified different variables as predictors of critical illness, including age, male sex, the presence of comorbidities (especially hypertension, COPD, cerebrovascular disease, and chronic kidney disease), unconsciousness, dyspnoea, fever, tachycardia, tachypnoea, SaO₂ <90%, high CRP levels, creatinine, LDH, neutrophil to lymphocyte ratio, and radiological confirmation of pneumonia. Likewise, the proportions of patients with a high COVID-GRAM score, WHO score ≥5, CURB65 score ≥2, and qSOFA score ≥2 were significantly higher in the group with a critical illness when compared to the group without a critical illness.

A high COVID-GRAM score at admission emerged as an independent predictor of critical illness, showing good sensitivity, specificity, and especially NPV. ROC curves showed good accuracy in predicting critical illness. Accuracy was even higher in the original study by Liang et al. (Liang et al., 2020); this difference in accuracy was perhaps influenced by the higher mean age and higher proportion with comorbidities among the present study patients. When the COVID-GRAM score was applied for predicting mortality, higher NPV and ROC curve values were obtained.

Interestingly, the accuracy of the CURB-65 score in predicting mortality was quite similar to that of the COVID-GRAM score. Although the AUC was slightly lower, the CURB-65 score showed a good NPV, and its simplicity of use makes it particularly attractive

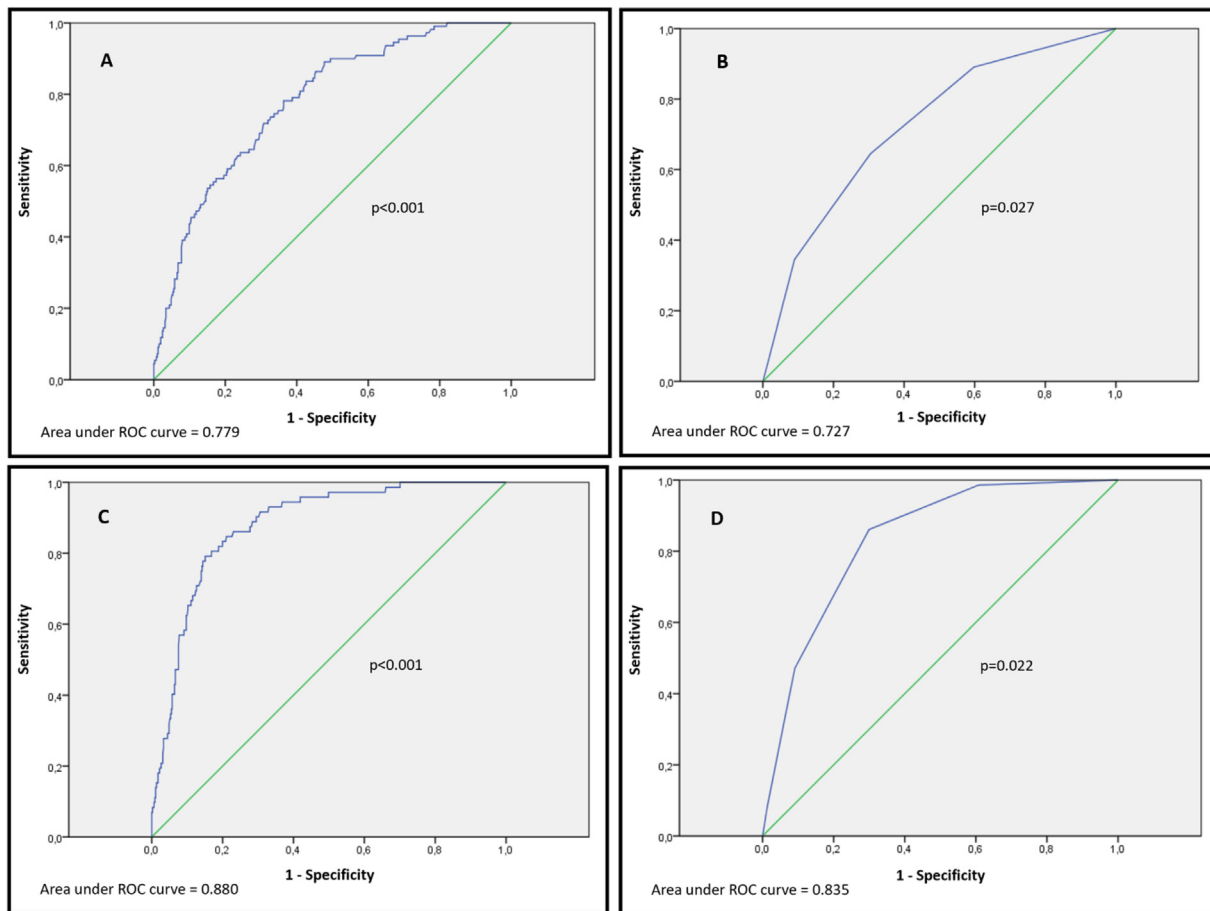


Figure 1. ROC curves to assess the accuracy of the COVID-GRAM score and CURB-65 score at admission for predicting critical illness and 30-day mortality in 523 patients hospitalized with COVID-19. (A) Accuracy of the COVID-GRAM score for predicting critical illness; (B) accuracy of the CURB-65 score for predicting critical illness; (C) accuracy of the COVID-GRAM score for predicting 30-day mortality; and (D) accuracy of the CURB-65 score for predicting 30-day mortality.

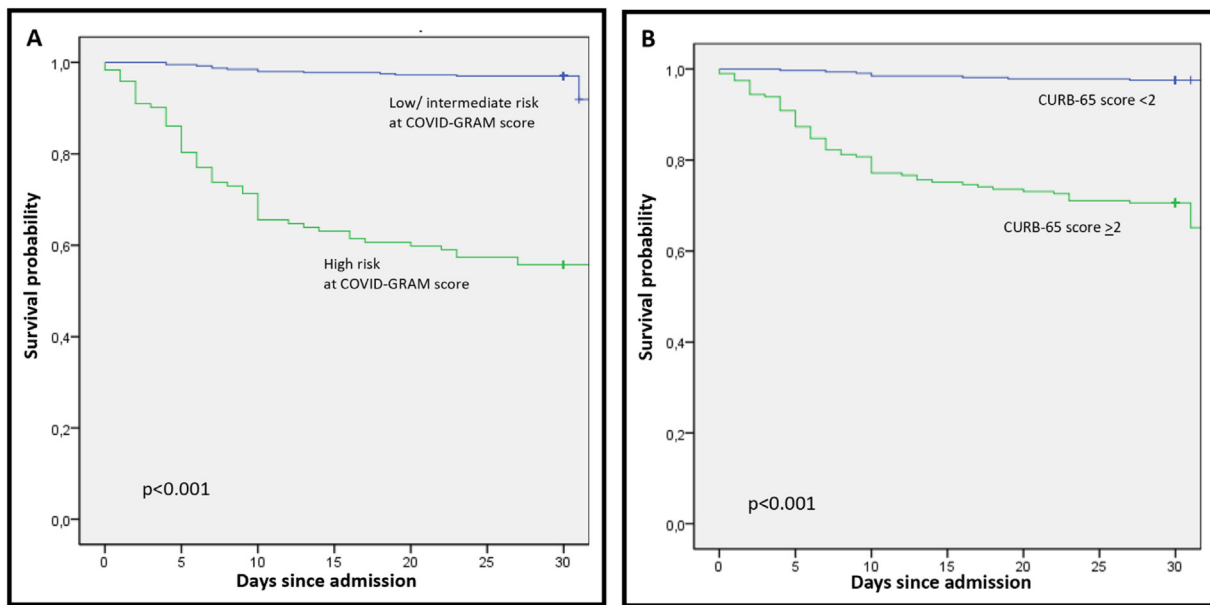


Figure 2. Kaplan–Meier curve for overall survival among 523 patients hospitalized with COVID-19 stratified by (A) COVID GRAM score and (B) CURB-65 score.

for routine clinical practice in COVID-19 patients, especially when quick decisions must be made, such as occurs in emergency departments. The results of this study on the accuracy of CURB-65 for mortality of patients with SARS-CoV-2 infection are similar to those reported in other publications (Guo et al., 2020; Ma et al., 2020; Fan et al., 2020; Satici et al., 2020; Wang et al., 2020; García Clemente et al., 2020).

This study has some limitations. First, the retrospective approach means that some variables were unknown from the COVID-GRAM and CURB-65 scores at admission. All unknown variables were assigned a value of normal, in order not to overestimate the results of the two scores. Second, all of the study participants were seen in the same hospital, and there may be differences among populations, even though similar patient characteristics as in other European and North American studies were observed (Richardson et al., 2020; Suleyman et al., 2020; Giacomelli et al., 2020; Guisado-Vasco et al., 2020). Finally, since all patients in this study were hospitalized, it is impossible to conclude if patients with a low risk of critical illness and mortality according to COVID-GRAM and CURB-65 could be safely discharged.

In summary, the COVID-GRAM score may be a useful tool for identifying Caucasian patients with SARS-CoV-2 infection who are at a low risk of critical illness and mortality. The CURB-65 score could be a good alternative, especially in situations of healthcare overload, where decisions must be made quickly. Further studies are needed to confirm whether these patients could be safely discharged and monitored on an outpatient basis.

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Ethical approval

Ethical approval was obtained from the Ethics Committee of Cantabria (internal code 2020.237).

Conflict of interest

The authors declare that they have no conflict of interest.

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