Characteristics and laboratory findings on admission to the emergency department among 2873 hospitalized patients with COVID-19: the impact of adjusted laboratory tests in multicenter studies. A multicenter study in Spain (BIOCOVID-Spain study)

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ABSTRACT
Identification of predictors for severe disease progression is key for risk stratification in COVID-19 patients. We aimed to describe the main characteristics and identify the early predictors for severe outcomes among hospitalized patients with COVID-19 in Spain. This was an observational, retrospective cohort study (BIOCOVID-Spain study) including COVID-19 patients admitted to 32 Spanish hospitals. Demographics, comorbidities and laboratory tests were collected. Outcome was in-hospital mortality. For analysis, laboratory tests values were previously adjusted to assure the comparability of results among participants. Cox regression was performed to identify predictors. Study population included 2873 hospitalized COVID-19 patients. Nine variables were independent predictors for in-hospital mortality, including creatinine (Hazard ratio [HR]:1.327; 95% Confidence Interval [CI]: 1.040-1.695,
Introduction

In December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the etiological agent for the pneumonia cases of unknown origin in Wuhan (Hubei Province, China), a disease designated as coronavirus disease 2019 (COVID-19) [1]. On March 11th, COVID-19 was characterized as a pandemic. Spain remains one of the European countries most severely affected by the ongoing COVID-19 pandemic both in terms of number of infected individuals and in terms of number of deaths [2].

The clinical presentation of COVID-19 varies from asymptomatic or mild upper respiratory tract symptoms to severe viral pneumonia with respiratory failure and death. The real challenge for the clinicians in an Emergency Department (ED) is to early identify COVID-19 patients at high risk for an unfavorable progression and to ensure optimal resource allocation. Therefore, there is a need to identify risk factors for early prediction of progression of COVID-19 patients.

The role of clinical laboratories in this viral outbreak includes staging, prognostication and therapeutic monitoring of individuals with COVID-19. A recent systematic review highlighted the most important biochemical and hematological alterations observed in these patients, with great interest for prognostic purposes [3]. In this line, different laboratory tests have been identified as outcome-related predictors, useful to support medical decision making [4,5]. Nonetheless, most studies referenced suffer from limitations, including small sample sizes, study population selection bias, great heterogeneity across the studies included in the reviews and meta-analysis and use of different endpoints of severity [5]. Besides, most of conclusions to date have been reported from studies performed in Chinese populations and variations in rates for COVID-19 hospitalizations and mortality across different locations suggesting differences in population characteristics have previously been reported [6].

In addition, much of the published investigation does not include information about analytical methods used for testing [5]. Hence, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Task Force in COVID-19 has recently urged caution when translating study findings to local laboratory practice. Of note, in multicenter studies, the use of a wide variety of methodologies and analyzers for measurement of biomarkers implies a high data heterogeneity and a poor reproducibility and only the use of adjusted results will enable the universal application of decision limits obtained from different methodologies undertaken in different locations [7,8].

BIOCovid-Spain study is an initiative by Laboratory Medicine professionals in Spain to generate a multicenter cohort database focusing on laboratory tests. From this information, we aimed to describe the characteristics and main laboratory findings of hospitalized COVID-19 patients in Spain and identify early clinical and laboratory predictors of in-hospital mortality.

Material and methods

Study design

BIOCovid-Spain study is a multicenter, retrospective observational study including patients hospitalized with a diagnosis of COVID-19 recruited in 32 hospitals of Health National System in 9 autonomous communities of Spain. The recruitment period was from 1 March 2020, to April 30, 2020. The follow-up censoring date was 20 May 2020. The study was approved by the Ethics Committee of all participating hospitals. Because of the retrospective design, we received the approval for data collection with waiver of informed consent.

This study was endorsed by Spanish Association of Medical Biopathology and Laboratory Medicine (AEBM-ML), Spanish Association of Clinical Laboratory (AEFA) and Spanish Society of Laboratory Medicine (SEQC-ML).

Study population

All consecutive adult patients (≥14 years) discharged or dead after hospital admission, with SARS-CoV-2 infection, were eligible for inclusion in the study. COVID-19 was diagnosed either by positive result of real-time reverse transcriptase-polymerase chain reaction (RT-PCR) testing of a nasopharyngeal specimen, or by a positive result of serological testing and a clinically compatible presentation.

Exclusion criteria were: (a) patients <14 years; (b) pregnant women; (c) patients transferred from or to another hospital; (d) patients transferred from nursing homes; (e) patients discharged from the ED for at home treatment; and (f) patients with Intensive Care Unit (ICU) admission criteria who were not admitted due to lack of availability.

Data collection

Data collection was performed retrospectively from electronic medical records and laboratory information systems by two researchers for each hospital. For eligible patients, we extracted the demographic information, comorbidities, laboratory test results, and disposition (discharge to home and in-hospital mortality). Laboratory data depicted the first test result occurring within the first 24h from presentation.

\[ p = .023, \text{ troponin (HR: 2.150; 95% CI: 1.155-4.001; } p = .016, \text{ platelet count (HR: 0.994; 95% CI: 0.989-0.998; } p = .004) \text{ and C-reactive protein (HR: 1.037; 95% CI: 1.006-1.068; } p = .019). ]
to the ED. A multicenter database was prepared for register of collected data and all patient identities were coded for blindness.

**Outcome measures**

The outcome was all-cause in-hospital mortality occurring during follow-up.

**Adjustment of laboratory tests**

To achieve an adjustment of laboratory test values, a harmonization factor was calculated for each methodology and analyzer, using a category 1 external quality assurance (EQA) scheme, provided by the Spanish Society of Laboratory Medicine (SEQC-ML), which includes results that are interchangeable and traceable to reference standards [9]. The value measured with the most common methodology and analyzer among participating laboratories was considered as reference to generate the factor. For those biochemical tests not included in this quality control material (albumin, C-reactive protein [CRP], ferritin, urea and lactate), a correction factor was calculated from other non-conmutable EQA schemes of the SEQC-ML (See Supplementary Material). To assure the comparability in a wide measurement range, a mean factor was calculated from the factors calculated in 6 EQA materials send to laboratories during 2019. A similar approximation has been recently performed by Kurstjens et al. [10] in a study evaluating the role of biochemical and hematological tests for a rapid identification of SARS-CoV-2-infected patients, in which significant differences were observed for ferritin measurement when different analyzers were used.

For cardiac troponin, only high sensitivity assays were included and the levels were dichotomized according to sex-stratified 99th-percentile. For procalcitonin, only Brahms-like methods were included.

For D-dimer, according to Favaloro et al., results were converted to a single unit of measurement (ng/mL Fibrinogen Equivalent Units [FEU]) [11]. Adjustment of all other hematological and coagulation tests was considered as not necessary according to the EQA scheme provided by the Spanish Society of Hematology and Hemothapy (SEHH).

**Statistical analysis**

Continuous variables were tested for normal distribution using the Kolmogorov-Smirnov’s test. Data are summarized as numbers and frequencies for categorical variables and or medians with interquartile ranges (IQRs) for continuous data. Comparisons between groups were performed with Chi-squared test for categorical data and Mann-Whitney U tests for continuous data. Cox regression analysis was performed to identify variables associated with in-hospital mortality. To obtain the predictors, we performed a block-wise forward procedure allocating the predictor variables into three clusters: demographics, comorbidities and laboratory tests. A multivariable regression analysis was fitted within each block using statistical significance (p-value <.10) as criterion to achieve the best set of predictors. Statistical significance was set at 5%. SPSS software version 20 (IBM Corporation, USA) was used for all statistical analyses.

**Results**

**Characteristics of study subjects**

During the study period, a total of 2981 COVID-19 patients admitted to 32 Spanish hospitals were recruited. One-hundred and eight patients who were still hospitalized on May 20, 2020 were excluded from analyses. The study population finally included 2873 hospitalized COVID-19 patients.

In-hospital mortality rate was 14.3%, which was seen to be significantly higher in male compared to female sex (16.4% vs. 11.3%; p < .001). ICU admission was required for 504 patients (17.3%); in these patients in-hospital mortality rate was 35.1%, significantly higher than in non-admitted to ICU (9.9%; p < .001). The median time from ED admission to ICU admission was 2 days (IQR: 1–4), while in-hospital length of stay and ICU length of stay were 22 days (IQR: 15–34) and 12 days (IQR: 6–20), respectively.

Patients’ characteristics, stratified by previously defined outcomes, are summarized in Table 1. Median age was 66 years (IQR: 54–76), ranging from 15 to 98 years and 41.7% were ≥70 years; 1699 patients were male (59.1%). The most common comorbidity was hypertension (45.8%), followed by diabetes mellitus (24.3%) and cardiovascular disease (CVD) (22.6%) and 1722 (59.9%) patients presented at least one comorbidity.

Patients who died were older and with a higher frequency of male sex and all comorbidities; 339 (82.3%) had at least one comorbidity. In-hospital mortality increased with age, reaching a percentage of 29.9% for patients over 80 years.

**Laboratory findings**

Individuals with altered baseline laboratory tests are presented in Table 2, also stratified according to the outcomes. The most common laboratory alterations were increased

| Table 1. Demographics and comorbidities of 2873 COVID-19 patients grouped according to in-hospital mortality at study censoring date. |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Total population | Survivors (%)    | Non-survivors (%) | p Value   |
| Age, years [Median (IQR)] | n = 2873 | n = 2461 (85.7%) | n = 412 (14.3%) | <.001 |
| Distribution    | <30 years | 45 (1.6%) | 44 (1.8) | 1 (0.2) | <.001 |
|                 | 30–39 years | 131 (4.6) | 128 (5.2) | 3 (0.7) | <.001 |
|                 | 40–49 years | 343 (11.9) | 338 (13.7) | 5 (1.2) | <.001 |
|                 | 50–59 years | 511 (17.8) | 484 (19.7) | 27 (6.6) | <.001 |
|                 | 60–69 years | 674 (23.5) | 593 (24.1) | 81 (19.7) | <.001 |
|                 | 70–79 years | 678 (23.6) | 530 (21.5) | 148 (35.9) | <.001 |
|                 | ≥80 years | 491 (17.1) | 344 (14.0) | 147 (35.7) | <.001 |
| Sex, male [n (%)] | 1699 (59.1) | 1420 (57.7) | 279 (67.7) | <.001 |
| Hypertension [n (%)] | 1317 (45.8) | 1043 (42.4) | 274 (66.5) | <.001 |
| Diabetes mellitus [n (%)] | 697 (24.3) | 548 (22.3) | 149 (36.2) | <.001 |
| COPD [n (%)] | 247 (8.6) | 182 (7.4) | 65 (15.8) | <.001 |
| CVD [n (%)] | 649 (22.6) | 485 (19.7) | 164 (39.8) | <.001 |
| CKD [n (%)] | 247 (8.6) | 161 (6.5) | 86 (20.9) | <.001 |

COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; CKD: chronic kidney disease.
In univariate analysis, the following variables showed a significant hazard ratio (HR) for in-hospital mortality and were included in the multivariate analysis: stratified-age, male sex, hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), CVD, chronic kidney disease (CKD), urea, creatinine, albumin, AST/GOT, bilirubin, creatine kinase (CK), LDH, troponin, CRP, procalcitonin, D-dimer, ferritin and hemoglobin levels, NLR, INR and white blood cell, neutrophil, lymphocyte and platelet counts. Independent predictors for in-hospital mortality are presented in Table 4. In the final adjusted analysis by Cox regression analysis, we found 9 variables independently associated with an increased hazard of in-hospital mortality: older age, male sex, hypertension, CVD, CKD, creatinine, CRP and troponin levels and platelet count.

**Discussion**

Alterations in laboratory tests can be used in clinical practice to predict the severity of COVID-19 and could improve prognosis and decrease the mortality rates, but further worldwide research is needed to better understand these changes and their relations with prognosis [15]. In this

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**Table 2.** Frequency of altered laboratory tests, measured on hospital admission, in 2873 COVID-19 patients grouped according to in-hospital mortality at study censoring date.

| Variable | Total population | Survivors | Non-survivors |
|----------|------------------|-----------|---------------|
|          | N = 2873         | n = 2461 (85.7%) | n = 412 (14.3%) |
| Lactate ≥ 2.0 mmol/L | 1948 | 1670 | 278 |
| Urea ≥ 8.16 mmol/L | 2748 | 2356 | 392 |
| Creatinine, μmol/L > 68.63 (female) > 91.51 (male) | 2859 | 2450 | 409 |
| Albumin < 35 g/L | 1366 | 1167 | 199 |
| ALT/GPT, U/L > 41 (male) > 33 (female) | 2687 | 2305 | 382 |
| AST/GOT, U/L > 40 (male) > 32 (female) | 2068 | 1771 | 297 |
| Bilirubin > 20.52 μmol/L | 2253 | 1934 | 319 |
| CK, U/L > 190 (male) > 170 (female) | 1644 | 1406 | 238 |
| LDH, U/L > 241 (male) > 225 (female) | 2477 | 2122 | 355 |
| Troponin ≥ 99th percentile (sex-stratified) | 1280 | 1078 | 202 |
| CRP > 5.0 mg/L | 2788 | 2386 | 402 |
| Procalcitonin ≥ 0.25 μg/L* | 2120 | 1808 | 312 |
| Ferritin > 500 μg/L* > 2000 μg/L† | 1806 | 1581 | 225 |
| Hemoglobin, g/L < 130 (male) < 120 (female) | 2869 | 2457 | 412 |
| WBC count > 11.00 * 10³/L | 2870 | 2459 | 411 |
| Neutrophil count > 7.50 * 10⁹/L | 2870 | 2459 | 411 |
| Lymphocyte count < 1.00 * 10⁹/L NLR > 5.0 (Median) > 5.82 (Quartile 4) | 2870 | 2459 | 411 |
| Platelet count < 150 * 10⁹/L | 2870 | 2458 | 412 |
| INR > 1.2 | 2646 | 2265 | 381 |
| D-dimer > 500 μg/L FEU* | 2663 | 2299 | 364 |

*Ref. [12]; †Ref. [13]; ‡Ref. [14].

*For patients >50 years, threshold was defined according to the formula proposed by Douma et al.*

ALT/GPT: alanine aminotransferase; AST/GOT: aspartate aminotransferase; CK: creatine kinase; CRP: C-reactive protein; FEU: Fibrinogen Equivalent Units; INR, International normalized ratio; LDH, lactate dehydrogenase; NLR: neutrophil-to-lymphocyte ratio; WBC: white blood cell.
Concerning to demographics, age in our cohort was similar to that reported in other national studies [16–18], although lower than that found by Docherty et al. [21] in United Kingdom, with a median age of 73 years. Of note, Chinese studies have reported even clearly lower ages, below 50 years [19]. Similar to the findings recently highlighted by Bonanad et al. [22], an increase of age-related mortality, with the highest mortality rate among patients older than 80 years, was described in this cohort.

Male sex has been also reported as a risk factor for severity of COVID-19 [24]. As described in previous studies [16–18,21], the number of male patients was higher than female and death was significantly higher in men. It would be related with sex differences in immune response that might impact on the inflammatory response and outcomes of COVID-19 [25].

Pre-existing conditions are described as significant predictors of COVID-19 disease outcomes in the literature [26]. Similar to previous findings described in Western and Asian cohorts [16–21], the main comorbidities in our study were a history of hypertension and diabetes mellitus. Unfortunately, other common comorbidities in COVID-19, such as dyslipidemia or obesity, were not collected in this study. Besides, a high proportion of patients, almost 60%, had at least one comorbidity, although this proportion was lower than that reported recently by Berenguer et al. [16], reaching a rate of 73.8%, likely due to the inclusion of a greater number of comorbidities. Similar to previous studies, comorbidities such as hypertension, CVD and CKD were predictors of in-hospital mortality [16]; however, of note, diabetes mellitus was not a predictor for this outcome, as Pugliese et al. recently suggested [27].

Concerning to laboratory tests, the clinical laboratories involved in this study used different analyzers from the major in vitro diagnostic device suppliers. Although several multicenter studies have reported the main blood

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**Table 3. Laboratory findings on admission of 2873 COVID-19 patients grouped according to in-hospital mortality at study censoring date.**

| Variable, median (IQR) | Total population n = 2873 | Survivors n = 2461 (85.7%) | Non-survivors n = 412 (14.3%) | p Value |
|------------------------|---------------------------|----------------------------|-------------------------------|---------|
| Lactate (mmol/L)       | 1.51 (1.10–1.98)          | 1.40 (1.08–1.89)           | 1.80 (1.30–2.50)              | <.001   |
| Urea (mmol/L)          | 5.99 (4.33–8.33)          | 3.99 (4.33–7.66)           | 8.66 (6.49–13.49)            | <.001   |
| Creatinine (µmol/L)    | 79.56 (64.53–101.66)      | 77.79 (63.65–96.36)        | 102.54 (78.68–138.79)        | <.001   |
| Albumin (g/L)          | 38 (34–41)                | 38 (35–42)                 | 35 (31–39)                   | .001    |
| ALT/GPT (U/L)          | 28 (18–46)                | 28 (18–46)                 | 26 (17–45)                   | .162    |
| AST/GOT (U/L)          | 35 (25–53)                | 34 (24–51)                 | 43 (29–64)                   | <.001   |
| Bilirubin (µmol/L)     | 8.38 (5.99–12.65)         | 8.38 (5.99–12.65)          | 8.89 (6.33–13.34)            | .139    |
| CR (U/L)               | 88 (53–163)               | 85 (51–150)                | 116 (65–247)                 | <.001   |
| LDH (U/L)              | 306 (237–408)             | 295 (222–387)              | 392 (290–555)                | <.001   |
| Platelet count (10^11/L)| 400 (31.3)                | 280 (120)                  | 120 (59.4)                   | <.001   |
| Troponin ≥99th percentile (sex-stratified) | 400 (31.3) | 280 (120) | 120 (59.4) | <.001 |
| CRP (mg/L)             | 77.8 (33.7–147.9)         | 68.7 (30.0–135.8)          | 136.4 (75.1–205.9)           | <.001   |
| Procalcitonin (µg/L)   | 0.10 (0.06–0.23)          | 0.10 (0.05–0.19)           | 0.10 (0.01–0.68)             | <.001   |
| Ferritin (µg/L)        | 674 (325–1368)            | 647 (310–1306)             | 924 (500–1815)               | <.001   |
| Hemoglobin (g/L)       | 139 (127–150)             | 14 (129–130)               | 135 (119–147)                | <.001   |
| WBC count (10^9/L)     | 6.60 (4.94–9.00)          | 6.50 (4.90–8.63)           | 7.90 (5.50–11.04)            | <.001   |
| Neutrophil count (10^9/L) | 4.90 (3.41–7.10)    | 4.72 (3.32–6.75)           | 6.56 (4.17–9.53)             | <.001   |
| Lymphocyte count (10^9/L) | 1.00 (0.70–1.33) | 1.00 (0.70–1.39) | 0.77 (0.51–1.10) | <.001 |
| NLR                    | 5.0 (3.06–8.52)           | 4.66 (2.89–7.76)           | 8.43 (4.80–14.65)            | <.001   |
| Platelet count (10^9/L) | 195 (152–256)             | 197 (154–259)              | 187 (137–245)                | <.001   |
| INR                    | 1.12 (1.03–1.23)          | 1.12 (1.03–1.23)           | 1.13 (1.04–1.28)             | .010    |
| D-dimer (µg/L FEU)     | 700 (436–1241)            | 660 (422–1127)             | 1118 (582–2319)              | <.001   |

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; CRP: C-reactive protein; FEU: Fibrinogen Equivalent Units; INR, International normalized ratio; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio; WBC, white blood cell.

**Table 4. Independent predictors for in-hospital mortality.**

| Demographics | Multivariate HR | CI 95% | p Value |
|--------------|-----------------|-------|---------|
| Sex, male    | 1.391           | 1.128–1.714 | .002  |
| Age (ref. group: <50 years) | 3.441 | 1.712–6.914 | .001  |
| 50–64 years  | 8.370           | 4.286–16.348 | <.001 |
| 65–79 years  | 15.495          | 7.894–30.416 | <.001 |
| ≥80 years    | 1.582           | 1.272–1.967 | <.001  |
| Comorbidities |                |       |         |
| Hypertension | 1.458           | 1.343–2.047 | <.001  |
| CVD          | 1.898           | 1.477–2.440 | <.001  |
| CKD          | 1.327           | 1.040–1.695 | .023   |
| Laboratory tests |      |       |         |
| Creatinine   | 2.150           | 1.155–4.001 | .016   |
| Troponin ≥99th percentile | 1.037 | 1.006–1.068 | .019  |
| CRP          | 0.994           | 0.989–0.998 | .004  |

CVD: Cardiovascular disease; CKD: Chronic kidney disease; CRP: C-reactive protein; HR: Hazard ratio; CI: Confidence interval.

In our study, in-hospital mortality was 14.3%; whereas the reported mortality rate in other multicenter Spanish populations for hospitalized patients has ranged from 11.9 to 28% [16–18]. This variability is also observed for international cohorts of hospitalized COVID-19 patients, with mortality rates varying from 1.4% in Chinese series [19] to 17% [20] and 26% [21] in Western populations. Differences in mortality rate reported have been attributed to causes as the different demographic characteristics and prevalence of comorbidities, the differing strategies used for SARS-CoV-2 RT-PCR testing and how COVID-19-related deaths were identified [22]. However, differences between Spanish series only could be explained by different criteria for inclusion of patients in the studies and for admission to hospitals, according to differences in the availability of health resources.
biochemical, hematologic and coagulation features of COVID-19, no prior adjustment of the results was performed to ensure the comparability of the results between the participating laboratories [16–19]. This lack of adjustment can generate data misinterpretation and compromise the robustness of conclusions reported [28]. Laboratory tests such LDH [7], ferritin [10] and albumin [29], reported as predictors of severity in COVID-19 patients, are strongly affected by the analytical method used to measure its blood levels. Therefore, to apply an adjustment factor contributes to the comparability of results.

We describe the presence of altered values for laboratory tests since the initial stage of early infection was a common finding. The most frequent alterations were increased values of CRP, LDH, ferritin and D-dimer, as well as a decreased lymphocyte count, considered as a signature for severe COVID-19 [30]. In our study, the rate of patients with abnormalities in these inflammatory markers was higher in patients who died. This finding could be related to the cytokine storm, already known in patients with severe to critical disease, in which lymphocyte count sharply decreased alongside with elevations of D-dimer, CRP and ferritin [31]. A high number of patients also had alterations in other laboratory tests since the early stages of infection, with abnormalities of renal, hepatic, cardiac or coagulation markers. Similar findings were found for procalcitonin, in agreement with previous studies [17], whose circulating levels should be in normal range, as expected for a viral infection, and lactate levels, for which a potential role for prognosis has hardly been analyzed so far.

The significant difference detected for most of laboratory tests levels in patients with a poor outcome is a consistent finding with other reports [16,17,21] and suggest a potential role for prognosis of COVID-19 patients. We identified several routine laboratory markers as predictors of in-hospital mortality, such as creatinine, troponin, CRP and platelet count, which have been suggested as predictors in previous studies and reviews [32–35]. We would like to highlight the role of creatinine as predictor for in-hospital mortality, suggested in previous studies [36]. Acute or pre-existing renal disease have been previously reported as predictors for the development of severe COVID-19 [36]. Although the kidney injury in COVID-19 is multifactorial, SARS-CoV-2 using angiotensin converting enzyme 2 (ACE2) receptor for renal cell entry and the virus-induced cytokines causing indirect effects on renal cells via shock or hypoxia have been proposed as mechanisms to explain the acute renal injury in these patients [37].

Strengths of this study, in addition to the sample size, are the previous estimation of this and the effort to adjust the results to guarantee their comparability. To our knowledge, only Kurstjens et al., performed a similar approach, calculating a harmonization factor to correct the observed differences for ferritin levels measured in different analyzers [10]. Besides, laboratory test levels were stratified by sex and age, as appropriate and recommended for tests such as D-dimer [38].

Our study has a number of limitations. First, this is a retrospective study and subject to the limitations of this design, including selection bias, errors in data entry, and residual confounding. Second, during the COVID-19 outbreak, a standardized analytical profile for ED or admission to ward or ICU was not established at onset or during the pandemic in all the participating centers and the available laboratory tests for physicians varied widely between hospitals; therefore, some cases had incomplete documentation of laboratory testing and the number of available results for each laboratory test was variable. Third, the role of IL-6, previously reported as predictor of COVID-19 severity [39], was not evaluated in our study, because it was measured in a small number of patients and with a great methodological variability.

Conclusion
In summary, analysis of laboratory data in multicenter studies requires a previous adjustment of results to assure the comparability of results reported by different laboratories. In our cohort, including a large number of hospitalized COVID-19 patients, we identified early risk factors for a poor outcome, including laboratory tests available in most of laboratories. These findings could help in the proper hospital management from the ED in patients with SARS-CoV-2 infection to early identify those at a high risk for severe disease progression.

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Author contributions
LGGR conceived and designed the study and supervised the conduct of the trial and data collection. DMG and ABB provided statistical advice on study design and analyzed the data. LGGR and DMG drafted the article, and CMI, JMBR and MJAM contributed substantially to its revision. All the authors contributed to data collection in the participating hospitals and final approval of this article.

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