A predictive score at admission for respiratory failure among hospitalized patients with confirmed 2019 Coronavirus Disease: a simple tool for a complex problem

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Abstract
Coronavirus Disease 2019 (COVID-19) pandemic has implacably stricken on the wellness of many countries and their health-care systems. The aim of the present study is to analyze the clinical characteristics of the initial wave of patients with COVID-19 attended in our center, and to identify the key variables predicting the development of respiratory failure. Prospective design study with concurrent data retrieval from automated medical records of all hospitalized adult patients who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rRT-PCR assay performed on respiratory samples from March 2nd to 18th, 2020. Patients were followed up to May 1st, 2020 or death. Respiratory failure was defined as a PaO2/FiO2 ratio ≤ 200 mm Hg or the need for mechanical ventilation (either non-invasive positive pressure ventilation or invasive mechanical ventilation). We included 521 patients of whom 416 (81%) had abnormal Chest X-ray on admission. Median age was 64.6 ± 18.2 years. One hundred eighty-one (34.7%) developed respiratory failure after a median time from onset of symptoms of 9 days (IQR 6–11). In-hospital mortality was 23.8% (124/521). The modeling process concluded into a logistic regression multivariable analysis and a predictive score at admission. Age, peripheral pulse oximetry, lymphocyte count, lactate dehydrogenase and C-reactive protein were the selected variables. The model has a good discriminative capacity with an area under the ROC curve of 0.85 (0.82–0.88). The application of a simple and reliable score at admission seems to be a useful tool to predict respiratory failure in hospitalized COVID-19 patients.

Keywords
Respiratory failure · SARS-CoV2 · COVID-19 · Coronavirus · Score · Outcome

Introduction
Coronavirus Disease 2019 (COVID-19) pandemic has implacably stricken on the wellness of many countries and their health-care systems.

COVID-19 has rapidly spread over the world, the incidence curve being overwhelmingly steep in Mediterranean countries such as Italy or Spain [1]. The first case in Madrid
was reported on February 25th 2020 [2], and our center
diagnosed the first patient in March 1st. In spite of the efforts
for flattening the epidemic curve, more than 3000 patients
have been attended over the following weeks in our hospital.
The number of subjects needing critical-care assistance grew
enormously, this picture being the rule in the metropolitan
area of Madrid and in some other highly populated Span-
ish regions. The magnitude of the epidemic, the uncertain
benefit-harm balance of available treatments, and the ethi-
cal responsibility for fairly allocating medical resources has
generated great stress among physicians [3].

In such scenario, a rapid and early assessment of patients’
risk to progress to respiratory failure is essential to wisely
manage hospital resources. Recent studies have reported
that elderly patients with high blood pressure and present-
ing with high C-reactive protein (CRP), Sequential Organ
Failure Assessment index, lymphopenia or d-dimer are at
higher risk of severe disease and death [4–10]. Still, these
parameters may lack sensitivity and specificity, and they
should be adjusted by other strategies aiming to avoid or
delay respiratory support. The ideal evaluation of patients
at baseline should be simple and executive, but also should
lead to right decisions. The aim of this study was to analyze
the clinical characteristics of the initial wave of patients with
COVID-19 attended in our center, and to create an easy-to-
perform score to rapidly identify patients at risk of develop-
ing respiratory failure.

**Methods**

**Study Population and design**

This prospective and observational study included all
consecutive adult (≥ 18 years) patients with confirmed
COVID-19 and hospitalized at the University Hospital “12
de Octubre” from March 2nd to 18th, 2020. Our center is
a 1200-bed teaching hospital, including 56 ICU-beds and
referral to a population of around 470,000 inhabitants in
southern Madrid (Spain). Patients were enrolled at the time
diagnosis of COVID-19 and followed up to May 1st, 2020
or death, whatever came first.

Clinical characteristics, baseline features measured by
Charlson Comorbidity Index [11], vital signs, respiratory
status, radiological data, and laboratory values at admission,
along with patient progress and complications during hos-
pitalization were recorded in electronic medical records and
concurrently extracted.

Vital signs were obtained in the Emergency Depart-
ment triage and the first available laboratory data from each
patient were used to calculate the score. Study data were
collected and managed using REDCap electronic data cap-
ture tools hosted at the Research Institute of Hospital 12
de Octubre (imas+12). REDCap (Research Electronic Data
Capture) is a secure, web-based software platform designed
to support data capture for research studies [12, 13].

The protocol was approved by the Hospital 12 de Octubre
Clinical Research Ethics Committee (reference 20/117) and
granted a waiver of informed consent due to its observa-
tional design.

**Microbiological methods**

For the molecular diagnosis of SARS-CoV-2 infection, naso-
pharyngeal swabs [flocked swabs in UTM™ viral transport
medium (Copan Diagnostics, Brescia, Italy)] were obtained
from suspected cases and processed by automatized extrac-
tion and specific PCR methods [14]. For real-time reverse
transcription polymerase chain reaction (rRT-PCR), the
LightCycler 480 System instrument (Roche Life Science,
Indianapolis, IN, USA) was used.

**Endpoint definition**

Respiratory failure was defined as a partial pressure of arte-
rial oxygen/fraction of inspired oxygen PaO2/FiO2 (PaO2/
FiO2) ratio ≤ 200 mmHg [15], or the need for mechanical
ventilation (either non-invasive positive pressure ventila-
tion—Continuous (CPAP) or Bilevel positive pressure ven-
tilation- or invasive mechanical ventilation), including those
patients who had a clinical indication for ventilatory support
but for any reason were finally not ventilated. If PaO2 was
not available, the estimated PaO2/FiO2 (ePaO2/FiO2) ratio
was calculated using the pulse oximetry saturation/fraction
of inspired oxygen (SpO2/FiO2) ratio applying the formula
SpO2/FiO2 = 64 + 0.84 × PaO2/FiO2 [16].

**Statistical methods**

The presence or absence of respiratory failure was blindly
defined to clinical information. We did not calculate formal
sample size. Instead, all available data were used to maxi-
mize the power of the study.

Outcome (respiratory failure) was recorded in all patients.
In the predictive model of respiratory failure [age, lympho-
cytes, SpO2 %, CRP and lactate dehydrogenase (LDH)] only
18 patients had missing data, representing 3.45% of the
entire cohort. Given the low percentage of patients excluded
from the multivariate model, no imputation of data was per-
formed and only complete-cases were included for the devel-
opment of the model.

Quantitative variables were described using median and
interquartile range (IQR) or means ± standard deviation
(SD), and compared by Student’s t test for independent sam-
ple tests or Mann–Whitney U test, as appropriate. All param-
eters were tested for normality of distribution by means of
During the recruitment period, 521 patients were included, of whom 181 (34.7%) developed respiratory failure after a median time from the onset of symptoms of 9 days [interquartile range (IQR): 6–11]). Supplementary Fig. 1 shows the number of patients hospitalized at 12 Octubre University Hospital in medical wards and ICU during the study period.

Demographic and clinical characteristics of the patients are shown in Table 1. Median age was 64.6 ± 18.2 years, with 317 patients (60.8%) over 60 years (77.9% in respiratory failure group vs 51.8% in non-respiratory failure, \( p < 0.0001 \)). Median Charlson Comorbidity index was ≥ 1 in 50% of patients, being higher among cases with respiratory failure group [1 (IQR 0–2) vs 0 (IQR 0–1), \( p < 0.0001 \)]. The most frequent previous medical condition was hypertension (42%).

**Patients’ characteristics at admission**

The median time between the onset of symptoms to the first positive rRT-PCR was 5 days (IQR 3–7), it being above 7 days in 116 patients (22.5%). Clinical, radiological and laboratory findings at admission are shown in Table 1. At admission, initial chest X-ray showed abnormal findings in 416 cases (81.1%) (87.8% in respiratory failure vs 77.5% in non-respiratory failure, \( p = 0.004 \)). The most common radiologic finding was bilateral ground-glass opacities (41.9%).

**Hematologic and biochemical abnormalities**

As shown in Table 1, significant differences were observed in most laboratory parameters between those who developed respiratory failure in comparison with those did not. Partial pressure of arterial oxygen (\( \text{PaO}_2 \)) on room air was determined in 262 cases whereas pulse oximetry saturation (\( \text{SpO}_2 \)) on room air was used in 512 patients. \( \text{SpO}_2(\%) \) at admission was 93 ± 6, and \( \text{SpO}_2 < 90\% \) was present in 101 cases (19.7%). Median values of LDH, CRP, and lymphocyte count at admission were 328 UI/l (IQR 265–413), 7.6 mg/dl (IQR 3.1–15), and 0.9 × 10³ cells/µl (IQR 0.62–1.2), respectively.

**Management and outcome**

In the course of hospitalization, 347 patients (68%) received oxygen therapy during a median of 6 days (IQR 3–11). Four hundred seventy-six patients were treated with antibiotics (91.5%), being azithromycin used in 292 cases (56%). Likewise, Lopinavir/ritonavir, hydroxychloroquine, interferon-\( \beta_1b \), corticosteroids, tocilizumab and remdesivir were prescribed in 60% (314), 75% (393), 24% (128), 25% (131), 8% (44), and 0.2% (1) patients, respectively.

As shown in Supplementary Table 1, ICU admission occurred in 52 patients (10%), of whom 51 belonged to the respiratory failure group (28% vs 0.3%, \( p < 0.0001 \)). Median length of stay in ICU was 12.5 days (IQR 6–18).

**Results**

**Baseline and clinical characteristics**

During the recruitment period, 521 patients were included, of whom 181 (34.7%) developed respiratory failure after a
Table 1  Demographic, clinical, radiological, and laboratory findings at admission according to the development of respiratory failure

| Variable                                      | Total (n = 521) | Respiratory failure (n = 181) | Non-respiratory failure (n = 340) | p value  |
|-----------------------------------------------|----------------|------------------------------|----------------------------------|---------|
| **Baseline characteristics**                  |                |                              |                                  |         |
| Age (years)                                   | 64.66 ± 18.2   | 71.73 ± 14.91                | 60.89 ± 18.69                    | < 0.0001|
| Gender (male)                                 | 299 (57.6)     | 125 (69.1)                   | 174 (51.5)                       | < 0.0001|
| Charlson comorbidity index score              | 1 (0–2)        | 1 (0–2)                      | 0 (0–1)                          | < 0.0001|
| Hispanic ethnicity (vs. others)               | 98 (19.3)      | 31 (17.3)                    | 67 (20.3)                        | 0.41    |
| Nursing-home or extended-care facility        | 17 (3.3)       | 11 (6.1)                     | 6 (1.8)                          | 0.008   |
| Smoker (current or former)                    | 131 (25.7)     | 64 (35.8)                    | 67 (20.3)                        | < 0.0001|
| Obesity                                       | 150 (34.2)     | 61 (38.1)                    | 89 (32)                          | 0.19    |
| Diabetes mellitus                             | 95 (18.3)      | 43 (23.8)                    | 52 (15.3)                        | 0.018   |
| Hypertension                                  | 217 (42.1)     | 97 (54.2)                    | 120 (35.7)                       | < 0.0001|
| Coronary heart disease                        | 40 (7.7)       | 19 (10.5)                    | 21 (6.2)                         | 0.078   |
| Congestive heart failure                      | 33 (6.3)       | 16 (8.8)                     | 17 (5)                           | 0.087   |
| Peripheral artery disease                     | 21 (4)         | 12 (6.6)                     | 9 (2.6)                          | 0.028   |
| Asthma                                        | 40 (7.7)       | 6 (3.3)                      | 34 (10)                          | 0.006   |
| Chronic obstructive pulmonary disease         | 41 (7.9)       | 26 (14.4)                    | 15 (4.4)                         | < 0.0001|
| Pulmonary hypertension                        | 16 (3.2)       | 11 (6.3)                     | 5 (1.5)                          | 0.004   |
| Sleep apnea syndrome                          | 37 (7.1)       | 21 (11.6)                    | 16 (4.7)                         | 0.004   |
| Cerebrovascular disease                       | 31 (6)         | 20 (11)                      | 11 (3.2)                         | < 0.0001|
| Dementia                                      | 53 (10.2)      | 30 (16.6)                    | 23 (6.8)                         | < 0.0001|
| Chronic kidney disease                        | 35 (6.7)       | 18 (9.9)                     | 17 (5)                           | 0.032   |
| Chronic liver disease                         | 25 (4.8)       | 12 (6.7)                     | 13 (3.8)                         | 0.14    |
| Malignancya                                   | 72 (14.3)      | 38 (21.8)                    | 34 (10.3)                        | < 0.0001|
| Previous use of steroidsb                     | 34 (6.6)       | 18 (9.9)                     | 16 (4.7)                         | 0.023   |
| **Clinical findings at admission**            |                |                              |                                  |         |
| Duration of illness prior to confirming the infection (days) | 5 (3–7) | 5 (3–7) | 5 (3–7) | 0.68 |
| > 7 days                                      | 116 (22.5)     | 36 (20.2)                    | 80 (23.7)                        | 0.36    |
| Temperature (°C)                              | 37.73 ± 0.97   | 37.63 ± 0.97                 | 37.7 ± 0.96                      | 0.38    |
| Systolic BP (mm Hg)                           | 124 (114–138)  | 125 (114–140)                | 124 (114–138)                    | 0.72    |
| Heart rate (beats per minute)                 | 90 (79–103)    | 90.5 (78–102)                | 90 (80–104)                      | 0.34    |
| Respiratory rate (breaths per minute)         | 18 (15–22)     | 20 (16–26.2)                 | 18 (15–18)                       | < 0.0001|
| > 20 breaths per minute                       | 138 (27.8)     | 80 (47.1)                    | 58 (17.7)                        | < 0.0001|
| Altered consciousness                         | 53 (10.2)      | 34 (18.8)                    | 19 (5.6)                         | < 0.0001|
| Dyspnea                                       | 278 (53.5)     | 126 (69.6)                   | 152 (44.8)                       | < 0.0001|
| **Radiological findings**                     |                |                              |                                  |         |
| Abnormal Chest X-ray                          | 416 (81.1)     | 158 (87.8)                   | 258 (77.5)                       | 0.004   |
| PaO2 (mmHg)c                                  | 67 (55–86.25)  | 57 (50.5–70.5)               | 79 (62–96)                       | < 0.0001|
| SpO2 (%)                                      | 92.95 ± 6.55   | 88.72 ± 8.56                 | 95.22 ± 3.46                     | < 0.0001|
| ePAFI ratio                                   | 376 (282–457)  | 285 (241–376)                | 409.5 (333–471)                  | < 0.0001|
| Leukocytes (× 109 cells/µl)                   | 5.6 (4.4–7.59) | 6.4 (4.7–8.75)               | 5.4 (4.3–7.1)                    | < 0.0001|
| Neutrophils (× 109 cells/µl)                  | 4 (2.9–5.8)    | 5 (3.5–7.35)                 | 3.6 (2.7–5.2)                    | < 0.0001|
| Lymphocytes (× 109 cells/µl)                  | 0.9 (0.6–1.2)  | 0.7 (0.5–1)                  | 1 (0.7–1.3)                      | < 0.0001|
| Monocytes (× 109 cells/µl)                    | 0.5 (0.3–0.7)  | 0.4 (0.3–0.7)                | 0.5 (0.4–0.7)                    | 0.013   |
| Platelets (× 109/µl)                          | 182 (145.2–233)| 169 (131.5–213.5)           | 187 (153–238)                    | 0.007   |
| Hemoglobin (g/dl)                             | 13.84 ± 1.88   | 13.57 ± 1.99                 | 13.98 ± 1.8                      | 0.018   |
| Lactate (mmol/l)                              | 1.4 (1–1.8)    | 1.45 (1.1–2)                 | 1.2 (1–1.6)                      | 0.004   |
| Creatinine (mg/dl)                            | 0.9 (0.71–1.12)| 0.99 (0.8–1.4)               | 0.84 (0.69–1.06)                 | < 0.0001|
| Triglyceride levels (mg/dl)                   | 120 (96–159)   | 123 (94–160.5)               | 120 (97–159)                     | 0.9     |

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Median time from admission to respiratory failure was 3 days (IQR 1–6). In the respiratory failure group, 27% (49/181) of patients were treated with invasive mechanical ventilation for a median duration of 12 days (IQR 7–17), whereas 31 patients (17%) were managed with non-invasive mechanical ventilation. Extracorporeal membrane oxygenation and prone position were used in 1 and 43 patients, respectively.

Median time from admission to clinical improvement was 5 days (IQR 3–9), with a significant difference between groups [14.5 days (IQR 9–20) in the respiratory failure group vs. 5 days (IQR 3–7) in the non-respiratory failure group, \( p < 0.0001 \)].

Overall mortality occurred in 23.8% (124/521), with a significant difference between groups [65.7% (119/181) vs. 1.5% (5/340), \( p < 0.0001 \)]. Median time from admission to discharge or death was 9 days (IQR 6–14 days), [11 days (IQR 7–19) vs. 8 days (IQR 5–12), \( p < 0.0001 \)]. Among survivors, median hospital stay was 22 days (IQR 16.5–31) in respiratory failure group vs. 8 days (IQR 5–12) in non-respiratory failure one (\( p < 0.0001 \)).

To analyze medical complications happening in the course of hospitalization, patients were followed up for 1 month or until death (see Supplementary Table 1).

### Risk estimation of respiratory failure

As Table 2 shows, a reduced model identifying respiratory failure was generated. Five variables remained independently associated with the primary endpoint: age (OR 1.026; 95% CI 1.019–1.042, \( p = 0.0004 \)), \( \text{SpO}_2(\%) \) (OR 0.853; 95% CI 0.804–0.906, \( p < 0.0001 \)), lymphocyte count (OR 0.414; 95% CI 0.232–0.737, \( p = 0.0029 \)), LDH (OR 1.004; 95% CI 1.002–1.006, \( p = 0.0001 \)) and CRP (OR 1.048; 95% CI 1.018–1.078, \( p = 0.0013 \)). LOESS smoothing curve plotting the probability of respiratory failure against variables included in the score are depicted in Fig. 1.

A score predicting the occurrence of respiratory failure was created as visualizations of the logistic regression model (Table 3). As an example, a patient with age 60 years, 800 lymphocytes/µl, \( \text{SpO}_2(\%) \) of 93%, LDH of 315 U/l and a CRP of 5 mg/dl, receives a score of 11. Therefore, using this model, this patient would have an estimated probability of 58.4% of respiratory failure.

This reduced model provided good discriminative ability (bootstrap-corrected c index 0.85) as Fig. 2 and Supplementary Table 2 shows and goodness-of-fit (Hosmer and Lemeshow \( p = 0.49 \)). According to Youden’s Index J the optimal cut-off for the score was 9 points (sensitivity of 82.66% and
Table 2 Regression coefficients of the logistic regression model

| Intercept and risk factors | Regression coefficient | p value | OR | 95% CI of OR |
|---------------------------|------------------------|---------|----|--------------|
| Intercept                 | 11.0424                | 0.0003  | − | −            |
| Age (years)               | 0.0264                 | 0.0004  | 1.026 | 1.0118–1.0419 |
| Lymphocytes (cells/µl)    | −0.8777                | 0.0029  | 0.414 | 0.2324–0.7376 |
| LDH (U/l)                 | 0.0044                 | 0.0001  | 1.0044 | 1.0022–1.0066 |
| CRP (mg/dl)               | 0.047                  | 0.0013  | 1.048 | 1.0185–1.0784 |
| SpO2 (%)                  | −0.1585                | <0.0001 | 0.8537 | 0.8045–0.9059 |

The linear predictor can be calculated as 11.042 + 0.0264 × each year (age) − 0.1585 × each unit of SpO2(%) − 0.8777 × each lymphocyte (×10^3 cells/µl) + 0.0044 × each unit of LDH + 0.047 × each unit of C-reactive protein (mg/dl). The predicted probability of respiratory failure can be calculated with the formula 1/(1+exp(−linear predictor))

OR odds ratio; CI confidence interval; SpO2 peripheral pulse oximetry; LDH lactate dehydrogenase; CRP C-reactive protein

specificity of 71.96%). The corresponding sensitivity, specificity, positive, and negative likelihood ratios of different points are detailed in Supplementary Table 4.

Calibration plot for the score is shown in Supplementary Fig. 2. The c-statistic (area under ROC curve) for internal validation was 0.84.

Discussion

During the recruitment period of the study, our hospital experimented an exponential growth of COVID-19 patients in medical wards and ICU in a short period of time, as shown in Supplementary Fig. 1. This circumstance forced an adaptive restructuring aimed to rapidly increase medical, respiratory intermediate care, and ICU beds. In a situation of overload such as the one we suffered during the first wave of the pandemic, the early identification of patients at high risk of respiratory failure seems mandatory to ensure appropriate infrastructure for respiratory support. In this context, a score with the ability of facilitating the early triage of these patients is essential. Furthermore, this score should be simple and easily implemented, even in resource-limited settings.

In this regard, we present a simple and quick 5-item score which can be easily calculated at patients’ bedside at admission. A large proportion of subjects at a high risk of respiratory failure would be identified by this tool with a high discriminative ability (C-statistic = 0.85). Having this information at an early stage would allow a sound planning of hospital beds and use of respiratory resources. Of note, this score would also select patients who would benefit from the early use of anti-inflammatory drugs to manage the characteristic dysfunctional immune response in patients with severe SARS-CoV-2 infection.

As shown in Supplementary Table 2, Charlson Comorbidity index substituting age could slightly increase the accuracy of the score, but the use of age is much simpler and practical, and the discrimination of the final model and the predictive ability was similar (pairwise comparison of ROC curves, p = 0.3). The score also includes SpO2% which is easier to determine than PaO2, and therefore was collected in the majority of cases. It should also be noted that arterial blood gas diagnostics could be inaccessible in resource-constrained settings, being pulse oximetry a reliable alternative to achieve a validated estimation of PaO2/FIO2, as proposed by the Kigali modification of Berlin criteria [18]. We also believe that SpO2% is a more reliable parameter than dyspnea, since this symptom may not be reported by patients even in presence of severe hypoxemia, probably because of the persistence of spared, normal compliant lung tissue surrounding affected areas with extreme intrapulmonary shunt [19].

The other three variables included in the score are laboratory values. Lymphopenia is described as a prognostic marker in SARS-CoV-2 [20]. Others, like interleukin-6, D-dimers, procalcitonin, and ferritin [10, 21] have been also associated with a poor outcome, but their availability in many Emergency Departments is scarce, this needing to be considered in a resource shortage scenario. In our score, the laboratory values related with respiratory failure were LDH and CRP, which performed soundly for predicting respiratory failure (Fig. 3). As shown in Supplementary Table 2, ferritin did not improve the model accuracy.

Different outcomes have been proposed in COVID-19 observational studies, being mortality the most frequently reported [7, 9, 10, 21]. Only one study reported the risk factors associated with acute respiratory distress syndrome, although it did not propose a score [10].

A recently published Chinese report [23] proposed a 10-item score for predicting the need of invasive ventilation, as part of a composite endpoint (which also included death and ICU admission). While of interest, the population analyzed was significantly different from that of our cohort regarding age and baseline features, COVID-19 respiratory involvement, and mortality. Our study may be more representative of the situation experienced in most Western countries. In this regard, our endpoint focuses on the most frequent and serious complication associated with COVID-19. Development of respiratory failure frequently leads to the need for invasive ventilation, ICU admission, and death (Liang’s study endpoints), but it also adds the use of non-invasive mechanical ventilation outside ICU, which needs trained staff and sophisticated facilities, too. In addition, it also includes a significant number of patients with respiratory failure who would finally not be
Fig. 1 LOESS smoothing curve plotting the probability of respiratory failure against variables included in the score.
suitable for ventilation, but would still benefit from optimized medical therapy and medical resources for a long time. We believe that our primary endpoint offers a more realistic picture of the situation experienced in overloaded hospitals.

We want to point out that despite the majority of chest X-ray were abnormal, the score was verified in the subgroup with normal X-ray, being the AUC 0.81 ($p < 0.0001$). These data might be of interest, since it could facilitate the use of the score even in less severe population, although this recommendation should be taken with caution.

An important strength of our study was that possible biases have been minimized by including all consecutive adult hospitalized patients with confirmed COVID-19 and presenting a very low percentage of missing data in the main variables of the study, especially in vital signs and analytical values, as they were gathered automatically by electronic records.

Conversely, this single center study has the inherent limitations of potential selection bias, depending on the main demographic features of the population attended. Additional

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**Table 3** Proposed score for predicting respiratory failure

| Variable            | Cut-off and associated points | Points | Probability of respiratory failure |
|---------------------|-------------------------------|--------|-----------------------------------|
| Age                 | < 55 years                    | 0 points | 1.1%                             |
|                     | 55–75 years                   | 2 points | 1.6%                             |
|                     | > 75 years                    | 3 points | 4.9%                             |
| Lymphocyte count    | < 500 (cells/dl)              | 4 points | 4%                               |
| (cells/dl)          | 500–1000                     | 3 points | 6%                               |
|                     | > 1000                        | 0 points | 9.1%                             |
| SpO2%               | < 92                          | 9 points | 13.5%                            |
|                     | 92–96                         | 1 point  | 19.4%                            |
|                     | > 96                          | 0 points | 27.3%                            |
| LDH (U/I)           | < 280                         | 0 points | 36.8%                            |
|                     | 280–380                       | 1 point  | 47.5%                            |
|                     | > 380                         | 4 points | 58.4%                            |
| CRP (mg/dl)         | < 4                           | 0 points | 68.6%                            |
|                     | 4–12                          | 1 point  | 77.2%                            |
|                     | > 12                          | 3 points | 84%                              |
|                     | > 12                          | 0 points | 89.1%                            |

$SpO_2$ peripheral pulse oximetry; $LDH$ lactate dehydrogenase; $CRP$ C-reactive protein

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**Fig. 2** Receiver operating characteristic (ROC) curve of the score in discriminating the presence of respiratory failure

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**Fig. 3** Predicted probability of respiratory failure
prospective multicenter validation studies of the proposed score for predicting the occurrence of respiratory failure should be completed before clinical use. The only laboratory value with a high percentage of missing data was D-dimers, so we failed in demonstrating if it could be an independent risk factor. This parameter has been associated with worse prognosis in some studies [10] but not in all of them [9, 21] and its high cost and, in our case, unavailability of enough test at some moments of the wave, limited its use.

Summing up, we believe that the proposed score may have significant clinical implications. In comparison with other scores proposed for predicting an unfavorable outcome for COVID-19 patients, this has the advantage of its simplicity and the fact that it can be calculated at the bedside of the patient on his arrival at the Emergency Department. It would be a useful tool to optimize the scarce resources available in a pandemic situation by identifying, at admission in the Emergency Department, patients at risk to develop respiratory failure. As some authors pointed out, adoption of straightforward triage algorithms might be useful to optimize the management of hypoxic patients with severe disease [24]. Additionally, our endpoint includes patients with respiratory failure (and not only invasive ventilation). This fact gives us an accurate idea of a subgroup of more severe and life-threatening patients in which early immunomodulatory drugs may be considered.

Conclusions

We propose a simple score to early predict the development of respiratory failure in COVID-19 to optimize antiviral and immunomodulatory therapy and to adequate health-care resources, including respiratory support in such a pandemic situation.

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Author contributions All authors meet the requirements for authorship. A.L., J.L–T., G.M., V.V., JM. A. and C.L. design the study. A.L., G.M., J.S. screened the patients. A.L., J.L–T., G.M., E.A., B.M., R. D., C.C., M.M., A.M., A.G. M.F., J.S., R.S-J., R.G., M.C. did acquisition of data. A.L., J.L–T., D.L. performed the statistical analysis. D.F., A.S. and M.M., A.M., A.G. M.F., J.S., R.S-J., R.G., M.C. did acquisition of data. A.L., J.L–T., D.L. performed the statistical analysis. D.F., A.S. and M.M., A.M., A.G. M.F., J.S., R.S-J., R.G., M.C. did acquisition of data. A.L., J.L–T., D.L. performed the statistical analysis. D.F., A.S. and M.M., A.M., A.G. M.F., J.S., R.S-J., R.G., M.C. did acquisition of data. A.L., J.L–T., D.L. wrote the final draft of the article and made all the changes suggested by the coauthors. All authors had access to the clinical study report, reviewed the article, and approved the submission of the article.

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Declarations

Conflict of interest The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

Human and animal rights statement The study protocol was approved by the University Hospital 12 de Octubre Review Board.

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