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SCIENTIFIC LETTER

Characteristics and results of a series of 59 patients with severe pneumonia due to COVID-19 admitted in the ICU☆

Características y resultados de una serie de 59 pacientes con neumonía grave por COVID-19 ingresados en UCI

To the Editor:

Since the first cases of pneumonia due to a new beta-coronavirus discovered in Wuhan, province of Hubei (China) were reported back in December 2019,[1] the spread of the infection has been growing nonstop worldwide. The World Health Organization (WHO) declared the situation of pandemic back in March 11, 2020 and now we are facing the biggest challenge in the history of intensive medicine. The correct characterization of the patients and the risk factors involved in the serious clinical signs seen should help at the present time and in the coming years to provide better healthcare and keep the infection under control.

This is a retrospective, cross-sectional study of 59 cases of severe pneumonia due to COVID-19 admitted to an intensive care unit (ICU) from a total of 525 hospitalized patients (11.24%). Patients were recruited from March 12 through May 1, 2020. Three of them still remained at the ICU when the study was submitted with a mean stay of 21 days (median of 19). A statistical analysis was conducted of the patients' clinical and demographic characteristics and of the data derived from the management of respiratory failure, use of mechanical ventilation, complications, and mortality. Fisher's exact test was used to compare the categorical variables and Mann-Whitney *U* test was used to compare the continuous ones. This study has been approved by our center ethical committee of clinical research.

The median of age of the patients included in the study was 63.0 years (standard deviation [SD] 11.2), 45 of them were males (76.3%), and arterial hypertension was the most prevalent comorbidity (n = 35 [59.3%]). Table 1 shows the patients' clinical and demographic characteristics.

Diagnosis was established using the reverse transcriptase polymerase chain reaction test (RT-PCR) that tested positive in 56 (94.9%) of the patients while in the remaining 3 (5.1%) it was only serological. In 33 cases (55.9%), the RT-PCR only tested positive in the nasopharyngeal exudate, in 18 (30.5%) both in the exudate and lower respiratory tract samples, in 3 (5.1%) it tested positive in the tracheal aspirate or brochoalveolar lavage and in 2 (3.4%) it tested positive in sputum. Since some of the patients had been transferred from the hospital conventional wards, a lower respiratory tract sample was collected if the previous RT-PCR in exudate had tested negative. The later application of the ELISA technique for serological diagnosis tested 35 patients only (59.3%), 27 (77.1%) of whom tested positive for both IgM and IgG. From the very moment it became available, both the patients admitted to the ICU and those already hospitalized were tested during their disease progression.

Of the total number of cases, 49 (83.1%) received invasive mechanical ventilation (IMV) at some point, 30 (61.2%) exclusively and 19 (38.8%) following high-flow nasal cannula (HFNC) oxygen therapy failure. The median of days on IMV was 19 (IQR, 9.5–26), 61.2% of the patients required ventilation in the prone position with a median of 2 cycles (IQR, 1–3.25). Twenty-nine patients underwent a percutaneous tracheostomy, 59.2% of those ventilated with a median of days from intubation until the procedure was performed of 11 days (IQR, 9.5–15). Tracheostomies were performed early on given the beneficial effects of this procedure in ventilated patients with long hospital stays and the fact that it is an already established procedure for the management of COVID-19 related pneumonia. The remaining cases, 9 (15.3%) and 1 (1.7%) received HFNC and conventional oxygen therapy, respectively, with no need for IMV. Regarding other life-support therapies, 8 patients (13.6%) required extrarenal depuration therapy and 4 (6.8%) received inhaled nitric oxide. Table 2 shows the ventilatory and analytical parameters of patients at admission.

We analyzed the thromboembolic complications that occurred during the ICU stay and found 10 events (16.9%) including pulmonary thromboembolism (n = 3 [5.1%]), deep venous thrombosis (n = 3 [5.1%]), ischemic stroke (n = 3 [5.1%]), and acute myocardial infarction (n = 1 [1.7%]). All patients received thromboembolic prophylaxis and only those with a confirmed diagnosis received therapeutic doses. The recommendations established by the Spanish Society of Thrombosis and Hemostasis (SETH)[2] were followed.

The overall mortality at the ICU setting was 33.9% (20 patients) with a median of age that was significantly higher in non-survivors ($P = .049$). Studying the different age groups, a growing tendency with older age was confirmed. Patients were categorized into 5 different groups: <40 years

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Table 1 Clinical and demographic characteristics of mechanical ventilation and related complications.

	Total (n = 59)	Survivors (n = 39)	Non survivors (n = 20)	*P* value[a,b]
Age; median (IQR)	63 (54–70)	58 (50–69)	65 (58–70)	.049
Sex; n (%)				
Males	45 (76.3%)	30 (76.9%)	15 (75.0%)	>.99
Women	14 (23.7%)	9 (23.1%)	5 (25.0%)	
Comorbidities; n (%)				
Arterial hypertension	35 (59.3%)	22 (56.4%)	13 (65.0%)	.59
Diabetes mellitus	19 (32.2%)	11 (28.2%)	8 (40.0%)	.39
Ischemic heart disease	6 (10.2%)	4 (10.3%)	2 (10.0%)	>.99
COPD	3 (5.1%)	2 (5.1%)	1 (5.0%)	>.99
Asthma	8 (13.6%)	5 (12.8%)	3 (15.0%)	>.99
SAHS	7 (11.9%)	3 (7.7%)	4 (20.0%)	.21
Liver disease	7 (11.9%)	4 (10.3%)	3 (15.0%)	.68
Chronic kidney disease	6 (10.2%)	3 (7.7%)	3 (15%)	.40
Cerebrovascular disease	4 (6.8%)	1 (2.6%)	3 (15%)	.11
HIV	0 (0%)	0 (0%)	0 (0%)	NA
HBV	0 (0%)	0 (0%)	0 (0%)	NA
HCV	0 (0%)	0 (0%)	0 (0%)	NA
Flu	0 (0%)	0 (0%)	0 (0%)	NA
Malignant neoplasm (actual or previous)	2 (3.4%)	2 (5.1%)	0 (0%)	.54
Malignant blood disease (actual or previous)	1 (1.7%)	0 (0%)	1 (5.0%)	.34
Solid organ transplant	1 (1.7%)	0 (0%)	1 (5.0%)	.34
Obesity	30 (50.8%)	18 (46.2%)	12 (60.0%)	.41
Body mass index ($\geq$ 30 kg/m^2), median (IQR)	30.21 (27.85–33.02)	29.09 (28.05–33.28)	30.35 (27.40–32.46)	.78
Active smoker; n (%)	2 (3.4%)	1 (2.6%)	1 (5.0%)	>.99
Former smoker; n (%)	20 (33.9%)	12 (30.8%)	8 (40.0%)	.57
Active alcohol use; n (%)	4 (6.8%)	2 (5.1%)	2 (10.0%)	.60
RASS antihypertensive drugs; n (%)	30 (50.8%)	21 (53.8%)	9 (45.0%)	.59
ACEI	14 (23.7%)	11 (28.2%)	3 (15.0%)	.34
ARA-II	16 (27.1%)	10 (25.6%)	6 (30.0%)	.76
APACHE II; median (IQR)	13 (10–17)	12 (9–14)	16 (13–20)	.001
SOFA; median (IQR)	8 (4–9)	6 (4–8)	8 (8–9)	.006
Days at the ICU; median (IQR)	19 (11–31)	25 (12–37)	17 (7–21)	.02
Mechanical ventilation; n (%)	49 (83.1%)	30 (76.9%)	19 (95.0%)	.14
Days on mechanical ventilation; median (IQR)	19.0 (9.5–26.0)	20.5 (12.0–32.8)	18.0 (6.0–21.0)	.031
Ventilation in the prone position; n (%)	30 (50.8%)	17 (43.6%)	13 (65.0%)	.17
Thromboembolic complications; n (%)	10 (16.9%)	8 (20.5%)	2 (10.0%)	.47

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; ARA-II, angiotensin-2 receptor antagonists; COPD, chronic obstructive pulmonary disease; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; NA, non-applicable; RASS, renin-angiotensin-aldosterone system; SAHS, sleep apnea-hypopnea syndrome.

P values $\leq$.05 were considered statistically significant.

[a] The Mann–Whitney *U* test was used to compare the continuous variables (medians).

[b] Fisher's exact test was used to compare the qualitative variables.

Table 2 Ventilatory and analytical parameters at admission; median (IQR).

	Total (n = 59)	Survivors (n = 39)	Non survivors (n = 20)	*P* value[a]
PaO_2/FiO_2 ratio	97.5 (87.0–157.6)	126.5 (88.5–175.8)	92.5 (63.5–115.0)	.29
FiO_2 (%)	80 (70–100)	80 (70–95)	88 (64–100)	.58
PEEP (cm H_2O)	14.5 (13–16)	14 (12–16)	15.5 (14–16)	.19
Lymphocytes ($\times 10^9$/mL)	0.60 (0.38–0.85)	0.58 (0.37–0.83)	0.65 (0.43–1.07)	.52
D-dimer (mg/L)	1.45 (0.65–2.93)	1.08 (0.60–3.04)	1.82 (1.02–5.92)	.09
Ferritin (ng/mL)	1.458 (664–2.819)	1.430 (527–2.704)	1.496 (945–3.330)	.44
LDH (IU/L)	531 (424–659)	520 (394–586)	622 (437–802)	.032
IL-6 (pg/mL)	72 (13–556)	72 (8–556)	121 (17–801)	.41

P values $\leq$.05 were considered statistically significant.
[a] The Mann-Whitney *U* test was used to compare the continuous variables (medians).

(n = 0 [0%]), from 41 years to 50 years (n = 1 [10%]), from 51 years to 60 years (n = 5 [35.7%]), from 61 years to 70 years (n = 10 [43.5%]), and over 70 years (n = 4 [40%]). The mortality rate associated with ventilatory support of those who received IMV was only 46.7% while the mortality rate of those who were previously treated with HFNC was 26.3%. Both subgroups had a similar APACHE II score at admission, a median of 14 (IQR 11.5–17.5) for the group that received IMV only and a median of 13 (RIQ 11–15) for the group that received HFNC followed by IMV. This suggests that an initial conservative approach in certain patients may not lead to higher mortality rates. The APACHE II and SOFA scores at admission were higher in non-survivors (*P* = .001 and *P* = .006, respectively).

Although the study has some limitations, the results are consistent with other results published to this date regarding previous comorbidities[3,4] and the possibility that the D-dimer is a risk factor for mortality,[3] which shows a trend towards statistical significance but is not statistically significant *per se*. Our rate of thromboembolic complications was lower compared to the one obtained in the study conducted by Klok et al.[5] (31%) and similar to that from other series of thromboembolic disease reported in critically ill patients.[6,7] Similarly, the mortality rate seen in our patients (33.9%) was lower compared to the mortality rate of series previously published such as the study conducted by Yang et al.[8] (61.5%) and other studies (49%–67%).[9,10]

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Conflicts of interest

None reported.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;Feb 20; 382(8):727–33, http://dx.doi.org/10.1056/NEJMoa2001017.
2. Sociedad Española de Trombosis y Hemostasia. https://www.covid-19.seth.es/recomendaciones-de-tromboprofilaxis-y-tratamiento-antitrombotico-en-pacientes-con-covid-19/, 2020 [Accessed 20 May 2020].
3. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;Mar; 13:e200994, http://dx.doi.org/10.1001/jamainternmed.2020.0994.
4. Blake A, Collins D, O'Connor E, Bergin C, McLaughlin AM, Martin-Loeches I. Clinical and biochemical characteristics of patients admitted to ICU with SARS-CoV-2. Med Intensiva. 2020;May 16, http://dx.doi.org/10.1016/j.medin.2020.05.003 [Epub ahead of print].
5. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;Apr 10, http://dx.doi.org/10.1016/j.thromres.2020.04.013. S0049-3848(20)30120-30121. [Epub ahead of print].
6. Minet C, Potton L, Bonadona A, Hamidfar-Roy R, Somohano CA, Lugosi M, et al. Venous thromboembolism in the ICU: main characteristics, diagnosis and thromboprophylaxis. Crit Care. 2015;Aug 18; 19:287, http://dx.doi.org/10.1186/s13054-015-1003-9.
7. McLeod AG, Geerts W. Venous thromboembolism prophylaxis in critically ill patients. Crit Care Clin. 2011;Oct; 27:765–80, http://dx.doi.org/10.1016/j.ccc.2011.07.001.
8. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;May; 8:475–81, http://dx.doi.org/10.1016/S2213-2600(20)30079-5.
9. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;Feb 24, http://dx.doi.org/10.1001/jama.2020.2648 [Epub ahead of print].
10. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. JAMA. 2020;Mar 19; 323:1612–4, http://dx.doi.org/10.1001/jama.2020.4326 [Epub ahead of print].

J.L. Serrano-Martínez*, J.F. Machado-Casas, M. Redondo-Orts, F. Manzano-Manzano, J. Castaño-Pérez, J.M. Pérez-Villares
Servicio de Medicina Intensiva, Hospital Universitario Virgen de las Nieves, Granada, Spain

Corresponding author.
E-mail address: jlserranouci@gmail.com (J.L. Serrano-Martínez).
2173-5727/

Novel coronavirus (2019-nCov): do you have enough intensive care units?

Nuevo coronavirus (2019-nCov): ¿tiene suficientes unidades de cuidados intensivos?

Recently, the World Health Organization declared the novel coronavirus (2019-nCov) a global health emergency due to its global implications for the health care system and its economic impact. Italy was one of the first European countries with registered clustered cases of acute pneumonia. On February 23, 2020, the Italian government declared the first set of quarantine measures to slow the spread of the virus.[1] Estimations show that 2019-nCoV is a high-diffusion virus with a 2% fatality rate; approximately 20% all hospital admissions were directly to the ICU.[2] National health care systems could collapse if this spread of pneumonia continues at the current rate. This study aims to analyze official Italian data to build a predictive model.[3] From February 23, 2020 to March 15, 2020, daily data from the cumulative reports of the *Protezione Civile Italiana* (Italian Civil Protection) were collected, including the number of positive subjects, hospital admissions, ICU admissions, deaths, and full recovery. Statistical programs were used for the analysis. Different models were tested, and forecast values were calculated, and the best model, with a p-value <0.05, was considered to calculate the predicted values. The number of positive subjects (PS) follows a non-linear regression with $p < 0.001$ for the number of PS and hospital admissions, PS and ICU admissions, PS and deaths, and PS and recovered subjects. Simultaneously, the number of people admitted to hospitals follows a non-linear regression with $p < 0.001$ (Table 1). Among the 46.7% of PS admitted in hospitals, 10.0% were admitted to the ICU. The ratio of hospitalized patients to those admitted to the ICU is 22.3%, the death rate is 5%, and the recovery rate is 8%. The relationship between hospital admissions and ICU admissions follows a linear regression, with $p < 0.001$. Recent data on 2019-n CoV present different non-linear growth patterns, besides the rapidly increasing number of PS, which are very susceptible to public health rules. It is fascinating to observe the constant ratio of hospitalized and ICU admissions. If, in the next few weeks, infections reach 1% of the Italian population, over 60.000 ICU beds will be required, which may be the breaking point for the system. These results could be confirmed and highlighted by the increasing trend of ICU admissions, and the relationship between hospitalized patients and ICU admitted subjects. The national health care system needs more time to adapt to and deal with this challenge. The 2019 n-CoV transmission probability presents the following relationship. $y = ax^3bx^2 + cx + d$. Here, y indicates infected subjects, x is the intrinsic potential reproducing number, and the constants a, b, c and d are the intercepts. With environmental strategies and adequate medical treatments, infection and death rates reduced, while recovery rates increased (Fig. 1a and b). Observing Italy's data, this equation is applicable to hospital and ICU admission, and to the rate of death and recovery. As in China, quarantine and environmental strategies have a positive, but slow effect. They can reduce the rate of infection, admissions to ICU, and death, and can change the model.[4] Furthermore, this is a preliminary interpretation, and not the end of this *phenomenon*. It will be possible to analyze, customize, and fit the best model.[5] However, in this context, it is important not to forget the emergency; necessary medical and surgical procedures should be guaranteed. A possible solution is to try to re-organize the mission of the hospital as happened in different and less dramatic events.[6] This model has the potential to predict the worst-case scenario. With this knowledge, we are ready to do the best to prevent the system from reaching the breaking point and to change the 2019 nCoV curve now!