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SHORT COMMUNICATION

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Factors associated with mechanical ventilation in SARS-CoV-2 patients treated with high-flow nasal cannula oxygen and outcomes

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Abstract

Five percent of patients infected with SARS-CoV-2 require advanced respiratory support. The high-flow nasal cannula oxygenotherapy (HFNCO) appears to be effective and safe to reduce the need for mechanical ventilation. However, the factors associated with HFNCO failure as well as the outcomes of patients receiving this noninvasive respiratory strategy remain unclear. Thus, we performed this study to determine factors leading to intubation of SARS-CoV-2 patients treated with HFNCO and patients' outcomes. We retrospectively analyzed the medical charts of patients admitted in our ICU center for acute respiratory failure due to SARS-CoV-2 infection and who initially benefited from HFNCO, between September 1, 2020, and March 1, 2021. We included all adults patients who received HFNCO and compared two groups: those treated with HFNCO alone and those who failed HFNCO. Patients treated with HFNCO and secondarily limited to the use of mechanical ventilation were excluded from the analysis. Sixty-nine patients were included, 33 were treated with HFNCO alone and 36 failed HFNCO. We found more patients with shock in the HFNCO failure group ($p = 0.001$). The mean IGSII score was higher in the HFNCO failure group ($p < 0.001$). The minimum PaO_2/FiO_2 was lower in the HFNCO failure group ($p = 0.024$). The length of stay in ICU was higher in the HFNCO failure group ($p < 0.001$). The mean duration of HFNCO before intubation was 1.77 days. Six-week mortality was higher in the HFNCO failure group ($p = 0.034$). Ten patients had a complication during intubation. The HFNCO leads to reduce the intubation rate, the length of stay in ICU, and the mortality. Determining the factors associated with HFNCO failure is important to avoid complications following late intubation.

KEYWORDS

COVID-19, high-flow nasal cannula, intensive care unit, mechanical ventilation, SARS-CoV-2

1 | BACKGROUND

Infection with SARS-CoV-2 is associated with a clinical presentation ranging from asymptomatic or paucisymptomatic forms (80%) to hypoxemic forms requiring oxygen therapy (14%), and up to forms requiring more advanced respiratory support (5%).[1] Initially, the high-flow nasal cannula oxygenotherapy (HFNCO) was not used because of the potential virus aerosolization risk, however, in the absence of evidence of increased risk of contamination most societies allowed HFNCO.[2–4] Thus, the use of HFNCO led to a decrease in intubation rate and did not increase mortality.[3,5–7] Some studies found a decrease in the length of stay and a decrease in mortality for patients treated with HFNCO.[6,8] However, the use of HFNCO on patients not infected with SARS-CoV-2 and presenting acute respiratory failure is associated with greater mortality when HFNCO fails within 48 h after its initiation. [9] Therefore, we performed a study to determine the predictive factors of HFNCO failure and the outcome of patients treated with this respiratory support when infected with SARS-CoV-2.

2 | METHODS

We retrospectively analyzed the medical charts of patients admitted in our ICU center for acute respiratory failure due to SARS-CoV-2 infection and who initially benefited from HFNCO, between September 1, 2020, and March 1, 2021. Laboratory confirmation of SARS-CoV-2 was defined as a positive result of a nucleic acid amplification test of nasopharyngeal swabs. We included all adults patients who received HFNCO for at least 2 h and compared two groups: those treated with HFNCO alone and those who failed HFNCO. HFNCO failure was defined as the subsequent need for invasive mechanical ventilation. Patients treated with HFNCO and secondarily limited to the use of mechanical ventilation were excluded from the analysis. Intubation criteria were left at the discretion of physicians and most often consisted, over the duration of the study, in the persistence of hypoxemia associated with respiratory distress signs despite the use of HFNCO with FiO_2 greater than 80%. For each patient we collected demographic data, underlying diseases, clinical characteristics at admission, IGSII score, clinical course, and patients' outcomes. The groups were compared using a Student's *t* test and a Fischer's exact test for quantitative and qualitative variables, respectively. The study was approved by the Ethical Committee of Medicine Odontology and Pharmacy Faculties and Hospitals (University Hospital of Strasbourg) No. CE-2020-32.

3 | RESULTS

Sixty-nine patients were included, 33 were treated with HFNCO alone and 36 failed HFNCO. Three patients were treated with HFNCO and secondarily limited to the use of mechanical ventilation. These three patients were highly comorbid. The first patient was 59 years old and had a stage four emphysematous chronic obstructive pulmonary disease (COPD); the second was 76 years old and had high blood pressure, diabetes mellitus, Stage 4 renal disease, and ischemic heart disease; the last patient was 77 years old and had high blood pressure, diabetes mellitus, morbid obesity (body mass index [BMI] at 40), cirrhosis, and loss of autonomy. Patients' characteristics are presented in Table 1. The patients' mean age was 63.5 and 65.3 years in the HFNCO alone group and failure group, respectively. The patients were predominantly male and obese in both groups. Patients in the HFNCO alone group had less comorbidity without significant difference (odd ratio [OR] = 0.245 [0.0230; 1.435], $p = 0.148$). All patients were treated with dexamethasone on admission. For one patient, the prone position was used, but still required mechanical ventilation. For 27 patients, noninvasive ventilation was used, 18 (66.7%) were intubated. Among the clinical characteristics on admission, we found more patients with shock in the HFNCO failure group (OR = ∞ [2.507; ∞], $p = 0.001$). In addition, the mean IGSII score was higher in the HFNCO failure group ($p < 0.001$). The minimum PaO_2/FiO_2 was lower in the HFNCO failure group ($p = 0.024$). The length of stay in ICU was higher in HFNCO failure group ($p < 0.001$). The mean duration of HFNCO before use of mechanical ventilation was 1.77 days ±0.381, with a confidence level of 95% and the standard deviation was 1.15. Six-week mortality was higher in the HFNCO failure group (OR = 5.370 [1.067; 53.155], $p = 0.034$). Among the 36 patients with HFNCO failure, 10 (31.3%) had a complication during intubation, in particular: seven ventilation collapses, two hypoxic cardiac arrests, and one extreme bradycardia.

4 | DISCUSSION

The use of HFNCO avoided the need for intubation in 47.8% of the cases in our study. Several studies, mostly with smaller cohorts, found a decreased intubation rate of patients treated with HFNCO. However, the HFNCO failure rate ranges from 32% to 71.6%.[7,8,10–12] The differences in HFNCO failure could be explained by more frequent use of the prone position which improves SpO_2, PaO_2, and lower PCO_2, or noninvasive ventilation in combination with HFNO, which can be used in salvage therapy.[11,13] Indeed, in our study, the use of noninvasive ventilation in 27 patients allowed to avoid mechanical ventilation in 33.3% of cases.

In line with other studies, we found that patients with shock were significantly more intubated.[5,8,12] We also found a lower minimal PaO_2/FiO_2 in the HFNCO failure group. This association was described by other studies with fewer patients.[8,10] Rather than following the PaO_2/FiO_2, the use of the ROX index, the ratio of pulse oximetry (SpO_2)/FiO_2 to the respiratory rate, which was initially developed to predict HFNCO failure in hypoxemic patients, seems interesting.[14] Several studies evaluated the ROX index in SARS-CoV-2 infected patients with acute respiratory failure and treated with HFNCO. They found an association between a high ROX score within 24 h of HFNCO initiation and intubation rate.[8,11] However, Blez et al. single-center and the prospective study suggested that the monitoring of the respiratory rate is efficacious to predict the HFNCO

TABLE 1 Patients' demographics data, clinical characteristics and outcome

Patients' characteristics	HFNCO alone (%) *n* = 33 (47.8%)	HFNCO failure (%) *n* = 36 (52.2%)	*p*
Mean age (min–max)	63.5 (50–87)	65.3 (36–80)	0.435
Male	26 (78.8)	26 (72.2)	0.585
Mean BMI (min–max)	30.5 (21–45)	30.8 (21–43)	0.839
Underlying disease			
Chronic respiratory failure	4 (12.1)	9 (25.0)	0.224
Tobacco use	6 (18.2)	6 (16.7)	1
Chronic kidney disease	2 (6.1)	5 (13.8)	0.431
Chronic heart failure	5 (15.2)	4 (11.1)	0.728
Diabetes mellitus	11 (33.3)	16 (44.4)	0.460
Solid cancer	2 (6.1)	3 (8.3)	1
Blood cancer	2 (6.1)	3 (8.3)	1
Solid-organ transplantation	0 (0.0)	1 (2.8)	1
Immunosuppressive therapy	1 (3.0)	4 (11.1)	0.359
Absence of underlying disease	7 (21.2)	2 (5.6)	0.148
Clinical characteristics at admission			
Days from symptom onset to hospitalization (min–max)	9.2 (1–23)	7.8 (1–22)	0.270
Chest CT-scan damage >50%	12 (36.4)	17 (47.2)	0.465
Acute kidney failure	4 (12.1)	11 (28.3)	0.083
Acute heart failure	4 (12.1)	3 (8.3)	0.702
Acute liver failure	1 (3.0)	1 (2.8)	1
Acute neurological failure	0 (0.0)	0 (0.0)	1
Acute circulatory failure	0 (0.0)	10 (27.8)	0.001
Mean IGSII score (min–max)	29.5 (12–50)	39.5 (22–62)	<0.001
Clinical course			
Minimal PaO_2/FiO_2 (mmHg) with HFNCO (min–max)	112.5 (53–344)	85.3 (36–220)	0.024
Duration of ICU stay (days) (min–max)	6.4 (1–12)	19.6 (2–54)	<0.001
Death at 1 week	1 (3.03)	2 (5,6)	1
Death at 6 weeks	2 (6.06)	12 (33.3)	0.034

Abbreviations: BMI, body mass index; HFNCO, high-flow nasal cannula oxygenotherapy; ICU, intensive care unit.

failure, in particular in the first hour and that the monitoring of other respiratory parameters like the ROX score did not provide any value in addition to the respiratory rate.[15] The presence of shock and the respiratory rate is among the five variables, together with the Glasgow coma scale, the number of comorbidities, and the age, present in the nomogram proposed by Liu et al. to predict the failure of non-invasive respiratory strategy.[12]

We found a higher IGSII score in the HFNCO failure group and we noticed that the HFNCO mean duration before failure was 1.77 days. Other studies also found that HFNCO failure occurs early and usually within 48 h.[8,11] The IGSII score assessing the severity within the first 24 h of patients admitted in ICU appears to be an interesting predicting factor for HFNCO failure.

We found that patients successfully treated with HFNCO had a shorter length of stay in ICU. However, the impact of HFNCO on the length of stay in ICU diverges in the literature.[6,8,11] These differences could be explained by a higher frequency of patients presenting less severe infection or by the achievement of early therapeutic limitation in patients treated with HFNCO in our cohort. However, the patients in the HFNCO alone group still presented an average PaO_2/FiO_2

ratio inferior to 150, testifying to the severity of their pneumonia. Thus, the ICU length of stay reduction in SARS-CoV-2 patients treated with HFNCO seems particularly important during the current pandemic.

Regarding mortality, we found greater mortality at six weeks in the HFNCO failure group (OR = 5.370 [1.067; 53.155], $p = 0.034$). Studies with smaller cohorts found a decrease in mortality in patients treated with HFNCO.[6,8,11] The higher mortality in the HFNCO failure group in our cohort could be explained by a high rate of complications following the intubation. We found 19.4% ventilation collapse, which is similar to what is found in patients not infected with the SARS-CoV-2, which found a ventilation collapse in 9.6%–29% of cases.[16,17] Cardiac arrest occurred in 5.6% of patients in our study, which is a higher rate than in patients uninfected with SARS-CoV-2 which is of the order of 2%.[18] These complications could be related to the delay of intubation.[9] Indeed, Zirpe et al. found better survival in patients with SARS-CoV-2 when they were intubated early.[19] However, other studies did not find excess mortality depending on the timing of intubation.[7,20]

Despite its retrospective and monocentric character, our study provides new insights into the understanding of HFNCO usage in severe SARS-CoV-2 pneumonia. Thus, the HFNCO leads to reduce the intubation rate, the length of stay in ICU, and the mortality at 6 weeks. However, there were a large number of complications following intubation, which required us to determine factors associated with HFNCO failure. The presence of shock, high IGSII score, and low PaO_2/FiO_2 seem to be good markers that should be evaluated through a prospective and multicenter study.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTION

Xavier Leroux collected and analyzed data and revised the manuscript. Maud Schock wrote the manuscript, collected data, analyzed data, and revised the manuscript. Olivier Augereau collected data and revised the manuscript. Henry Lessire collected data and revised the manuscript. Charles Bouterra collected data and revised the manuscript. Lounis Belilita collected data and revised the manuscript. Pierre Rerat collected data and revised the manuscript. Antonio Alvarez collected data and revised the manuscript. Martin Martinot collected data, analyzed data, and revised the manuscript. Victor Gerber designed the study, wrote the manuscript, collected and interpreted data, and revised the manuscript. All authors read and approved the final version of the paper.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

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