

Discriminating between CPAP success and failure in COVID-19 patients with severe respiratory failure

Pietro Arina^{1,2}, Beatrice Baso^{1,2}, Valeria Moro^{1,2}, Hemani Patel¹, Gareth Ambler^{3,4} et al for the UCL Critical Care COVID-19 Research Group

¹Intensive Care Unit, University College London Hospitals NHS Foundation Trust, London UK

²Bloomsbury Institute of Intensive Care Medicine, Division of Medicine, University College London, London, UK

³NIHR UCLH/UCL Biomedical Research Centre, London, UK

⁴Dept of Statistical Science, University College London, London, UK

Address for correspondence: Prof Mervyn Singer, Bloomsbury Institute of Intensive Care Medicine, University College London, Cruciform Building, Gower St, London, WC1E 6BT, UK
E-mail: m.singer@ucl.ac.uk Orcid no: 0000-0002-1042-6350

Take-home message: Biomarker-based prediction of CPAP success or failure (death if ceiling of treatment or subsequent need for mechanical ventilation) in COVID-19 patients with moderate-to-severe respiratory failure

Funding: Gareth Ambler and David Brealey received funding from the NIHR UCLH/UCL Biomedical Research Centre

Study approval: Approval received from the London-Westminster Research Ethics Committee (REC ref 20/HRA/2505, IRAS ID 284088) and the Health Research Authority on 2nd July 2020.

Keywords: COVID-19; respiratory failure; continuous positive airways pressure (CPAP); invasive mechanical ventilation; non-invasive mechanical ventilation; biomarkers

Dear Editor

Continuous positive airways pressure (CPAP) treatment was used increasingly in the UK and elsewhere for COVID-19 respiratory disease to avoid the need for mechanical ventilation (1-3). Early identification of patients benefitting from CPAP would assist decision making however we found that ICU admission respiratory parameters (rate, PaO₂:FiO₂ ratio) were poorly discriminatory. Using electronic healthcare records we retrospectively studied COVID-19 patients admitted to the University College London Hospital ICU between 8 March and 5 June 2020 in moderate-to-severe respiratory failure who received initial management with CPAP to see whether better prognosticators could be identified.

Comparison of demographic, clinical and biochemical parameters measured on ICU admission was made between patients adjudged CPAP success (hospital survival with CPAP alone) or failure (either death where CPAP was a ceiling of treatment, or need for mechanical ventilation regardless of hospital outcome). Requirement for other organ support was also compared. Patients managed on CPAP in non-ICU wards were excluded as detailed clinical and lab data were often lacking.

Of 108 within-hospital admissions, 93 (86%) received CPAP as initial respiratory failure management (median[IQR] PaO₂:FiO₂ ratio 13 [10-18] kPa) (Supplementary Figure 1). Thirty-two (34%) were adjudged CPAP successes and 61 (66%) failures (14 deaths (23%) with CPAP as ceiling of treatment, 47 (77%) requiring invasive ventilation of whom 26 died).

Demographics and ICU admission values of respiratory rate, inspired oxygen concentration and PaO₂:FiO₂ ratio were similar between groups (Supplementary data). Admission values of C-reactive protein (CRP) (p<0.0001), NT-brain natriuretic peptide (NT-proBNP) (p<0.001), troponin-T (p<0.001) and D-dimers (p<0.05) were significantly higher in CPAP failure patients (Fig 1). Other organ support was only required for CPAP failure patients receiving invasive ventilation (46 vasopressor, 28 renal replacements), but none for CPAP successes. At 6 hours post-CPAP the PaO₂:FiO₂ ratio rose by 76.7% (37.9-99.8%) in CPAP success patients but only by 38.1% (-24.4-100.5) in the failure group (p=0.015).

For outcome prediction (CPAP failure), sixteen potential predictor physiological or biochemical variables were assessed. Details are provided in the supplementary index. In brief, separate univariable logistic regression models were fitted for each predictor, with p-values <0.05 determining variables entered into a multivariable logistic regression model. A model combining elevated CRP and NT-proBNP predicted CPAP failure with a sensitivity of 0.75 (95% CI: 0.62-0.86), specificity of 0.83 (0.61-0.95), positive predictive value of 0.91 (0.78-0.97) and negative predictive value of 0.59 (0.41-0.76).

Failure of CPAP to avert death or invasive mechanical ventilation was associated with increased blood levels of thrombo-inflammatory and cardiac injury/dysfunction biomarkers on ICU admission. This may reflect an increased incidence of pulmonary thrombi either identifiable on imaging or multiple microthrombi, with subsequent right heart strain. The much increased requirement for vasopressor and renal support in invasively ventilated patients reflects disease severity, but a significant iatrogenic contribution from high airway pressures, heavy sedation and hypovolaemia cannot be excluded. The high positive predictive value using elevated CRP and NT-proBNP may identify patients likely to fail CPAP. If validated, this could be gainfully used in management pathways and to stratify patients for intervention studies.

Acknowledgements:

The UCL Critical Care COVID-19 Research Group members involved in this research comprised Pietro Arina^{1,2}, Beatrice Baso^{1,2}, Valeria Moro^{1,2}, , Hemani Patel¹, Gareth Ambler^{3,4}, Petra Voegelé¹, Nishkantha Arulkumaran^{1,2}, David Brealey^{1,2,3}, Mervyn Singer^{1,2})

¹Intensive Care Unit, University College London Hospitals NHS Foundation Trust, London UK

²Bloomsbury Institute of Intensive Care Medicine, Division of Medicine, University College London, London, UK

³NIHR UCLH/UCL Biomedical Research Centre, London, UK

⁴Dept of Statistical Science, University College London, London, UK

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Figure 1: Biomarkers and variables recorded on ICU admission in patients receiving CPAP

Shaded area denotes normal range. The normal range for C-Reactive Protein (≤ 5 mg/L) is not indicated, FiO_2 = fraction of inspired oxygen concentration; PaO_2/FiO_2 = ratio of arterial partial pressure to fraction of inspired oxygen concentration. Shaded area denotes normal range except for PaO_2/FiO_2 where the increasing shades of grey denotes mild, moderate and severe respiratory failure according to the Berlin definition, NT-proBNP = N type -pro B-natriuretic peptide.