



## Early View

Research letter

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## Is CPAP therapy in COVID-19 associated with an increased rate of pulmonary barotrauma?

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To the Editor:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 150 million people worldwide, with over 3 million deaths as of 6th<sup>th</sup> May 2021<sup>1</sup>. In the United Kingdom (UK) approximately 15% of individuals affected by coronavirus disease 2019 (COVID-19) have required admission to hospital<sup>2</sup> and those with severe disease require advanced respiratory support including invasive mechanical ventilation (IMV).<sup>3</sup> Due to the considerable scale of the pandemic, non-invasive continuous positive airway pressure (CPAP) has been utilised for COVID-19-related type I respiratory failure as a therapeutic strategy to improve patient outcomes<sup>4,5</sup> and also to preserve IMV capacity during a challenging time for acute healthcare providers. Its exact role is however unclear and is the subject of a UK multicentre trial.<sup>6</sup>

The UK, to date, has observed discrete surges of SARS-CoV-2 infection rates. We compared data from March to June 2020 (wave 1) with August to November 2020 (wave 2).<sup>1</sup> For wave 1, there are limited reports of pneumothorax, pneumomediastinum and surgical emphysema (collectively referred to as pulmonary barotrauma) relating to positive pressure support in patients with COVID-19<sup>7,8</sup>. Martinelli *et al* conducted a retrospective multi-centre UK case series of patients admitted to hospital with COVID-19 in wave 1 and identified 71 patients with barotrauma (60 pneumothorax, 6 with co-developed pneumomediastinum and 11 with pneumomediastinum alone). 3 of the patients were diagnosed on CPAP and 38 on IMV. Overall the authors estimated a pneumothorax incidence of 0.91%.<sup>7</sup>

Our organisation, a large University Hospital comprising two acute teaching hospitals in Liverpool, UK, delivered CPAP therapy both in established Critical Care areas and a dedicated COVID-19 Respiratory Support Unit managed by respiratory and infectious diseases teams. In wave 1, we retrospectively recorded one case of secondary pneumothorax from 112 patients (0.9%) in which the patient received CPAP, mirroring the incidence seen in the aforementioned case series. During wave two, we observed a marked increase in pulmonary barotrauma cases with 9/136 (6.6%) patients developing this complication whilst on CPAP (*Table 1*). Before commencing CPAP therapy, all 9 patients had a high oxygen requirement, with a median p/f ratio of 72mmHg (Range 55-122mmHg) and median respiratory rate of 28 breaths per minute. All patients had radiographic evidence of COVID-19 pneumonia and an absence of pneumothorax on initial chest imaging. All diagnoses were made with subsequent chest radiographs or computed tomography imaging. Pneumothoraces were seen in 5/9 patients (4 bilateral, 1 unilateral) and 3/5 patients required intercostal chest drain insertion. All 9 patients had radiological evidence of pneumomediastinum. None of the patients were known to have significant underlying structural respiratory disease; additionally none were active smokers and only 3 had previously smoked. Development of

barotrauma was a marker of poor outcomes with 100% mortality in all 5 patients who developed pneumothorax.

During pulmonary barotrauma, alveolar rupture leads to air leakage in to the surrounding tissues and air spaces.<sup>9</sup> The mean duration from commencing CPAP to the diagnosis of barotrauma is 6.3 days (range 3-10 days, median 6 days) with affected patients receiving a median maximum CPAP pressure of 12.5cmH<sub>2</sub>O (range 10-15cmH<sub>2</sub>O, mean 12.1cmH<sub>2</sub>O). The pathophysiological explanation for the apparent increased rate of barotrauma in wave 2 is unclear; the combination of relatively high airway pressures and time on CPAP may be a precipitating factor for barotrauma. Additionally, withdrawal of CPAP therapy for short breaks followed by re-application of pressure was an observed theme in wave 2 and may contribute to alveolar hyperinflation with increased alveolar pressures. In contrast to wave 1, all patients escalated to CPAP in wave 2, including the 9 who developed pulmonary barotrauma, were also prescribed dexamethasone in keeping with the evidence base that emerged in wave 1 from the RECOVERY trial<sup>10</sup>.

However, despite prior experience in treating patients with COPD exacerbations on oral steroids with non-invasive ventilation at high pressures, we have not seen barotrauma to the extent that we have seen in COVID-19 patients and therefore postulate that treatment with dexamethasone combined with the acute inflammatory insult of COVID 19 pneumonitis may contribute to increased lung tissue friability.

Overall, CPAP appears to have been a beneficial intervention in the outcome of patients with COVID-19 seen at our centre during both wave 1<sup>5</sup> and 2. However, given our observations, caution and vigilance regarding the risk of pulmonary barotrauma should be undertaken. A low threshold for a chest radiograph after starting CPAP and routine examination for surgical emphysema may aid early recognition of barotrauma. Daily review of progress, including time on CPAP, delivered pressure, and response to therapy is mandatory. In particular, we would suggest that increased work of breathing should prompt review of therapy and discussion about the transition to IMV; barotrauma may be seen as a type of patient self-induced lung injury (PSILI) and IMV with sedation and paralysis may allow driving pressures to be reduced and lung injury to be limited.

Observing data from patients at our centre has enabled a descriptive analysis of a possible increased risk of pulmonary barotrauma associated with CPAP in patients with COVID-19 pneumonitis. Our small sample size precludes meaningful statistical analysis and we recognise that this is an important limitation of this study. Outcome data of the RECOVERY-RS trial<sup>6</sup>, comparing CPAP, high flow nasal oxygen and standard care may support our observations. The possible association of a higher rate of barotrauma with the widespread use of dexamethasone may also require further exploration. CPAP therapy is an important intervention for patients with COVID-19 pneumonitis within healthcare settings; therefore awareness of potential development of pulmonary barotrauma is key for acute clinicians managing this patient cohort.

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**Table 1.** Characteristics of COVID-19 patients on CPAP with pulmonary barotrauma, wave 2

<b>Summary</b>	
Number of patients receiving CPAP	136
Number of Barotrauma cases	9
Incidence	6.6%
<b>Demographics</b>	
Age (years)	median 64 (range 27-82)
Gender	6 male, 3 female
BMI (kg/m <sup>2</sup> )	median 28 (range 24-36)
Smoking Status	6 never-smoker, 3 ex-smoker
Underlying Respiratory Diagnosis	7 none, 1 asthma, 1 pleural plaques
<b>Baseline Characteristics before commencing CPAP</b>	
Respiratory Rate (breaths/minute)	median 28 (mean 29.5, range 20-40) ( <i>Data for 8 patients</i> )
p/f ratio (mmHg)	median 72 (mean 80.0, range 55-122)
<b>CPAP Therapy</b>	
Time from commencing CPAP to barotrauma diagnosis (days)	median 6 (range 3-10)
Maximum CPAP pressure received (cmH <sub>2</sub> O)	median 12.5 (range 10-15)
<b>Barotrauma cases</b>	
Pneumothorax	5 (4 bilateral, 1 unilateral)
Requirement of intercostal chest drain insertion	3
Pneumomediastinum	9
Surgical Emphysema (radiological diagnosis)	8
Outcome	5 died, 1 inpatient, 3 discharged