



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Have we improved the management of COVID-19 patients admitted in intensive care between the two waves?

Michaël Piagnerelli ^{a,b,*}, David Fagnoul ^a, Eric Carlier ^a, Lauréline De Visscher ^a, Patrick Biston ^a, Karim Zouaoui Boudjeltia ^b

^a Intensive Care, CHU-Charleroi, Université Libre de Bruxelles, 6042 Charleroi, Belgium

^b Laboratory of Experimental Medicine (ULB 222), Faculty of Medicine, Université Libre de Bruxelles, CHU-Charleroi, 6110 Montigny-le-Tilleul, Belgium

To the Editor,

Since the description of first cases of patients admitted in intensive care unit (ICU) for Coronavirus disease-19 (COVID-19) acute respiratory distress syndrome (ARDS) in China in December 2019, the knowledge about the physiopathology, the management and the potential treatments are source of many publications [1].

As other countries in Europe [2,3], we experienced two distinct waves (from March to Augustus and September to December 2020) of patients with COVID-19 admitted in our 40 bed ICU in CHU-Charleroi, Belgium.

During the first wave, we adapt our local practices in the management of these patients, by applying the results of the major studies, sometimes endorsed by the WHO [1]. We treat hypoxic patients with dexamethasone in place of hydroxychloroquine, despite few data on the severity of the patients enrolled in the RECOVERY trial [4]. We also increased dose of thromboprophylaxis due to higher risk of thrombotic events [5], we specially applied ultra-protective mechanical ventilation and have reserved venovenous extracorporeal membrane oxygenation (vvECMO) only in selected patients [6].

We, therefore, aimed to evaluate the impact of our adaptive practice on ICU mortality between both waves.

We collected and compared data of all adult patients admitted in our ICU for hypoxia due to COVID-19. Higher number of patients was admitted during the second wave (40 versus 134 patients). ICU mortality was identical in the second compared to the first wave for all patients (39 versus 30%; $p = 0.3$). Approximately 70% of the patients required mechanical ventilation in both waves (71.8 versus 70.9%). In these more severe patients, more co infections were diagnosed at ICU admission but no differences on demographic, duration of symptomatology before ICU admission, delays for ICU admission and intubation were observed between patients (Table 1). Mortality in patients on mechanical ventilation was higher during the second wave (48 versus 36%; $p = 0.28$).

In a multiple logistic regression, no variables were associated with mortality in ventilated patients during the first wave. In contrast, age (odds ratio: 1.08 [1.03–1.13]; $p = 0.001$); lactate concentrations at ICU admission (odds ratio: 1.64 [1.09–2.47]; $p = 0.01$);

Table 1

Characteristics of the ICU COVID-19 patients on mechanical ventilation.

	Wave 1 (n = 28)	Wave 2 (n = 95)	P values
Sex (male) (%)	18 (72)	65 (68)	0.73
Age (years)	60 (55–67)	66 (59–73)	0.1
BMI	29.6 (27.6–31.4)	30.1 (26.4–34.2)	0.78
COPD (%)	4 (14)	10 (11)	0.57
Arterial hypertension (%)	15 (54)	52 (54)	0.96
Diabetes mellitus (%)	10 (36)	34 (36)	0.98
Chronic immunosuppression (%)	2 (7)	8 (8)	0.84
Cirrhosis (%)	1 (4)	2 (2)	0.6
Apache II	13 (12–19)	14 (11–17)	0.79
SOFA at day 1	6 (5–8)	6 (4–8)	0.96
Delays:			
symptoms-hospital admission (days)	7 (3–10)	7 (4–8)	0.46
Hospital-ICU admission	1 (0–4)	0 (0–3)	0.08
ICU-intubation	0 (0–1)	0 (0–0)	0.23
Treatments:			
Hydroxychloroquine (%)	18 (64)	0 (0)	< 0.001
Corticoids (%)	5 (18)	94 (99)	< 0.001
Co infection at ICU admission	2 (7)	24 (25)	0.03
PaO ₂ /FiO ₂ at intubation	63 (55–78)	64 (55–88)	0.77
Lactate (mmol/L)	1.3 (0.9–1.9)	1.8 (1.3–2.4)	0.014
Mechanical ventilation:			
Pplateau (cmH ₂ O)	25 (23–28)	25 (22–27)	0.74
Driving Pressure (cmH ₂ O)	16 (14–17)	15 (13–18)	0.75
Compliance pulmonaire (mL/cmH ₂ O)	29 (23–35)	31 (23–38)	0.46
Complications:			
Thrombotic events (%)	5 (18)	22 (23)	0.56
Dialysis (%)	5 (18)	11 (12)	0.49
Vasopressors (%)	13 (47)	67 (71)	0.87
Nosocomial infections (%)	14 (50)	68 (72)	0.1
Outcome			
Duration of MV	12 (8–17)	11 (7–18)	0.51
ICU length of stay (days)	14 (11–21)	12 (9–20)	0.39
Hospital length of stay (days)	20 (11–29)	19 (13–25)	0.79
Mortality (%)	10 (36)	46 (48)	0.28

Data were obtained at ICU admission and are presented as n (%) or median [IQR]. P-values were calculated using Chi-square or Kruskal-Wallis tests.

BMI: Body Mass Index.

COPD: Chronic obstructive pulmonary disease.

SOFA: Sequential Organ Failure Assessment.

* Corresponding author at: Intensive Care, CHU-Charleroi, Université Libre de Bruxelles, 140, chaussée de Bruxelles, 6042 Charleroi, Belgium.

E-mail address: Michael.piagnerelli@chu-charleroi.be (M. Piagnerelli).

thromboembolic complications (odds ratio: 4.04 [1.41–11.5]; $p = 0.009$) and use of vasopressors (odds ratio: 5.53 [1.98–15.4]; $p = 0.001$) were associated with ICU mortality in the second wave.

Despite modifications of treatments, thromboembolic complications and length of mechanical ventilation were the same between both waves (Table 1).

As others studies, we reported in our cohort the same risk factors associated on mortality (age and thrombotic events) [7,8]. Nevertheless, and despite modifications of our therapies during the first wave in agreement with the literature, no improvement on morbidities (requiring and length of mechanical ventilation in hypoxic patients, incidence of thrombotic events) and mortality were observed.

In summary, while management and therapies performed on ICU patients with COVID-19 were modified, ICU mortality didn't change, especially in mechanically ventilated patients.

This teaches us that the results obtained on large cohorts of patients are difficult to translate into current practice. We need rapidly multicentric comparisons between the two waves to adapt our management.

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the ISPPC Charleroi Ethics Committee (OM008).

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Funding

None.

Authors' contributions

MP, DF and KZB designed the study. MP, DF, EC, LDV collected the data. MP, DF, PB and KZB analyzed and interpreted the data. MP and KZB drafted the manuscript. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no competing interests.

Acknowledgements

All doctors and nurses of the ICU CHU-Charleroi for their dedication and sacrifice during this long pandemia.

References

- [1] Tsang JLY, Binnie A, Fowler RA, et al. Twenty articles that critical care clinicians should read about COVID-19. *Intensive Care Med.* 2021 Mar;47(3):337–41.
- [2] Karagiannidis C, Windisch W, McAuley DF, Welte T, Busse R. Major differences in ICU admissions during the first and second COVID-19 wave in Germany. *Lancet Respir Med.* 2021 May;9(5):e47–8. [https://doi.org/10.1016/S2213-2600\(21\)00101-6](https://doi.org/10.1016/S2213-2600(21)00101-6).
- [3] Contou D, Fraissé M, Pajot O, Tirolien JA, Mentec H, Plantefève G. Comparison between first and second wave among critically ill COVID-19 patients admitted to a French ICU: no prognostic improvement during the second wave? *Crit Care.* 2021; 25:3.
- [4] Horby P, Lim WS, Emberson JR, et al, RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with COVID-19. *N Engl J Med.* 2021.Feb 25;384(8):693–704.
- [5] Piagnerelli M, Cauchie P, Wautrecht JC. Optimizing the risk-benefit balance of thromboprophylaxis in critically ill patients with coronavirus disease 2019. *Crit Care Med.* 2020 Oct;48(10):e988–9.
- [6] Schmidt M, Hajage D, Lebreton D, Monsel A, Voiriot G, Levy D, et al. Combes A for the Groupe de Recherche Clinique en Réanimation et Soins intensifs du Patient en Insuffisance Respiratoire aiguë (GRC-RESPIRE) Sorbonne Université, and the Paris-Sorbonne ECMO-COVID investigators. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. *Lancet Respir Med.* 2020 Nov;8(11):1121–31.
- [7] Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: A multicenter prospective cohort study. *Intensive Care Med.* 2020 Jun;46(6):1089–98.
- [8] COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: A prospective cohort study. *Intensive Care Med.* 2021 Jan;47(1):60–73.