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Use of protracted CPAP as a supportive treatment for COVID-19 pneumonitis and associated outcomes: a national cohort study

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Abstract

Background

Continuous positive airway pressure (CPAP) has been increasingly deployed to manage patients with COVID-19 and hypoxemic respiratory failure, often for protracted periods. However, concerns about protracted CPAP have been raised. This study aims to examine the use of CPAP for patients with COVID-19 and the outcomes after protracted use.

Methods

This is a national cohort study of all adults admitted to Scottish critical care units with COVID-19 from 01/03/20 to 25/12/21 that received CPAP. Protracted CPAP was defined as ≥5 continuous days of CPAP. Outcomes included CPAP failure rate (institution of invasive mechanical ventilation (IMV) or death), mortality, and outcomes following institution of IMV. Multivariable logistic regression was performed to assess the impact of protracted CPAP on mortality after IMV.

Results

1961 patients with COVID-19 received CPAP for COVID pneumonitis with 733 patients (37.4%) receiving protracted CPAP. CPAP failure occurred in 891 (45.4%): 544 patients (27.7%) received IMV and 347 patients (17.7%) died in critical care without IMV. Hospital mortality rate was 41.3% for the population. For patients that subsequently commenced IMV, hospital mortality was 58.7% for the standard duration CPAP group and 73.9% for the protracted duration CPAP group (p=0.003), however, there was no statistical difference in hospital mortality after adjustment for confounders (OR 1.4, (95% CI 0.84, 2.33, p=0.195).

Conclusions

Protracted CPAP was used frequently for managing patients with COVID-19. Whilst it was not associated with worse outcomes for those patients who subsequently required IMV, this may be due to residual confounding and differences in processes of care.

Keywords

COVID-19; Continuous positive airway pressure; CPAP; Non-invasive ventilation; Pneumonitis; ARDS

Editor's key points

- Face-mask Continuous positive airway pressure (CPAP) is a key treatment option in acute respiratory failure
- Many clinicians are concerned that prolonged use of CPAP may lead to worse outcomes amongst patient who then require invasive mechanical ventilation
- This analysis did not show a significantly higher mortality rate for patients who received prolonged CPAP before invasive ventilation
- There may still be a mortality association with prolonged CPAP but there are likely to be several causes for this including treatment limitation decisions
- Clinicians should reflect carefully on the next treatment steps for patients who require CPAP for more than 48 hours

Introduction

Infection with SARS-CoV 2 can lead to a severe acute respiratory failure from pneumonitis, acute respiratory distress syndrome (ARDS) and pulmonary micro-thrombi. One in six hospitalised patients in the ISARIC 4C cohort, required admission to a critical care unit[1]. Respiratory support varied and initial concerns regarding non-invasive ventilation (NIV) were overcome as this mode became increasingly utilised. By the second pandemic wave, the majority of patients in a critical care unit had received NIV during their stay, with continuous positive airway pressure (CPAP) the commonest mode of choice, supported by early results from RECOVERY-RS trial suggesting a reduction in invasive mechanical ventilation (IMV) or death with CPAP[2]. Unlike NIV, CPAP does not provide any additional ventilatory support, but instead a set level of continuous positive pressure is applied throughout the respiratory cycle. For some patients CPAP was used as a ceiling of therapy as IMV was unlikely to be successful. Other patients were commenced on CPAP in the hope that IMV could be avoided. This resulted in some patients receiving CPAP for protracted periods in a manner not previously utilised in critical care.

Clinicians and researchers have expressed concerns about this increasing use of protracted CPAP. Evidence for ventilatory strategies in patients with ARDS have shown benefit from controlled tidal volume and pressure strategies[3]. CPAP does not allow for tight control of these parameters, and patient self-inflicted lung injury (P-SILI), from spontaneous ventilation on CPAP, might worsen respiratory failure and subsequent outcomes for these patients[4]. Several studies have now demonstrated higher mortality rates for COVID-19 patients who have been treated with CPAP for more than 2-3 days compared to those receiving CPAP for shorter durations[5,6]. However, some of these differences may be attributed to the use of CPAP as a “ceiling of treatment” where benefit of CPAP is less estabished[7]. Furthermore, supportive treatment of COVID-19 has led to many patients receiving CPAP for periods far beyond that assessed in these studies. Recent national reports describe half of COVID-19 patients managed with CPAP receive more than 5 days of support[8].

This study will describe the population with COVID-19 that received protracted CPAP (duration 5 days or more) in a critical care setting from a complete national dataset. We will describe the demographics, baseline characteristics, intubation rate and survival outcomes for these patients in comparison to patients who were managed with shorter-duration CPAP. In addition, the study will assess the association between protracted CPAP and outcomes following IMV for CPAP failure.

Methods

Study design, setting and databases

A cohort study design was used. The Scottish Intensive Care Society Audit Group (SICSAG) database captures all adult general intensive care (ICU) activity within Scotland. Data are entered prospectively and are subject to regular validation assessments[9]. The Community Health Index (CHI) number is used across Scottish health systems and uniquely identifies individuals. CHI was used to link the SICSAG database to the following national databases: Electronic Communication of Surveillance in Scotland (ECOSS) database, which captures all virology testing in Scotland; National Records of Scotland death records; Scottish Morbidity Record 01 (SMR01), which captures all acute hospitalisations.

Participants

The study population comprised Scottish residents aged ≥16 years with a positive polymerase chain reaction test for nucleic acid for SARS-CoV-2 before or during critical care admission, who were admitted to general ICUs, combined ICU/high dependency units (HDUs) and standalone HDUs in Scotland, and received CPAP from 01/03/2020 to 25/12/2021. CPAP was defined as receipt of continuous positive airway pressure with or without the use of high flow nasal oxygen as required for tolerance. Method and duration of CPAP delivery was determined by the bedside clinicians. Patients that only received CPAP following extubation from IMV were excluded. Records relating to patients transferred between HDUs and ICUs were combined to create a continuous critical care stay. Only

first admissions for patients with multiple, non-continuous critical care admissions were included. Follow-up was censored on 15/01/2022.

Variables

Primary exposure: Receipt of type of respiratory support was recorded in the SICSAG database on a daily basis. Duration of CPAP was taken from total number of consecutive days receiving CPAP in critical care (with or without HFNO as required) prior to critical care discharge or initiation of IMV (whichever occurred first). A hierarchy was employed so that if a patient received more than one type of respiratory support in the same day, only one was recorded (IMV > CPAP > HFNO). Protracted CPAP was defined as ≥5 days of receipt of CPAP, as this had been identified as the median value of all NIV modalities from the national cohort report[8]. The relationship between time on CPAP and hospital mortality was assessed using a logit plot and the threshold for protracted CPAP reviewed. Patients receiving only HFNO were excluded.

Outcomes: The primary outcome was hospital mortality. Secondary outcomes included CPAP failure (death or IMV during critical care stay), critical care unit mortality, organ support during critical care stay, and duration of critical care stay. Critical care outcomes were available for those patients discharged or dead on or before 15/01/2022.

Other variables: Demographic variables consisted of sex, age and ethnicity. Ethnicity was derived from Scottish Census 2011 categories, aggregating low frequencies[10]. The Scottish Index of Multiple Deprivation (SIMD Version 2020),[11] an area-based ranking index based on postcode of residence, was used to define socioeconomic deprivation represented as quintiles. Previous health status comprised the number of emergency acute hospital admissions in the year before admission, pre-admission Clinical Frailty Score (CFS), and comorbidities. Charlson-defined comorbidities and SICSAG-defined severe comorbidities were combined as previously described[12,13]. Acute illness variables comprised the number, type and duration of organ systems supported (cardiovascular, respiratory and renal

support). Information pertaining to treatment limitations or clinician decision making were not available as part of the routinely collected data.

Statistical analysis

We used R Version 3.6.1[14] with the packages *tidyverse, survminer, finalfit, mice* and *splines,* to analyse data. We used a significance level of 5%, 95% confidence intervals (95% CI) and two-sided p values. Measures of central tendency and dispersion were presented for continuous variables. The number of admissions to Scottish critical care units determined the sample size.

Baseline characteristics and outcomes were stratified by CPAP duration status (<5 days vs ≥5 days CPAP) and outcomes and were compared using Mann-Whitney U and chi-square tests. Daily frequency of bed occupancy and organ support activity was derived from Augmented Care Period (ACP) data and presented stratified by CPAP status[8,12].

Kaplan-Meier plots were used to demonstrate mortality following institution of IMV following CPAP and groups compared with log-rank test. We evaluated the univariable and multivariable association between protracted CPAP and hospital mortality using logistic regression models, restricted to patients who transitioned from CPAP to IMV. This ensured that all patients were deemed suitable for escalation to IMV. Multiple imputation using chained equations was used to impute missing values under an assumption that data were missing at random for the following variables: frailty, SIMD, ethnicity and hospital mortality. Five imputed datasets were created and estimates pooled using Rubin's rules[15]. The remaining variables in the model were complete, with no missing data. Admission date was used as a measure of time. Its relationship with mortality was non-linear (Supplementary Figure 1) likely due to changes in admission patterns and patient demographics over time, and so the term was entered into the model as a natural spline, with 5 degrees of freedom. We undertook a series of sensitivity analyses: 1. We assessed the relationship between duration of CPAP prior to IMV

(as a continuous variable) and hospital mortality; 2. We repeated analyses with a threshold of CPAP ≥7 days to assess the threshold of longer duration CPAP; 3. We repeated analyses in the subgroup of patients defined as non-frail using the CFS (1-3), as this group were less likely to have treatment limitations in place; 4. We repeated analyses in the subgroup of units located in hospitals in which non-invasive respiratory support for COVID-19 was provided in critical care rather than wards for the vast majority of patients (see Supplement) to evaluate the impact of periods of CPAP delivered in ward environments not captured in the SICSAG database.

Approvals

The Public Benefit and Privacy Panel for Health and Social Care (1920-0093) granted SICSAG approval to undertake work relating to the COVID-19 pandemic.

Results

Descriptive analysis of all patients that received CPAP in critical care

Between 1 March 2020 and 25 December 2021, a total of 4829 patients with COVID-19 disease were admitted to Scottish critical care units. Of these 1961 (40.6%) received CPAP as the initial ventilatory strategy (Supplementary Figure 2). 1228 (65.7%) of those had a duration of CPAP therapy of less than 5 consecutive days (standard duration) and 733 (37.4%) had a duration of 5 or more days (protracted CPAP).

Baseline characteristics of patients who received CPAP are outlined in table 1 and stratified according to standard or protracted duration of CPAP. All baseline features were similar between the standard and protracted CPAP groups. Median age was 61 years and a majority (64.3%) were male. 36.4% of patients were from the most deprived SIMD quintile and 9.8% from the least deprived. A majority (95.8%) were white. Most patients (55.8%) had no co-morbidities and the most common co-morbidity was respiratory disease (17.5%). The majority of patients (69.2%) had no emergency admissions to

hospital in the preceding year, 22.3% had experienced a single emergency admission with multiple admissions uncommon (8.5%). Clinical frailty scores were available for 86.7% of the population, with the majority (56.8% overall) classified as non-frail. At presentation to critical care, P:F ratios were available for 481 (24.5%) of the total population, and 305 of these patients (63.4%) were classified as severe ARDS with P:F <13.3kPa. Similar rates of severe ARDS were noted between the two groups (62.8% and 64.8%) although there was a higher proportion of patients with missing values in the protracted CPAP group.

The median (IQR) duration of CPAP therapy was 4 (IQR 2,7) days. The trend in use of respiratory support over the first 30 days following commencement of respiratory support is outlined in Figure 1. Following initiation of CPAP, 936 patients (47.7%) also received HFNO, with more HFNO utilisation in the protracted CPAP group (60.6% vs. 40.1%, p <0.001) (Table 2). There was a rapid decline in the use of CPAP over the first 10 days such that only 10% of patients that commence CPAP remain on CPAP/ HFNO at day 10.

The proportion of patients receiving CPAP for 5 or more days was small in the first wave of the pandemic between March and May 2020. It gradually increased through the pandemic and was highest in November 2021. Trends in use of respiratory support by calendar month are outlined in Supplementary Figure 3.

Outcomes for all patients following CPAP

Outcomes following CPAP are described in Table 2. Critical care mortality was similar between those managed with protracted CPAP and those that received a shorter CPAP course (32.4% vs. 34.3%, p=0.385). Hospital mortality was also similar between the two groups at 38.8% vs. 42.8% (p=0.102).

CPAP failure, defined as escalation from CPAP to IMV or death in critical care, occurred less frequently in the protracted CPAP duration group (39.6% vs. 48.9%, p<0.001). This was attributable to a lower rate of invasive mechanical ventilation (IMV) in the protracted duration CPAP group compared to the

standard CPAP group (21.1% vs. 31.7%, p<0.001). The unit mortality rate without IMV was comparable between groups (23.4% vs. 25.3%, p=0.479).

Patients that received protracted CPAP were less likely to require additional organ support in the form of cardiovascular support (24.7% vs. 33.5%, p<0.001) or renal replacement therapy (5.7% vs. 8.9%, p=0.012). With the exception of CPAP/ HFNO duration, the duration of additional organ support was similar between the two groups.

Impact of protracted CPAP on subsequent IMV outcomes

Baseline characteristics of patients who received IMV following a period of initial CPAP are outlined in Supplementary Table 1 and stratified according to standard or protracted duration of CPAP. The protracted CPAP group had a higher median age (62 years vs. 59 years) and a higher proportion of males (76.1% vs. 68.6%). Median duration of CPAP and HFNO prior to IMV for those with standard and protracted CPAP were: CPAP 2 days (1,3) vs 6 days (4,8), and HFNO 2 days (1,3) vs 3 days (2,5) respectively. Critical care unit and hospital mortality for patients who received IMV after CPAP was 57.4% and 63.0% respectively (Table 2). Patients that had received protracted CPAP had higher unadjusted mortality rates when compared to standard duration CPAP; unit mortality 66.4% vs. 53.9% (p=0.004) and hospital mortality 73.9% vs. 58.7% (p=0.002). Kaplan Meier survival after institution of IMV demonstrates poorer unadjusted survival for those managed with protracted CPAP (Figure 2).

After adjusting for age, sex, deprivation, ethnicity, number of comorbidities, previous emergency admissions, frailty, P:F ratio and ICU admission date, protracted CPAP prior to IMV was not associated with increased odds of hospital mortality with an odds ratio (OR) 1.40 (95% CI 0.84,2.33, p=0.195) (Table 3). A sensitivity analysis using individual comorbidities did not demonstrate any difference in odds of hospital mortality (Supplementary Table 2).

Sensitivity analyses

The association between CPAP duration and hospital mortality varied during the first three days following commencement of CPAP, becoming more linear thereafter (Supplementary Figure 4.). A protracted CPAP threshold of ≥7 days (Supplementary Tables 3 and 4). Outcomes were similar with an adjusted OR 1.53 (0.76, 3.08, p=0.225) for hospital mortality following IMV after protracted CPAP of ≥7 days. The duration of CPAP +/- HFNO prior to IMV as a continuous variable was assessed after adjustment for variables (Supplementary Table 5). There was no statistically significant association between protracted CPAP (≥5 days) and hospital mortality in either the subgroup of non-frail patients (adjusted OR 1.32, 95%CI 0.74,2.35, p=0.340) (Supplementary Tables 6-8) or the subgroup of patients receiving treatment in hospitals which provided most non-invasive respiratory support in critical care areas rather than wards (adjusted OR 1.68, 95%CI 0.88,3.20, p=0.117) (Supplementary Tables 9-11).

Discussion

One third of patients in this national cohort study that commenced CPAP for COVID pneumonitis received protracted CPAP of greater than five days duration. Patient features, including baseline demographics, comorbidities, and measures of frailty, were remarkably similar between those who received protracted CPAP compared to those who received CPAP for a shorter duration. One in four patients commenced on CPAP ultimately received invasive mechanical ventilation. While overall hospital mortality was similar between the two CPAP groups, protracted CPAP prior to IMV was associated with higher unadjusted hospital mortality. After adjusting for demographic confounders and the impact of changes in CPAP utilisation practices over time, there was no statistically significant difference in mortality noted for patients managed with protracted CPAP prior to IMV when compared to patients treated with a shorter duration of CPAP prior to IMV. This was also confirmed in subgroups non-frail patients and those managed in hospitals which limited provision of non-invasive respiratory support to critical care units. However, these findings may be due to residual confounding and differences in processes of care between the two groups.

Previous research suggests that CPAP can be a useful strategy to manage COVID patients in need of extended respiratory support[2,16]. Our study demonstrated that invasive mechanical ventilation was required for fewer patients managed with protracted CPAP. However, this may reflect systematic differences between the two groups, such as a lower severity of disease for those who managed to stabilise on CPAP during the initial 5 days of support. In addition, there may be a higher proportion of patients in the protracted CPAP group who were considered poor candidates for IMV. Our dataset was limited as it did not include contextual data about clinician decision making in relation to escalation of care for individual patients. However, the baseline features between the two groups were similar in terms of age, comorbidities and frailty. Additionally, mortality in those who did not receive IMV was similar between the two groups. There were no formal escalation policies in place in Scotland at the time of this study, however, guidelines from the British Thoracic Society and Intensive

Care Society in January 2021, suggested that a lack of improvement following three days of CPAP management would be indicative of CPAP failure. It is unlikely that during the peak periods of COVID activity that CPAP as a ceiling of treatment was continued indefinitely and, therefore, patients unsuitable for IMV may have progressed to end of life care prior to the five-day threshold for protracted CPAP.

The RECOVERY-RS trial has provided the most robust evidence regarding non-invasive ventilation for COVID patients to date. This study randomised patients to either conventional oxygen therapy or CPAP and demonstrated a lower intubation rate in those receiving CPAP (41.3% vs. 33.4%)[2]. Due to randomisation, the findings of the study have a substantially lower likelihood of being affected by residual bias, in contrast to our study. However, the impact of duration of CPAP was not evaluated as part of that study.

Vaschetto et al described a cohort of COVID-19 patients treated with CPAP in respiratory intermediate care units across Northern Italy[6]. They found that over one third of patients commenced on CPAP outside of ICU subsequently required IMV, and that duration of CPAP therapy prior to IMV was associated with an increasing risk of mortality. The overall mortality rate was higher for those patients that received CPAP for greater than three days (51% vs 35%). The authors report concerns about delays in intubation leading to this increased mortality rate. While this study demonstrated similar intubation rates to our study, we did not find the same impact of protracted CPAP on outcomes following IMV. However, our study differs in that the patient population were being managed in a critical care setting with immediate IMV availability. This may have mitigated any delay to intubation when necessary.

A subsequent study conducted in 25 ICUs in Italy demonstrated that, when restricted to a population who received NIV followed by IMV, only duration of NIV administered before ICU admission and age, but not duration of NIV administered within ICU, were associated with in-hospital mortality[5]. Our study found that hospital mortality was lower for the overall population treated with protracted CPAP

compared to standard duration, but for those that required IMV, the unadjusted mortality rate was higher. This increased mortality might be expected for patients who have deteriorated in spite of in-hospital treatment and support. Following adjustment for additional confounders, protracted CPAP was not associated with a statistically significantly increased odds of hospital mortality. The differences in outcomes between this study and the Italian study may be related to the differing covariates entered in multivariable models, differing patients transitioning to IMV, as well as differences in baseline characteristics between the study populations. Furthermore, it should be noted that all of the patients in our cohort received CPAP in a critical care setting.

This study observed a high CPAP failure rate affecting nearly half of all patients. A study reporting outcomes for 390 patients treated with NIV for COVID-19 in the HOPE COVID-19 registry demonstrated a similar proportion with failure of non-invasive respiratory support (44%) as that seen in our cohort (45%)[17]. However, in-hospital deaths contributed 64% to this composite outcome in the HOPE study compared with 44% in our cohort. The reason for this may be attributable to differences between the cohorts, with the HOPE registry population studying all hospitalised patients rather than restricted to critical care, and having an older median age and burden of comorbidities than that observed in this study. Therefore, there have been a higher proportion of frail patients for whom IMV was deemed non-beneficial.

There are number of strengths to this study. Firstly, by linking ICU, hospitalisation records, and national death records, we are confident that we have near complete data for the cohort of patients managed within an ICU or HDU environment in Scotland. Additionally, by linking with the ECOSS database, which records all patients with a positive COVID-19 polymerase chain reaction swab, we can be definite that all patients included had confirmed COVID-19. During the time period analysed, COVID pneumonitis accounted for the vast majority of SARS-CoV-2 positive critical care admissions.

A weakness of the study is that the dataset only contains a limited amount of data regarding a patient's chronic health state and no information relating to limitations of therapy. As a result, there is a lack

of granularity around why some patients were escalated to invasive ventilation or not. Furthermore, the dataset is unable to give indications about decision making around the time of intubation and the reasoning behind a decision to intubate, therefore making it difficult to say why clinicians decided to intubate, despite a protracted period on CPAP. Factors pertaining to disease severity such as respiratory rate or respiratory effort were not available for any of the patients, and there was no measure of degree of hypoxia at the point of commencing CPAP. P:F ratios at admission to critical care were available for one quarter of the population. These data were only collected for those patients admitted to units that provide level 3 or combined level 2/3 care and therefore, might be expected to have a higher severity of illness. The proportion of missing data was not distributed equally with more missing data in the protracted CPAP group. However, where data was available, the median values between the two groups were similar. P:F ratios were included in the adjusted analysis of mortality following IMV. However, with such a large proportion of missing data in the missing indicator category, the likelihood of residual confounding due to inadequate adjustment for severity of disease persists.

While the SICSAG database was adapted to respond to rapidly changing service configurations such that all areas of the hospital providing ICU level care were captured, it is recognised that some hospitals were deploying CPAP in ward environments beyond that recorded by SICSAG. It is likely that there will be a small proportion of patients that received CPAP in an external environment prior to being managed in a critical care unit. However, a sensitivity analysis reported similar findings when restricted to units in hospitals which limited the provision of CPAP to critical care units. Finally, the study has not assessed complications from protracted CPAP. The RECOVERY-RS trial reported the highest rate of adverse events in the CPAP group, affecting over a third of these participants[2]. Moreover, poor ventilation strategies have been shown to impact longer-term outcomes in ARDS survivors[18].

The role of NIV modalities such as CPAP in acute hypoxaemic respiratory failure is controversial with concerns regarding uncontrolled and potentially injurious high tidal volumes exacerbating existing lung injury[4], delaying intubation and leading to worse outcomes[19,20]. Concerns have been raised during the COVID pandemic regarding the role of protracted CPAP causing increased barotrauma leading to adverse outcomes on extra-corporeal ventilation[21]. Furthermore, the increased lung stress and strain may be associated with the development or worsening of P-SILI as suggested by experts in this field[22]. However early intubation in COVID-19 pneumonitis may have contributed to ICU strain and resource depletion during surges of pandemic activity[23]. This study provides detailed descriptive information relating to the outcomes for patients receiving protracted CPAP in COVID-19 pneumonitis, but is limited in drawing firm conclusions relating to the relative benefits and harms of protracted CPAP compared with intubation. Whilst randomisation is the most robust approach to evaluating alternative interventions, such a study would be challenging to undertake due to logistical and ethical issues. The effects of avoiding intubation, such as less ICU-acquired weakness, dysphonia, delirium or sedation related complications, compared to the potential increased mental health burdens of protracted CPAP, have not been evaluated by this study and are important considerations. In addition to addressing these issues, further research should explore features such as physiological variables or patient characteristics associated with CPAP failure, in addition to exploring longer-term mortality alongside functional outcomes such as quality of life and respiratory function, to fully understand the impact of utilising protracted CPAP in this cohort.

Conclusion

In this national cohort study of patients with COVID-19 managed with CPAP, one third of patients commenced on CPAP for respiratory support received protracted CPAP. CPAP failure was common affecting nearly half of those managed with CPAP. Protracted CPAP was not associated with higher mortality rates, but this may be due to residual confounding and differences in processes of care.

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Declarations

Declaration of interests

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Author contributions

All authors contributed to the study conception and design. Material preparation and data collection were performed by Martin Paton, Ros Hall and Lorraine Donaldson. Data analysis was performed by Michael Blayney. The first draft of the manuscript was written by Kathryn Puxty and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Table/Figure legends

Table 1: Characteristics of patients that received CPAP for COVID-19

Table 2: Outcomes for patients that received CPAP for COVID-19

Table 3: Factors associated with hospital mortality following invasive mechanical ventilation

Figure 1: Utilisation of respiratory support for COVID pneumonitis during the first 30 days after critical care admission

Continuous positive airway pressure (CPAP), High flow nasal oxygen (HFNO), Invasive mechanical ventilation (IMV). No support includes patients on standard facemask oxygen, nasal prongs, no oxygen, and those who have died prior to 30 days.

Figure 2: Survival following institution of IMV after CPAP for COVID pneumonitis

Table 1: Characteristics of patients that received CPAP for COVID-19

		All	CPAP <5 days	CPAP ≥5 days
	n	1961	1228	733
Age (years)	Median (IQR)	61 (52,69)	61 (52,69.25)	61 (53,69)
Sex	Female	700 (35.7%)	452 (36.8%)	248 (33.8%)
	Male	1261 (64.3%)	776 (63.2%)	485 (66.2%)
Socioeconomic status quintile (SIMD)	1 - Most deprived	680 (36.4%)	424 (36.0%)	256 (37.1%)
	2	438 (23.4%)	277 (23.5%)	161 (23.3%)
	3	298 (15.9%)	185 (15.7%)	113 (16.4%)
	4	270 (14.4%)	181 (15.4%)	89 (12.9%)
	5 - Least deprived	183 (9.8%)	112 (9.5%)	71 (10.3%)
Ethnicity	White	1686 (95.0%)	1037 (94.4%)	649 (96.0%)
	Other	89 (5.0%)	62 (5.6%)	27 (4.0%)
Comorbidity count	0	1095 (55.8%)	685 (55.8%)	410 (55.9%)
	1	414 (21.1%)	265 (21.6%)	149 (20.3%)
	2 plus	452 (23.0%)	278 (22.6%)	174 (23.7%)
Comorbidities	Cardiovascular	277 (14.1%)	177 (14.4%)	100 (13.6%)
	Respiratory	344 (17.5%)	221 (18.0%)	123 (16.8%)
	Diabetes Mellitus	294 (15.0%)	196 (16.0%)	98 (13.4%)
	Cancer	158 (8.1%)	86 (7.0%)	72 (9.8%)
	Other	302 (15.4%)	185 (15.1%)	117 (16.0%)
Emergency hospital admissions in previous year	0	1357 (69.2%)	834 (67.9%)	523 (71.4%)
	1	438 (22.3%)	276 (22.5%)	162 (22.1%)
	2 plus	166 (8.5%)	118 (9.6%)	48 (6.5%)
Clinical frailty score (CFS)	Non-frail	1114 (56.8%)	659 (53.7%)	455 (62.1%)
	Vulnerable	328 (16.7%)	203 (16.5%)	125 (17.1%)
	Frail	258 (13.2%)	169 (13.8%)	89 (12.1%)
	Not known	261 (13.3%)	197 (16.0%)	64 (8.7%)
Time from hospital admission to critical care admission (days)	Median (IQR)	1 (0,2)	1 (0,2)	0 (0,2)
P:F ratio at admission to critical care	**n (%)**	481 (24.5%)	339 (27.6%)	142 (19.4%)
	Median (IQR)	11.4 (9.1,15)	11.3 (9.0,14.8)	11.7 (9.4, 15.3)
	≤13.3kPa	305 (63.4%*)	213 (62.8%*)	92 (64.8%*)

CPAP indicates first set of consecutive days of CPAP prior to invasive ventilation, death or critical care discharge. 92 records have an unknown SIMD quintile. 186 records have unknown ethnicity. *PF ratios are only available for patients admitted to Level 3 or combined Level 2/3 areas on the first day of their Critical Care stay and percentages given for those with data available.

Table 2: Outcomes for patients that received CPAP for COVID-19

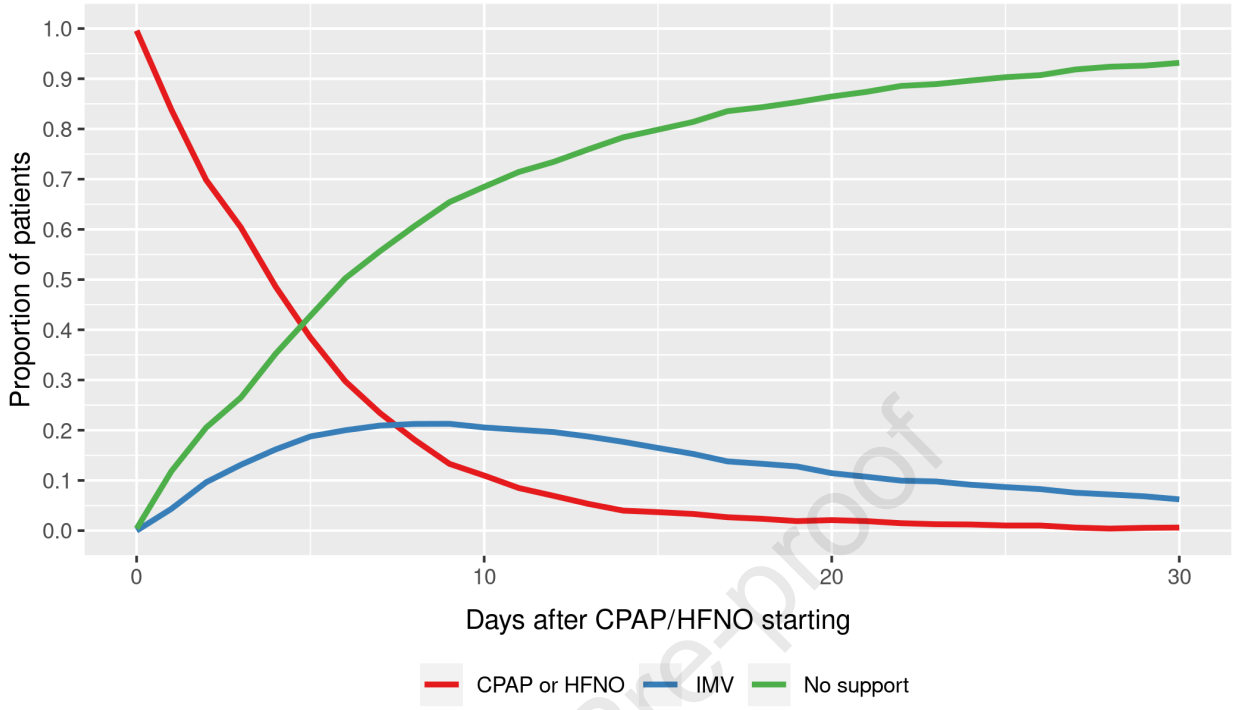
		All	CPAP <5 days	CPAP ≥5 days	p-value
		1961	1228	733	
Outcome, n (%)					
Unit mortality		657 (33.6%)	421 (34.3%)	236 (32.4%)	0.385
Hospital mortality		756 (41.3%)	491 (42.8%)	265 (38.8%)	0.102
CPAP failure		891 (45.4%)	601 (48.9%)	290 (39.6%)	<0.001
Required IMV		544 (27.7%)	389 (31.7%)	155 (21.1%)	<0.001
Died in critical care without IMV		347 (17.7%)	212 (17.3%)	135 (18.4%)	0.479
Outcome without IMV, n (%)					
Unit mortality without IMV		347 (24.5%)	212 (25.3%)	135 (23.4%)	0.479
Hospital mortality without IMV		436 (33.0%)	276 (35.3%)	160 (29.6%)	0.033
Outcome following IMV, n (%)					
Unit mortality following IMV		310 (57.4%)	209 (53.9%)	101 (66.4%)	0.004
Hospital mortality following IMV		320 (63.0%)	215 (58.7%)	105 (73.9%)	0.002
Length of stay in days, Median (IQR)					
Critical care length of stay		8 (4,14)	6 (3,14)	9 (6,14)	<0.001
Post-critical care hospital stay*		6 (3,14)	6 (3,13.2)	6 (3,15.2)	0.398
Total hospital length of stay		13 (8,23)	13 (7,22)	15 (10,25)	<0.001
Organ support during critical care stay, n (%)					
HFNO	n (%)	936 (47.7%)	492 (40.1%)	444 (60.6%)	<0.001
Cardiovascular support	n (%)	592 (30.2%)	411 (33.5%)	181 (24.7%)	<0.001
Renal support	n (%)	151 (7.7%)	109 (8.9%)	42 (5.7%)	0.012
Duration of organ support in days, Median (IQR)**					
CPAP		4 (2,7)	3 (2,4)	7 (6,10)	NA
HFNO		2 (1,4)	2(1,3)	3 (2,5)	<0.001
IMV		14 (8.8,24)	14 (9,24)	14 (8,24)	0.841
Cardiovascular support		6 (3,12)	7 (3,12)	6 (3,12)	0.663
Renal support		7 (3,14)	7 (3,15)	6 (3,13)	0.396

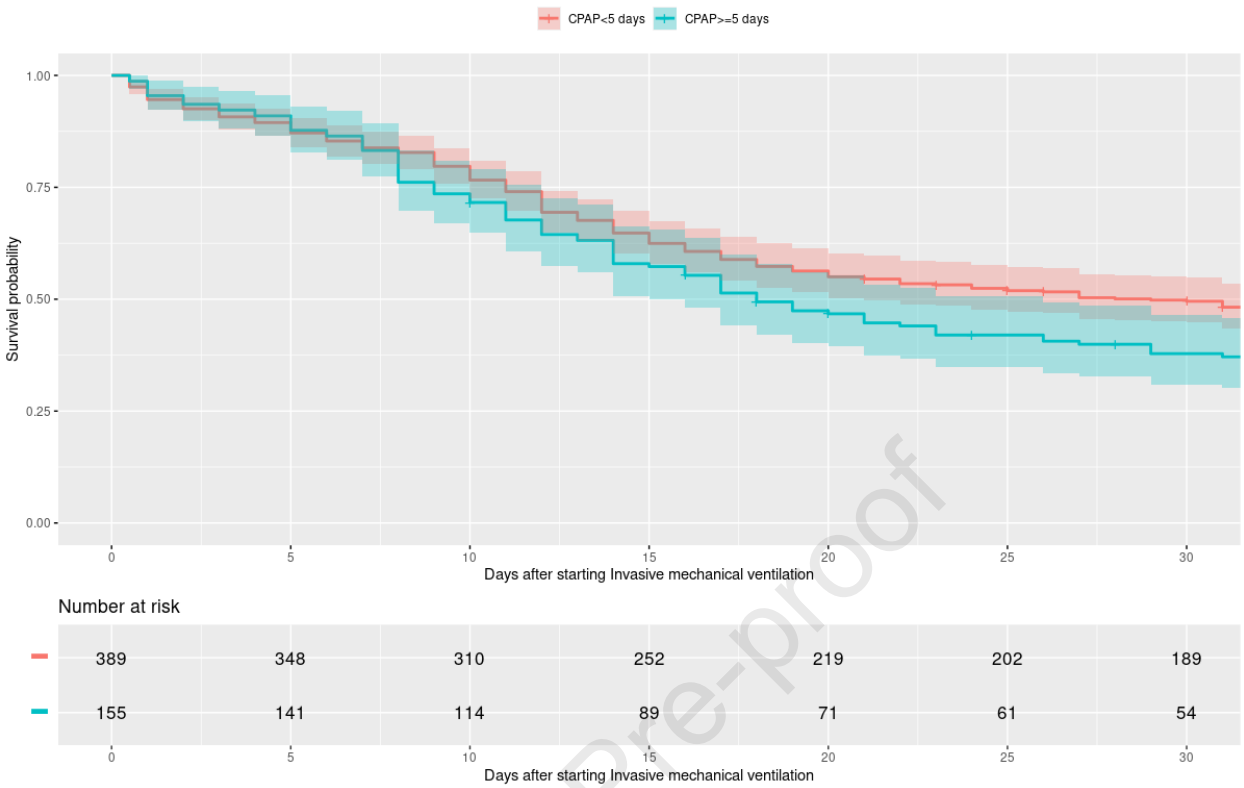
Continuous Positive Airway Pressure (CPAP), Invasive Mechanical Ventilation (IMV), High Flow Nasal Oxygen (HFNO). This table includes data from 12 patients who were still in critical care at the time of the data extract. *For patients discharged alive **Indicates data for patients who required organ support.

Table 3: Factors associated with hospital mortality following invasive mechanical ventilation

	Univariable model		Multivariable model	
	Odds ratio (95% CI)	**P-value**	**Odds ratio (95% CI)**	**P-value**
Protracted CPAP prior to IMV	1.94 (1.25,3.01)	0.003	1.40 (0.84, 2.33)	0.195
Age*	1.06 (1.04,1.08)	<0.001	1.07 (1.05,1.09)	<0.001
Male sex	1.59 (1.07,2.38)	0.022	1.38 (0.89,2.14)	0.155
Ethnicity (ref=White)				
Other**	0.65 (0.33,1.29)	0.218	1.11 (0.48,2.56)	0.811
SIMD (ref=5 - Least deprived)				
4	1.95 (0.5,2.23)	0.897	0.92 (0.4,2.08)	0.836
3	1.01 (0.5,2.04)	0.986	0.86 (0.39,1.89)	0.708
2	1.01 (0.51,2.02)	0.970	1.04 (0.49,2.21)	0.914
1 - Most deprived	0.82 (0.43,1.57)	0.545	0.92 (0.45,1.89)	0.828
Comorbidity (ref= None)				
Single comorbidity	0.98 (0.62,1.53)	0.914	0.97 (0.58,1.62)	0.899
Multiple comorbidities	1.47 (0.88,2.45)	0.142	1.31 (0.71,2.44)	0.387
PF ratio (ref=Unavailable)				
>13.3kPa	1.09 (0.59,2.02)	0.790	1.17 (0.56,2.45)	0.674
≤13.3kPa	0.99 (0.65,1.49)	0.944	0.88 (0.54,1.42)	0.595
Prior Emergency Admission	0.89 (0.59,1.34)	0.569	0.77 (0.48,1.25)	0.290
Frailty (ref=Non-frail)				
Vulnerable or Frail	0.98 (0.63,1.52)	0.925	0.8 (0.49,1.25)	0.365
Natural Spline Admission Date				
1	2.22 (1.00,4.93)	0.051	2.27 (0.94,5.48)	0.067
2	0.58 (0.12,2.80)	0.493	1.08 (0.19,6.17)	0.932
3	1.50 (0.38,5.90)	0.558	2.20 (0.46,10.5)	0.319
4	0.88 (0.13,6.21)	0.899	1.36 (0.16,11.63)	0.780
5	7.52 (2.11, 26.72)	0.002	14.98 (3.49, 64.3)	<0.001

Number of Observations = 540. Multiple imputation has been used to supplement missing data for Ultimate Hospital Mortality (n=32 (5.9 %)), SIMD (n=24 (4.4 %)), Frailty (n=77 (14.3 %)) and Ethnicity (n=40 (7.4 %). Admission date was assessed using a Natural Spline with 5 degrees of freedom. Continuous Positive Airway Pressure (CPAP), Invasive Mechanical Ventilation (IMV), Scottish Index of Multiple Deprivation (SIMD). *Age analysed as a continuous variable in years. **Includes patients with unknown ethnicity





Number at risk

CPAP<5 days	389	348	310	252	219	202	189
CPAP>=5 days	155	141	114	89	71	61	54

0 5 10 15 20 25 30

Days after starting Invasive mechanical ventilation