Survival of a cohort of COVID-19 patients on mechanical ventilation in the ICU of a Level III hospital in Bogotá, Colombia

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ABSTRACT

Background & Objective: The COVID-19 mortality varies from country to country. The pandemic has enriched our knowledge about the pathogenesis of the viral diseases in the human race. We aimed to establish survival curves based on a population of patients with confirmed diagnosis of COVID-19 who received mechanical ventilation in ICU of our level-III hospital.

Methodology: It is an observational study with a prospective cohort. All patients with a positive RT-PCR test for SARS-CoV-2 after the nasopharyngeal swab and who needed mechanical ventilation were identified. Kaplan–Meier survival estimates were calculated until the follow-up date of September 26, 2020.

Results: We included 62 patients in the study. The bivariate analysis found that congestive heart failure, kidney injury, dysnatremia, acid-base disorders, delta CO₂, and lactate levels were associated with higher mortality. When performing backward-type Cox regression, it was observed that the CO₂ delta [Hazard Ratio (HR) = 14.78, 95% CI: 2.1-100.5, P = 0.00] and lactate levels (HR = 6.15, 95% CI: 1.1-34.2, P = 0.038), were associated with an increase in mortality, for the admission variables. And only dysnatremia (HR = 5.28, 95% CI: 1.8-15.3, P = 0.00) and acid-base disorders (HR = 12.04: 95% CI: 4.1-35.3, P = 0.00) for the follow-up variables.

Conclusions: Among the factors associated with increased mortality in COVID-19 patients on mechanical ventilation in the first 24 h, parameters related to tissue hypoperfusion were identified. For the variables associated with mortality at 14 days, dysnatremia and acid-base disorders were identified.
1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is the name given to the disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which was first described in December 2019 in patients from Wuhan city, Hubei province, China. From December 2019 to the present, the causative organism, SARS-CoV-2, has spread worldwide, infecting 548,990,094 people and causing 6,341,637 deaths, making this disease a public health problem at the global level.

Epidemiological studies have shown that 6-10% of patients develop more severe form of COVID-19 and require admission to an intensive care unit (ICU) for acute hypoxemic respiratory failure. These patients also require mechanical ventilation, resulting in a prolonged hospital stay and an increased likelihood of mortality; there are also reports of higher infection rates contributing to mortality.

To date, few studies have been carried out in critically ill patients in Colombia; additionally, differences in demographics and population behavior may limit the generalizability of some findings. Therefore, it is imperative to evaluate the risk factors associated with mortality and survival of patients diagnosed with COVID-19 in a cohort of patients who were hospitalized and received mechanical ventilation in the ICU of a Level III hospital in the city of Bogotá, Colombia.

2. METHODOLOGY

An observational study was carried out with a prospective cohort of patients admitted to the ICU at a Level III institution in Bogotá, Colombia.

Patients’ electronic medical records were reviewed and collected by trained intensive care physicians following a standardized protocol. Each researcher entered the data into an online data acquisition system explicitly predesigned for this purpose [CICERO (CovId-19 meChanical vEntilation Research grOup)].

All consecutive COVID-19 patients included in the dataset from March 1, 2020 to September 26, 2020, and who met the following inclusion criteria: ≥18 y of age, intubated and mechanically ventilated, confirmed SARS-CoV-2 infection by evidence-based RT–PCR analysis of a respiratory tract sample. The following patients were excluded: patients with unconfirmed SARS-CoV-2 disease, those without data at the beginning of the study, those without ventilator parameter information, or patients who were not intubated.

All the data were collected within the first 24 h of admission to the ICU. Data from days 3, 5, 7, and 14 were used to estimate a measure of central tendency relative to follow-up. The collected data included demographic characteristics, comorbidities, symptoms at the ICU admission, vital signs, paraclinical studies, ventilator parameters, complementary therapies, such as prone position and pharmacological treatments, and severity assessment scores.

Statistical analysis

The selected predictors of mortality were used as dichotomous variables, and the cutoff points were based on previous studies and included the following: creatinine (> 2 mg/dL), sodium (135-145 mEq/L; values outside this range indicated dysnatremia), potassium (3.5-5 mEq/L), pH (7.35-7.45; values outside this range indicated acid-base disorders), PaO₂ (< 65 mmHg), PaCO₂ (30-35 mmHg), bicarbonate in arterial blood (18-22 mEq/L), oxygen extraction (20-30%), arterial saturation (< 90%), venous saturation (70-80%), lactate levels (< 2 mmol/L) and sepsis-induced coagulopathy (SIC) score < 2).

Survival analysis was performed using the Kaplan–Meier method; the onset of symptoms was considered the time point when monitoring began. The dates were available in the database, and the following was used to create time intervals for the survival analysis: time (T1) from the beginning of symptoms to death/end of follow-up (discharge from the ICU) in days (d). There were no losses to follow-up, and competitive risks were ignored when assuming that all the deaths were influenced by COVID-19 infection within their causal complex; thus, the only censor in patients who did not present the event was the cutoff date of the study. Considering that the exact moment of the day at which each patient enrolled in or left the investigation is unknown, the days of follow-up were counted in a non-inclusive way; that is,
individual regression coefficients reliably- www.statistics.com). Additionally, the McNemar test was performed to identify the modifications of the categorical variables over time.

All analyses were performed in the SPSS program (IBM® SPSS® Statistics 24.0). An $\alpha \leq 0.05$ was used for all cases, with a one-tailed $P$ for the log-rank test and a two-tailed $P$ for the Wald test.

### Ethical aspects

This study received ethical approval (Ethics Committee Letter No. 200-057; Dated October 6, 2020) from the Ethics Committee of Integrated Subnetwork of Health Services Central East of the Santa Clara Hospital, Bogotá, Colombia. This research followed the international ethical standards for biomedical research with human beings established in the Declaration of Helsinki, and the regulations of the Ministry of Social Protection of Colombia, Resolution 8430 of 1993.

### 3. RESULTS

In total, 62 patients with COVID-19 were analyzed. The mean age was 62.7 ± 11.1 y, with an average age of 65.4 vs. 58.5 y for patients who died versus patients who survived. At admission, the most frequent comorbidity was hypertension (38.7%). The most common symptom at admission to the ICU was respiratory distress, which was observed in 43(69.4%) of the patients (Table 1).

The laboratory abnormalities observed in this cohort were (in order of frequency) lymphopenia (62.9%), elevated lactate dehydrogenase levels (46.8%), and elevated ferritin levels (29%). Regarding the relevant findings by ventilator monitoring, we found compromised dynamic compliance (67.7%), increased resistance in the airway (51.6%), the use of a high PEEP (46.8%), severe pulmonary dysfunction according to the Berlin classification (45.2%), and compromised static compliance (38.7%). Concerning the parameters related to protective ventilation (plateau pressure, conduction pressure, and tidal volume), we found a low frequency of changes in these parameters from admission to follow-up (Table 2).

During follow-up, the significantly altered variables were lymphocyte count, tidal volume, LDH level,
Creatinine level, acid-base status, sodium level, potassium level, PaCO₂ level, and PaO₂ level (Table 2). During the follow-up period 37 (59.7%) patients died. A progressive decrease was observed in the overall survival function, reaching a survival of 50% on Day 25. Generally, the highest mortality rate occurred between Days 0 and 30 of follow-up; after that, the mortality rate decreased to zero beginning on Day 62. When evaluating the Kaplan–Meier survival function, a 99.9% probability of survival was observed on the first day, a 68% probability was observed on the tenth day, and a 78% probability was observed on the twelfth day. As of Day-30, of the course of the disease, the survival rate was approximately 69% (Figure 1).

Survival associated with risk factors
With the LogRank tests, it was possible to identify the differential survival associated with the presence or absence of selected factors, such as concurrence with decompensated heart failure at admission, elevated creatinine level, dysnatremia, acid-base disorders (diagnosed by a change in pH), increased delta CO₂ and increased lactate level. The associations were statistically significant when each factor was evaluated in the first 24 h after admission (Figure 2). By averaging the values within the first 14 days of the hospital stay, the log-rank tests identified differential survival associated with the presence or absence of selected factors, such as dysnatremia, acid-base disorders, and elevated levels of lactate (Figure 3). For the other variables, no statistically significant differences were identified (Tables 1 and 2).

Cox regression
Under the backward-type Cox regression, it can be observed that after controlling for the effect of the other factors, the HR of increased lactate and delta CO₂ levels remained statistically significant (Table 3). Similarly, a backward-type Cox regression was carried out for the follow-up variables. It was observed that after controlling for the effect of the other factors, the HR for dysnatremia and acid-base disorders remained statistically significant (Table 3).

4. DISCUSSION
To date, numerous studies have identified risk factors associated with mortality from COVID-19; this is a relevant document because it allows us to determine the outcomes of a cohort of patients from a Level III hospital in Bogotá, Colombia, and to estimate COVID-19 survival in a critically ill and vulnerable Colombian population. Thus, this study provides an essential insight into the reality of the Latin American people.

In this cohort of patients, the mean age was 63 ± 11 y, the SOFA score was 6 ± 3.5, and the NEW2 score was 8 (IQR 7-11). Additionally, 51.6% of the patients required vasopressor support, and 48.4% required prone therapy. The median hospital stay was 38 vs. 17 days, the median ICU stay was 25 vs. 17 days, and the median mechanical ventilation duration was 9 vs. 8.5 days among survivors vs. non-survivors. These patients were treated with high ventilator parameters (a median FiO₂ of 80% (IQR 50-100) and a PEEP of 13 (IQR 10-14)) and received protective mechanical ventilation (a median tidal volume 6.9 mL/kg (IQR 6.5-7.4), a driving pressure of 10 (IQR 6-14), and a plateau pressure of 21 (IQR 17-24).

Patients severely affected by COVID-19 usually present with the first phase of illness characterized by acute viremia (fever, cough, and myalgia); the second phase is then characterized by a pulmonary injury caused mainly by severe inflammation due to a massive cytokine response, also called “cytokine storm”, which can lead to elevated serum lactate levels and could be mediated by tissue hypoperfusion. However, Giuseppe Nardi et al. found that high delta lactate levels may be an early marker of biological damage mediated by virus-related inflammation rather than low output. In contrast, Thirumalaisamy P et al. found that serum lactate levels...
Table 2: Variables of the cohort at admission and follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>First 24 h</th>
<th>Follow-up</th>
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<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>HR</td>
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<tr>
<td><strong>Laboratory results</strong></td>
<td></td>
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<tr>
<td>D-dimer (&gt;1 mcg/ml)</td>
<td>15 (24.2)</td>
<td>1.22</td>
</tr>
<tr>
<td>Troponin (&gt; 0.05 ng/dl)</td>
<td>27 (43.5)</td>
<td>1.18</td>
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<tr>
<td>Lymphocyte count (&lt;1000 mm³)</td>
<td>39 (62.9)</td>
<td>1.36</td>
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<tr>
<td>LDH (&gt; 350 UI/L)</td>
<td>29 (46.8)</td>
<td>0.45</td>
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<tr>
<td>Ferritin (&gt;1000 mcg/L)</td>
<td>18 (29)</td>
<td>1.50</td>
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<tr>
<td>Creatinine</td>
<td>19 (30.6)</td>
<td>2.30</td>
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<tr>
<td>Sodium</td>
<td>23 (37.1)</td>
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<tr>
<td>Potassium</td>
<td>16 (25.8)</td>
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<tr>
<td><strong>Ventilatory parameters</strong></td>
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<td></td>
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<tr>
<td>Tidal volume (&gt; 6 ml/kg)</td>
<td>7 (11.3)</td>
<td>1.24</td>
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<tr>
<td>FiO₂ &gt; 60%</td>
<td>37 (59.7)</td>
<td>1.25</td>
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<tr>
<td>PEEP &gt; 12</td>
<td>29 (46.8)</td>
<td>1.18</td>
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<tr>
<td>Plateau pressure &gt; 30</td>
<td>3.2 (2)</td>
<td>1.70</td>
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<tr>
<td>Driving pressure &gt; 15</td>
<td>7 (11.3)</td>
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<tr>
<td>Peak Pressure &gt; 35</td>
<td>15 (24.2)</td>
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<tr>
<td>Dynamic compliance ml/cmH₂O &lt; 40</td>
<td>42 (67.7)</td>
<td>1.51</td>
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<tr>
<td>Static compliance ml/cmH₂O &lt; 40</td>
<td>24 (38.7)</td>
<td>1.83</td>
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<td>Ventilatory Ratio &gt; 2</td>
<td>4 (6.5)</td>
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<td>PAFI &lt; 100</td>
<td>28 (45.2)</td>
<td>1.36</td>
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<td><strong>Gasometric parameters</strong></td>
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<tr>
<td>pH</td>
<td>32 (51.6)</td>
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<td>PaO₂</td>
<td>24 (38.7)</td>
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<td>PaCO₂</td>
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<td>Bicarbonate in blood</td>
<td>32 (51.6)</td>
<td>1.17</td>
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<td>Venous saturation</td>
<td>17 (27.4)</td>
<td>1.19</td>
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<td>Tissue oxygen extraction</td>
<td>15 (24.2)</td>
<td>1.19</td>
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<tr>
<td>Delta CO₂</td>
<td>7 (11.3)</td>
<td>10.99</td>
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<tr>
<td>Arterial saturation</td>
<td>13 (21.6)</td>
<td>1.13</td>
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<td>Lactate</td>
<td>15 (24.2)</td>
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<td><strong>Complementary therapies</strong></td>
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<tr>
<td>Prone position</td>
<td>30 (48.4)</td>
<td>1.40</td>
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<tr>
<td>Vasopressors</td>
<td>32 (51.6)</td>
<td>1.08</td>
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<tr>
<td><strong>Images</strong></td>
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<td></td>
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<tr>
<td>Chest X-ray (4 quadrant infiltrates)</td>
<td>35 (56.5)</td>
<td>1.41</td>
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<tr>
<td><strong>Scales</strong></td>
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<tr>
<td>NEWS2 &gt; 7</td>
<td>35 (56.5)</td>
<td>1.01</td>
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<tr>
<td>SOFA score &gt; 4</td>
<td>29 (46.8)</td>
<td>1.14</td>
</tr>
<tr>
<td>SIC</td>
<td>7 (11.3)</td>
<td>2.55</td>
</tr>
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</table>

* = McNemar statistic; Abbreviations: ng = nanogram; FiO₂ = Inspired oxygen fraction; PAFI = index of PaO₂/FiO₂; Delta CO₂ = Venous-to-arterial carbon dioxide difference; SIC = Sepsis-induced coagulopathy; SOFA Sequential Organ Failure Assessment; NEWS2 = National Early Warning Score 2; HR = Hazards Ratio.
Figure 2: Survival at admission
an increase in mortality, regardless of whether it corresponds to lactic or non-lactic acidosis or alkalosis (mediated by increased aldosterone levels). In this cohort, it was found that acid-base alterations (HR = 12.04, 95% CI: 4.1-35.3, P = 0.00) were associated with an increase in mortality. However, further studies with physicochemical approaches are required to characterize the disorder better.

Dysnatremia is a common disorder in critically ill patients. It is often acquired in the hospital, which explains why this disorder corresponds to findings in the late stage of the disease. Multiple mechanisms have been postulated to explain these findings; for example, the inappropriate secretion of antiuretic hormones, associated with drugs. These findings are consistent with the results from this cohort, where higher mortality was observed to be associated with sodium disorders (HR =

On the other hand, numerous investigations have been carried out during the pandemic on serum biomarkers associated with COVID-19-related mortality, but few studies have investigated the acid-base status. It is known that acid-base alterations are frequently observed in the ICU. These alterations have been associated with

Figure 3: Survival at follow-up

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COVID-19 patients on mechanical ventilation
The mortality rate in this disease is variable since it could range from 20% to 60%, depending on the type of studies. In this cohort of patients, the mortality rate was 59.7%, suggesting that a high mortality rate is expected, given that the study included critically ill patients who received mechanical ventilation and vasopressor support and had a high rate of multiorgan dysfunction. Myocardial dysfunction, measured by increased troponin levels, was observed in a significantly high percentage of patients at admission and follow-up (43.5% and 48.4%, respectively). The same was true for renal dysfunction (30.6% and 56.6%) and hematological dysfunction (24.2% and 53.2%). When the follow-up variables were analyzed, it was found that in this cohort of patients, kidney injury, electrolyte alterations, lactate levels, PaO₂ levels, PaCO₂ levels, and radiological findings significantly worsened during follow-up. The above explains why these mortality rates were similar to those reported in the literature for this type of condition. On the other hand, a progressive decrease in overall survival was observed, reaching a survival of 50% on Day 28; generally, the highest mortality rate was observed between Days 0 and 35 of follow-up, with a median survival of 29 days (95% CI: 21–36). These data suggest the need for early identification and timely treatment of critical patients, and these approaches should be considered crucial for reducing the number of deaths and increasing survival.

5. LIMITATIONS

The current study has some limitations. First, in some cases, there was incomplete documentation of antecedents, symptoms, or laboratory findings in the database, even after efforts to find and collect these data. Some diagnoses of disease coexistence were based on the self-reports of patients or relatives at admission, leading to a recall bias. Second, with the limited number of patients, it is difficult to assess the risk factors associated with mortality with adjusted multivariate methods; the preceding explains the wide confidence intervals described in this study. It could be said that this is a cohort with a modest number of patients admitted to the hospital, with a collection of standardized data. Nevertheless, larger cohorts would help to define better the clinical presentation, natural history, and risk factors of such patients. More studies on patients hospitalized in ICUs are needed to obtain a complete picture of the spectrum of the clinical severity of the disease in Colombia and Latin America. Additionally, the statistical findings should be interpreted with caution, and nonsignificant P values do not necessarily rule out the absence of an association.

6. CONCLUSION

Patients admitted to a Level III hospital with a diagnosis of COVID-19 and who received mechanical ventilation had a mortality rate of 59.7%. Among the factors associated with increased mortality in the first 24 hours, parameters related to tissue hypoperfusion, such as increased lactate and CO₂ delta levels, were identified. For variables associated with mortality at 14 days, dysnatremia and acid-base disorders were identified. For the most part, these results are consistent with what have been observed by other researchers in other countries. However, studies with a larger sample size are possibly needed to confirm these findings. This study is one of the first to estimate the survival of critically ill Colombian patients diagnosed with COVID-19.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

We gratefully thank Faculty of Medicine

9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors’ contribution

GO: Conceptualization, Validation, Writing - Review & Editing
MG: Writing - Review & Editing, Supervision
11. REFERENCES


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