Letter to the Editor

First, second and third wave of COVID-19. What have we changed in the ICU management of these patients?

To the editor

Since the appearance of the coronavirus disease 2009 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in December 2019, the COVID-19 has spread throughout the world, occurring in forming several peaks in waves. We read with interest the recent article published by Saito et al.,[1] where they compared the severity and characteristics of the first and second waves in Japan. In Spain we have seen three waves: a first wave during March-April 2020, a second wave during September-November 2020, and a third wave during January-February 2021. There are very few articles comparing clinical characteristics of COVID-19 patients between the different waves.[1–3] The objective of the present study was to compare clinical characteristics, treatments administered, and the evolution of critically ill COVID-19 patients during the three waves suffered in an Intensive Care Unit (ICU) in the northwestern of Spain.

We prospectively evaluated patients admitted to the Clinical University Hospital of Santiago, Spain, in the three waves, with laboratory-confirmed COVID-19 disease who had severe acute respiratory distress syndrome (ARDS) needing ICU admission. The following information were collected in all patients: age, sex, comorbidities, inflammatory biomarkers, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, PaO2/FiO2, ICU treatments, prone position (PP) sessions, need of mechanical ventilation (MV), duration of ICU admission and ICU outcomes. Data was presented as number (percentage), and mean ± standard deviations or median and interquartile range as appropriate considering variable distribution. Chi-square and Wilcoxon rank-sum test were used to test for differences between categorical or numeric variables. Descriptive statistics were calculated, non-parametric tests were used for comparison of groups. Data were analysed using SPSS program (v. 22.0). The study protocol was approved by the ethics committee of Galicia (code No. 2020-184), and all participating subjects provided informed consent.

A total of 89 ICU patients with ARDS by Covid-19 were included. Demographic details and treatments are summarized in Table 1. Contrary to the first wave, higher proportion of patients in the second and third wave were not intubated, receiving high flow nasal oxygen (HFNO) or noninvasive mechanical ventilation (NIMV) (Table 1). In the third wave more patients were treated with corticosteroids compared with fist wave (100% vs 80%, $p = 0.007$) and in more patients were used awake prone positioning compared with first wave (91% vs 45%, $p = <0.001$) and second wave (91% vs 56%, $p = 0.001$). In patients who needed MV, the duration between ICU admission and tracheal intubation was longer during the third wave compared with the first wave. Nosocomial infections, complications, duration of ICU admission and mortality were similar in the three waves (Table 1).

In conclusion, we observed that during the third wave there was a tendency to use corticosteroids,[4] NIMV, HFNO, and awake PP, with lower use of MV compared with first wave. A limitation of the study is that present study only included patients admitted of one hospital. Thus, the results may not reflect the experience and results in hospital of other regions. Multicenter studies with a greater number of patients will be able to confirm whether there is a trend towards less use of MV and whether this may influence the decrease in the incidence of nosocomial infections, complications associated with MV, length of stay in the ICU and mortality.

Summary statement

During the third wave there was a tendency to use corticosteroids, NIMV, HFNO, and awake PP, with lower use of MV compared with first wave.

CRediT authorship contribution statement

Manuel Taboada: Conceptualization, Writing – original draft, Data curation, Writing – review & editing. **Mariana González:** Writing – original draft, Data curation, Writing – review & editing. **Antía Alvarez:** Writing – original draft, Data curation, Writing – review & editing. **María Eiras:** Writing – original draft, Data curation, Writing – review & editing. **Jose Costa:** Writing – original draft, Data curation, Writing – review & editing. **Julián Álvarez:** Writing – original draft, Data curation, Writing – review & editing. **Teresa Seoane-Pillado:** Formal analysis, Data curation, Writing – original draft, Writing – review & editing.

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Table 1

Demographics, clinical characteristics, treatments, and outcomes of COVID-19 patients admitted in ICU during the three waves.

Demographics	First Wave (1) N=20	Second Wave (2) N=23	Third Wave (3) N=46	P value (1 vs. 2)	P value (1 vs 3)	P value (2 vs 3)
Age, mean (SD)	64.85 (12.39)	69.57 (12.44)	65.02 (12.42)	0.188	0.840	0.108
Male sex, No. (%)	11 (55.0)	16 (69.6)	34 (73.9)	0.324	0.130	0.703
BMI, mean ± SD,	29.99 (4.93)	30.30 (5.9)	30.88 (7.53)	0.733	0.983	0.619
Coexisting conditions, No. (%)						
Hypertension	9 (45.0)	14 (60.9)	23 (50.0)	0.298	0.709	0.393
Hyperlipidemia	9 (45.0)	9 (39.1)	23 (50.0)	0.697	0.709	0.393
Diabetes	4 (20.0)	6 (26.1)	10 (21.7)	0.728	0.999	0.687
Asthma	1 (5.0)	3 (13.0)	3 (6.5)	0.610	0.999	0.393
Chronic obstructive pulmonary disease	3 (15.0)	1 (4.3)	4 (8.7)	0.323	0.425	0.658
Heart disease	5 (25.0)	4 (17.4)	4 (8.7)	0.711	0.116	0.426
Obesity (BMI ≥ 30 Kg m^{-2})	6 (30.0)	14 (60.9)	18 (39.1)	0.067	0.479	0.088
Cancer	2 (10.0)	5 (21.7)	4 (8.7)	0.420	0.999	0.148
Trasplant	1 (5.0)	2 (8.7)	3 (6.5)	0.999	0.999	0.999
Not comorbidity	4 (20.0)	1 (4.3)	3 (6.5)	0.167	0.189	0.999
Home treatments, No. (%)						
ACE inhibitors	4 (20.0)	0 (0.0)	1 (2.2)	0.039	0.027	0.999
Antiplatelets	0 (0.0)	5 (21.7)	7 (15.2)	0.051	0.092	0.517
Statins	5 (25.0)	10 (43.5)	28 (60.9)	0.205	0.007	0.171
Laboratory parameters, median (IR)						
Lymphocyte count, /μL	510(277–670)	560 (320–720)	500 (297–665)	0.770	0.928	0.765
Lactate dehydrogenase, U/L,	635 (341–901)	437 (329–561)	567(381–794)	0.051	0.748	0.027
D-dimer, ng/mL,	1064(692–1834)	1000 (454–4114)	968 (679–3781)	0.644	0.978	0.693
C-reactive protein, mg/L.	14 (13–25)	5 (3–19)	11 (6–18)	0.008	0.040	0.140
Procalcitonin	0.13 (0.10–0.67)	0.21 (0.07–0.77)	0.13 (0.07–0.25)	0.457	0.111	0.460
Serum Ferritin, μg/L	864 (561–1592)	951 (455–1612)	1048 (472–1616)	0.770	0.999	0.770
ICU Medical treatments, No. (%)						
Lopinavir-ritonavir	20 (100.0)	0 (0.0)	0 (0.0)	<0.001	<0.001	–
Hydroxychloroquine	20 (100.0)	0 (0.0)	0 (0.0)	<0.001	<0.001	–
Remdesivir	1 (5.0)	8 (34.8)	7 (15.2)	0.024	0.418	0.063
Tocilizumab	8 (40.0)	4 (17.4)	21 (45.7)	0.099	0.671	0.021
Anakinra	0 (0.0)	4 (17.4)	3 (6.5)	0.111	0.548	0.211
Corticosteroids	16 (80.0)	21 (91.3)	46 (100.0)	0.393	0.007	0.108
Anticoagulant intermediate dose	8 (40.0)	8 (34.8)	14 (30.4)	0.724	0.449	0.715
Anticoagulant high dose	10 (50.0)	15 (65.2)	30 (65.2)	0.313	0.245	0.999
Characteristics during ICU admission						
APACHE II, median (IR)	16 (13–10)	14 (10–20)	14 (12–17)	0.625	0.109	0.740
Time from illness onset to ICU admission, days median (IR)	11 (10–14)	9 (7–11)	9 (5–11)	0.033	0.002	0.506
PaO2:FiO2 ratio at ICU admission, median (IR)	113 (85–144)	95 (68–123)	92 (69–106)	0.219	0.009	0.624
Patients needing mechanical ventilation (MV), No. (%)	14 (70.0)	6 (26.1)	18 (39.1)	0.004	0.021	0.284
Duration between ICU admission and MV, days, median (IR)	0 (0–1)	2 (0 –4)	5 (2–9)	0.091	<0.001	0.066
Duration of MV, days, median (IR)	13 (8–25)	13 (7–26)	14 (9–17)	0.968	0.722	0.871
Patients treated with VMNI or HFNO. No. (%)	4 (20.0)	19 (82.6)	44 (95.7)	<0.001	<0.001	0.090
Use of awake prone positioning, No. (%)	9 (45.0)	13 (56.5)	42 (91.3)	0.451	<0.001	0.001
Use of intubated prone positioning, No. (%)	12 (85.7)	4 (66.7)	13 (72.2)	0.549	0.426	0.9999
Patients needing tracheostomy, No. (%)	5 (25.0)	1 (4.3)	9 (19.6)	0.081	0.745	0.148
Nosocomial infection, No. (%)	9 (45.0)	5 (21.7)	14 (30.4)	0.104	0.254	0.446
Pneumothorax. No. (%)	2 (10.0)	1 (4.3)	3 (6.5)	0.590	0.635	0.999
Renal replacement therapy, No. (%)	1 (5.0)	0 (0.0)	4 (8.7)	0.465	0.999	0.293
Length of ICU stay, days, median (IR)	15 (6–31)	12 (6–22)	10 (6–21)	0.421	0.258	0.637
ICU mortality, No. (%)	5 (25.0)	4 (17.4)	10 (21.7)	0.711	0.759	0.760

Date are number (percentage (%)), median (interquartile range (IR)); ICU: Intensive Care Unit; COPD, chronic obstructive pulmonary disease; ACE: Angiotensin-converting-enzyme inhibitors; APACHE II: Acute Physiology and Chronic Health Evaluation II, BMI: Body mass index;; VMNI: noninvasive mechanical ventilation; HFNO: High flow nasal oxygen; FiO2: inspired oxygen fraction.

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