Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Short communication

High-flow cannula for frail patients with SARS-CoV-2 infection non-eligible for intensive care unit management

L. Bouetard a,b,1, T. Flamand c,1, D. Vignes a, A. Robert e, R. Sterpu a, L. Lemonnier c, M. Mion d, V. Gerber e, S. Abgralla b, M. Martinot c,⇑

a Infectious Diseases Department, Antoine Beclere University Hospital, APHP, Paris, France
b Université Paris-Saclay, UVSQ, INSERM U1018, CESP, Le Kremlin-Bicêtre, France
c Infectious Diseases Department, Hôpitaux Civils de Colmar, Colmar, France
d Geriatrics Department, Antoine Béclère University Hospital, APHP, Paris, France
e Intensive Care Department, Hôpitaux Civils de Colmar, Colmar, France

Article history:
Received 29 August 2022
Revised 22 October 2022
Accepted 18 November 2022
Available online 24 November 2022

Keywords:
COVID-19
High-flow oxygen
High-flow nasal cannula
Elderly
Tocilizumab

ABSTRACT

Objectives: High-flow nasal cannula (HFNC) was widely used during the COVID-19 pandemic in intensive care units (ICU), but there is no recommendation for elderly patients non-eligible for ICU management. We aimed to describe the outcomes of HFNC treatment in patients with COVID-19 who are not eligible for ICU management.

Methods: Retrospective bicentric cohort study performed between September 1, 2020 and June 30, 2021 in two infectious diseases departments of Colmar Hospital and Antoine Beclere University Hospital, France.

Results: Sixty-four patients were treated with HFNC: 33 in Colmar and 31 in Beclere hospital (median age: 85 years; IQ, 82–92). Of these, 16 patients survived (25%). Surviving patients had a lower Charlson comorbidity index score than deceased patients (five vs six; p = 0.02).

Conclusions: Despite a high death rate, with survivors being younger and having fewer comorbidities, HFNC is an easy tool to implement in non-ICU wards for the frailest patients.

1. Background

Coronavirus disease 2019 (COVID-19) is a polymorphic disease that mainly affects the respiratory tract [1], with a risk for acute respiratory distress syndrome (ARDS) associated with a need for high amounts of oxygen. Mechanical ventilation (MV) was favored for critical COVID-19 cases during the first wave. Elderly patients and patients with comorbidities are the most affected by mortality [1,2], but they were usually not eligible for intensive care unit (ICU) management [2], especially those with ARDS due to its poor prognosis in older patients. New methods of oxygen delivery rapidly emerged, especially high-flow nasal cannula (HFNC). HFNC is a form of respiratory support that delivers high flow, heated, and humidified controlled concentrations of oxygen via the nasal route. This method was implemented in ICUs [3] to lower the pressure on ICU beds by avoiding unnecessary MV and to reduce the time spent in ICUs. We hypothesized that HFNC could be beneficial in non-ICU wards for patients who are not eligible for treatments in the ICU. Since September 2020, HFNC has been implemented in infectious diseases wards for elderly or very frail patients infected with COVID-19 and not eligible for treatment in the ICU. Effectiveness of HFNC and risk factors for poor outcomes were assessed.

2. Methods

This study was conducted in two French infectious diseases wards that regularly used HFNC for patients not eligible for treatment in ICUs at the Hôpitaux Civils de Colmar (HCC) and at Antoine Beclere University Hospital (ABUH) between September 1, 2020 and June 30, 2021. Patients infected with systemic acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) confirmed by a positive test to reverse transcriptase polymerase-chain-reaction (RT-PCR) test from a nasopharynx swab, who were not eligible for admission to ICUs due to age and/or comorbidities, were considered for HFNC. The non-eligibility for ICU was either based on a collegial discussion between the physicians in charge of the patients and the ICU physicians or on the patient’s choice.

In our wards, the criterion for implementing HFNC was the necessity for oxygen by mask either over 6 to 10 L/min or in case

https://doi.org/10.1016/j.idnow.2022.11.004
of poor tolerance to classic oxygen therapy over 6 L/min with a high-concentration mask. HFNC was initiated with a gas flow rate of 50/60 L/min (HCC/ABUH), a fraction of oxygen (FiO₂) of 0.7/1.0, and at a temperature of 37 °C with a nasal cannula of suitable size to maintain oxygen saturation over 92%–95%. High-flow oxygen was continued until it could be switched to standard oxygen therapy after a progressive decrease in the gas flow rate to 30/40 L/min and in FiO₂ to 0.3/0.4 with oxygen saturation maintained at more than 95% or until death.

Demographic and clinical data were retrieved from medical records, the Charlson comorbidity index (CCI) was calculated, and the frailty score was determined using the Clinical Frailty Scale (CFS), which defines nine classes from Very Fit to Terminally Ill [4]. Details of SARS-CoV-2 infection chest computed tomography (CT) scans, laboratory data, and medical prescriptions were collected and analyzed. Primary outcomes were survival and hospital discharge or death.

Variables are presented as medians, together with the first and third quartiles (Q1–Q3). Categorical data are presented as the number of missing values and absolute and relative counts. Continuous variables were compared using Wilcoxon test, while categorical data were compared using chi-square test or Fisher’s exact test, as appropriate.

3. Results

Between September 2020 and June 2021, 64 patients (35 females and 29 males) were hospitalized for SARS-CoV-2 pneumonia and were treated with HFNC in our wards. Clinical details and outcomes are shown in Table 1. Sixteen patients survived (25%) — 6 in HCC and 10 in ABUH — while 48 died (75%).

All patients benefited from standard care (SOC) treatments for COVID-19 comprising antipyretic therapy, prevention of thrombotic complications, and dexamethasone (6 mg/day for 10 days). Seventeen patients (27%) received intravenous infusions of tocilizumab (8 mg/kg) at the time of significant increases in oxygen requirement. Infusions were repeated in ABUH 12 to 24 hours later. Of the patients who received tocilizumab, 7 out of 17 (41%) survived. When survivors and non-survivors were compared, the CCI was significantly lower in survivors than in non-survivors (Table 1). All 48 patients who died had ARDS, but seven of them died from other causes: two patients experienced a sudden death, three had an identified superinfection (one had Staphylococcus aureus bacteremia, one had Escherichia coli bacteremia with septic shock, and one had Pneumocystis jirovecii infection), one had a hematological malignancy with tumor lysis, and one presented end-stage cardiorenal syndrome.

4. Discussion

Mortality among elderly and frail patients infected with SARS-CoV-2 is very high. Accordingly, there is an urgent clinical need for therapies that may improve the prognosis of these patients. HFNC seems to improve the prognosis of patients aged over 80 years eligible for admission in ICUs [5]. Programs of HFNC were implemented in conventional medical wards for critically ill patients who may benefit from admission to ICUs, thereby saving resources for ICUs [6]. Few studies have evaluated the use of HFNC in elderly patients not considered eligible for admission to ICU, but HFNC appears to improve survival and to lower maximal breathing frequency compared with conventional oxygen therapy with high-concentration masks [7,8]. However, the number of patients treated in these two studies was low (41 and 9 patients, respectively). Furthermore, two other retrospective studies performed by Lagier et al. on 44 patients with a median age of 84 and a median CCI of 7, and by van Steenkiste et al. on 32 patients with a median age of 79 and a median frailty score of 4, showed quite similar survival rates: 36.4% and 25%, respectively [9,10]. Conducted at two centers and comprising a large cohort of 64 patients, the findings of the present study demonstrate that HFNC is easy to implement and to monitor in conventional medical wards. Since the implementation of HFNC only necessitated a short one-hour training of nurses and physicians and allowed for a monitoring similar to that of other patients not on HFNC, it seemed easy to implement in these patients not eligible to ICU management.

We were also able to compare our results with those of the HCC ICU wards that used HFNC over a similar period. During the same period, a study conducted in the HCC ICU ward demonstrated that among 69 younger patients with a median age of 64 years treated with HFNC, 30 patients (43.5%) were successfully treated with HFNC alone without MV and/or death [11]. Findings of this study show that even in younger patients, HFNC implementation for critically ill patients with COVID-19 is associated with a high rate of failure. A previous study conducted at ABUH during the first wave of the pandemic reported that among 296 hospitalized patients, 30 patients aged over 70 years (median age 83 years, IQR 79–86 years) were treated with corticosteroids and required an oxygen flow of at least 9 L/min. When the required oxygen flow was 12 L/min or more, 6 out of 25 patients (24%) treated with corticosteroids survived [12]. Even though the present study included slightly older patients (median age 85 years, IQR 82–92 years), survival was similar between our study and the previous study at the ABUH.

In the present study, the risk factors for poor outcomes were difficult to assess due to the low number of patients included. However, the CCI was lower in survivors; thus, the survivors tended to be younger and with fewer comorbidities especially renal insufficiency and cancer, which could be an important factor in selecting eligible patients for HFNC in medical wards. Interestingly, CCI has already been reported to be useful as a prognosis marker in cases of COVID-19 in a previous study on HFNC in a large Danish population cohort [13] and in patients with acute respiratory failure of any cause who received provided HFNC in general wards [14]. The frailty score was not associated with death in our analysis, but previous studies reported that the use of a clinical frailty score was probably better than using age alone in predicting the outcomes of old patients [2]. Regarding biomarkers and chest CT scans, none were statistically different between survivors and non-survivors.

HFNC also has undeniable comfort advantages with a reduction in the severity of dyspnea and a decreased respiratory rate due to reduced respiratory distress, possibly explaining the higher survival rate with HFNC than with high-concentration mask. However, no scale was used to measure the comfort of patients with HFNC in this study. Thus, the comfort related to HNCF rather derived from the medical teams and nurses’ overall impression. However, studies focusing on patient’s comfort reported similar improvement [13,15,16]. Reduction in dyspnea and respiratory distress could not only be attributed to direct improvement of hypoxemia but also to the heating and humidification of inspired gas, which prevents thick secretions and subsequent atelectasis. It could also be attributed to the low levels of positive end expiratory pressure (PEEP) generated by high gas flow rates and flushing of upper-airway dead space [8]. HFNC also allows patients to maintain oral nutrition and hydration. Anxiety and stress also appeared to be reduced. This notion of comfort is also important to help healthcare workers better adapt as the management of death and critical conditions are a major occupational hazards for people working in ICUs. Accordingly, the use of HFNC may reduce emotional fatigue, depression, anxiety, and stress [17].
Finally, although all patients benefited from standard-of-care treatments, we observed a trend towards increased survival in patients treated with tocilizumab; however, this did not reach statistical significance. In France, tocilizumab was recommended in cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort. Int J Epidemiol 2020;49(5):1468–81. https://doi.org/10.1093/ije/dya016

The main limit of our study is its retrospective, non-comparative, bicentric design with a small number of patients, preventing multivariate analysis. To validate the potential effect of HFNC on mortality, a comparative study with conventional oxygen therapy is necessary.

5. Conclusion

HFNC is an interesting option for patients with severe SARS-CoV-2 infection and is easy to implement in non-ICU medical wards, although more precise criteria based on comorbidity scores rather than age alone may help select patients most likely to benefit from HFNC.

Ethics statement

The Ethics Committee of Medicine Odontology and Pharmacy Faculties and Hospitals (University Hospital of Strasbourg; N ° CE-2022-101) approved this study under a consent waiver.

Authors’ contribution

MM, TF, LB, and SA conceived and designed the study, analyzed the data, and drafted the manuscript. MM, TF, LB, SA, and VG reviewed the manuscript for content. All authors collected and analyzed the data. All authors read and approved the final version of the manuscript.

Funding

None to report.

Conflicts of Interest

The authors report no conflict of interest.

References

[1] Reilev M, Kristensen KB, Pottegard A, Lund LC, Hallas J, Ernst MT, et al. Characteristics and predictors of hospitalization and death in the first 1122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort. Int J Epidemiol 2020;49(5):1468–81. https://doi.org/10.1093/ije/dya016.
[2] Prendini V, Tiseo G, Falcone M. Caring for older adults during the COVID-19 pandemic. Clin Microbiol Infect 2022;28(6):785–91.
[3] Demoule A, Veillard Baron A, Darmon M, Beurton A, Géri G, Voisriot G, et al. High-flow nasal cannula in critically ill patients with severe COVID-19. Am J Respir Crit Care Med 2020;202(7):1039–42.
[4] Abraham P, Courvoisier DS, Annweiler C, Lenoir C, Millien T, Dalmaz F, et al. Validation of the clinical frailty score (CFS) in French language. BMC Geriatr 2019;19(1). https://doi.org/10.1186/s12877-019-1215-z.

[5] Oba S, Altinay M, Salkaya A, Turk HS. Evaluation of the effect of clinical characteristics and intensive care treatment methods on the mortality of covid-19 patients aged 80 years and older. BMC Anesthesiol 2021;21(1):291. https://doi.org/10.1186/s12871-021-01511-d.

[6] Issa I, Soderberg M. High-flow nasal oxygen (HFNO) for patients with Covid-19 outside intensive care units. Respir Med 2021;187:106554. https://doi.org/10.1016/j.rmed.2021.106554.

[7] Hacquin A, Perret M, Manckoundia P, Bonniaud P, Beltramo G, Georges M, et al. High-flow nasal cannula oxygenation in older patients with SARS-CoV-2-related acute respiratory failure. J Clin Med 2021;10(16):3515.

[8] Willems RAL, Spaetgens B, Conemans LH, Wesseling G, Stehouwer CDA, Alnima T. High flow nasal cannula in older vulnerable COVID-19 patients: A missed opportunity? Respir Med 2021;189: https://doi.org/10.1016/j.rmed.2021.106666.

[9] Lager J-C, Amrane S, Mailhe M, Gainnier M, Arlotti S, Gentile S, et al. High-flow oxygen therapy in elderly patients infected with SARS-CoV2 with a contraindication for transfer to an intensive care unit: A preliminary report. Int J Infect Dis 2021;108:1–3.

[10] van Steenkiste J, van Herwerden MC, Weller D, van den Bout CJ, Ruiter R, den Hollander JG, et al. High-flow Nasal Cannula therapy: A feasible treatment for vulnerable elderly COVID-19 patients in the wards. Heart Lung 2021;50 (5):654–9.

[11] Leroux X, Schock M, Augereau O, Lessire H, Bouterra C, Belilila L, et al. Factors associated with mechanical ventilation in SARS-CoV-2 patients treated with high-flow nasal cannula oxygen and outcomes. J Med Virol 2022;94 (3):1236–40.

[12] Beaumont A-L, Vignes D, Sterpu R, Bussone G, Kansau J, Pignon C, et al. Factors associated with hospital admission and adverse outcome for COVID-19: Role of social factors and medical care. Infect Dis Now 2022;52(3):130–7.

[13] Christensen DM, Strange JE, Gislason G, Tarp-Pedersen C, Gerds T, Fosbøl E, et al. Charlson Comorbidity Index Score and risk of severe outcome and death in Danish COVID-19 patients. J Gen Intern Med 2020;35(9):2801–3.

[14] Colombo SM, Scaravilli V, Cortegeani A, Corcione N, Guzzardella A, Baldini L, et al. Use of high flow nasal cannula in patients with acute respiratory failure in general wards under intensivists supervision: a single center observational study. Respir Res 2022;23(1). https://doi.org/10.1186/s12931-022-02090-y.

[15] Rochwerg B, Granton D, Wang DX, Helviz Y, Einav S, Frat JP, et al. High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: a systematic review and meta-analysis. Intensive Care Med 2019;45(5):563–72. https://doi.org/10.1007/s00134-019-05590-5.

[16] Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. Respir Care 2010;55(4):408–13.

[17] Chahraoufi K, Biyo A, Cras E, Gilles F, Laurent A, Valache B, et al. Psychological experience of health care professionals in intensive care unit: a qualitative and exploratory study. Ann Fr Anesth Reanim 2011;30(4):342–8. https://doi.org/10.1016/j.anfar.2011.01.020.

[18] Ouissa R, Le Guillou C, Broudic M, Markowicz S, Curlier E, Roger P-M. Successful high flow nasal cannula therapy for severe COVID-19 pneumonia is associated with tocilizumab use. Infect Dis Now 2022;52(3):145–8.