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Factors related to mortality of patients with COVID-19 who are admitted to the ICU

Prognostic mortality factors of COVID-19 patients

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Abstract

During the severe acute respiratory syndrome coronavirus 2 pandemic, hospital resources, particularly critical care units, were overburdened and this had a significant impact on both the therapies and the prognosis of these patients. This study aimed to identify factors and therapies that may improve prognosis and other factors associated with increased mortality. A secondary objective was to evaluate the impact that obesity had on these patients. An observational study was conducted on 482 patients aged 18 years or older who were diagnosed with SARS-CoV-2 pneumonia and admitted to the Intensive Care Units of 3 national hospitals registered in the CIBERESUCICOVID database between September 2020 and March 2021. After identifying the sample profile, risk factors were analyzed, the predictive model was constructed, and crude odd ratios were calculated for each factor. Additionally, logistic regression was used to build the multivariate model adjusting for potential confounders. The final model included only the variables selected using the Backward method. A sample of 335 men (69.5%) and 145 women (30.08%) aged 61.94 ± 12.75 years with a body mass index (BMI) of 28.05 (25.7; 31.2) was obtained. A total of 113 patients received noninvasive mechanical ventilation. The most common comorbidities were: high blood pressure (51.04%), obesity (28%), diabetes mellitus (23.44%), other metabolic diseases (21.16%), chronic heart failure (18.05%), chronic obstructive pulmonary disease (11.62%), and chronic kidney disease (10.16%). In-hospital, 3-month and 6-month post-discharge mortality in patients with BMI > 30 (n = 135) versus BMI ≤ 30 (n = 347) was significantly different (P = .06). Noninvasive mechanical ventilation failed in 42.4% of patients with BMI > 30 compared to 55% of patients with BMI ≤ 30. This study identified the factors associated with failure of mechanical ventilation. The most common comorbidities were congestive heart failure, high blood pressure, chronic kidney disease, severe liver disease, diabetes mellitus, and solid organ transplantation. In terms of ventilatory support, patients who received high-flow nasal oxygen therapy on admission had lower mortality rates. The use of renal replacement therapy was also significantly associated with higher mortality.

Abbreviations: BMI = body mass index, FiO2 = fraction of inspired oxygen, ICU = intensive care unit, IMV = invasive mechanical ventilation, NIV = noninvasive mechanical ventilation, OR = odds ratios.

Keywords: COVID-19, ICU, mortality factors, obesity, prognosis, SARS-COV2, seriously ill patient

1. Introduction

The COVID-19 pandemic posed a challenge to all health care systems worldwide in terms of material and human resources. Although the incidence of COVID-19 has declined today, respiratory viral infections are still a high-profile problem that consume considerable resources in intensive care units. It is therefore essential to analyze the data obtained in order to establish associations that will allow prediction of the behavior of the disease according to the different risk factors and treatments used. With this knowledge, resources will be allocated more effectively and the prognosis for future patients will be improved.

During the critical phase of the pandemic, the surge of critically ill COVID-19 patients imposed unprecedented pressure

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

The research was exempted from the requirement to obtain informed consent owing to the fact that it was a study with data previously collected from clinical records, strictly adhering to the criteria of anonymisation, security, and confidentiality of data required for this type of research. However, the Ethics Committee of the Campo de Gibraltar was consulted to approve this exemption.

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on healthcare resources, including the availability of beds, ventilators, and specialized healthcare staff.[1] This saturation of intensive care units (ICUs) led to the creation of triage protocols for the ethical and efficient allocation of resources.[2] These protocols involved objective clinical criteria and other factors, such as likelihood of survival, expected duration of the need for additional resources, and severity of the illness. In addition, committees were established for the allocation of medical resources to ensure that allocation decisions were fair and transparent.[3]

The pandemic also led to an increased demand for specialized critical care staff, resulting in the reassignment and training of noncritical care clinicians and even the recruitment of retired professionals. The use of telemedicine has also been enhanced to facilitate the provision of advice from highly qualified intensive care specialists to remotely support and monitor less experienced ICU staff. In addition, mandatory and appropriate use of personal protective equipment and activation of isolation protocols were introduced to adapt to the challenges of infection and spread prevention within the hospital.[4]

Also, the COVID-19 health crisis has inspired the development of new therapies and treatment approaches for critically ill patients. Both clinical research[5] and collaboration between healthcare professionals have been crucial in identifying effective treatments, such as the administration of corticosteroids in patients with severe disease or the implementation of protective ventilation strategies.

Overall, the COVID-19 pandemic has had a significant impact on critical care services. In this regard, while ICUs have faced major challenges,[6] significant progress has also been made in the understanding and treatment of COVID-19.

On the other hand, increased collaboration between health professionals and the scientific community has led to the rapid generation and dissemination of shared knowledge. This collaborative effort has facilitated the identification of effective treatments and therapies,[7] as well as the development of best practices for the management of critically ill COVID-19 patients. This action is therefore considered essential not only in this specific case, but also as a strategic line for the future.

The resilience and adaptability of health systems and professionals working in them were also crucial in meeting the said challenges, as illustrated by the examples discussed above.[8] However, as the pandemic evolved and control improved, ICUs had to continue to adapt to the various changes brought about by this global crisis.[9]

On the other hand, when it comes to predicting prognosis, one of the most important aspects is to identify the factors that can influence the development and course of the disease. The main hypothesis is that the presence of certain risk factors together with the initial response in terms of parameters will have an impact on patients and their prognosis. Patients at risk for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) have been characterized by risk factors such as high blood pressure, cardiovascular disease, diabetes, chronic respiratory disease, or cancer.[10,11]

In relation to obesity, it has been identified as a severity factor leading to a more severe clinical course and greater complications.[12,13] In particular, it is associated with ventilatory dysfunction at the base of the lung, resulting in a deficit in pulmonary ventilation with a consequent decrease in blood oxygen transport and saturation.[14] In turn, obesity alters the balance of adipocytes and immune cells, resulting in a disruption of immune surveillance. This results in a dysregulated immune response, increased macrophage chemotaxis and differentiation, which affect the lung parenchyma and bronchi.[15,16] Overall, it seems likely that obesity itself is an independent risk factor for the severity of severe respiratory SARS-CoV-2 infection. Several studies[17,18] have found an association between body mass index (BMI) and prognosis in SARS-CoV2 infection, with a negative impact on mortality and short and long-term complications.

Therefore, identifying the factors associated with poorer prognosis is of paramount importance in clinical practice, as this knowledge may contribute to more efficient decision making and resource reallocation. Additionally, identifying the factors associated with failure of mechanical ventilation may allow prediction of the choice of the most appropriate ventilatory support for each patient. In this way, the aim of this investigation was to examine which factors and comorbidities are associated with increased mortality and, secondarily, to define the impact that obesity, measured as BMI ≥ 30, has on the prognosis of severe COVID-19 disease.

2. Material and methods

2.1. Design

A multicenter, observational cohort study without a control group was conducted on patients with severe acute respiratory syndrome coronavirus 2 lung pathology admitted to the ICU and included in the CIBERESUCICOVID study. Patients requiring invasive mechanical ventilation (IMV) on admission were excluded so as to investigate predictive factors of failure of noninvasive ventilation (NIV). The failure of noninvasive ventilation was defined as the need for orotracheal intubation and initiation of invasive mechanical ventilation.

2.2. Ethical aspects

The study was conducted in accordance with the ethical principles of the Universal Declaration of Helsinki and the relevant Spanish legislation on biomedical research. These include the Law on Biomedical Research (Law 14/2007 of 3 July), Organic Law 3/2018 on the Protection of Personal Data and the Guarantee of Digital Rights, the General Data Protection Regulation, and the Law on Patient Autonomy (Law 41/2002 of 14 November).

Confidentiality and anonymity were ensured by recording initials and age and then assigning a code for identifying the patient. Electronic storage of data that could lead to direct patient identification was avoided. After verification and cleaning of the data matrix, and prior to statistical analysis, patients' initials were removed from the dataset.

The contents of the data collection sheets and documents generated throughout the study were protected from unauthorized use by anyone outside the research, except for inspection by health authorities.

This study had a valid and beneficial research purpose, with no risk to participants. It was also reviewed by an Ethics Committee of the Campo de Gibraltar to ensure that it met acceptable ethical standards (COV20_001100).

The research was exempted from the requirement to obtain informed consent owing to the fact that it was a study with data previously collected from clinical records, strictly adhering to the criteria of anonymization, security, and confidentiality of data required for this type of research. However, the Ethics Committee was consulted to approve this exemption.

2.3. Study population

Patients included in the CIBERESUCICOVID database were the focus of this study. This is a multicentre, observational cohort study of patients with SARS-CoV-2 infection admitted to 55 Spanish Intensive Care Units between September 2020 and March 2021.

The sample was obtained in a non-probabilistic and purposive way according to the established criteria of cases from the CIBERESUCICOVID database that met the requirement of being a patient > 18 years of age, with a diagnosis of severe SARS-CoV-2 pneumonia confirmed by real-time polymerase chain reaction, admitted to the ICU, and registered in CIBERESUCICOVID. Cases with the following conditions were excluded: (a) patients with life expectancy < 24 hours or limitation of life support (limitation of therapeutic effort); (b) patients with voluntary refusal of invasive measures; (c) patients with contraindication and/or intolerance to NIV; (d) patients requiring orotracheal intubation and connection to IMV on admission to ICU (first 24 hours).

2.4. Sample size

Published studies on the efficacy of NIV in patients with COVID-19 were reviewed, reflecting a failure rate dependent on the severity of respiratory failure, ranging from 25% to 50%. Assuming a worst-case failure rate of 50%, 95% confidence, and 5% precision, the required sample size would be 384 patients (288 patients for a 25% failure rate).

2.5. Data collection

The data were extracted from the RedCap database, compliant with the CIBERESUCICOVID study, without the need for direct access to the patients' medical records.

This research protocol was approved by the Executive Committee of the CIBERESUCICOVID study, who provided the data anonymized by code, limiting any other patient information that could lead to their identification. Only the main researcher of the CIBERESUCOVID study was allowed to relate the information collected in this study to each patient's clinical history.

Subsequently, a data matrix was completed by entering the study variables and the parameters obtained. A coding system was developed for the variables in order to detect and correct errors and inconsistencies in the parameters collected. Finally, the data were analyzed.

2.6. Definition of variables

Data were collected for the following variables:

1. Epidemiological history of the patient.
2. Clinical, biological, and treatment data on admission to hospital.
3. Clinical, biological, and treatment data on admission to the ICU and sequentially until discharge from the ICU or death.
4. Specific data on oxygen therapy and invasive and noninvasive ventilatory support.
5. Clinical and biological parameters at discharge from hospital.
6. Clinical follow-up data for patients surviving up to 6 months, including pulmonary function tests, chest radiography, and quality of life questionnaires.
7. In-hospital and intra-ICU mortality data at 28 days, 90 days, 6 months, and 1 year.
8. In order to objectify the concept of obesity, the BMI was applied. The formula is BMI = weight (kg)/height (m^2). Specifically, BMI < 30 and obesity BMI ≥ 30 were dichotomized.

2.7. Statistical analysis

Data were analyzed using R software version 4.2.2 for MacOS 10.13. Quantitative variables were presented as mean, standard deviation or median with interquartile range, and qualitative variables as absolute frequencies and percentages.

To analyze the normality of the distribution of quantitative variables, the Kolmogorov-Smirnov test (with Lilliefors correction) was applied, represented by distribution functions (histogram, Q-Q plot, box-plot).

Different statistical tests were used to analyze the data according to their type and hypotheses, including the chi-squared test to compare observed proportions between groups and Fisher test when expected frequencies were ≤5. Student *t* test was used to compare means between 2 independent groups. In the absence of normality of the data, nonparametric Mann–Whitney test for independent samples and Wilcoxon signed-rank test for paired samples were used.

Several analyses were performed to identify risk factors and develop a predictive model by calculating crude odds ratios (OR) for each factor. A multivariate model was applied using logistic regression and adjusting for potential confounders. The backward method was used to select the variables to be included in the final model.

The model's predictive ability was evaluated using the area under the ROC curve and its 95% confidence interval. Additionally, the optimal cutoff points for estimating diagnostic sensitivity and specificity were determined, with a significance level of $P < .05$.

3. Results

3.1. Clinical-epidemiological characteristics of patients with severe SARS-CoV-2 pneumonia admitted to the ICU

A total of 482 patients were admitted to intensive care units due to acute respiratory failure caused by severe SARS-CoV-2 pneumonia. Of these, 335 (69.5%) were male and 145 (30.08%) were female. The mean age of the patients was 61.94 ± 12.75 years and the median BMI was 28.05 [25.7; 31.2].

The most frequent comorbidities (Table 1) were: high blood pressure (51.04%); obesity (28%); diabetes mellitus (23.44%); chronic heart failure (18.05%); chronic obstructive pulmonary disease (11.62%); and chronic kidney disease (10.16%).

The most prevalent symptoms on admission were fever (82.78%); dyspnea (63.9%); dry cough (58.51%); fatigue/asthenia (31.53%); diarrhea (22.82%); myalgia (19.09%); and productive cough (15.35%). Patients were on statins (30.7%); non-steroidal anti-inflammatory drugs (17.63%); antibiotics (11.62%); and oral steroids (10.79%). Antihypertensive drugs were the most commonly used, followed by ARA II (21.37%); diuretics (18.46%); angiotensin-converting enzyme inhibitors (15.35%); beta-blockers (14.52%); and calcium antagonists (13.07%).

On admission, 306 patients (63.48%) required conventional oxygen therapy with fraction of inspired oxygen (FiO2) (median 60 [40; 80]). Regarding hemodynamic parameters (Tables 2–4), the mean values were: heart rate (85.48 ± 18.71 beats/minute); respiratory rate (28.82 ± 7.55 breaths/minute); systolic blood pressure (132.7 ± 26.59 mm Hg); diastolic blood pressure (72.64 ± 16.58 mm Hg); and mean blood pressure (91.92 ± 19.3 mm Hg).

The multivariate regression model (Table 5) showed the following associated statistics: sensitivity 72.6%, specificity 80.3%, negative pressure ventilator 77%, and positive pressure ventilator 76.3%.

The ROC curve of the obtained model showed an AUC–ROC of 86.1% (95% CI, 79.9–92.4%), indicating an excellent predictive ability (Fig. 1).

3.2. Evaluation of the impact of BMI on the prognosis of patients with severe SARS-CoV-2 pneumonia admitted to the ICU

Patients with a BMI ≥ 30 (n = 135) were compared with patients with a BMI < 30 (n = 347). Both in-hospital mortality and mortality at 3, 6, and 12 months after discharge were lower in patients with a BMI ≥ 30. As shown in Table 6, the differences observed in mortality at 6 and 12 months after discharge

Table 1

Factors and comorbidities associated with mortality.

Mortality	Alive (n = 340)	Exitus (n = 130)	*P*-value
Sex			
Male	237 (69.7)	91 (70.5)	.949
Female	103 (30.3)	38 (29.4)	
Age	60 [51; 68]	70.5 [64; 76]	<.001
BMI	28 [25.8; 31.5]	28 [25.3; 30.6]	.371
Comorbidities			
Congestive heart failure	50 (14.7)	35 (26.9)	.003
High blood pressure	153 (44.9)	88 (67.7)	<.001
Asthma	13 (3.8)	4 (3.1)	1
Chronic kidney disease	26 (7.6)	23 (17.7)	.002
Moderate-severe liver disease	2 (0.6)	3 (2.3)	.132
Mild liver disease (cirrhosis without portal hypertension)	11 (3.2)	4 (3.1)	1
Obesity (BMI > 30)	105 (30.8)	28 (21.5)	.060
Chronic neurological disease	21 (6.1)	9 (6.9)	.926
Dementia	0 (0)	4 (3.1)	.006
Rheumatologic disease	15 (4.4)	9 (6.9)	.379
Diabetes mellitus	63 (18.5)	47 (36.1)	<.001
Active malignant neoplasm	11 (3.2)	18 (13.8)	<.001
Solid organ Tx	11 (3.2)	9 (6.9)	.128
HIV or AIDS	4 (1.2)	1 (0.8)	1
Immunosuppression, other causes	5 (1.5)	6 (4.6)	.079

Table 2

Mortality according to clinical parameters.

Clinical parameters on ICU admission	Alive (n = 340)	Exitus (n = 130)	*P*-value
FiO2	60 [40; 70]	60 [50; 90]	.002
PaO2	71.6 [62.3; 86]	66 [56; 78.8]	.018
PaCO2	33.7 [30.5; 37.6]	34.3 [30; 38]	.496
pH	7.45 [7.42; 7.48]	7.44 [7.41; 7.48]	.136
HCO3, mean (SD)	23.4 (±3.7)	23.4 (4.5)	.945
SaO2	94 [91; 96.1]	90 [86; 94]	<.001
Glasgow Coma Scale	15 [15; 15]	15 [15; 15]	.001
Temperature, mean (SD)	36.8 (±1.02)	36.5 (±1.02)	.007
Heart rate, mean (SD)	84.9 (±18.9)	87 (±17.9)	.260
Respiratory rate, mean (SD)	28.5 (± 7.6)	29.6 (±7.5)	.166
Systolic blood pressure, mean (SD)	132.4 (± 25.2)	133.9 (±30.3)	.599
Mean blood pressure, mean (SD)	92.3 (±19.1)	91.1 (±19.6)	.545
Diastolic blood pressure, mean (SD)	73.5 (± 16.5)	69.9 (±15.9)	.031
Time from symptom onset to hospital admission	7 [5; 10]	6 [4; 7]	<.001
Time from symptom onset to ICU admission	9 [6; 12]	8 [6; 11]	.107
Time from hospital admission to ICU admission	1 [0; 3]	2 [0; 4]	.122
Time from hospital admission to IMV	3 [2; 5.5]	5 [3; 9]	<.001
Time from ICU admission to IMV onset	2 [1; 3]	2.5 [1; 4.2]	.002
HFNC at ICU admission	254 (74.5)	68 (52.3)	<.001
NIV at ICU admission	38 (11.1)	50 (38.5)	<.001
PCR	119.6 [58.9; 201.6]	161.5 [74.7; 257]	.008
SOFA score	3 [3; 4]	4 [3; 6]	<.001
APACHE II score	10 [7; 13]	13 [10; 18]	<.001
PAFI at ICU admission	126 [94.2; 194.2]	124.2 [89.9; 168.1]	.262
NIV failure (or requiring IMV after 24 hours of ICU admission)	79 (26.1)	83 (69.2)	<.001

APACHE = acute physiology and chronic health evaluation, HFNC = high-flow nasal cannula, ICU = intensive care unit, IMV = invasive mechanical ventilation, NIV = noninvasive mechanical ventilation, PAFI = ratio of arterial oxygen partial pressure (PaO2) to fractional inspired oxygen (FiO2), PCR = polymerase chain reaction, SOFA = sequential organ failure assessment.

showed a trend towards statistical significance ($P = .066$ and $P = .06$, respectively). On the other hand, NIV failed in 42.4% of patients with BMI ≥ 30 (Table 7), compared with 55% of patients with BMI < 30, although this was not statistically significant ($P = .313$).

4. Discussion

With regard to socio-demographic factors, the results of this study are consistent with those of other studies,[19,20] showing that older patients have a higher mortality rate. The most common comorbidities follow the same pattern as those published in the scientific literature,[10,11] which indicate that congestive heart failure, high blood pressure, chronic kidney disease, severe liver disease, diabetes mellitus, and solid organ transplantation are the most common in this type of patient. Among the comorbidities that are found to increase mortality, those of rheumatological etiology, malignant neoplasms, and immunosuppressive processes should be highlighted. This admission history is consistent with that reported in the literature.[21–23]

Among the clinical parameters quantified on admission to the ICU and associated with mortality,[24–27] a greater need for a high inspiratory fraction (FiO2) should be highlighted. This is expected to be associated with greater hypoxemia and lower oxygen saturation in the peripheral pulse wave, reflecting greater hypotension at the hemodynamic level.[28]

In terms of ventilatory support, patients who received high-flow nasal oxygen therapy on admission had lower mortality rates, while those who received NIV on admission had higher mortality rates. These results may be due to the fact that in most hospital centers the use of NIV was reserved for the most severely ill patients, whereas virtually all patients requiring ICU admission were started on HFNO therapy. Consistent with the scientific literature,[29–31] those patients requiring IMV had higher mortality rates, which was quite expected, as these patients were the most severely ill.

In similarity to the scientific evidence,[32] multivariate analysis showed that the independent factors associated with higher mortality were the use of NIV on admission to the ICU, the presence of diabetes mellitus as a preexisting condition, and the time elapsed between hospital admission and NIV initiation, with OR increasing with each day of admission. The risk also increased per unit of polymerase chain reaction and creatinine value. However, a higher ratio of arterial oxygen partial pressure (PaO2) to FiO2 was identified with a lower OR.

Consistent with other studies,[33,34] on the third day of ICU admission, morbidity was associated with the higher need for FIO2, more frequent hypotension, and consequently a higher need for inotropes. Both the need for muscle relaxants and the use of the prone position were more common in patients with higher mortality.[35,36] These data reflect the fact that the most common criteria for the use of these 2 therapies were greater patient severity in terms of PAO2/FiO2 index (ratio of arterial oxygen partial pressure [PaO2] to fractional inspired oxygen [FiO2]). That is, patients with a higher probability of exitus.

The use of renal replacement therapy was also significantly associated with higher mortality, which is in line with available data and experience.[35] Another notable finding was the increased incidence of ventilator-associated pneumonia.

Undoubtedly, one of the most relevant data obtained from this research is the association of respiratory pathology with obesity, which has also been reflected in other studies.[32,36] However, the present results show a decrease in mortality and failure of mechanical ventilation in patients with a BMI ≥ 30. These findings are to be treated with caution, as one of the exclusion criteria of the study was the need to initiate invasive mechanical ventilation within the first 24 hours of admission to the ICU, bearing in mind that, in accordance with the literature reviewed to date, these patients who received early mechanical ventilation were those with greater severity, a higher number of complications and, probably, a higher BMI.[37,38]

According to the meta-analysis by Huang, Y et al,[21] obesity plays an especially significant role in the risk of death due to COVID-19, especially in male patients. Specifically, it increases the risk of hospitalization, ICU admission, need for IMV, and death in patients with COVID-19. In addition, excessive visceral adiposity appears to be associated with severe COVID-19 outcomes.

In another prospective cohort study conducted in Italy,[22] it was reported that patients with obesity had a 3-fold increased risk of death compared to those with a BMI < 30 kg/m^2. Similarly, research in the Bronx borough of New York City found that severe obesity (defined as BMI ≥ 30 kg/m^2) was associated with increased in-hospital mortality, independent of other factors.[19] Yet, in line with the present findings, a prospective cohort study in New York involving 1150 adults hospitalized for COVID-19 excluded severe obesity as a risk factor for in-hospital mortality.[23]

Other studies[17,38,39] have suggested that increased visceral fat is associated with a worse prognosis in patients with COVID-19, suggesting a possible positive association between visceral obesity and COVID-19 severity. Similarly, a study by Simonnet A, et al[40] found that obesity (BMI ≥ 30) and severe obesity (BMI > 35) were present in 47.6% and 28.2% of cases, respectively. A total of 85 patients (68.6%) required IMV. The proportion of patients requiring IMV increased with BMI category ($P < .01$, $\chi2$ test for trend) and was highest in patients with BMI > 35 (85.7%).[21]

Table 3

Parameters of mortality at onset of NIV.

At onset of NIV	Alive (n = 340)	Exitus (n = 130)	*P*-value
PEEP	12 [10; 14]	12 [10; 14]	.063
Plateau pressure	23 [21; 26]	23.1 [21; 27]	.996
Tidal volume per (ml/kg)	6.77 [6.08; 7.22]	6.66 [6.12; 7.33]	.860
FIO2	90 [70; 100]	94.9 [70; 100]	.766
PAFI	105.9 [67.7; 162]	79.4 [36.8; 135.8]	<.001
SOFA score	4 [3; 5]	7 [5; 8]	<.001

FiO2 = fraction of inspired oxygen; PAFI = ratio of arterial oxygen partial pressure (PaO2) to fractional inspired oxygen (FiO2); PEEP = positive end-expiratory pressure; SOFA = sequential organ failure assessment.

Table 4

Mortality parameters at the third day in ICU.

Parameters at third day in ICU	Alive (n = 340)	Exitus (n = 130)	*P*-value
Fio2	50 [40; 66.5]	75 [53; 90.5]	<.001
PaO2	71.5 [60.5; 86.1]	75 [59.5; 96.3]	.199
Vasopressors	93.5 [90; 96]	93 [89; 95.9]	.585
SBP	128.4 (±27.7)	132.1 (± 32.6)	.281
MBP	89.7 (±19.2)	87.8 (± 19.8)	.390
DBP	70.7 (±16.7)	66.1 (± 16.8)	.010
Inotropes	55 (17.8)	45 (36.9)	<.001
Neuromuscular relaxants	43 (13.9)	28 (23.1)	.029
PCR	34 [16.1; 75]	84 [37.4; 221.9]	<.001
SOFA score	4 [3; 5]	7 [4; 8]	<.001
Prone position	73 (21.7)	37 (45.1)	<.001
Renal replacement therapy	11 (3.2)	14 (16.3)	<.001
Ventilator-associated pneumonia	16 (84.2)	30 (90.9)	.656
Pulmonary thromboembolism	50 (14.7)	8 (6.3)	.022
PAFI	138 [100.7; 206.6]	126.3 [75.5; 175.9]	.009

DBP = diastolic blood pressure, MBP = mean blood pressure, PAFI = ratio of arterial oxygen partial pressure (PaO2) to fractional inspired oxygen (FiO2), PCR = polymerase chain reaction, SBP = systolic blood pressure, SOFA = sequential organ failure assessment.

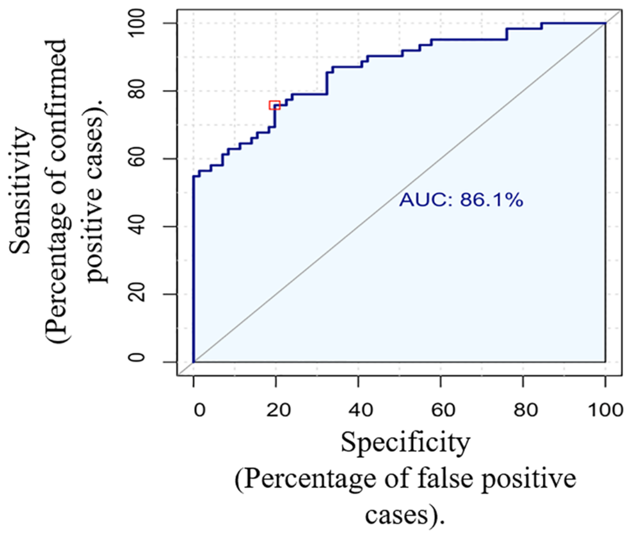

Figure 1. ROC curve.

Table 5

Predictive factors of mortality. Multivariate logistic regression.

	OR	CI 95%	*P*-value
NIV at ICU admission	12.16	3.60–48.08	<.001
Diabetes mellitus	3.97	1.47–11.37	.008
Time from hospital to IMV	1.24	1.08–1.45	.003
PCR at ICU admission	1.003	1.001–1.007	.039
PAFI at day 3	0.98	0.97–0.99	<.001
Creatinine at day 3	4.78	2.23–12.73	<.001

CI = confidence interval, ICU = intensive care unit, IMV = invasive mechanical ventilation, NIV = noninvasive mechanical ventilation, OR = odds ratio, PAFI = ratio of arterial oxygen partial pressure (PaO2) to fractional inspired oxygen (FiO2), PCR = polymerase chain reaction.

In this regard, the OpenSAFELY study[41] conducted in the United Kingdom in over 17 million adults with COVID-19 infection, although not specifically on critical patients, showed that obesity and diabetes were independently associated with mortality. A BMI > 40 kg/m^2 was associated with almost double the COVID-19-related mortality compared to patients without obesity. In the ICU setting, several studies[24,33,34] have reported an association between increased incidence of adverse prognosis and obesity.

4.1. Limitations

This study has some limitations that need to be acknowledged. Firstly, the limitations inherent to observational study designs using medical records, namely the possibility of loss of information due to the fact that the data were collected after the event occurred and that the information recorded was incomplete. The second limitation is that the time during which patients received NIV was not recorded, nor was the time elapsed before this therapy failed, which is undoubtedly relevant since delaying intubation and mechanical ventilation has been proven to have a negative impact on mortality. Thirdly, the potential impact of limiting the therapeutic effort, especially during the worst moments of the pandemic, was not considered and cannot be assessed. Fourth, therapeutic strategies changed over the course of the pandemic, resulting in different treatment depending on the wave to which each patient belonged, among other factors, and thus making it difficult to estimate the impact on the morbidity and mortality observed. Fifth and finally, in the assessment

Table 6

Obesity and mortality.

Obesity (BMI ≥ 30) Mortality	Alive (n = 347)	Exitus (n = 135)	*P*-value
Hospital discharge	107 (29.8)	28 (22.8)	.166
3 months	106 (30.5)	29 (22.3)	.107
6 months	106 (30.5)	28 (21.5)	.066
1 year	105 (30.8)	28 (21.5)	.060

BMI: body mass index.

Table 7

Relationship between BMI and success or failure of NIV.

	BMI ≥ 30	BMI < 30	*P*-value
NIV failure	135 (42.4%)	347 (55%)	.313

BMI = body mass index, NIV = noninvasive mechanical ventilation.

of mortality, patients receiving invasive mechanical ventilation on admission to the ICU were excluded from the study, as their mortality rates were higher than those of patients who did not require mechanical ventilation. In addition, important variables such as race or certain socio-economic variables may not have been collected, which could have affected the fit of the models.

5. Conclusions

This study does serve as an epidemiological study about COVID in Spain, which has identified the factors associated with failure of mechanical ventilation that may allow prediction of the choice of the most appropriate ventilatory support for each patient. The most common comorbidities were congestive heart failure, high blood pressure, chronic kidney disease, severe liver disease, diabetes mellitus, and solid organ transplantation. Among the comorbidities that are found to increase mortality, those of rheumatological etiology, malignant neoplasms, and immunosuppressive processes should be highlighted. In terms of ventilatory support, patients who received high-flow nasal oxygen therapy on admission had lower mortality rates. The use of renal replacement therapy was also significantly associated with higher mortality.

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