careful consideration must be given to protection of the elbow, upper arm, and shoulder given the distribution of injuries reported here (Fig 1b). Reduction in the mechanical loads on peripheral nerves, specifically avoiding positions of prolonged focal compression, stretching of nerves, or both should be an immediate focus. There are undoubtedly lessons to be learned from perioperative medicine[10] to optimise positioning, frequency of repositioning, unloading, and cushioning of susceptible nerve compression sites. Ultrasound elastography may prove to be a useful quantitative measurement tool for assessment of nerve tension and stiffness.[11] Limitations of this study include missing clinical data for some patients, lack of a control group, and the retrospective design, which precludes establishment of a causal relationship between prone positioning and peripheral nerve injury. Additionally, many of these patients spent significant time in the supine position on neuromuscular blocking agents which could also increase susceptibility to tissue injury.

In conclusion, peripheral nerve injury after prone positioning for management of severe COVID-19-related ARDS patients is surprisingly common. Physicians must be aware of an increased susceptibility to peripheral nerve injury in severe COVID-19 and refine standard protocols in order to reduce the risk.

Authors' contributions

Conception and design: GRM, ARW, RS, LR, LFW, SD, JHK, JMW, PJ, CKF
Acquisition of data: GRM, ARW, RS, LR, SD, RPN, SDD, CKF
Analysis and interpretation of data: GRM, ARW, JMW, CKF
Manuscript proof reading and editing: all authors

Declarations of interest

The authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.08.045.

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Outcomes in mechanically ventilated patients with hypoxaemic respiratory failure caused by COVID-19

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Editor—Acute hypoxaemic respiratory failure (AHRF) is a key manifestation of acute coronavirus disease 2019 (COVID-19), caused by severe acute respiratory distress syndrome due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. COVID-19-related AHRF ranges from a mild self-limiting condition to severe progressive hypoxaemia requiring mechanical ventilation, with or without radiological evidence of bilateral consolidation and diffuse ground-glass lesions,[1] fulfilling the Berlin acute respiratory distress syndrome (ARDS)[2] criteria. The severity of hypoxaemia in COVID-19 is often disproportionate to the reduction in lung volumes,[3] which may be a consequence of the effects of SARS-CoV-2 on pulmonary vascular tone, inflammation, and thrombosis.[4–6]

The aim of this study was to compare respiratory parameters and outcomes for COVID-19 patients with ARDS from other causes of similar severity of hypoxaemia using aggregate data from the LUNG-SAFE (Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure) study.[7] We present the clinical characteristics, lung mechanics, gas exchange, and outcomes of a cohort of critically ill COVID-19 patients with AHRF receiving invasive mechanical ventilation with partial pressure of oxygen/inspired oxygen concentration ratio (Pa_{o2}/Fio_2 ratio) <300 mm Hg during their first critical care admission in a format similar to that of the LUNG-SAFE study.[7] We grouped (COVID-19 *vs* LUNG-SAFE) patients based on the severity of oxygenation alone based on the Berlin definition of ARDS.[2] Chest radiogram characteristics were not considered in the inclusion criteria.

The study was a single-centre, retrospective, observational cohort study of adult patients admitted with confirmed COVID-19 AHRF to the Critical Care Department at Guy's and St Thomas' Hospital (GSTT) in London, UK, between March 3 and May 22, 2020. The study had institutional approval and with waiver of individual informed consent (reference number 10796).

Baseline patient data, clinical characteristics, lung mechanics, gas exchange, and outcomes were obtained from clinical information systems (CareVue Rev.F.01, Philips, Eindhoven, The Netherlands; and other electronic patient records) using Microsoft SQL Server Management Studio v18.4 (Microsoft, Redmond, WA, USA). Actual or temperature-corrected partial pressure of carbon dioxide (Pa_{co2}), Pa_{o2}, and pH were merged with contemporaneous ventilation parameters and measurements. We used the worst Pa_{o2}/Fio_2 ratio on critical care admission day to categorise hypoxaemia into mild (Pa_{o2}/Fio_2 ratio 200–300 mm Hg), moderate (Pa_{o2}/Fio_2 ratio 100–200 mm Hg) and severe (Pa_{o2}/Fio_2 ratio ≤100 mm Hg) as per the Berlin ARDS definition.[2] There were no missing data. All analyses were conducted in R version 3.6.1 (http://www.R-project.org).

Amongst the 317 critical care admissions over the study period attributable to COVID-19, 213 patients met our inclusion criteria of AHRF receiving invasive mandatory mechanical ventilation with Pa_{o2}/Fio_2 ratio <300 mm Hg, during their first critical care admission. We excluded patients receiving noninvasive respiratory support (n=48) or extracorporeal membrane oxygenation (ECMO; n=51), or readmissions (n=9). The mean (95% confidence interval [CI]) age of the cohort was 56 (54–57) yr, 72.8% (n=155) were male, 40.4% (n=86) had hypertension, and 33.8% (n=72) had diabetes mellitus as comorbidities.

There were 23 (10.8%) patients with mild, 122 (57.3%) with moderate, and 68 (31.9%) with severe ARDS, based on Pa_{o2}/Fio_2 ratio categories. Mean tidal volumes were ~7 ml kg^{-1} of predicted body weight (PBW) for all three severity categories, with similar total minute ventilation. Mean PEEP was 10 (95% CI, 9.6–10.4) cm H_2O, which increased from 8 (95% CI, 7.4–9.1) cm H_2O in mild disease to 11 (95% CI, 10.5–11.9) cm H_2O in severe disease. Values of peak inspiratory pressure and driving pressure increased with disease severity, with peak inspiratory pressures of 21 (95% CI, 19.4–22.6) cm H_2O in mild, 24 (95% CI, 23.6–25.1) cm H_2O in moderate, and 28 (95% CI, 26.4–28.7) cm H_2O in severe disease. Delta pressure was 13 (95% CI, 11.3–14.4) cm H_2O in mild, 14.7 (95% CI, 14.2–15.3) cm H_2O in moderate, and 15.4 (95% CI, 14.6–16.3) cm H_2O in severe disease.

The majority of patients in all categories of severity had a peak airway pressure <30 cm H_2O and received tidal volumes <8 ml kg^{-1} PBW (Fig. 1a). Compliance of the respiratory system decreased from 41.2 (95% CI, 34.7–47.8) ml cm H_2O^{-1} in the mild group to 31.9 (95% CI, 28.4–35.4) ml cm H_2O^{-1} in the severe group, and 24% of patients in the moderate or severe AHRF groups had compliance >40 ml cm H_2O^{-1} (Fig. 1b). Overall, the mean (95% CI) duration of mechanical ventilation was 15 (13.5–16.5) days, with longer duration of mechanical ventilation associated with more severe disease (Fig. 1c). The critical care length of stay was longer in the moderate and severe categories compared with the mild category, but similar in the moderate and severe categories owing to higher and earlier mortality in the severe category. ICU mortality was 9% in mild disease, 27.5% in moderate disease, and 55.7% in severe disease, with significant differences among the three severity categories (P<0.01 log-rank; Fig. 1d).

Overall ICU mortality of 34.2% in our cohort was similar to the overall mortality reported in the LUNG-SAFE (35.3%)[7] cohort and in the COVID-19 cohort receiving mechanical ventilation (35%).[8] Similar to the LUNG-SAFE cohort and the Berlin ARDS predictive validity analyses, there was a dose–response relationship between mortality and severity of hypoxaemia, albeit with lower mortality in the mild category.

These results illustrate that although the characteristics of the COVID-19 AHRF population largely overlap with the LUNG-SAFE cohort, the COVID-19 cohort had a greater predominance of moderate (57% *vs* 47%) and severe (31% *vs* 23%), and a lower proportion of patients with mild hypoxaemia (10.8% *vs* 30%)

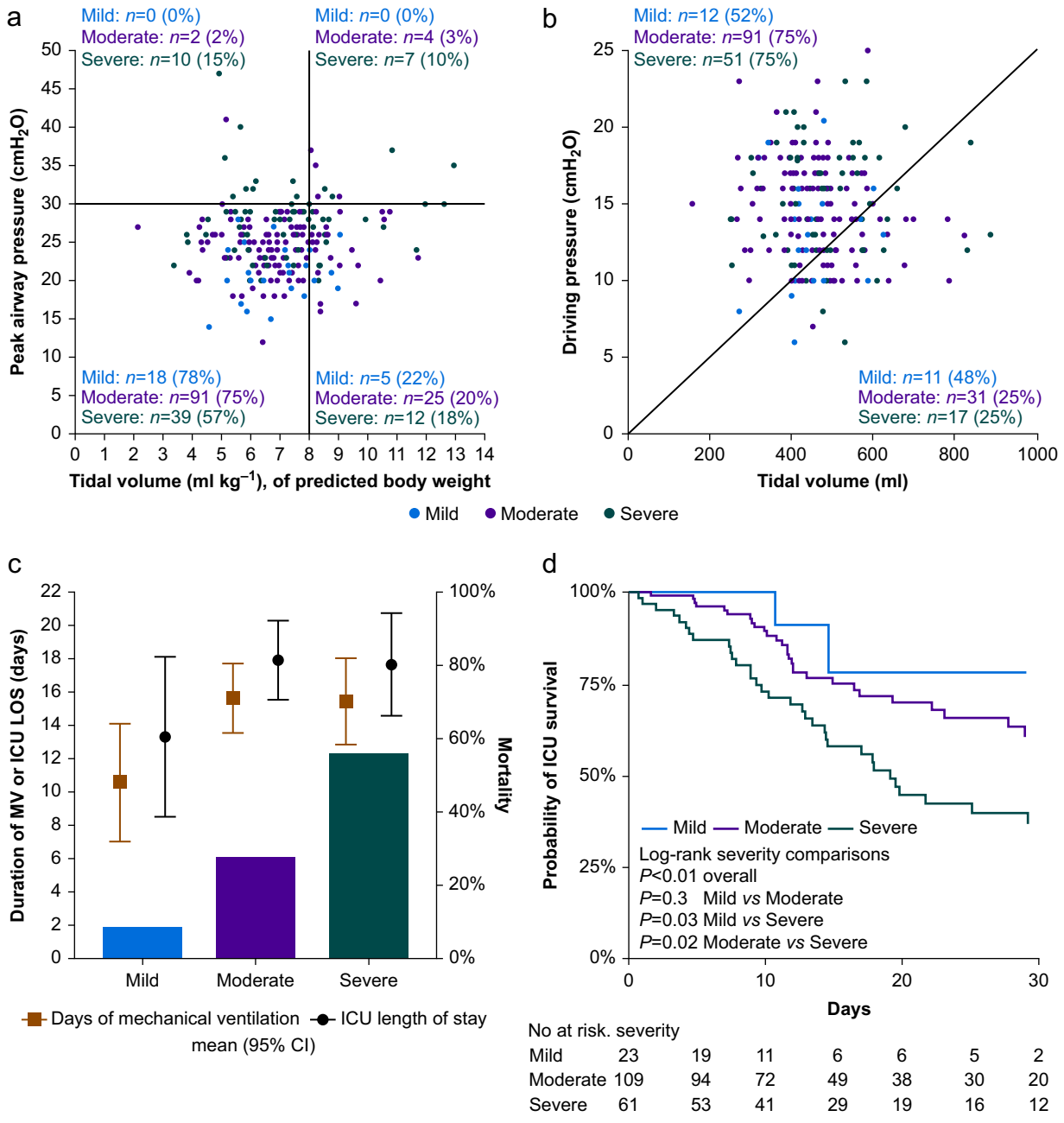

Fig 1. Distribution of ventilation parameters on day 1 by acute respiratory distress syndrome (ARDS) severity and outcome. (a) Distribution of tidal volume *vs* peak airway pressure. (b) Distribution of tidal volume and driving pressure. The black diagonal line represents a compliance cut-off of 40 ml cm H_2O^{-1}. The upper-left triangle represents the distribution of patients with compliance <40 ml cm H_2O^{-1}. The lower-right triangle represents the distribution of patients with compliance >40 ml cm H_2O^{-1}. (c) Mortality (right Y-axis) and duration of mechanical ventilation (MV) or ICU length of stay (LOS) by disease severity. Data are shown as mean (95% confidence interval [CI]). (d) Probability of ICU survival by disease severity.

compared with the LUNG-SAFE cohort.[7] Despite the greater severity of hypoxaemia compared with LUNG-SAFE, a greater proportion of patients with COVID-19 were ventilated within protective boundaries.

In conclusion, despite initial data showing high mortality in mechanically ventilated COVID-19 patients, our data show that with comparable degrees of hypoxaemia and lung mechanics to ARDS from other causes, the mortality is similar to ARDS as survival is high in mild disease. More detailed characterisations of patient phenotypes may help us understand the factors associated with severity of hypoxaemia and lung parenchymal involvement.

Declarations of interest

The authors declare that they have no conflict of interests. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research, or the Department of Health and Social Care.

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Effect of entraining oxygen at different locations in a noninvasive ventilator

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Keywords: continuous positive airway pressure; COVID-19; mechanical ventilation; noninvasive ventilation; oxygen therapy

Editor—Guidance on using noninvasive ventilation produced by NHS England,[1] and the Association for Respiratory Technology and Physiology (ARTP) COVID Group[2] suggests that oxygen can be entrained into the breathing system at the patient end, directly into the heat and moisture exchange (HME) filter or through an oxygen entrainer. This is contrary to manufacturer guidance (for the Breas Vivo 2, the system in use at the Nightingale Hospital), which recommends entraining the oxygen into the dedicated port at the back of the machine.

The aim of this study was to determine whether entraining oxygen at the patient end or machine end of the breathing system caused a difference in delivered fractional oxygen (FiO_2) or pressure to the patient. This was done using continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP) modes to also assess if this was dependent on ventilation mode.

The following experiments took place in the Nightingale Hospital (London, UK) in an unused ward adjacent to the patient ward. The named experimenters were assisting clinical staff in a technical support role. Experiments were conducted largely at night when the ward activity was at its quietest. Consequently, the experimenters wore full personal protective equipment (PPE). They had limited access to measurement instrumentation that they may have used in a more standard setting.

The Vivo 2 (Breas, Sweden) Noninvasive Ventilator was set up as if it were being used on a patient, including a heat and moisture exchange (HME) filter. In addition, a second filter (high-efficiency particulate air [HEPA] filter) was placed in series with the usual filter. The extra filter was added so that FiO_2 could be measured via a sampling line using a Penlon 465 anaesthetic machine (Penlon Ltd, Oxfordshire, UK). A test lung (Drager Ltd, Lubeck, Germany) was attached in place of a patient.

Initially, oxygen was entrained through the dedicated port on the Vivo 2. Using the CPAP mode, pressure was set sequentially to 5, 10, and 15 cm H_2O. For each CPAP pressure setting, oxygen flow rate was incrementally increased from 0 to 15 L min^{-1} (via a flow regulator attached to the piped oxygen supply), and FiO_2 was recorded. The whole process was then repeated with oxygen entrained directly into the HME filter. The experiment was then repeated with one