

# Clinical characteristics and post-intensive care outcomes of COVID-19 pneumonia.

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## Research

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# Abstract

**Background:** COVID-19 can result in a severe viral pneumonia, with high reported mortality rates in patients requiring mechanical ventilation. There is controversy as to whether established therapeutic approaches to acute respiratory distress syndrome are optimal in this condition, and numerous novel therapies have been used, often outside the context of randomised trials. In addition, longer term quality of life outcomes associated with COVID-19 are as yet unknown. The aim of this case series is to describe demographic, physiological and outcome data of patients with COVID-19 admitted to our intensive care units who were treated according to evidence-based guidelines for acute respiratory distress syndrome.

**Methods:** We retrospectively reviewed the records of all patients admitted to intensive care units in our institution with COVID-19 between March and June, 2020. Physiological and laboratory data were recorded at baseline and daily until intensive care discharge or death. Quality of life was assessed at a virtual post-intensive care follow-up clinic around 10 weeks after ICU discharge.

**Results:** 45 patients with COVID-19 were included, 37 (82.2%) of whom were male, with a mean age of 55 years. 42 (93.3%) of this cohort met criteria for acute respiratory distress syndrome at time of admission. Clinical management was consistent with evidence based institutional guidelines introduced for acute respiratory distress syndrome. Median length of intensive care stay was 14 days. The intensive care mortality rate was 8.9%. Functional and psychological morbidity post intensive care was significant: 45.2% of respondents had at least moderate impairment of mobility and 35.5% described at least moderate symptoms of anxiety or depression at the time of follow up.

**Conclusions:** This case series demonstrates low mortality in a cohort of patients treated according to an established evidence-based approach for acute respiratory distress syndrome. However, COVID-19 survivors have a marked functional and psychological morbidity impacting quality of life following ICU admission. The therapeutic goal in the future will be to achieve similar survival outcomes while minimizing the significant morbidity associated with COVID-19 related critical care admission.

## Background

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the novel betacoronavirus that causes coronavirus disease 2019 (COVID-19) (1, 2). A minority of patients develop a severe viral pneumonia precipitating acute respiratory distress syndrome (ARDS), multi-organ failure and death (3,4). The mortality of patients requiring admission to Intensive Care Units (ICUs) is high, reported at between 26% and 50% worldwide (4, 5, 6, 7). Prompted by this, numerous therapies have been used on a compassionate basis in the absence of robust evidence, including antivirals and immune modulators, with mixed results (8, 9). Furthermore, it has been suggested that COVID-19 pneumonia represents a sufficiently novel disease entity that standard evidence-based approaches to ARDS are not applicable or even deleterious (10, 11, 12).

This retrospective case series describes clinical and physiological features, treatment strategies, and clinical and functional outcomes for patients with COVID-19 admitted to Intensive Care Units in the Belfast Health and Social Care Trust between 1st March and 1st June 2020 and treated according to evidence-based guidelines for ARDS (13).

## Methods

### Population and Setting

All patients admitted to Intensive Care Units within Belfast Health and Social Care Trust with a primary diagnosis of COVID-19 from March 1 to June 1, 2020 were included in this case series. COVID-19 infection was defined by a positive result on reverse transcriptase polymerase chain reaction (RT-PCR) assay together with a compatible clinical history.

Clinical management and investigations were at the discretion of the treating clinical team according to an institutional guideline (available online, additional file 1) which utilized a standard evidence-based approach to ARDS including low tidal volume ventilation and conservative fluid management (13). The use of novel therapies outside the context of clinical trials was actively discouraged. The exception to this approach was anticoagulation. Patients were initially treated with low molecular weight heparin according to a standard institutional guideline for venous thromboembolism prophylaxis. Due to frequent and recurrent thrombosis of continuous renal replacement therapy filters despite regional citrate anticoagulation, however, dosing was increased using an algorithm based on patient weight, fibrinogen level, renal function and anti-Xa levels.

### Data collection and definitions

Data collection comprised a comprehensive retrospective review of electronic and paper-based notes. Baseline demographic details were noted for all patients and comorbidities were defined using the Charlson Comorbidity Index (14). Acute Physiology And Chronic Health Evaluation (APACHE) II scores were calculated based on the initial 24 hours of ICU admission (15). ARDS was defined according to the Berlin criteria (16).

For the first 24 hours, ventilatory parameters were matched to corresponding arterial blood gases. On subsequent days, all data were collected at 0800 hours. Sequential Organ Failure Assessment (SOFA) scores were calculated daily (17): for the purposes of calculating the neurological component, pre-sedation Glasgow Coma Scale was assumed to be 15 for all intubated patients.

### Data recording and outcomes

All data were recorded in Microsoft Excel (Microsoft, 2020). Statistical analysis was performed on Microsoft Excel or Graphpad Prism software v8.0 software. Early outcomes included ICU and hospital mortality, duration of mechanical ventilation, and ICU and hospital length of stay. Surviving patients were invited to attend a virtual follow-up clinic at 6–8 weeks following hospital discharge as part of routine

clinical care. Prior to attending the clinic, patients were asked to complete online questionnaires to assess quality of life and functional status (EQ-5D-L) (18).

To give context and for comparison, demographic, clinical and outcome data generated were presented alongside data from (i) data from a critically-ill COVID-19 cohort within the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme, a long-standing national clinical audit of patient outcomes from adult critical care units in England, Wales and Northern Ireland (up to date as of 24/07/2020) (19) and (ii) data from the Large observational study to UNderstand the Global impact of Severe Acute respiratory FailurE (LUNGSAFE) study, a recent large worldwide cohort study of patients with ARDS (20).

## **Ethics**

The Belfast Health and Social Care Trust Research and Development department deemed this work not to require research ethics approval.

## **Results**

### **Baseline Characteristics**

Over the period March 1st to June 1st, 45 patients met criteria for inclusion. Baseline demographic and clinical characteristics are summarized in Table 1. The majority of patients (N = 32, 76.1%) had received non-invasive Continuous Positive Airway Pressure (CPAP) at ward level prior to ICU admission, and 43 of 45 patients (95.6%) underwent invasive mechanical ventilation within the first 24 hours of ICU admission: the remaining 2 patients were not intubated.

Table 1. Baseline demographic and clinical characteristics of patient cohort.

	Study cohort (n=45)	ICNARC Report 24/07/2020 (n=10667)	Bellini et al (20) ARDS cohort (n=3022)
Age at admission			
Mean (SD)	55 (11.2)	58.8 (12.7)	61.5 (12.4)
Sex, n (%)			
Female	8 (17.8)	3141 (29.8)	1151 (38.1)
Male	37 (82.2)	7409 (70.2)	1871 (61.9)
Ethnicity, n (%)			
White	32 (71.1)	6704 (66.1)	-
Mixed	0 (0)	185 (1.8)	-
Asian	5 (11.1)	1586 (15.6)	-
Black	0 (0)	981 (9.7)	-
Other	8 (17.8)	692 (6.8)	-
Body Mass Index			
Mean (SD)	32.8 (7.4)	-	-
<18.5	0 (0)	75 (0.8)	-
18.5-25	6 (14.3)	2556 (25.6)	-
25.1-30	9 (21.4)	3436 (34.4)	-
30.1-40	21 (50)	3135 (31.4)	-
>40	6 (14.3)	790 (7.9)	-
Comorbidities, n (%)			
Ischaemic Heart Disease	1 (2.2)	-	-
Congestive Heart Failure	2 (4.4)	-	-
COPD	0 (0)	-	-
Chronic Kidney Disease	6 (13.3)	-	-
Hematological malignancy	2 (4.4)	-	-
Charlson Comorbidity Index, median (IQR)	1 (1,3)	-	-
Hospital stay prior to admission (Days), median (IQR)	1 (0,3)	1 (0,3)	-
APACHE II score, mean (SD)	12.0 (4.5)	15.1 (5.3)	-
Admission SOFA score, mean SD)	4.9 (1.9)	-	10.1 (4.2)

Maximal respiratory support prior to ICU admission, n (%) (N=42)			
CPAP			
HFNO	32 (76.1)	-	-
Facemask/Non-rebreather	1 (2.3)	-	-
	9 (21.4)	-	-
Mechanical ventilation in first 24 hours, n (%)	43 (95.6)	6037 (58.8)	-

### Physiology and pathophysiology

Respiratory physiological parameters are shown for intubated patients in Table 2. Mean PF ratio in the first 24 hours of presentation to ICU was 183.2 mmHg. All patients had bilateral infiltrates on chest radiograph at time of referral, and 42 patients (93.3%) met Berlin criteria for ARDS, predominantly of moderate severity.

Table 2. Baseline respiratory physiologic parameters for invasively ventilated patients (first 24 hours of ICU admission).

	Study cohort (N=42)	ICNARC Report (n=7355*) 26/07/2020	Bellini et al (20) ARDS+IMV cohort (n=2377)
PaO <sub>2</sub> /FiO <sub>2</sub> ratio (mmHg)			
Lowest, median (IQR)	121.1 (87.2, 154.7)	113.3 (81, 158.3)	-
Mean (SD)	183.2 (67.5)	-	161.3 (62.2)
ARDS (Berlin criteria) <sup>†</sup> , n (%)			
Mild (PFR 200-300mmHg)	3 (7.1)	-	714 (30.0)
Moderate (PFR 100-200mmHg)	25 (59.5)	-	1106 (46.6)
Severe (PFR <100mmHg)	14 (31.1)	-	557 (23.4)
FiO <sub>2</sub> (%)	55.6 (15.7)		65.0 (12.4)
PEEP (cmH <sub>2</sub> O), mean (SD)	11.9 (2.4)	-	8.4 (3.7)
Estimated driving pressure (cmH <sub>2</sub> O), mean (SD)	12.2 (3.7)	-	-
Tidal Volume (ml/kg IBW), mean (SD)	6.7 (1.1)	-	7.5 (2.5)
Dynamic compliance (ml/cmH <sub>2</sub> O) (Mean [SD])	40.4 (15.6)	-	-

\* Advanced respiratory support (ICNARC definition).

In the first 24 hours of ICU admission, the mean PEEP applied was 11.9 cmH<sub>2</sub>O and a mean estimated driving pressure of 12.2 cmH<sub>2</sub>O was required to achieve average tidal volume of 6.7 ml/kg of ideal body weight. Mean dynamic compliance of patients was 40.4 ml/cmH<sub>2</sub>O (additional file 1). Sequential PF ratios for the cohort appeared relatively static for the first 10 days of admission, with sustained improvements evident between days 10 and 14 (Fig. 1).

Therapeutic modalities used are shown in Table 3. No patients received extra-corporeal membrane oxygenation (ECMO). One patient who was deemed unsuitable for ECMO was treated with airway pressure release ventilation as a rescue measure and survived.

Table 3. Organ Support Measures.

	Study cohort (n=45)	ICNARC Report 24/07/2020 (n=10228)	Bellini et al (20) ARDS + IMV cohort (n=2377)
Prone positioning, n (%)	18 (40)	-	187 (7.9)
No of episodes, median (IQR)	2 (1, 3.75)	-	-
Mean duration of episode, (hours), mean (SD)	14.9 (4)	-	-
Neuromuscular blocker use, n (%)	29 (64.4)	-	516 (21.7)
Duration (days), mean (SD)	4.9 (3.4)	-	-
Inhaled pulmonary vasodilators, n (%)	2 (4.4)	-	182 (7.7)
Airway pressure release ventilation (APRV), n (%)	1 (2.2)	-	-
Vasopressor use, n (%)	33 (73.3)	-	-
Duration (days), median (IQR)	3 (2,8)	-	-
Renal replacement therapy, n (%)	14 (31.1)	2707 (26.6)	-
Duration (days), mean (SD)	12.8 (7.8)	-	-
Antibiotic use, n (%)	38 (84.4)	-	-
No of days antibiotics, median (IQR)	7.5 (4, 14)	-	-

Cardiovascular support was required in 33 patients (73.3%) for a median duration of 5.4 days. Furthermore, 14 patients (31.1%) required renal replacement therapy during ICU admission. 14 patients were enrolled in clinical trials (21, 22). Other than low dose Hydrocortisone for septic shock, no patients received immune modulator or antiviral drugs outside the context of a clinical trial.

### **Patient outcomes**

Outcome data were available for all patients in the study cohort (Table 4). Median duration of mechanical ventilation for survivors was 13 days and length of stay in ICU for survivors was 14 days. 4 patients (8.9%) died during their ICU admission. 7 patients (15.6%) required tracheostomy to facilitate weaning from mechanical ventilation. One patient subsequently died in hospital following ICU discharge.

Table 4. Patient outcomes.



	Study cohort (n=45)	ICNARC report 24/07/20 (n=10228)	Bellini et al (20) ARDS cohort (n=3022)
ICU mortality, n (%)	4 (8.9)	4078 (39.9)	1028 (34)
Hospital mortality, n (%)	5 (11.1)	-	1196 (39.6)
Length of ICU stay (days), median (IQR) All patients Survivors	14 (7.5, 20.5) 14 (8, 20.5)	- 12 (5, 28)	10 (5,20) 11 (7,21)
Hospital length of stay (days), N=43, median (IQR) All patients Survivors	21 (14,35) 21 (14,38)	- -	23 (14, 40) -
Duration of mechanical ventilation (days), median (IQR)	13 (8,19)	13 (7, 23)	8 (4,16)
Tracheostomy, n (%)	7 (15.6)	-	-
Quality of life (EQ-5D score) N=31, n (%) reporting moderate to severe problems with each domain Mobility Self-Care Usual activities Anxiety/depression Pain/Discomfort	14 (45.2) 9 (29.0) 19 (61.3) 11 (35.5) 16 (51.6)	-	-

Quality of life outcome data were available for 31 patients at mean of 65 days following ICU discharge (Table 4). 14 patients (45.2%) described at least a moderate problem with their mobility and 11 patients (35.5%) reported moderate to severe problems with anxiety and depression following ICU discharge.

## Discussion

In this case series, we describe the cohort of critically ill patients with COVID-19 admitted to ICU for acute hypoxemic respiratory failure in our institution. Almost all fulfilled Berlin criteria (16) for moderate to

severe ARDS and were managed according to standard evidence-based approaches for ARDS with low mortality.

Physiological parameters were consistent with previous studies in ARDS: in particular, respiratory system compliance was reduced to a comparable degree to other cohorts of patients with ARDS (5, 7, 23). Our use of dynamic, rather than static, measures of lung compliance likely represents an over-estimation. Few patients exhibited the proposed 'L' phenotype with near normal compliance (12) (additional file 1).

The most striking clinical feature of this cohort was prolonged inflammation and hypoxemia, which were associated with prolonged mechanical ventilation and ICU stay, and with considerable post-discharge morbidity.

The ICU mortality rate of 8.9% is substantially lower than that previously reported, albeit our cohort is small. At the time of submission, the reported mortality for patients with COVID-19 in ICUs in England, Wales and Northern Ireland was 39.9% (19), which is consistent with other series thus far (5, 7) and similar to the published 34% mortality for a cohort of patients with all-cause ARDS (20). The reasons for the lower mortality observed in our cohort are not entirely clear. Our patients were slightly younger and appear to have had less severe systemic derangement at time of presentation than those included in other cohorts (19). Nevertheless, the majority of our cohort had failed CPAP by the time of ICU admission and almost all were mechanically ventilated within 24 hours. Baseline respiratory physiology is comparable both with ICNARC and LUNGSAFE cohorts (19, 20). Furthermore a comparable proportion of patients required renal replacement therapy to those in the published ICNARC report (31.1% vs 26.6%) (20).

Other factors which may have contributed to the low mortality rate in this cohort include the relatively late epidemiological surge of COVID-19 in our region. This allowed sufficient opportunity for adequate resource allocation to ICUs, introduction of institutional guidelines, and staff training. Heterogeneity of clinical management was minimized and there was a high level of adherence to evidence-based guidelines for ARDS (13). Critical care capacity was never exceeded and predicted rationing of ICU resources was never required.

Neuromuscular blockade was used in the majority of patients, for a mean duration of 4.9 days, longer than has previously been tested within the confines of clinical trials (24, 25), and likely reflective of prolonged hypoxemia. Prone positioning was widely used within our cohort, often repeatedly, with a mean 39.1% increase in PF ratio immediately post proning (additional file 1). This magnitude of therapeutic effect is comparable to that published previously in ARDS (23).

Post-discharge quality of life data were available for just over two thirds of our cohort, with all respondents reporting a problem in at least one dimension of mobility, self-care, usual activities, pain/discomfort and anxiety/depression post-ICU discharge. 45.2% of patients had at least moderate issues with mobility and 61.3% had moderate to severe problems participating in previous activities. These results are comparable to those published previously for outcomes after all cause ICU admission

(28). Anxiety and depression were at least a moderate problem with 35.5% of responders; a feature well documented in post-ARDS survivors. The incidence in this cohort is congruent with previous reported rates (29). These data illustrate the major burden on rehabilitation services which will follow the COVID-19 pandemic, and the clear need for evidence-based approaches to management of the post-intensive care syndrome (29).

The complex pathophysiology and heterogenous disease spectrum associated with COVID-19 mean there is an ongoing urgent need for investigation of novel therapies such as antivirals and immune modulating agents. While clear benefit has emerged for some (30, 31), our data support our belief that evidence-based supportive measures as refined over decades of research into ARDS remain key to the critical care management of COVID-19.

## Conclusion

COVID-19 pneumonia results in clinically similar respiratory physiology to that previously described for ARDS. In our cohort, we demonstrated that strict adherence to evidence-based ARDS treatment can be associated with good outcomes without the use of novel therapies. The burden of the disease extends much longer than the initial ICU admission and the challenge of future critical care management of COVID-19 will be to minimize the considerable resource burden and morbidity, while achieving similar or better survival outcomes.

## Abbreviations

COVID-19: Coronavirus disease. RT-PCR: Reverse Transcriptase Polymerase Chain Reaction. APACHE: acute physiology and chronic health evaluation. SOFA: Sequential Organ Failure Assessment. PF ratio:  $PaO_2$ :  $FiO_2$  Ratio. ICNARC: Intensive care national audit and research centre. IMV: invasive mechanical ventilation. LUNGSAFE: Large observational study to UNDERstand the Global impact of Severe Acute respiratory Failure. BMI: Body Mass index. CPAP: Continuous Positive Airway Pressure. CRP: C-Reactive Protein. REMAP-CAP: Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia. REALIST COVID-19: Repair of Acute Respiratory Distress Syndrome by Stromal Cell Administration in COVID-19.

## Declarations

**Ethics approval:** Belfast Health and Social Care Research and Development Department deemed this case series not to constitute research and that formal research ethics approval was not required.

**Consent for Publication:** Not applicable.

**Availability of data and materials:** All data generated and/or analysed during this study are available from the corresponding author on reasonable request. The data are not publicly available due to containing information that could compromise patient privacy.

**Competing Interests:** The authors have no financial or non-financial competing interests.

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**Authors' contributions:** *Conception and design:* NC, SL, SMcM, MD, ROR, JS. *Acquisition and Analysis:* NC, SL, McM, MD, MD, CS, MD, ROR, PJ, JS. *Drafting of Manuscript:* NC, SL, SMcM, JS.

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## References

1. World Health Organization. Novel coronavirus – China. January 12, 2020. Available online at <https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/>
2. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation report -38. Available online at <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>.
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395: 497–506.
4. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L et al. Features of 20133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ* 2020;369:m1985.
5. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020; 323 (16): 1574-1581.
6. Potere, N., Valeriani, E., Candeloro, M. et al. Acute complications and mortality in hospitalized patients with coronavirus disease 2019: a systematic review and meta-analysis. *Crit Care* 24, 389 (2020). <https://doi.org/10.1186/s13054-020-03022-1>
7. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. *N Engl J Med* 2020; 382: 2012-2022
8. Van de Veerdonk F & Netea M. Blocking Il-1 to prevent respiratory failure in COVID-19. *Crit Care* 24, 445 (2020). <https://doi.org/10.1186/s13054-020-03166-0>
9. Stallmach, A., Kortgen, A., Gonnert, F. et al. Infliximab against severe COVID-19-induced cytokine storm syndrome with organ failure—a cautionary case series. *Crit Care* 24, 444 (2020). <https://doi.org/10.1186/s13054-020-03158-0>

10. Laverdure, F., Delaporte, A., Bouteau, A. et al. Impact of initial respiratory compliance in ventilated patients with acute respiratory distress syndrome related to COVID-19. *Crit Care* 24, 412 (2020). <https://doi.org/10.1186/s13054-020-03133-9>
11. Tsolaki, V., Zakyntinos, G.E. & Makris, D. The ARDSnet protocol may be detrimental in COVID-19. *Crit Care* 24, 351 (2020). <https://doi.org/10.1186/s13054-020-03081-4>
12. Gattinoni L, Chiumello D, Caironi P Gattinoni L, Chiumello D, Caironi P et al. COVID-19 pneumonia: different respiratory treatment for different phenotypes? *Intensive Care Med* (2020) 46:1099–1102
13. Griffiths MJD, McAuley DF, Perkins GD, Barrett N, Blackwood B, Boyle A et al. Guidelines on the management of acute respiratory distress syndrome. *BMJ Open Res* 2019; 6:e000420.
14. Charlson M, Pompeii P, Ales K, Mackenzie R. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J. Chron. Dis.*, 40 (5) (1987), 373-383
15. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13(10):818-829.
16. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E et al. Acute respiratory distress syndrome: The Berlin definition. *JAMA* 2012;307:2526-2533
17. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Brunining H et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med*. 1996;22(7):707-710. doi:10.1007/BF01709751
18. Rabin R, De Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med*. 2001;33(5):337–343. doi: 10.3109/07853890109002087
19. ICNARC Case Mix Programme Database. Available online at <https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports>. Accessed 29<sup>th</sup> July 2020.
20. Bellani G, Laffey JG, Pham T, Brochard L, Esteban A, Gattinoni L et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. 2016;315(8):788–800. doi:10.1001/jama.2016.0291
21. Gorman E, Shankar-Hari M, Hopkins P, Tunnicliffe W, Perkins G, Silversides J et al. Repair of Acute Respiratory Distress Syndrome by Stromal Cell Administration in COVID-19 (REALIST-COVID-19): A structured summary of a study protocol for a randomised, controlled trial. *Trials* 2020 21:462
22. Angus D, Berry S, Lewis R, Al-Beidh F, Arabi Y, Bentum-Puijk W et al. A Randomised, Embedded, Multifactorial, Adaptive Platform Trial for Community-Acquired Pneumonia Study: Rationale and Design. *Ann Am Thorac Soc* 2020. doi: 10.1513/AnnalsATS.202003-192SD. Online ahead of print.
23. Guerin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368:2159-2168.
24. Papazian L, Forel JM, Gacouin A, Penot-Ragon C, Perrin G, Loundou A et al. Neuromuscular blockers in Early Acute Respiratory Distress Syndrome. *N Engl J Med* 2010; 363:1107-1116

25. The National Heart, Lung and Blood Institute PETAL Clinical Trials Network. Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome. *N Engl J Med* 2019; 380:1997-2008
26. Ziehr DR, Alladina J, Petri CR, Maley J, Moskowitz A, Medoff B et al. [Respiratory Pathophysiology of Mechanically Ventilated Patients with COVID-19: A Cohort Study](#) [published online ahead of print, 2020 Apr 29]. *Am J Respir Crit Care Med*. 2020; doi:10.1164/rccm.202004-1163LE
27. Granga C, Teixeira-Pinto A, Costa-Pereira A. Quality of life after intensive care- evaluation with EQ-5D questionnaire. *Intensive Care Medicine* 2002; 28: 898-907.
28. Rawal G, Yadav S, Kumar R: Post-intensive care syndrome: an overview. *J Transl Int Med* 2017;5:90–2
29. Huang M, Parker A, Bienvenu O, Dinglas V, Colantuoni E, Hopkins R et al. Psychiatric Symptoms in Acute Respiratory Distress Syndrome Survivors: A 1-year National Multicenter Study. *Crit Care Med*. 2016 55(5):954-965
30. Horby PW, Lim WS, Emerson J, Mafham M, Bell J, Linsell L et al. Dexamethasone in Hospitalized Patients with COVID-19 – Preliminary Report. *N Engl J Med* 2020; doi: 10.1056/NEJMoa2021436
31. Beigl J, Tomashek KM, Dodd LE, Mehta A, Zingman B, Kalil A et al. Remdesivir for the Treatment of Covid-19 – Preliminary Report. *N Engl J Med*. DOI: 10.1056/NEJMoa2007764.

## Figures

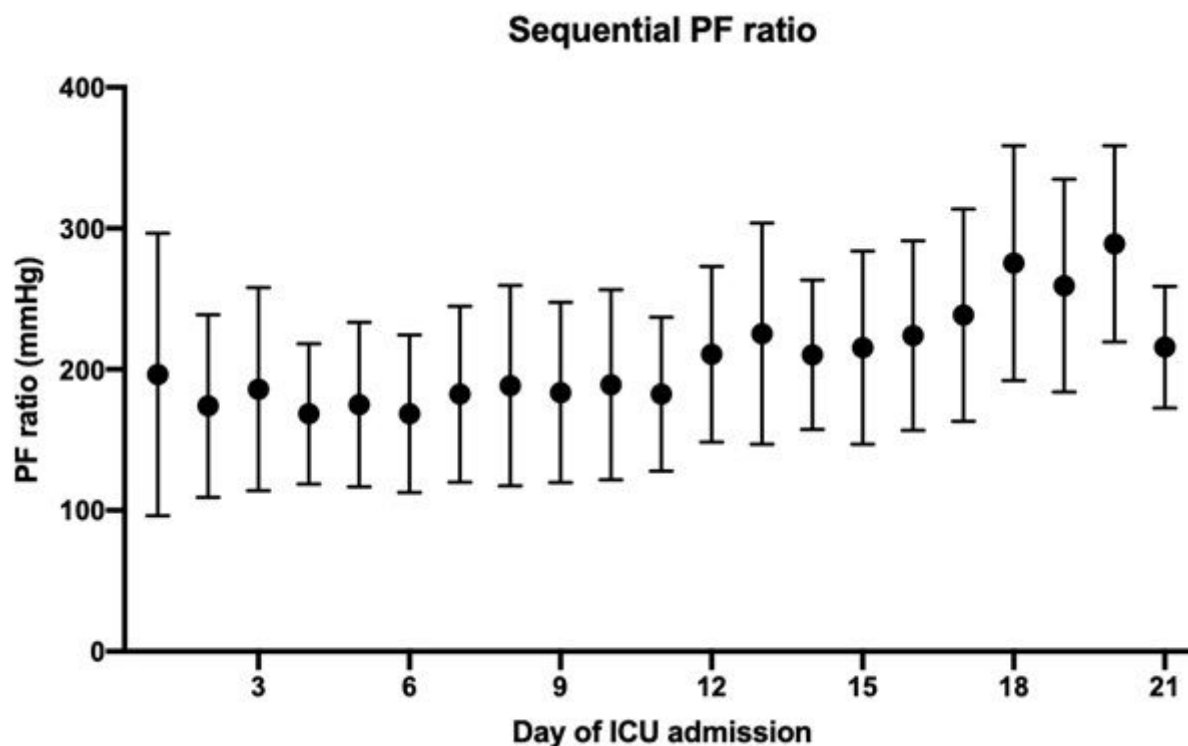


Figure 1

PaO<sub>2</sub>/FiO<sub>2</sub> ratios over time, mean+/- standard deviation (SD).

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [COVID19caseseriesCritCareAddFile120Aug2020JS.docx](#)