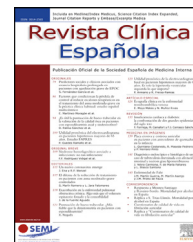




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## BRIEF ORIGINAL

## CURB-65 as a predictor of 30-day mortality in patients hospitalized with COVID-19 in Ecuador: COVID-EC study<sup>☆</sup>



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### KEYWORDS

Pneumonia;  
Coronavirus;  
SARS-CoV-2;  
COVID-19;  
CURB-65;  
Mortality

### Abstract

**Objective:** This article aims to assess the utility of CURB-65 in predicting 30-day mortality in adult patients hospitalized with COVID-19.

**Methods:** This work is a cohort study conducted between March 1 and April 30, 2020 in Ecuador.

**Results:** A total of 247 patients were included (mean age  $60 \pm 14$  years, 70% men, overall mortality 41.3%). Patients with  $\text{CURB-65} \geq 2$  had a higher mortality rate (57 vs. 17%,  $p < .001$ ) that was associated with other markers of risk: advanced age, hypertension, overweight/obesity, kidney failure, hypoxemia, requirement for mechanical ventilation, or onset of respiratory distress.

**Conclusions:**  $\text{CURB-65} \geq 2$  was associated with higher 30-day mortality on the univariate (Kaplan–Meier estimator) and multivariate (Cox regression) analysis.

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## PALABRAS CLAVE

Neumonía;  
Coronavirus;  
SARS-CoV-2;  
COVID-19;  
CURB-65;  
Mortalidad

## CURB-65 como predictor de mortalidad a 30 días en pacientes hospitalizados con COVID-19 en Ecuador: estudio COVID-EC

### Resumen

**Objetivo:** Valorar la utilidad del CURB-65 para predecir la mortalidad a 30 días en pacientes adultos hospitalizados con COVID-19.

**Métodos:** Cohorte realizada entre el 1 de marzo y el 30 de abril de 2020 en Ecuador.

**Resultados:** Se incluyeron 247 pacientes (edad media  $60 \pm 14$  años, 70% varones, mortalidad global 41,3%). Los pacientes con CURB-65  $\geq 2$  presentaron mayor mortalidad (57 vs. 17%,  $p < 0,001$ ), en asociación con otros marcadores de riesgo: edad avanzada, hipertensión arterial, sobrepeso/obesidad, fracaso renal, hipoxemia, requerimiento de ventilación mecánica o desarrollo de distrés respiratorio.

**Conclusiones:** En el análisis univariado (Kaplan–Meier) y multivariado (regresión de Cox) el CURB-65  $\geq 2$  se relacionó con una mayor mortalidad a 30 días.

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## Introduction

COVID-19, caused by coronavirus type 2 which causes severe acute respiratory syndrome (SARS-CoV-2), was the main cause of morbidity and mortality in 2020.<sup>1</sup> Approximately 15% of patients correspond to severe cases and 5% to critical illness, with mortality for this latter group being around 50%.<sup>2</sup>

Multiple risk factors associated with the onset of acute respiratory distress syndrome and death have been identified, including old age, organ dysfunction due to Sequential Organ Failure Assessment (SOFA), coagulopathy, and elevated D-dimer.<sup>3–5</sup> Early detection of patients likely to develop severe disease is highly important and can help ensure the provision of adequate care and appropriate distribution of resources.

To date, there are few tools for assessing the severity of COVID-19 in patients.<sup>2,6</sup> Various protocols have suggested the use of scales such as CURB-65 (Confusion, Urea, Respiratory rate, Blood pressure and 65 years of age and older), the Pneumonia Severity Index, and the quick SOFA score; however, there is little research into their utility in COVID-19.<sup>6–12</sup> Of the mentioned scores, CURB-65 is simple and useful for predicting 30-day mortality in adult patients with bacterial pneumonia.<sup>13,14</sup>

Therefore, this multicentre study assesses the utility of CURB-65 in predicting 30-day mortality in adult patients hospitalised with COVID-19.

## Methods

Retrospective cohort study that reviewed data from adult patients hospitalised at one of the six participating hospitals in the city of Guayaquil between 1 March and 30 April 2020, with confirmed or suspected COVID-19 diagnosis according to the protocols for the diagnosis and management of COVID-19 in Ecuador.<sup>15,16</sup> Only patients that were recorded by the study investigators were included and cases with a negative

SARS-CoV-2 nasal swab were excluded. The registry received ethical approval from the Comprehensive Health Innovation and Research Institute from the Medical School of Guayaquil Catholic University.

The variables from the COVID-EC study were previously published.<sup>17</sup> The investigators from each centre collected demographic data and clinical, analytical, radiological, microbiological, and therapeutic variables.

All-cause in-hospital death was recorded, and CURB-65 was calculated for all patients during their first contact in the Emergency Department.<sup>13</sup>

The primary outcome variable was in-hospital and 30-day all-cause death. The qualitative variables were expressed as absolute and relative frequencies. The quantitative variables were expressed in means and standard deviation. For comparisons, the Chi-squared test was used or Fisher's test for qualitative variables and Student's t-test was used for the quantitative variables. Kaplan-Meier curves were created for the primary outcome variable according to the CURB-65 classification and were compared using the log-rank test.

To evaluate the independent association between CURB-65 and mortality, a Cox regression model was adjusted which included variables associated with the outcome variable in the univariate analysis with  $p < 0.10$ . The effect measures were shown with hazard ratios (HR) and a 95% confidence interval (95% CI). The areas under the curve (AUC) for the prediction models were compared using the DeLong and Clarke-Pearson approach. The differences were considered statistically significant when the  $p$ -value was less than 0.05.

Statistical analyses were carried out using the SPSS statistical package (IBM, North Castle, New York, USA).

## Results

A total of 247 patients were included (mean age  $60 \pm 14$  years; 70% male; 47.4% admitted to the Intensive Care Unit; overall mortality 41.3%). The most common comorbidity was

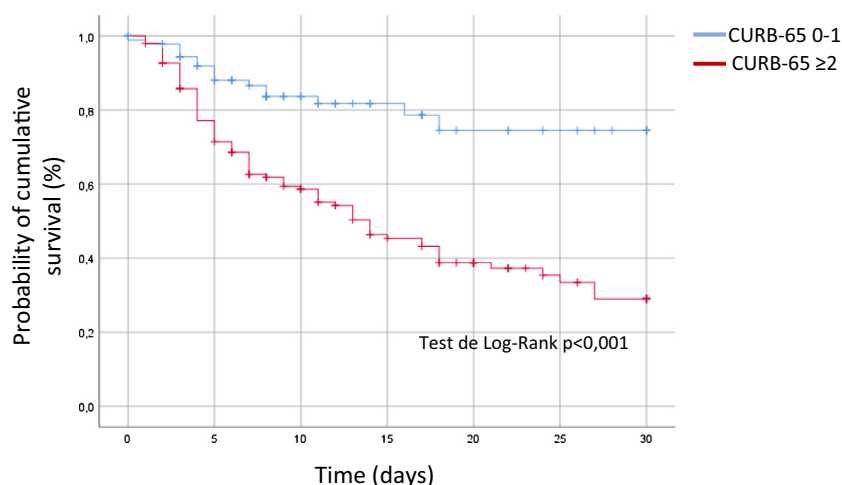


Fig. 1 Probability of cumulative survival at 30 days.

Table 1 Univariate and multivariate analysis of independent factors associated with mortality.

	Univariate			Multivariate		
	HR	95% CI	p	HR	95% CI	p
<i>Clinical variables</i>						
Age (>65 years)	1.22	0.91–1.65	0.189	–	–	–
Coronary artery disease	1.82	1.23–2.70	0.03	–	–	–
Immunosuppression	1.86	1.21–2.87	0.068	–	–	–
Ex-smoker	1.62	1.14–2.32	0.026	–	–	–
SO <sub>2</sub> < 92%	2.02	1.27–3.24	0.001	–	–	–
<i>Analytical variables</i>						
CRP (>150 mg/L)	1.87	1.20–2.91	0.002	–	–	–
D-dimer (>1500 ng/mL)	1.30	0.94–1.80	0.145	–	–	–
<i>Prognostic variables</i>						
CURB-65 ≥ 2	3.34	2.09–5.36	0.001	2.28	2.24–2.61	<0.01
<i>Therapeutic variables</i>						
Corticosteroids	0.66	0.49–0.88	0.009	–	–	–
Azithromycin	0.65	0.48–0.88	0.013	–	–	–
Tocilizumab	0.69	0.45–1.06	0.10	–	–	–
LMWH	1.07	0.83–1.36	0.69	–	–	–

CURB-65: confusion, urea > 42 mg/dL, respiratory rate > 30 rpm, blood pressure < 90 mmHg (systolic) or < 60 mmHg (diastolic), 65 years or older; LMWH: low-molecular-weight heparin at prophylactic doses (enoxaparin 40 mg/24 h or equivalent); HR: hazard ratio; 95% CI: 95% confidence interval; CRP: C-reactive protein; SO<sub>2</sub>: oxygen saturation.

high blood pressure (48.6%), followed by overweight/obesity which was present in 28.3% of cases.

The most reported COVID-19 symptoms were dyspnoea (90.7%), fever (85.4%), cough (84.2%), and weakness (81%). The most common radiology finding was the presence of bilateral pneumonia (76.1% of cases) and 35.2% of patients presented interstitial involvement in the chest tomography. SARS-CoV-2 infection was confirmed in 22% of patients by means a nasal swab using reverse transcription polymerase chain reaction technique. It was not possible to confirm infection with said technique in 193 patients due to a lack of test availability.<sup>18</sup>

After classifying the patients according to CURB-65 (0–1 vs. ≥2), those with CURB-65 ≥ 2 presented older age

(64 ± 13 vs. 54 ± 14.6 years, *p* < 0.001) and higher rate of comorbidity (high blood pressure 57 vs. 36.2%, *p* = 0.002; overweight/obesity 34 vs. 20.2%, *p* = 0.02; coronary artery disease 7.3 vs. 0%, *p* = 0.007). These patients presented lower oxygen saturation levels (81 ± 15% vs. 88 ± 9%, *p* < 0.001), required more support with mechanical ventilation (55 vs. 36.2%, *p* = 0.005), and presented more acute respiratory distress syndrome (68.9 vs. 49.8%, *p* = 0.002) and death (57 vs. 17%, *p* < 0.001). The general characteristics of the sample are presented in Annex 1 (Appendix B, see supplementary material).

The Kaplan-Meier survival curves showed significant differences between patients according to CURB-65 (0–1 vs. ≥2) for the 30-day mortality variable (Fig. 1). In the multi-

ivariate analysis, CURB-65  $\geq 2$  was independently associated with 30-day mortality due to COVID-19 (Table 1).

CURB-65  $\geq 2$  presented adequate discriminatory capacity to predict 30-day mortality with 84% sensitivity, 54% specificity, a PPV of 56% and a NPV of 83% (AUC 0.72, 95% CI 0.68–0.86;  $p < 0.001$ ) (Appendix B, annex 2. See supplementary material).

## Discussion

CURB-65 is probably the most widely used mortality prediction scale across the globe as it uses only five variables to determine disease severity, placing emphasis on physiological parameters and being easier to calculate than other scales such as the Pneumonia Severity Index.<sup>14</sup> These are the reasons why CURB-65 has been included in hospital protocols for the management of COVID-19 patients.<sup>19</sup>

Previous studies have identified risk factors for death in adults hospitalised with COVID-19; in particular, being over the age of 50, having cardiovascular diseases, D-dimer levels  $> 1000$  ng/mL and an elevated SOFA score at admission.<sup>3,10</sup>

In addition, elevated blood levels of IL-6, troponin I and LDH have frequently been observed in patients with severe disease.<sup>3</sup> A recent study with 681 patients reported that a CURB-65 score  $\geq 2$  presented adequate discriminatory capacity to predict 30-day mortality, similar to that found in our study.<sup>11</sup>

Other evidence shows that scales such as APACHE II and SOFA predict in-hospital mortality better than CURB-65 (AUC 0.96, 95% CI 0.94–0.99 for APACHE II; AUC 0.86, 95% CI 0.81–0.93 for SOFA, and AUC 0.84, 95% CI 0.78–0.91 for CURB-65, using cut-off points of 17, 3, and 1, respectively). This could be explained because the APACHE II variables include comorbidity and age, while CURB-65 only includes age. Therefore, the APACHE II and Pneumonia Severity Index scales could be more appropriate for stratifying mortality risk in patients with comorbidities.<sup>8,11</sup>

Our findings confirm that CURB-65 is a useful tool in patients with COVID-19, despite it having been originally designed as a tool for bacterial pneumonia.<sup>9,10,12</sup> Using a cut-off point of  $\geq 2$ , we have found significant differences in mortality in adult patients hospitalised with COVID-19. In our series, mortality for the CURB-65 0–1 group was 17%, which is contrasted with what was previously reported in bacterial pneumonia.<sup>14</sup>

In a recently published French series with 279 patients, it was observed that 21.1% of those with CURB-65 0–1 presented poor evolution.<sup>12</sup> This makes it possible to infer that the CURB-65 score is related to higher mortality, yet its relevance for guiding decision-making on hospital admission of patients with COVID-19 is uncertain: it does not adequately identify those who can be managed in an out-patient setting. This may be because there are epidemiological differences and differences in terms of severity between patients with COVID-19 and those with bacterial pneumonia. Therefore, if CURB-65 is used, prior to deciding whether or not to discharge the patient directly from the Emergency Department, the likelihood of presenting direct complications due to pneumonia should be considered, including respiratory failure, pleural effusion, worsening of underlying disease,

ability to take oral medication, and the availability of a caregiver.<sup>14</sup>

Despite the fact that a specific risk score has already been developed and validated for predicting the development of severe/critical disease in patients hospitalised with COVID-19 (AUC 0.88, 95% CI 0.84–0.93), this requires 10 variables, so using CURB-65 remains a simpler option.<sup>2</sup> For practical purposes, simplifying patient classification into intermediate-low or moderate-high risk groups can be adequate, and it is for that reason that we consider CURB-65 to be more feasible in actual clinical practice.

This study presents various limitations. First, those that are inherent to a non-randomised retrospective study. Second, COVID-19 diagnosis could not be confirmed in all cases given that there were not enough tests available in Ecuador for diagnosis<sup>18</sup> and, as in other countries, the diagnostic criteria changed over the course of time.<sup>20</sup> Third, not all the radiological and/or lab tests were available for all the patients. Nevertheless, despite the aforementioned limitations, it is a registry of real clinical practice, and the only multicentre one performed in hospitals in Guayaquil, Ecuador.<sup>17</sup>

## Conclusion

The CURB-65 scale is a useful and simple tool for predicting 30-day mortality in patients hospitalised with COVID-19, using a cut-off point of  $\geq 2$ .

## Funding

None.

## Conflicts of interest

The authors declare that they do not have any conflicts of interest.

## Appendix A. COVID-EC Research Group

Jorge Carriel, Roberto Muñoz-Jaramillo, Bella Morales-Cabezas, Osvaldo Seijas-Cabrera, Pamela Zea-Santillán, Herman Alarcón-Peralta, Giomary Nucette, Jorge Menéndez-Sanchón, Diana Guamán-Gutiérrez, Jorge Bucaram-Matamoros, Karim Larrea-Olivero, Daniel Tettamanti-Miranda, Pia Manrique-Acosta, Guillermo Bejarano-Wagner, Carlos Jaramillo-Sotomayor, Fausto Heredia-Villacreses, Julio Cevallos-Quiroz, Matías Altes-Ezequiel, Oswaldo Bolaños-Ladinez, Ana Castañares Perdigón, Jimmy Martin-Delgado, Alejandra Espinoza de los Monteros, Giuliana Roggiero Bueno, Peter Chedraui y Gustavo Ramírez Amat.

## Appendix B. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.rce.2020.10.001>.

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