Role of CPAP in management of patients with Covid-19 infections who are not suitable for mechanical ventilation: a real-world observational study

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Abstract

Background

The optimum management of respiratory failure in COVID-19 patients has been a challenge for physicians across the globe. Many scientific societies have suggested the use of CPAP (continuous positive airway pressure) in severe cases, in an effort to reduce invasive ventilation. We investigated mortality outcomes in patients who needed CPAP but were not suitable for invasive ventilation.

Methods

We retrospectively evaluated the mortality outcomes of all consecutive COVID-19 cases with severe type 1 respiratory failure requiring FiO2 >0.6 who were admitted to our hospital between 12th March and 04th May'20. British Thoracic Society guidelines were followed for identifying patients needing CPAP. Their outcomes were recorded and compared with a similar group of patients who had oxygen as a ceiling of care. Prospectively collected data between 5th May and 7th June'20 in similar but smaller group of patients was also analysed.

Results:

A total of 104 COVID-19 patients with documented Do Not Attempt Resuscitation (DNAR) decision required high fraction of inspired oxygen (FiO2) >0.6 to maintain peripheral oxygen saturation (SpO2)> 92% (SpO2> 88% in COPD). 24 received CPAP as the ceiling of care with a mortality rate of 92.5%. The remaining 80 patients who were on oxygen as a ceiling of treatment had 91.7% mortality.

Conclusion

CPAP did not appear to improve survival of patients with severe respiratory failure due to COVID-19 who were not suitable for invasive ventilation. Further studies are warranted to adequately inform appropriate management strategies for this group of patients.

Keywords

CPAP; non-invasive ventilation; COVID-19; critically ill; respiratory failure

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Background

Severe COVID-19 infection causing respiratory failure requiring high-level care is unfortunately an ongoing global problem, posing considerable strain on hospital resources. The optimum management of such cases with different modalities of respiratory support and their effectiveness in certain groups of COVID-19 patients has not been extensively reported.[1] This is mainly due to the uncharted waters we are all navigating in with this new virus. In England, expert groups and guideline committees have rolled-out clear concise guidance on patient selection regarding escalation of care and eligibility for invasive ventilation, however, the outcomes of patients who are not fit for escalation or invasive ventilation but require treatment with CPAP have not been yet reported.

Objectives

In our study, we investigated the mortality (in hospital) outcomes of CPAP use in patients with respiratory failure secondary to severe COVID-19 infection who were deemed not fit for invasive ventilation, and compared it to patients who were managed on oxygen alone.

Methods

No formal ethical approval for this study was sought as this was considered as a service evaluation. All interventions were carried out at Kettering General Hospital (United Kingdom) which is 600 bedded secondary care hospital. We retrospectively investigated all -19 (probable or confirmed) patients with severe respiratory failure who required FiO2> 0.6) and admitted to our hospital between 15th March and 4th May 2020. All confirmed cases had a positive rRT-PCR swab for COVID-19. Patients meeting the case definition of 'probable COVID-19' as per WHO case definition[2] were also included, if they were managed clinically as COVID-19 infection by the treating physician, as false negative results were common with rRT-PCR testing [3][4]. Patients requiring NIV for acute or chronic type 2 respiratory failure due to pre-existing conditions were excluded from the study. A decision on fitness for invasive ventilation including DNAR was recorded in the medical notes at the time of admission after senior clinician review and discussion with the patient as per national guidelines and did not interfere with the eligibility for CPAP. CPAP was considered for patients who met the BTS criteria for its initiation at the discretion of the attending physician in conjunction with the respiratory team and / or critical care outreach team [5]. Those who were deemed to be too ill to benefit from CPAP were managed with oxygen alone. We retrospectively analysed the data of all the patients admitted with suspected COVID-19 and also analysed their Vital Signs recorded online. Those meeting the criteria for CPAP {requiring FiO2> 0.6 to maintain SpO2 >92% (88-92% in COPD)} were analysed in greater depth. Patients who met the criteria for CPAP but were managed on oxygen therapy alone were included as the control group. CFS (clinical frailty score) and data on comorbidities well known to affect mortality in COVID-19 infection like hypertension, diabetes, cardiovascular disease (CVD), cerebro-vascular accident (CVA), Neutrophil / Lymphocyte ratio (NLR) on admission and chronic obstructive pulmonary disease (COPD) was collected to compare the two groups (Table 1).

To improve the validity of the study, whilst analysing the data for above two groups, we also prospectively collected data (at arm's length) for any patient who met the same criteria from 6th May to 8th June 2020. Combined data (retrospective and prospective) was also analysed to detect any statistically important differences between the groups (Table 2).

Inclusion criteria

- Age 18 and above
- rRT-PCR confirmed or clinically probable COVID-19
- Requiring FiO2 > 0.6 to maintain SpO2 >92% (88-92% in COPD)
- Not fit for ITU escalation or invasive ventilation with DNAR in place, based on Clinical Frailty Score (CFS) and existing guidelines. Decision recorded on admission, prior to treatment

Exclusion criteria

- Fit for ITU escalation / invasive ventilation
- Patients requiring BiPAP for 'acute' or 'acute on chronic' type 2 respiratory failure

Statistical analysis

The data was summarized using descriptive statistics and results are reported as means and standard deviations, and any differences between the two groups were analysed using a two tailed T test. Categorical variables are summarized numerically and percentages with any differences analysed using Chi squared test.

Results

Between 12th March and 04th May 2020, 71 patients fulfilled the inclusion criteria and were included in the study. 16 of them were treated with CPAP and the rest were treated with oxygen therapy alone. Their baseline characteristics are listed in (Table 1). A total of 55 patients were included in the control group and received standard oxygen administration methods ranging from Venturi, Humidified oxygen or non-rebreathe masks. Patients in the CPAP group were treated with either NIPPY 3® ventilator in the CPAP mode or StarMed Ventukit® Up CPAP hoods (Intersurgical SpA, Italy). Mortality in the CPAP group was 93.7% (n=16) compared to 92.7% in the control group (n=55). There was a statistically significant difference between the 2 groups in terms of age and clinical frailty score in favour of the CPAP group. Despite this, there wasn't any statistical or clinically significant difference in mortality between the two groups.

The prospective arm of the study included a total of 33 patients of which 8 patients received CPAP with the rest receiving high flow oxygen only. The mortality in this group was also high with 91% dying (7 CPAP and 23 in the oxygen group). Mortality remained above 90% when both the retrospective and prospective groups were combined. Similarly there was no difference in mortality in patients with proven COVID-19 infection and those 'highly suspected' cases who were treated clinically as COVID-19 infection.

	Retrospective CPAP group	Retrospective O2 group (control group)	P value
Number	16	55	NA
Average Age (SD)	72.7 (11.5)	82 (8.19)	0.0006**
Sex	43.7% male (7 male, 9 = female)	56.4% male (31 =male, 24 =female)	0.26
CFS	4.92	5.5	0.13
COPD	4 (25%)	11 (20.37%)	0.67
Diabetes	4 (25%)	21 (37%)	0 .33
Hypertension	4 (25%)	21 (37%)	0.33
CVA/CVD	8 (50%)	50%	0 .95

Mean Neutrophil/lymphocyte ratio of >3.3 (SD)	10.97	10.96	0.99
Mortality rate	93.75%	92.73%	0.89

Table 1. Comparison of baseline characteristics and outcomes of retrospective groups

	Combined CPAP group	Combined O2 group	P value
Number	24	80	NA
Average Age (SD)	74.16 (10.86)	82.05 (7.7)	.00006
Sex	37.5% male (9 = male, 15 = female)	50% male (40=male,40 = female)	0.28
CFS	5.0	5.64	0 .064
COPD	33.3%	20.78%	0.207
Diabetes	37.5%	37.6%	0.82
Hypertension	45.8%	40.5%	0.643
CVA/CVD	50%	51.28%	0.913
Mean Neutrophil/lymphocyte ratio (SD)	11.28	10.86	0.87
Mortality rate (in Hospital)	91.7%	92.5%	0.89

Table 2. Detailed analysis results of combined data (retrospective and prospective) groups of patients

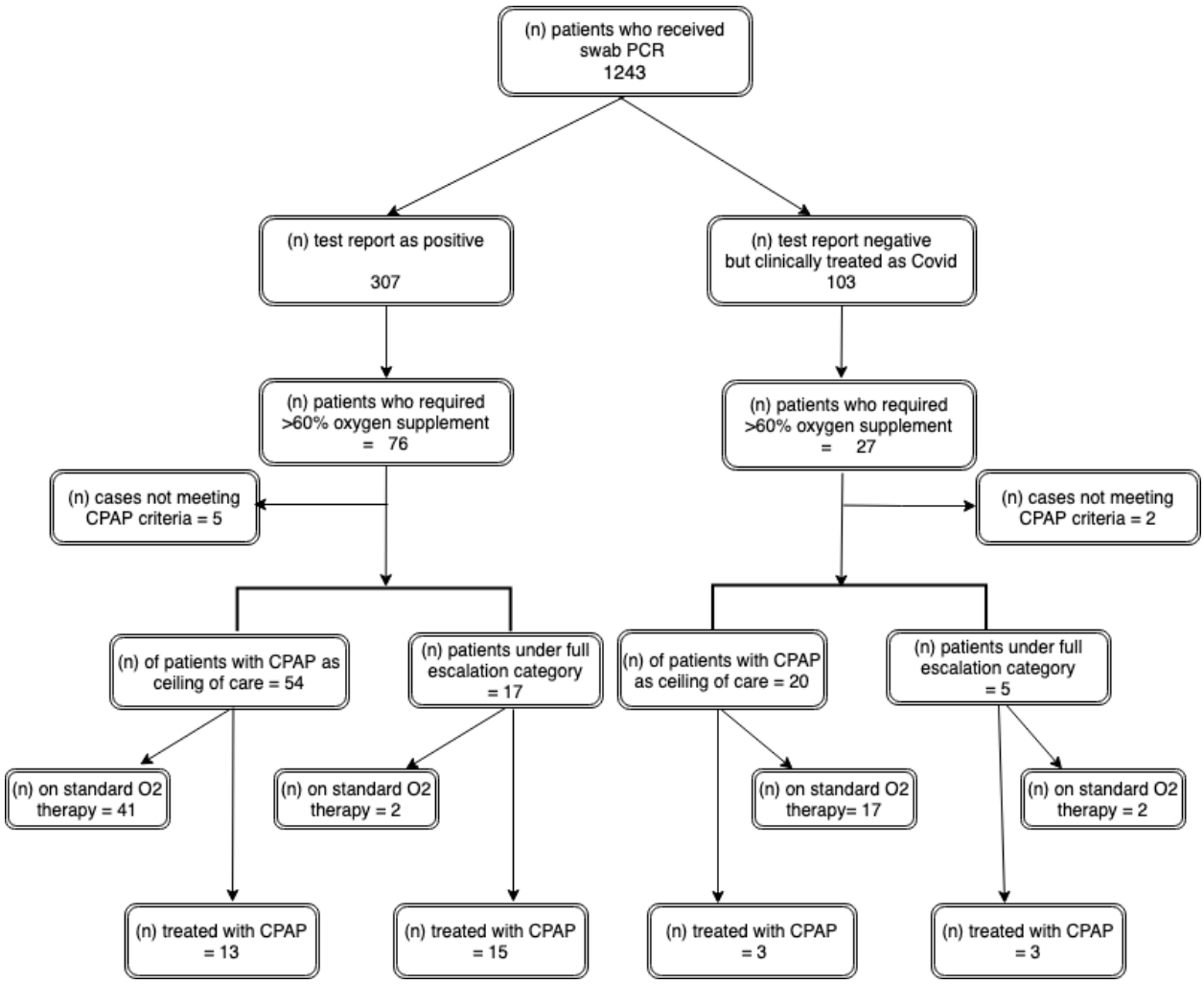

Figure 1: Figure 1. Flow chart for case selection in retrospective study group

Discussion

In our 'real-world' observational study, 15 out of 16 patients with severe COVID-19 infection requiring FiO2 > 0.6 who were deemed unsuitable for invasive ventilation and received CPAP therapy, did not survive (93.75% mortality). This was similar to the 92.73% mortality in the control group. Both groups of patients were similar, except for a significant age difference in favour of the CPAP group. With age being a strong predictor of mortality in COVID-19 infection, we would have expected the results to favour the CPAP group. Despite this, a similar percentage of patients survived in this group as in the CPAP group. The high mortality raises doubts about the effectiveness of this modality of treatment in patients who are not suitable for invasive ventilation, even if one were to disregard the oxygen group completely. It is possible that CPAP is not actually beneficial in this specific group of patients but would definitely require further large-scale studies to confirm this.

During the study period, a further 11 patients with COVID 19 infection required NIV for type 2 respiratory failure due to pre-existing respiratory conditions. Most of these patients had a documented DNAR decision on admission, however their survival rate was 66.7%. Therefore, our study results cannot be generalised to

patients requiring NIV for hypercapnic respiratory failure in the context of COVID-19 infection.

Our study, although small, apart from indicating the probable futility of CPAP in patients who are not fit for invasive ventilation, also points to a very high mortality in this group of patients who required high flow oxygen (FiO2 $>$ 0.6). However, in the 23 patients deemed suitable for intubation in our hospital (between 12th March and 8th June), CPAP prevented intubation in 13 (56.6%) patients and overall mortality in this group was 20.8%. It is not very clear as to why the CPAP which appeared beneficial in patients suitable for full escalation of treatment didn't appear to have any clinical benefit in the study patients who are not fit for invasive ventilation.

Our study is certainly not without weaknesses. It is a single centre retrospective study with its attendant biases. However, given the current uncertainty on the optimum management of the severe COVID-19 respiratory failure, as well as the lack of robust data on CPAP in patients who are not fit for ITU escalation, it would be unethical to randomise patients, potentially depriving them from a widely accepted form of treatment. Firstly, one might argue that the level of care for patients who had 'ward-based' CPAP was not 'on par' with those who received CPAP in an ITU environment in terms of monitoring and 'nurse-to-patient' ratio, potentially having an impact on outcomes. However, it must be noted that both the patients whose CPAP was managed in the ITU during the initial phase of the pandemic did not survive either. Outside of ITU, the patients were managed in designated areas with expertise in dealing with non-invasive ventilation. The mortality was also similarly high in the prospective group who were treated later on during the pandemic, when the breadth of expertise in dealing with CPAP was broader. In our hospital, during the COVID-19 pandemic we established a 1:3 'nurse-to-patient' ratio for our 'Level 2' areas, with continuous monitoring of vital signs and early warning score (EWS), allowing us to maintain high patient safety standards. To our knowledge, in recent published data referring to increased demand of care for COVID-19 patients in all areas, the 'nurse-to-patient' ratio has been either similar to ours or even less intense, even in ITU environments due to dilution of staff under the revised COVID recommendations, as well as the inevitable surge [5]. Additionally, one might argue that the patient selection might have been inappropriate, impacting outcomes. To minimise that possibility, we followed all current BTS and Intensive Care Society recommendations for CPAP patient selection and treatment strategies [6].

There were no previous studies which specifically looked at the outcomes of CPAP in patients not suitable for invasive ventilation. A very small retrospective study published recently by Oranger M,et al., [7] commented that in 7 such patients intermittent CPAP improved survival when used early. The limitation of this study is the very small number of participants and it might be possible that the threshold for commencement of CPAP in UK hospitals might differ from other European settings, as this study recruited patients who required just $>$ 6lts/min oxygen. It is clinically plausible that they might otherwise have survived with administration of higher concentration oxygen on its own.

In summary, in our study, patients with severe COVID-19 pneumonia who were not fit for invasive ventilation and treated with CPAP, had extremely high mortality which was comparable to those who were treated with high flow O2 alone. These findings were also confirmed in the prospective arm of the study. Our findings should be further validated by analysing larger datasets where available or through large-scale randomised controlled trials and may lead to a crucial change of practice and more sensible resource allocation for both staff and equipment.

Contributorship

H.A., E.A., Z.A., S.P, R.R., M.N, S.M, S.K., and N.K. collected and analyzed the data. R.R. and G.T. contributed to the concept of the study, supervised the process. R.R, G.T and H.A drafted the manuscript.

Conflicts of interest

No conflicts of interest were identified and no funding received.

Data Sharing Statement

The authors confirmed that all data underlying the findings are full available without restriction. All data are included within the manuscript. Further supporting data is available from the corresponding author on request.

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