

RESEARCH ARTICLE

Continuous Positive Airway Pressure (CPAP) face-mask ventilation is an easy and cheap option to manage a massive influx of patients presenting acute respiratory failure during the SARS-CoV-2 outbreak: A retrospective cohort study

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Abstract

Introduction

Because of the COVID-19 pandemic, intensive care units (ICU) can be overwhelmed by the number of hypoxemic patients.

Material and methods

This single centre retrospective observational cohort study took place in a French hospital where the number of patients exceeded the ICU capacity despite an increase from 18 to 32 beds. Because of this, 59 (37%) of the 159 patients requiring ICU care were referred to other hospitals. From 27th March to 23rd April, consecutive patients who had respiratory failure or were unable to maintain an SpO₂ > 90%, despite receiving 10–15 l/min of oxygen with a non-rebreather mask, were treated by continuous positive airway pressure (CPAP) unless the ICU physician judged that immediate intubation was indicated. We describe the characteristics, clinical course, and outcomes of these patients. The main outcome under study was CPAP discontinuation.

Results

CPAP was initiated in 49 patients and performed out of ICU in 41 (84%). Median age was 65 years (IQR = 54–71) and 36 (73%) were men. Median respiratory rate before CPAP was 36

(30–40) and median SpO₂ was 92% (90–95) under 10 to 15 L/min oxygen flow. Median duration of CPAP was 3 days (IQR = 1–5). Reasons for discontinuation of CPAP were: intubation in 25 (51%), improvement in 16 (33%), poor tolerance in 6 (12%) and death in 2 (4%) patients. A decision not to intubate had been taken for 8 patients, including the 2 who died while on CPAP. Two patients underwent less than one hour CPAP for poor tolerance. In the end, 15 (38%) out of 39 evaluable patients recovered with only CPAP whereas 24 (62%) were intubated.

Conclusions

CPAP is feasible in a non-ICU environment in the context of massive influx of patients. In our cohort up to 1/3 of the patients presenting with acute respiratory failure recovered without intubation.

Introduction

The pandemic of novel coronavirus disease 2019 (COVID-19) began in Wuhan, China in December 2019. As of August 2th 2020, the WHO reported a total of 17 660 523 COVID-19 cases globally, including 680 894 deaths. In a large UK cohort, death from COVID-19 was strongly associated with being male, older age, deprivation, uncontrolled diabetes and severe asthma [1].

The nature of the pulmonary lesions triggered by SARS-CoV-2 is still a matter of debate. Some histopathological studies suggest that diffuse alveolar damage is not the single pattern [2, 3]. Disorders of the pulmonary circulation (thrombosis, endothelial injury) and organizing pneumonia may also be present. The classical clinical features of ARDS after intubation such as low pulmonary compliance are not found in all patients [4, 5].

In terms of clinical management, initial recommendations suggested early intubation and ARDS-type ventilator settings [6]. Although some studies suggest a role for non-invasive ventilation (NIV) in mild ARDS [7–10], including a recent meta-analysis [11], invasive mechanical ventilation remains the standard of care, especially for severe cases. While CPAP in cardiogenic pulmonary oedema has been shown to reduce intubation rate [12], a randomized trial in acute hypoxemic respiratory failure, showed no effect of CPAP in reducing intubation rate and mortality, despite improved oxygenation [13]. However, during the Chinese and European COVID-19 outbreaks, a number of critical care teams proposed using high flow oxygen through nasal cannula (HFONC) or NIV at least for initial management [14–18]. Optimal respiratory support for COVID-19 patients presenting with acute hypoxemic respiratory failure, however, remains unknown.

The district of Seine Saint Denis has been the worst affected area during the 2020 SARS-CoV-2 outbreak in Parisian region, with a mortality in excess of 168.7% as compared to the same period in 2019 [19]. It is densely populated and has a high-deprivation index. From mid-March until end of April 2020, the Delafontaine Hospital, a large public hospital in Saint Denis, experienced a massive influx of patients requiring invasive ventilation. Both intensive care unit (ICU) and Emergency Department (ED) were quickly overwhelmed. The number of patients admitted in the wards (210 non-ICU beds, for 585 COVID-19 admissions) exceeded our ICU capacity (18 beds, increased to 32 during the crisis, for 100 admissions). Fifty-nine (37%) out of the 159 patients requiring ICU care during this period had to be referred to other hospitals (Fig 1). Therefore, we had an urgent need to delay the course of respiratory failure in

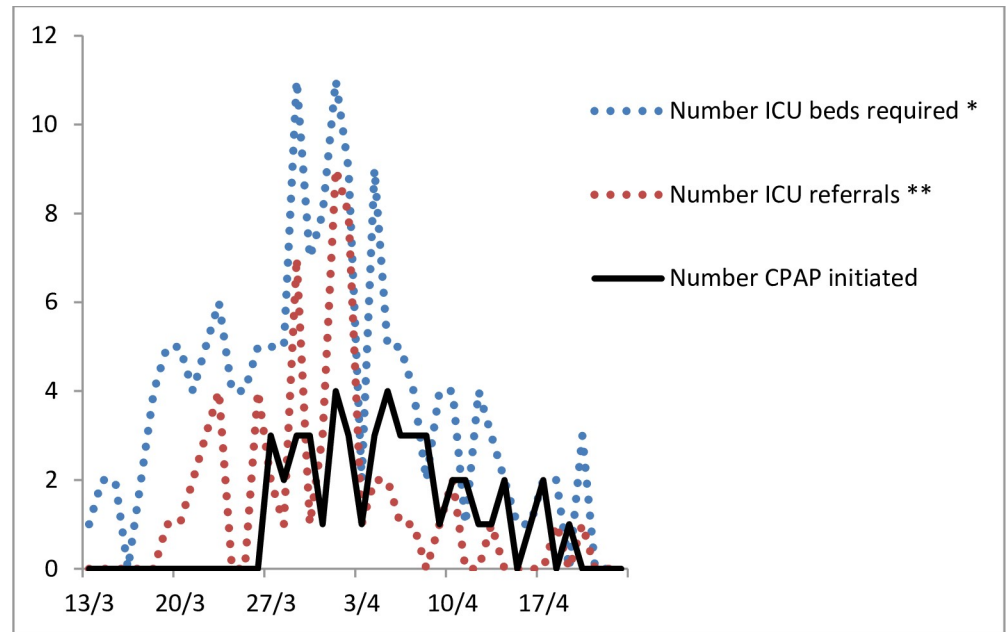


Fig 1. ICU patient load in Delafontaine Hospital during SARS-CoV-2 outbreak. * Total number of patients who were intubated in ED or wards, were admitted in ICU or for whom CPAP was initiated. ** Number of patients that required transfer in other hospitals by emergency medical retrieval service (SAMU).

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the less severe patients in order to manage the flow of patients in the ICU and the ED resuscitation room.

To achieve this, we considered face-mask CPAP because it does not require a ventilator. From 27th March onwards, patients with signs of respiratory failure despite 10 to 15 l/min of oxygen delivered by non-rebreather mask (NRM) were systematically assessed for face-mask CPAP or immediate intubation.

In this single centre retrospective observational cohort study, we describe the characteristics and outcomes of patients supported with CPAP in our hospital during the SARS-CoV-2 outbreak.

Materials and methods

Study design and participants

We reviewed the characteristics, clinical course and outcomes of all consecutive adults with proven COVID-19 treated with face-mask CPAP in ICU or in wards between 27th March and 23 April. During this 4 weeks-period, patients receiving 10–15 l/min oxygen through NRM who had clinical signs of respiratory failure or were unable to maintain an SpO₂ > 90% were treated with face-mask CPAP unless the ICU physician judged that immediate intubation was indicated. Every patient included had a thoracic CT scan suggestive of COVID-19 pneumonia and/or a positive SARS-CoV-2 PCR on naso-pharyngeal swab or broncho-alveolar lavage. The primary outcome under study was reason for CPAP discontinuation (poor tolerance, intubation, death or improvement). Poor tolerance was defined as a refusal by the patient to do more CPAP sessions, because of breathing discomfort.

Data collection

The following baseline patient characteristics were retrieved from patient electronic medical record: sex, age, comorbidities, body mass index (BMI), withholding / withdrawal of life-

sustaining therapies, associated COVID-19 therapies administered before the primary outcome under study occurred (antivirals, corticosteroids, immuno-modulating therapies, prone positioning), oxygen flow rate and SpO₂ before and after starting CPAP treatment, duration of CPAP treatment, medical unit where CPAP treatment was performed, duration of invasive mechanical ventilation, SAPS2 score for patients admitted in ICU, driving pressure and P/F ratio on first day of mechanical ventilation. The clinical outcomes (i.e. discharges from hospital, mortality) were recorded until the final day of follow-up on June 24th.

CPAP therapy

CPAP of 5 to 10 cm H₂O was delivered via a face-mask dedicated to NIV (Performa Track®) with one of 2 types of CPAP valve (Boussignac™ or CPAP-O-two™) or alternatively, an ICU ventilator (Servo I® or Evita Infinity V500®). Treatment was undertaken in a medical ward, the ED short-stay unit or the ICU. An electrostatic heat and moisture exchanger filter (DAR™) was placed between the mask and the CPAP valve to prevent aerosolization of virus through expired gases. All patients were admitted to a single room with implementation of contact and airborne precautions. Medical and nursing staff in wards, unfamiliar with NIV, were trained by the intensivist who was initiating the CPAP treatment. Patients received an initial prolonged session lasting at least 4 hours before being reassessed of their need of invasive mechanical ventilation. If the patient could be temporarily taken off CPAP without an immediate fall of SpO₂ below 90% (on O₂ 15l/min via NRM) or recurrence of clinical signs of acute respiratory failure, CPAP treatment was resumed for 2 hours every 4 hours. Progressive weaning of CPAP was performed according to clinical signs, pulse oximetry and arterial blood gases. When possible, patients were managed in the ICU (nurse/patient ratio 1:2). If no ICU bed was available (as in over 80% cases), patients with CPAP were shifted to the ED short-stay unit (8 beds) adjacent to the ICU (nurse/patient ratio 1:4) which allowed frequent re-evaluation of the patient's state by the intensivist on duty. In the eventuality of no available bed in the ED short stay unit, CPAP treatment was instituted and managed in the medical ward where the patient had been admitted (nurse/patient ratio 1:7 during the outbreak). Ward patients on CPAP were systematically reviewed overnight by the resident on duty responsible for the COVID-19 medical wards.

Statistics

No *a priori* statistical sample size calculation was performed. Sample size was equal to the number of patients treated during the study period. Quantitative values are expressed as the median (interquartile range, IQR), and qualitative values are presented as numbers (percentages). Univariate analysis was performed using Fisher exact test or Wilcoxon test, as appropriate. All tests were two-sided and a p value <0.05 was considered statistically significant. Because of alpha inflation due to multiple comparisons, findings should be interpreted as exploratory. A Cox hazard proportional model was fit for time to intubation, controlling for potential confounders in the cohort of 39 patients analysed. All variables available at baseline and associated with intubation in univariate analysis with a p-value <0.10 were selected. Variables selected are: CT-scan severity (<50% vs ≥50% of lung involved), SpO₂ at the time of CPAP initiation, dose of anticoagulant (simple, double or curative) and time between hospital admission and CPAP initiation. Because of the important differences in the proportion of patients on corticosteroids in the 2 groups (though statistically non-significant in univariate analysis) and the impact on mortality of corticosteroid treatment found in the Recovery trial [20], we included it as an additional variable in the model. Variables with more than 10% missing values were not implemented in the multivariate analysis. The analyses were carried out

using R version 3.6.2 (The R Project For Statistical Computing, Vienna, Austria; <http://www.R-project.org>).

Ethics

The study was approved by the national ethics review board (CNRIPIH—Commission Nationale des Recherches Impliquant la Personne Humaine) under the number 2020-A01396-33. The ethic committee waived the requirement for informed consent: patients or their next-of-kin were informed by mail about the data collection process and their right to oppose. The database was declared to the Commission Nationale Informatique et Libertés (CNIL) under the number 2217928. Electronic medical records of the Delafontaine hospital (Saint-Denis, France), concerning patients who sought care between March and April 2020, were accessed between May and June 2020. Statistical analyses were conducted on anonymised data.

Results

Forty-nine consecutive patients were treated with CPAP between 27th March and 23rd April 2020 (Fig 2). Initiation of CPAP occurred throughout the entire study period and followed the

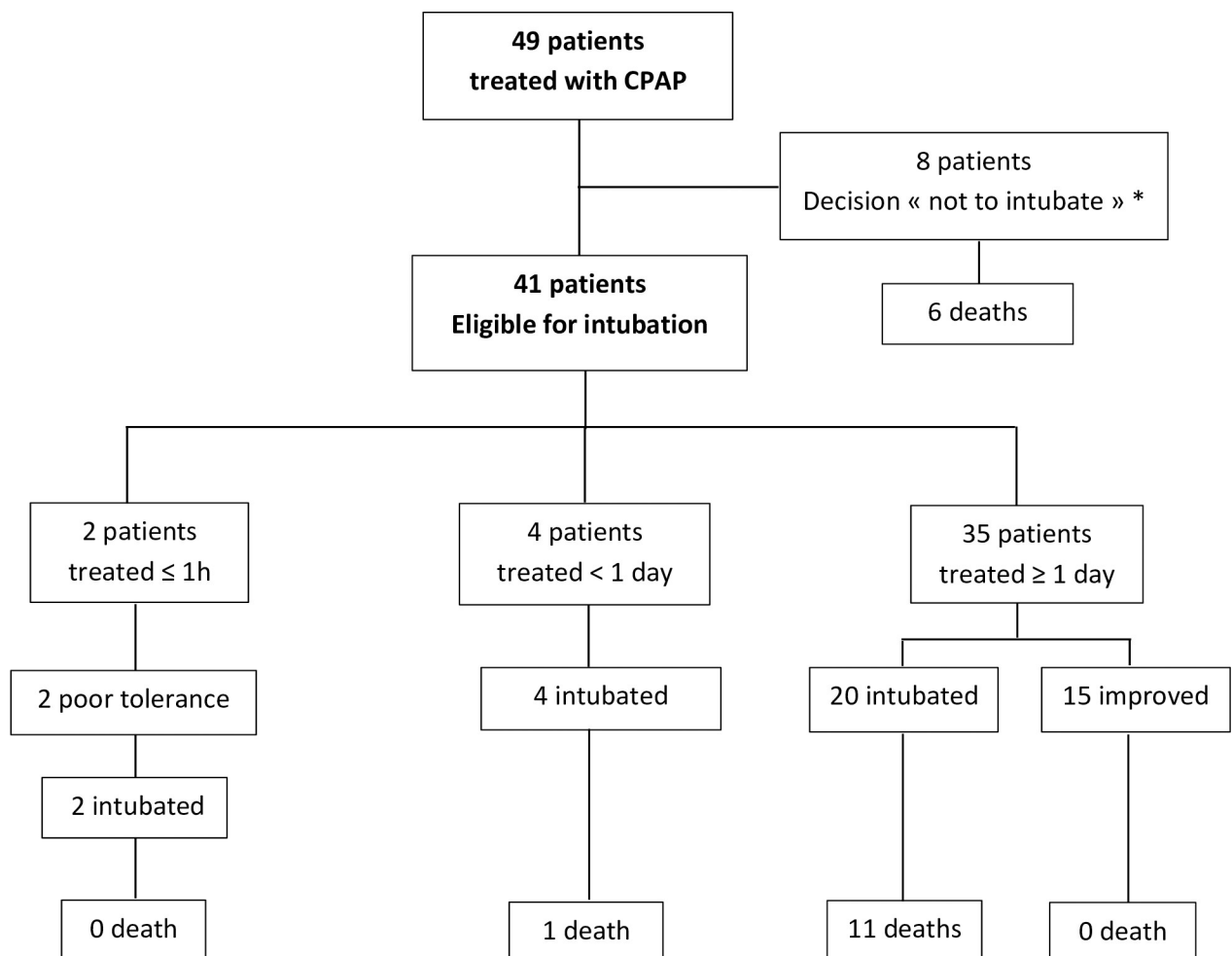


Fig 2. CPAP therapy—patient flow diagram. * CPAP discontinued for poor tolerance (5 patients), death during treatment (2 patients) and improvement (1 patient).

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epidemic curve (Fig 1). SARS-CoV-2 pneumonia was confirmed by PCR in 39 (79%) patients and by thoracic CT scan in all patients. Twenty-six (53%) patients were eventually intubated and a total of 18 (37%) died.

Patients' characteristics are presented in Table 1. The median age was 65 years (IQR = 54–71) and 36 (73%) were men. Forty-one (84%) patients had at least one comorbidity. The most frequent were hypertension (31 patients, 63%), obesity (13 patients, 34%) and diabetes (16 patients, 33%). The median duration of symptoms before hospital admission was 6 days (IQR = 5–9). Thoracic CT-scan at admission showed mild (10 to 25%), moderate (25 to 50%) or severe (>50%) lung involvement in 13 (27%), 23 (46%) and 13 (27%) patients respectively.

Table 1. Patients' characteristics.

Characteristics	All patients (n = 49)	Patients improved with CPAP (n = 15) *	Patients intubated after CPAP (n = 24) *	P value ^δ
Age in year ^e	65 (54–71)	67 (53–68.5)	62(54–69)	.79
Age categories [¶]				
0–39 yr	0	0	0	
40–49 yr	5/49 (10%)	1/15 (7%)	3/24 (12.5%)	1
50–59 yr	11/49 (22%)	4/15 (27%)	6/24 (25%)	1
60–69 yr	19/49 (39%)	8/15 (53%)	9/24 (37.5%)	.51
70–79 yr	10/49 (20%)	2/15 (13%)	5/24 (20%)	.69
≥80 yr	4/49 (8%)	0	1/24 (5%)	1
Female sex [¶]	13/49 (27%)	4/15 (27%)	5/24 (20%)	.71
BMI distribution [¶]				
< 24,9 kg/m ²	10/38 (26%)	3/11 (27%)	6/21 (29%)	1
25–29,9 kg/m ²	15/38 (40%)	3/11 (27%)	9/21 (43%)	.46
30–34,9 kg/m ²	8/38 (21%)	3/11 (27%)	4/21 (20%)	.67
35–39,9 kg/m ²	2/38 (5%)	0	1/21 (4%)	1
≥40 kg/m ²	3/38 (8%)	2/11 (19%)	1/21 (4%)	.27
Comorbidities [¶]				
Any	41/49 (84%)	11/15 (73%)	20/24 (83%)	.69
Hypertension	31/49 (63%)	9/15 (60%)	16/24 (67%)	.74
Diabetes	16/49 (33%)	6/15 (40%)	7/24 (29%)	.51
Cerebrovascular disease	3/49 (6%)	1/15 (7%)	2/24 (8%)	1
Coronary artery disease	2/49 (4%)	0	0	
Chronic renal failure	5/49 (10%)	2/15 (13%)	3/24 (12.5%)	1
Chronic lung disease	10 (20%)	2/15 (13%)	4/24 (17%)	1
Cancer	1 (2%)	0	0	
Immunodeficiency	0	0	0	
Delay between symptoms and hospital admission (days) ^e	6 (5–9)	6 (5.5–9.5)	6 (5–8.25)	.76
SARS-CoV-2 PCR positivity [¶]	39/47 (83%)	10/14 (71%)	21/24 (88%)	.39
Thoracic CT at admission [¶]				
10–25%	13/49 (27%)	7/15 (47%)	4/24 (17%)	.07
25–50%	23/49 (46%)	6/15 (40%)	13/24 (54%)	.75
>50%	13/49 (27%)	2/15 (13%)	7/24 (29%)	.15

* Patients excluded for analysis (n = 10): withdrawal/limitations of life-sustaining therapies (n = 8), <1 hour CPAP treatment (n = 2).

^e Median (IQR).

[¶] Number / total number (%).

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Table 2. CPAP therapy and other interventions (before or during CPAP period).

	All patients	Patients improved with CPAP (n = 15)*	Patients intubated after CPAP (n = 24)*	P value
Time between admission and CPAP initiation in days ^ε	3 (1–5)	4 (4–6.5)	2 (1–5)	.04
Care zone of initiation of CPAP				
ICU	8/49 (16%)	2/15 (13%)	5/24 (21%)	.69
ED short stay unit	29/49 (59%)	9/15 (61%)	16/24 (67%)	.74
COVID-19 ward	12/49 (25%)	4/15 (26%)	3/24 (12%)	.69
CPAP device				
Boussignac™ valve	41/49 (84%)	11/15 (74%)	20/24 (83%)	.69
CPAP-O-two™ valve	3/49 (6%)	2/15 (13%)	1/24 (4%)	.55
ICU ventilator	5/49 (10%)	2/15 (13%)	3/24 (13%)	1
Oxygen flow rate before CPAP initiation				
15L/min	42/47 (89%)	11/15 (73%)	22/22 (100%)	.05
11–12L/min	5/47 (11%)	4/15 (27%)	0	.05
SpO ₂ in % before CPAP initiation ^ε	92 (90–95) n = 44	95 (92.5–95.5) n = 15	92 (90–93) n = 21	.02
Respiratory rate per min before CPAP ^ε	36 (30–40) n = 36	38 (29–40) n = 13	32 (30–38) n = 19	.47
Oxygen flow on CPAP in L/min	25 (23–25) n = 21	25 (23–26) n = 5	25 (25–26) n = 12	1
SpO ₂ in % on CPAP ^ε	97 (94–98) n = 29	98 (96–98) n = 9	96 (93–98) n = 15	.14
Respiratory rate per min on CPAP ^ε	34 (29–37) n = 23	29 (23–32) n = 6	36 (30–37) n = 14	.46
CPAP duration in days ^ε	3 (1–5)	4 (3–7)	2 (2–3)	.002
<1h [¶]	4/49 (8%)	-	-	
1h - 1day [¶]	6/49 (12%)	0	4/24 (17%)	.15
1–5 days [¶]	30/49 (61%)	10/15 (67%)	19/24 (79%)	.46
>5 days [¶]	9/49 (18%)	5/15 (33%)	1/24 (4%)	.02
Other interventions				
Antibiotics [°]	45/49 (92%)	13/15 (87%)	23/24 (96%)	.55
Lopinavir/ritonavir	4/49 (8%)	1/15 (7%)	1/24 (4%)	1
Corticosteroids	29/49 (59%)	10/15 (67%)	11/24 (46%)	.32
Anakinra	7/49 (14%)	2/15 (13%)	3/24 (13%)	1
Hydroxychloroquine	17/49 (35%)	6/15 (40%)	9/24 (38%)	1
Therapeutic anticoagulation	14/49 (29%)	3/15 (20%)	7/24 (29%)	.71
Twice daily (double dose) prophylactic anticoagulation	19/49 (39%)	9/15 (60%)	6/24 (25%)	.04
Once daily (single dose) prophylactic anticoagulation	16/49 (32%)	3/15 (20%)	11/24 (46%)	.17

* Patients excluded for analysis (n = 10): withdrawal/limitations of life-sustaining therapies (n = 8), <1 hour CPAP treatment (n = 2).

^ε Median (IQR).

[¶] Number / total number (%).

[°] Antibiotics: Amoxicillin-clavulanic acid, Spiramycin, Azithromycin, Erythromycin, third generation cephalosporin, Piperacillin-tazobactam, Cefepim.

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Modalities of CPAP therapy and associated interventions are described in [Table 2](#). CPAP was performed out of ICU in 41 (84%) cases. Median duration of CPAP therapy was 3 days (IQR = 1–5). Reasons for discontinuation of CPAP were intubation for invasive mechanical ventilation in 25 (51%) patients, improvement in 16 (33%), poor tolerance in 6 (12%) and

death in 2 (4%). A decision not to intubate had been taken with the patient and their family for the 2 patients who died while on CPAP. All patients received at least once daily prophylactic anticoagulation. Twice daily (thus double dose) prophylactic anticoagulation, typically enoxaparin 40mg every 12 hours, was administered in 19 (39%) patients while 14 (29%) received therapeutic anticoagulation. Hydroxychloroquine was administered in 17 (35%) patients, Lopinavir/Ritonavir in 4 (8%), corticosteroids in 29 (59%) and Anakinra in 7 (14%). Awake prone positioning was used in 7 (14%) patients. Two of those were eventually intubated.

Eight patients had a withdrawal or limitation of life-sustaining therapies (“do-not intubate” decision). Of the 41 other patients, 2 had poor tolerance of CPAP, resulting in its discontinuation within less than one hour. We did not consider these patients as being significantly treated, which left 39 patients suitable for analysis of outcome. Fifteen patients (38%) out of 39 showed sustained clinical improvement with CPAP therapy and never required intubation, including 1 patient (25%) in the 40–49 years age category, 4 patients (40%) in the 50–59 years, 8 patients (47%) in the 60–69 years and 2 patients (29%) in the 70–79 years. The other 24 patients (62%) eventually required invasive ventilation (Fig 2). In this group, median time from CPAP initiation to intubation was 1 day (IQR = 1–2), median P/F immediately after intubation was 100 (IQR = 80–139), and median duration of mechanical ventilation was 17 days (IQR = 10–22).

Patients who improved with CPAP were compared to patients who required invasive mechanical ventilation. Characteristics regarding age, sex, comorbidities and disease presentation were similar in both groups. Patient who improved with CPAP were treated later in their hospital stay, had higher oxygen saturation before CPAP initiation, longer duration of CPAP and received more often concomitant double dose prophylactic anticoagulation. In multivariate analysis, only low oxygen saturation before initiation of CPAP was independently associated with a higher risk of intubation (Fig 3).

Twelve (46%) of the 26 intubated patients had a fatal outcome. Median SAPS 2 score of ventilated patients was 57 (IQR = 38–64), resulting in a standardized mortality ratio of 0.75. At the time of final follow up, 18/49 (37%) patients were dead, 30 (61%) were discharged (14 from the group of patients who improved with CPAP), 1 (2%) was still hospitalized in intensive care unit but weaned from mechanical ventilation.

Discussion

Our hospital experienced a massive influx of hypoxemic patients during the COVID-19 outbreak, 59 (37%) of the 159 patients requiring ICU care had to be referred to other hospitals for lack of ICU beds. In this context we tried CPAP as a temporizing treatment in the management of acute respiratory failure. We choose not to use bi-level pressure NIV for several reasons. First, the number of ventilators available could not ensure surge capacity in the context of massive patients influx, and the CPAP devices were cheap enough to be bought in a large amount (28€ for a Boussignac™, 62€ for a CPAP-O-two™). Second, bi-level pressure modes could have exposed patients who already have increased respiratory drive to the risk of ventilation induced lung injury through excessive tidal volume [21]. Third, the increase in positive pressure during inspiration was suspected to carry a greater risk of aerosolization of virus particles, hence increasing the risk of contamination of health care workers [22, 23]. The final reason was to keep pressure support ventilation as an option for pre-oxygenation before intubation when indicated [24]. Using bi-level pressure modes would have also required more intensive training of ward staff unfamiliar with NIV techniques. HFONC was also not considered because of the lack of high flow oxygen delivery devices during the outbreak period. In addition, there was also a concern about a greater risk of aerosolization, especially in non ICU settings where strict compliance with airborne precautions was more difficult to achieve.

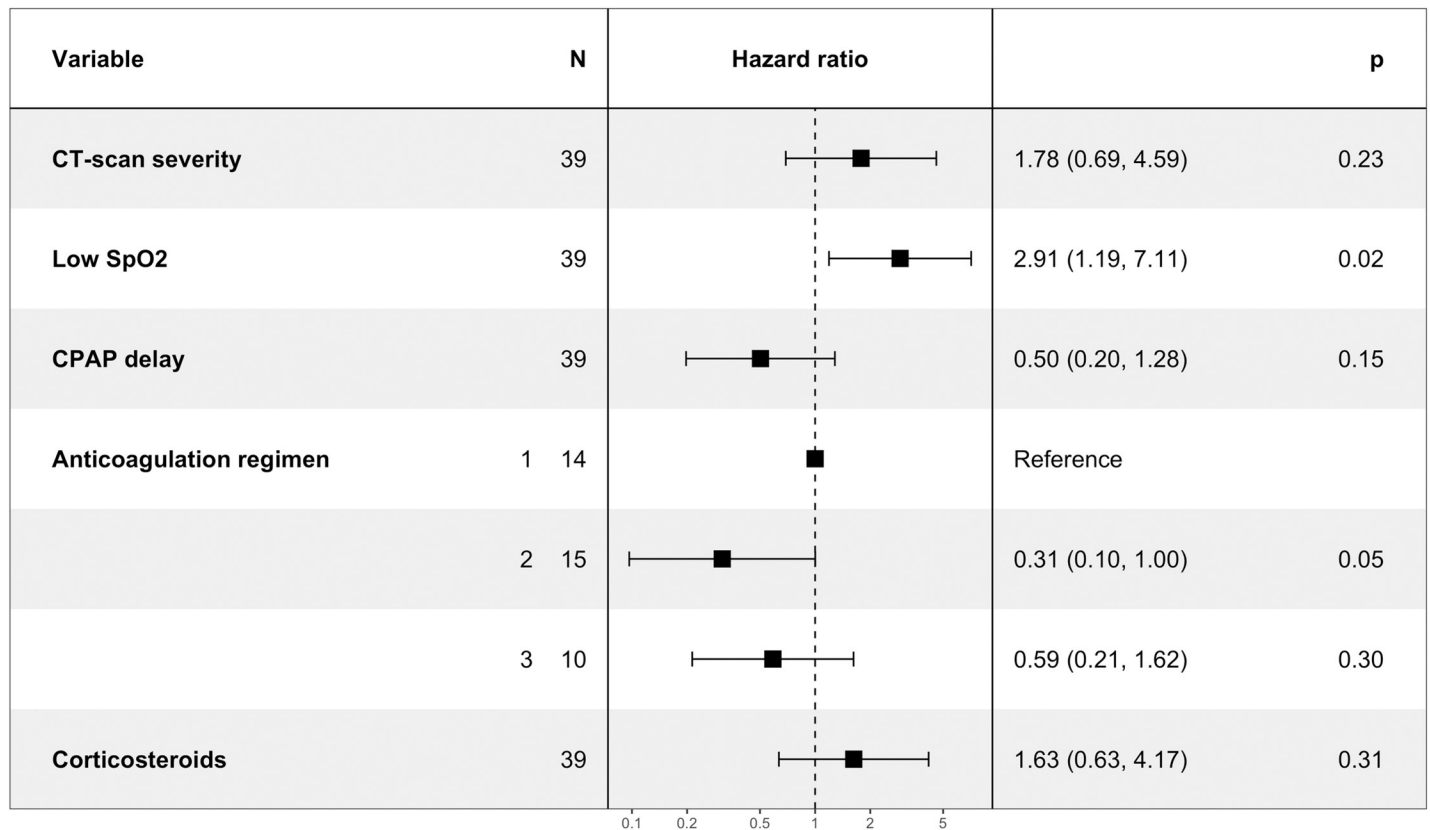


Fig 3. Factors associated with intubation. Hazard ratio of intubation adjusted for CT-scan severity (more or less of 50% of lung involved by SARS—CoV2 induced lesions), low saturation (SpO₂, < 92% or > 92%), delay in days between hospitalization and CPAP initiation (two groups based on the median value of CPAP delay), use of anticoagulant treatment grouped by dosage: simple dose prophylaxis (1), double dose prophylaxis (2) or curative treatment (3) and treatment with corticosteroids. *P* values are indicated as the result of likelihood-ratio test. The validity of the proportional hazards assumption was tested using `cox.zph()` function in R (*P* values > 0.05) and by visualization of Schoenfeld residuals.

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In this single center retrospective observational study, overall mortality of this cohort was 37% (18/49). Sixteen (33%) patients improved with face-mask CPAP, and eventually did not require invasive ventilation though they were very hypoxemic (11 (73%) of them required 15L/min oxygen). Apart from 2 patients with a do-not-intubate orders, no death occurred during CPAP therapy. Mortality rate was 46% in the patient group requiring invasive mechanical ventilation, which was consistent with a large cohort of 20133 patients from 208 hospitals in UK (International Severe Acute Respiratory and emerging Infections Consortium—ISARIC). Among 3001 admitted to critical care (high dependency unit or intensive care unit), mortality was 32% while 41% continued to receive care at the date of reporting. In the 1658 patients receiving invasive ventilation mortality was 37% while 46% were still in hospital [25]. This mortality rate was related to the severity of illness (median SAPS2 score of 57) but may also be due to delayed intubation.

Reports are emerging on the use of CPAP in situations similar to ours during the SARS—Cov-2 pandemic. In a single center in UK, CPAP was initiated in patients requiring more than 28% FiO₂ or 4l/mn oxygen in combination with awake proning [26]. When compared to the ISARIC cohort [25], there were reduced ICU admissions (7.2 versus 16.5%) and invasive ventilation rates (4.8 versus 9.8%), with comparable hospital mortality (33.3 versus 36.8%). Another single center retrospective study in UK suggest a positive effect of CPAP therapy, with a favourable outcome (i.e. survival without mechanical ventilation) in 14 (58%) patients, and an

intubation rate of 38%, which was similar to our results [27]. A French two period retrospective study favours CPAP over oxygen: intubation-free survival was 77% (29/38) with CPAP compared to 43% (6/14) with oxygen ($p = 0,043$). However it was performed in the absence of shortage of ICU beds, and CPAP was initiated in patients less hypoxemic than our population (oxygen flow > 6 L/min for $SpO_2 > 92\%$), those two points may be the reasons of a lower intubation rate compared to ours [28]. In an Italian prospective cohort, 157 patients underwent helmet CPAP with a 55% survival without mechanical ventilation. In this study, patients were less hypoxemic than in our cohort at CPAP initiation ($PaO_2/FiO_2 < 300$ mmHg). The helmet interface was well tolerated with discontinuation in only 4 patients [29].

On the whole, despite the fact that non-invasive ventilation techniques (HFONC, bi-level pressure ventilation or CPAP) have already been used in several respiratory virus outbreaks (SARS, MERS, H1N1), we lack strong evidence on their efficiency because studies were mainly retrospective, with inappropriate control for selecting or confounding bias, or without any control group [30, 31]. As a consequence, recommendations from scientific societies concerning non-invasive oxygen therapy in COVID-19 are heterogenous, some favouring HFONC, CPAP, or bi-level pressure, depending on the country [32].

It is not possible to infer from our study any definite conclusion on the role of CPAP to avoid invasive ventilation because of the small sample size and because we were unable to identify a population of patients that could have been a comparator. Our study has several other limitations. First, due to its retrospective design, we were unable to collect additional data that could have contributed to a better understanding of the role of CPAP in managing hypoxemic respiratory failure in COVID-19. Data on actual pressure levels delivered to each patient and the number of hours per day of CPAP could not be collected. It was also not possible to ascertain in all patients whether vital signs (SpO_2 , respiratory rate) and arterial blood gases were taken while on CPAP or while on NRM, hence a high rate of missing values. Patients with profound hypoxemia and high respiratory rate on CPAP may be exposed to self-induced lung injury. We attempted to collect the values for driving pressures immediately after intubation and positive expiratory pressure levels during CPAP therapy but these data were unfortunately only available in a few cases. This should be investigated in further studies.

Secondly, due to small sample size, the observed effect of CPAP in avoiding invasive mechanical ventilation within a sub-group of patients could be biased by concomitant treatments (drugs and/or prone positioning during spontaneous breathing) administered to spontaneously breathing-patients. However, in the multivariate analysis, corticosteroid treatment, the main therapy that has been shown to impact mortality [20], was not associated with the success of CPAP treatment. The absence of a control group does not allow us to make any firm conclusion on the role of CPAP in avoiding intubation. In addition, some patients treated with CPAP may simply have received higher FiO_2 because the seal of the mask is better and the O_2 flow higher as compared to patients on NRM: for example with a Boussignac™ CPAP, O_2 flow was usually set between 20 to 30 L/min to reach the target pressure of 5 to 10 cm H_2O . This could have contributed to their clinical improvement.

Third, there might be several selection bias. We chose to include all patients with findings highly suggestive of COVID-19 on thoracic CT scan among which only 79% had a positive PCR on respiratory samples. However, SARS Cov2 rt PCR on naso pharyngeal swabs is known to have an imperfect sensibility, and we considered that at the peak of the outbreak, alternative diagnosis were improbable [33]. The group of patients who did not need mechanical ventilation may have been less severe. This may be an important bias for their favourable outcome, which may not be due to the effect of CPAP only. This is suggested by the higher levels of SpO_2 at initiation of CPAP in the group of patients who improved compared with the group of patients who progressed to intubation. Response to CPAP could be used to identify patients

who do not require intubation despite being profoundly hypoxemic [34]. However, CPAP could also have worsened the condition of patients whose intubation was delayed. The high SAPS2 scores of the intubated patients in the study provide some evidence to this effect.

Fourth and finally, contamination of health care workers was not evaluated. Expired gases dispersion during CPAP seems to be limited if there is good mask interface fitting [35], but leaks do occur incidentally and NIV is considered an aerosol-generating procedure [23]. Potential benefit from face-mask CPAP should be weighed against the risk of contamination of health care workers, especially in settings where infection prevention and control precautions are difficult to maintain. Choosing the appropriate interface is critical to decrease leaks and minimize aerosolization and there may be some advantages to select full face masks [22, 36]. Helmet is another option but is more difficult to handle in a non-ICU setting [37].

The role of face-mask CPAP in managing acute hypoxemic respiratory failure in COVID-19 patients warrants further investigation in larger prospective studies and comparison with other ways to manage hypoxemic respiratory failure, such as high flow nasal oxygen cannula [14, 16, 17]. The simplicity and practicality of CPAP in a number of contexts, including massive patient influx and resource limited settings, is appealing [38]. However, the likely increased risk of contamination of health care workers, notably if personal protective equipment is inadequate, must be taken in account. CPAP could also be considered as a first-line respiratory support strategy in less hypoxemic patients without significant respiratory failure in association with other strategies to improve oxygenation, such as awake prone positioning [17, 26, 39–44].

Conclusion

We found that treatment with face-mask CPAP was feasible in a non-ICU environment and in the context of a massive influx of patients. In our situation, it was useful to post-pone intubation and to manage the flow of patient requiring invasive ventilation. We also found, that among patients who have low SpO₂ and /or signs of respiratory failure while on 15l/min O₂ via NRM more than one third eventually did not need invasive mechanical ventilation. Given the limitations of our study, the role of face-mask CPAP in managing patients with hypoxemic respiratory failure should be investigated in further research.

Supporting information

S1 Dataset.
(XLSX)

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