

LETTER



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

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Dear Editor,

Continuous positive airways pressure (CPAP) treatment was used increasingly in the UK and elsewhere for coronavirus disease 2019 (COVID-19) to avoid the need for mechanical ventilation [1–3]. Early identification of patients benefitting from CPAP would assist decision making however we found that intensive care unit (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 Fig. 1). Thirty-two (34%) were adjudged CPAP successes and 61 (66%) failures (14 deaths (23%) with CPAP as the ceiling of treatment, 47 (77%) requiring invasive ventilation of whom 26 died). Demographics and ICU admission values of respiratory rate, inspired oxygen concentration (FiO₂) and PaO₂/FiO₂ ratio were similar between groups (Supplementary data). Admission values of C-reactive protein (CRP) ($p < 0.0001$), N Terminal-pro-B-type 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 vasopressors, 28 renal replacement therapy), but none for CPAP successes. At 6 h post-CPAP the PaO₂/FiO₂ ratio rose by 76.7% (37.9 to 99.8%) in CPAP success patients but only by 38.1% (–24.4 to 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

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The members of the UCL Critical Care COVID-19 Research Group are listed in Acknowledgements.

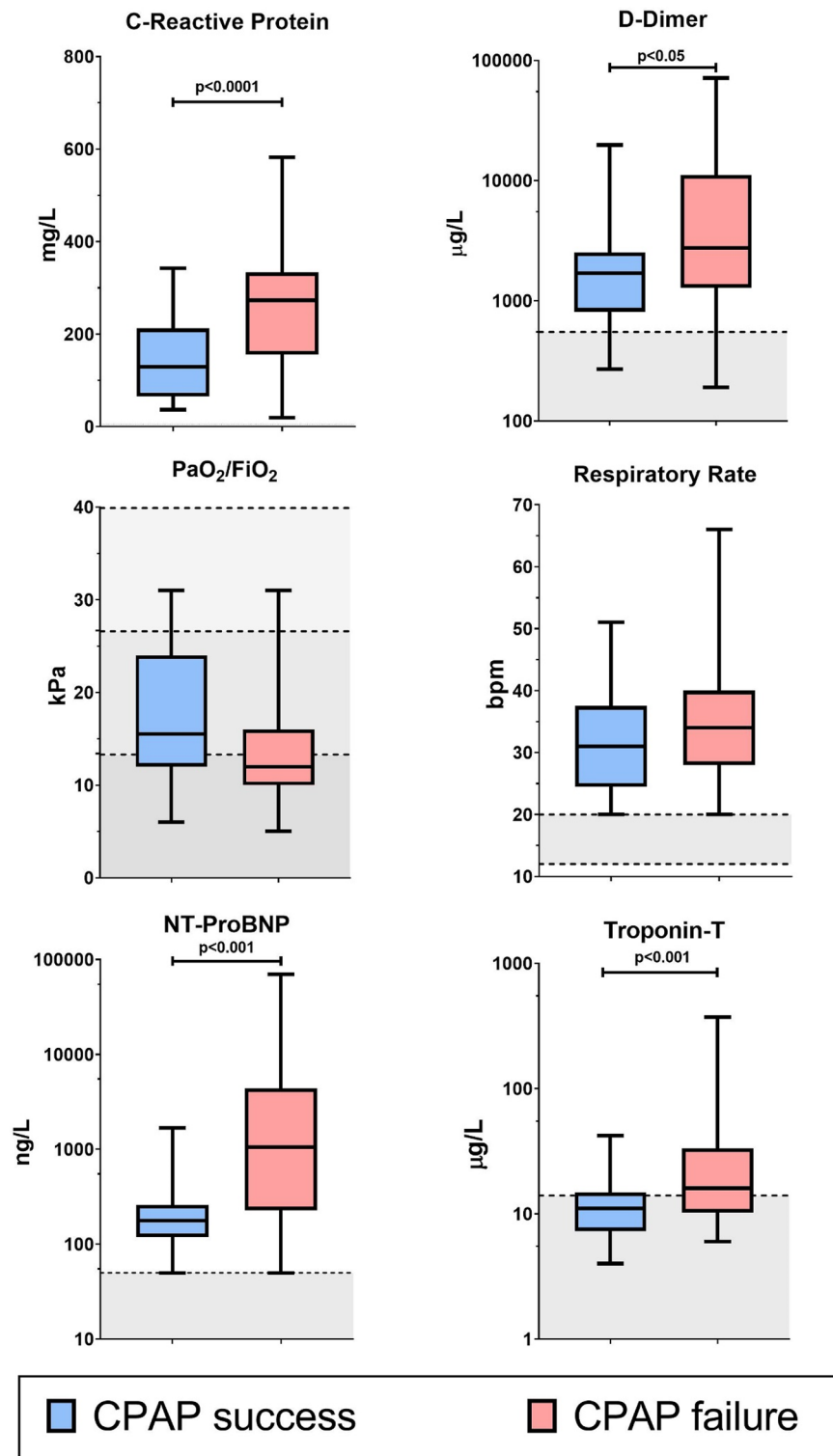


Fig. 1 Biomarkers and variables recorded on ICU admission in patients receiving CPAP. Shaded area denotes normal range. The normal range for C-Reactive Protein (≤ 5 mg/L) is not indicated, FiO_2 fraction of inspired oxygen concentration; PaO_2/FiO_2 ratio of arterial partial pressure to the fraction 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 terminal-pro B-type natriuretic peptide

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.

Electronic supplementary material

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Compliance with ethical standards

Conflicts of interest

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Ethical 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.

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References

1. Sun Q, Qui H, Huang M, Yang Y (2020) Lower mortality of COVID-19 by early recognition and intervention: experience from Jiangsu Province. *Ann Intensive Care* 10:33
2. Radovanovic D, Rizzi M, Pini S, Saad M, Chiumello DA, Santus P (2020) Helmet CPAP to treat acute hypoxemic respiratory failure in patients with COVID-19: a management strategy proposal. *J Clin Med* 22:1191
3. Doidge JC, Mouncey PR, Thomas K, Gould DW, Ferrando-Vivas P, Shankar-Hari M, Harrison DA, Rowan KM. Trends in intensive care for patients with COVID-19 in England, Wales and Northern Ireland. Preprints doi:<https://doi.org/10.20944/preprints202008.0267.v1>