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## High-flow oxygen therapy in elderly patients infected with SARS-CoV2 with a contraindication for transfer to an intensive care unit: A preliminary report

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26 **Abstract:**

27 **Objectives:** In a conventional hospital ward, we used high-flow nasal oxygen (HFNO) to treat  
28 elderly COVID-19 patients non eligible for intensive care unit transfer.

29 **Methods:** This study was conducted in the Institut Hospitalo-Universitaire Méditerranée  
30 Infection, Assistance Publique-Hôpitaux de Marseille (AP-HM), France. We used high-flow  
31 nasal oxygen (HFNO) in our conventional infectious disease ward from 15 September 2020 for  
32 elderly patients non eligible for intensive care unit transfer.

33 **Results:** Of the 44 patients (median age 83 years (57–94), mean: 80.25), 61.4% (27/44) were  
34 men. The median Charlson score was 7 (1-15). The median of the NEWS-2 score upon  
35 admission was 8 (3-11) and was 10 at the time of initiation of HFNO. The median PaO<sub>2</sub>/FiO<sub>2</sub>  
36 ratio was 103 (71–151) prior to HFNO initiation. Among the 44 patients, 16 patients (36.4%)  
37 had been weaned from HFNO, and 28 patients had died (63.6%).

38 **Conclusions:** In this preliminary report, we observed that HFNO saved the lives of one-third of  
39 elderly COVID-19 patients who would have systematically died.

## 40 **Introduction**

41 COVID-19 has emerged as world pandemic that has caused more than 2.7 million deaths  
42 and has infected 124 million people worldwide (John Hopkins University, 2021). Severe  
43 infections occur in patients over 65 years of age who are suffering from comorbidities and most  
44 deaths have occurred in patients over 80 years of age (Lagier et al. 2020). The most common  
45 complication is severe pneumonia with acute respiratory distress syndrome requiring admission  
46 to intensive care units which availability is limited in a pandemic context.

47 There is uncertainty in the management of COVID-19 between the need to conduct  
48 therapeutic trials and the need to focus on the quality of care. A considerable difference has  
49 emerged in the way in which Asian and Western countries have managed the pandemic,  
50 resulting in a conflict between a pragmatic approach and an almost virtual approach to a  
51 previously unknown disease. This may largely explain the higher mortality from COVID-19 in  
52 Western countries such as France at the beginning of the outbreak, where some patients were  
53 unfortunately offered either a therapeutic trial or the prospect of doing nothing and staying at  
54 home, to await the onset of dyspnoea (Lagier et al. 2020). However, patient management was  
55 considerably improved by the quality of care when an early diagnosis was reached (Risch et al.  
56 2020), when we evaluated “happy hypoxemia” and observed lesions by performing low-dose CT  
57 (Lagier et al. 2020, Brouqui et al. 2020), and when we detected coagulation disorders by  
58 measuring D-dimers independently of any antiviral treatment, regardless of whether they were  
59 are evaluated by a randomised clinical trial (Lagier et al. 2020). This pragmatic approach  
60 allowed us to maintain very low mortality in our institute (Lagier et al. 2020), as well as in our  
61 intensive care facility (<15%, personal data) (Lagier et al. 2020).

62 Nevertheless, one weak point remained the management of patients with comorbidities  
63 and/or who were of an age that did not allow them to be transferred to intensive care. For these  
64 patients non eligible for an ICU but who presented with refractory hypoxemia not responding to

65 conventional oxygen support, we used high-flow nasal oxygen (HFNO) in our conventional  
66 infectious disease ward from 15 September 2020. Here, we report the use of HFNO to manage  
67 these SARS-CoV2 patients.

## 68 **Material and Methods**

### 69 **Patients**

70 This study was conducted in the Institut Hospitalo-Universitaire Méditerranée Infection,  
71 Assistance Publique-Hôpitaux de Marseille (AP-HM). As previously described, we proposed  
72 early massive screening and standardised management of the patients in the day-care hospital or  
73 in one of the infectious diseases wards of our hospital (75 beds). From 15 September 2020, we  
74 were equipped with HFNO (Airvo2<sup>®</sup>, Fisher and Paykel Healthcare, Villebon sur Yvette,  
75 France) which became a standard therapy for acute hypoxemic non-hypercapnic respiratory  
76 insufficiency. Data were retrospectively collected and analysed from 15 September to 1  
77 December 2020. Severity was assessed using the National Early Warning Score adapted to  
78 COVID-19 patients (NEWS-2) as well as the Charlson score, as previously described (Liao et al.  
79 2020, Charlson et al. 1987).

### 80 **Inclusion criteria:**

81 Patients had to have been not eligible for an ICU transfer due to their age and/or severe  
82 comorbidities but, prior to their infection with COVID-19, had to be living independently at  
83 home. The decision for beginning HFNO was systematically taken by both infectious disease  
84 and ICU physicians.

### 85 **Ethics**

86 The study was conducted in the Institut Hospitalo-Universitaire (IHU) Méditerranée  
87 Infection (<https://www.mediterranee-infection.com/>), Assistance Publique-Hôpitaux de Marseille  
88 in the south of France. Data were collected retrospectively from the routine care setting using the  
89 hospital's electronic health recording system. According to European General Data Protection

90 Regulation No 2016/679, patients were informed of the potential use of their medical data and  
91 that they could refuse that their data be used. The analysis of collected data followed the MR-  
92 004 reference methodology registered under No. 2020-152 in the AP-HM register. The  
93 noninterventional retrospective nature of the study was approved by our institutional review  
94 board committee (Mediterranée Infection No.: 2020-021).

## 95 **Results**

96 Between 14 September 2020 and 1 December 2020, 44 patients were treated using 24  
97 hours a day HFNO. Patients were fed normally. One patient who died, had a potential  
98 contraindication (hypercapnia) for the use of HFNO, but the indication was decided jointly with  
99 ICU specialists because of absence of other therapeutics with the objective of increased comfort  
100 of the patient. Of the 44 patients, the median age of patients treated with HFNO was 83 years  
101 (57–94, mean: 80.25), and 61.4% (27/44) were men (**Table 1**). Patients were admitted to our  
102 ward within a median of seven days (1-14) after the first COVID-19 symptoms appeared. The  
103 median Charlson score was 7 (1-15) and only two patients had a score < 4. In the medical history  
104 of these two patients, one suffered from Down syndrome with obstructive sleep apnoea and  
105 obesity, and the other had polycythaemia complicated by acute pulmonary embolism. The  
106 median of the NEWS-2 score [2] upon admission was 8 (3-11) and was 10 at the time of  
107 initiation of HFNO. The median time from admission to HFNO initiation was three days (0–9  
108 days). The mean level of oxygen flow before initiation of HFNO was 12.7 L/min (7L/min to  
109 15L/min). The median PaO<sub>2</sub>/FiO<sub>2</sub> ratio was 103 (71–151) prior to HFNO initiation. C-reactive  
110 protein ranged from 28 to > 350 mg/L (mean of 146 mg/L). Among the 44 patients, 16 patients  
111 (36.4%) had been weaned from HFNO, and 28 patients had died (63.6%). Of the 16 patients who  
112 were weaned, the mean duration of HFNO treatment was 10 days (4-25 days). Ten of these 16  
113 patients were transferred to a rehabilitation unit, three were transferred in other hospitalization  
114 wards and three returned at home or to their retirement home.

115 **Discussion**

116 Here, we demonstrate that HFNO can be used as oxygen therapy supportive care for  
117 COVID-19 infection, outside the ICU, as recently highlighted in another French cohort (Guy et  
118 al. 2020). The specificity of our cohort is the severity of our patients non eligible for transfer to  
119 the ICU. In contrast to one recent report (Guy et al. 2020), we demonstrated that this technique  
120 may be effective in elderly patients and/or in patients with many comorbidities highlighted by an  
121 increased Charlson score, and who are contraindicated for an ICU transfer. Despite this, more  
122 than a third of such patients who would die in all cases without HFNO, were saved. In addition,  
123 patient comfort was optimised, as previously described.

124 This approach taken was pragmatic, focusing on improving the quality of care and  
125 outside of any randomised trial which would have been entirely unethical, given the severity of  
126 our patients' conditions and which is not useful in the context of an emerging pandemic, as  
127 previously described (Frieden et al. 2017). We chose a step-by-step implementation of our  
128 therapeutic management strategy. From the beginning of the disease, we decided to test patients  
129 at an early stage and on a massive basis, using PCR (Lagier et al. 2020). Secondly, we proposed  
130 the use of an antiviral treatment, followed by anticoagulation treatment and anti-inflammatory  
131 treatment for late stages of COVID-19 infections (Lagier et al. 2020). The use of HFNO is a new  
132 step in the care of these patients, further reducing mortality. Regarding the entire management of  
133 COVID-19 patients and to avoid the use of such techniques, the earliness of the diagnosis and  
134 the management remains the key. Some authors have reported that the use of supplemental  
135 oxygen in prehospital care can play a role to reduce risk of hospitalization and death  
136 (McCullough et al. 2021, Mc Cullough et al. 2020). Close monitoring is required for these  
137 patients (McCullough et al. 2021, Mc Cullough et al. 2020). In our experience, we prefer initiate  
138 oxygen supplementation during hospitalization.

139           This preliminary report demonstrated the contribution of HFNO for the management of  
140 elderly patients contraindicated for an ICU transfer. Future studies including larger number of  
141 patients and in depth clinical analysis will be interesting to confirm the contribution of HFNO in  
142 elderly COVID-19 patients. Issues to be addressed in the future will include a) optimising patient  
143 selection and being able to start HFNO earlier in order to increase the proportion of survivors; b)  
144 performing a long-term follow-up of elderly COVID-19 infected patients treated with HFNO.

145 **Table 1: Baseline characteristics of the 44 patients**

	N (%)
Age (Mean, Median)	80.25y (83y)
<65 y	3 (6.8%)
65-75y	7 (15.9%)
75-85	24 (54.6%)
>85y	10 (22.7%)
Charlson score	
1-5	9 (20.5%)
6-8	32 (72.7%)
>=9	3 (6.8%)
NEWS-2 score (admission)	
<= 3	4 (9.1%)
4-6	8 (18.2%)
7-10	27 (61.4%)
>10	5 (11.3%)
NEWS-2 score (at the time of HFNO initiation)	
<= 3	0
4-6	1 (2.3%)
7-10	22 (50%)
>10	21 (47.7%)

147 **Conflicts of interest**

148 The authors have no conflicts of interest to declare.

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