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## Correspondence

**High flow nasal cannula in older vulnerable COVID-19 patients: A missed opportunity?**

## ARTICLE INFO

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## Dear Editor,

We read with great interest the article by Issa and Söderberg [1], about how high flow oxygen through nasal cannula (HFNC) is feasible and efficient for patients with COVID-19 outside the ICU and therefore saves resources within the ICU, and the article by Ferrer et al. [2], in which they show the ROX index predicts HFNC success on the one hand and that HFNC successfully prevents endotracheal intubation (ETI) and death in patients with COVID-19. Both articles allow to take a moment to further reflect on the use of HFNC in patients with COVID-19 and in times of limited healthcare resources, especially in those who are older, vulnerable and/or frail.

It is undisputed that our older population is among the highest risk groups of poor outcome. Despite the tremendous success of the currently used vaccines, there is a clear unmet need to improve the management of older individuals with severe COVID-19 for various reasons. First, because of the emerging debates about waning vaccine immunity, failure to deliver vaccines to disadvantaged populations, and the fact that continued outbreaks are expected and indeed observed in larger population if vaccine efficacy does not reach 100%.

Apart from well-known risk factors for mortality and functional decline in older individuals, it is conceivable that decisions that intended to alleviate shortages of limited healthcare resources, such as ICU beds and mechanical ventilation capacity played an important role in further increasing mortality rates in older individuals [3]. As oxygen treatment remains the backbone of supporting critically ill COVID-19 patients, for older patients who are considered non-eligible for ETI, this also means that they may be withheld from other treatment than conventional oxygen delivery options.

We would like to grab the opportunity to share our promising experience with HFNC. However, for vulnerable patients who are considered not eligible for ETI or have a do-not-intubate order (DNI), HFNC may offer a rescue strategy in case of failure of conventional oxygen therapy (COT).

Generally, HFNC seems to reduce the need for invasive ventilation in patients with acute hypoxemic respiratory failure without impacting mortality [4]. However, evidence supporting the use of HFNC in hospitalized older COVID-19 patients with respiratory failure remains limited [1,2,5–8]. Anticipating shortages and providing optimal care for

older patients considered non-eligible for ETI, we have conducted a proof-of-principle study to compare the effect of HFNC with COT on 30-day survival (primary outcome), breathing frequency and peripheral oxygen saturation (secondary outcomes) in older patients with severe COVID-19.

We conducted a single center observational study. Patients with COVID-19 and respiratory insufficiency, non-eligible for mechanical ventilation, were included. Respiratory insufficiency was defined as needing a minimum flow of 10 L O<sub>2</sub> using Venturi or non-rebreathing mask to achieve a peripheral oxygen saturation (SpO<sub>2</sub>) of  $\geq 92\%$ . Patients were deemed non-eligible for mechanical ventilation due to comorbidities, frailty, or own preference. The patients receiving HFNC were retrospectively matched (based on age, Charlson Comorbidity Index (CCI) and Clinical Frailty Scale (CFS)) with controls treated with COT. Main exclusion criteria were use of immunosuppressive agents, COPD GOLD III/IV, and CFS > 6.

All patients were treated according to the prevailing standard of care consisting of dexamethasone, antibiotics and thromboprophylaxis. The target SpO<sub>2</sub> was set at  $\geq 92\%$ , and the fraction of inspired oxygen was adjusted accordingly. We refer to the Supporting Information for a full description of the study population and methods.

Twenty-three patients (9 receiving HFNC and 14 controls) with proven COVID-19 and respiratory insufficiency were included. Mean age was 75 years (SD 3.69) in the HFNC group and 78 years (SD 4.46) in the COT group. 55% and 71% of the patients were male in the HFNC group and COT group, respectively. The mean CCI was 5 in both groups. The CFS was 4 in 33% of the HFNC group and 36% of the COT group. All patients received dexamethasone, antibiotics and thromboprophylaxis. Three patients in the HFNC group additionally received tocilizumab due to alterations in guidelines. The baseline characteristics did not significantly differ between both groups (see Supporting Information).

Fig. 1A shows the 30-day survival, demonstrating a striking and statistically significant difference between HFNC and COT (89% vs. 29%,  $p$ -log-rank = 0.009). Fig. 1B and C shows that the maximal breathing frequency was significantly lower in the HFNC group (Fig. 1B,  $p < 0.001$ ), although no difference was observed in the maximal SpO<sub>2</sub> (Fig. 1C).

HFNC is a treatment modality that should be applied in the older

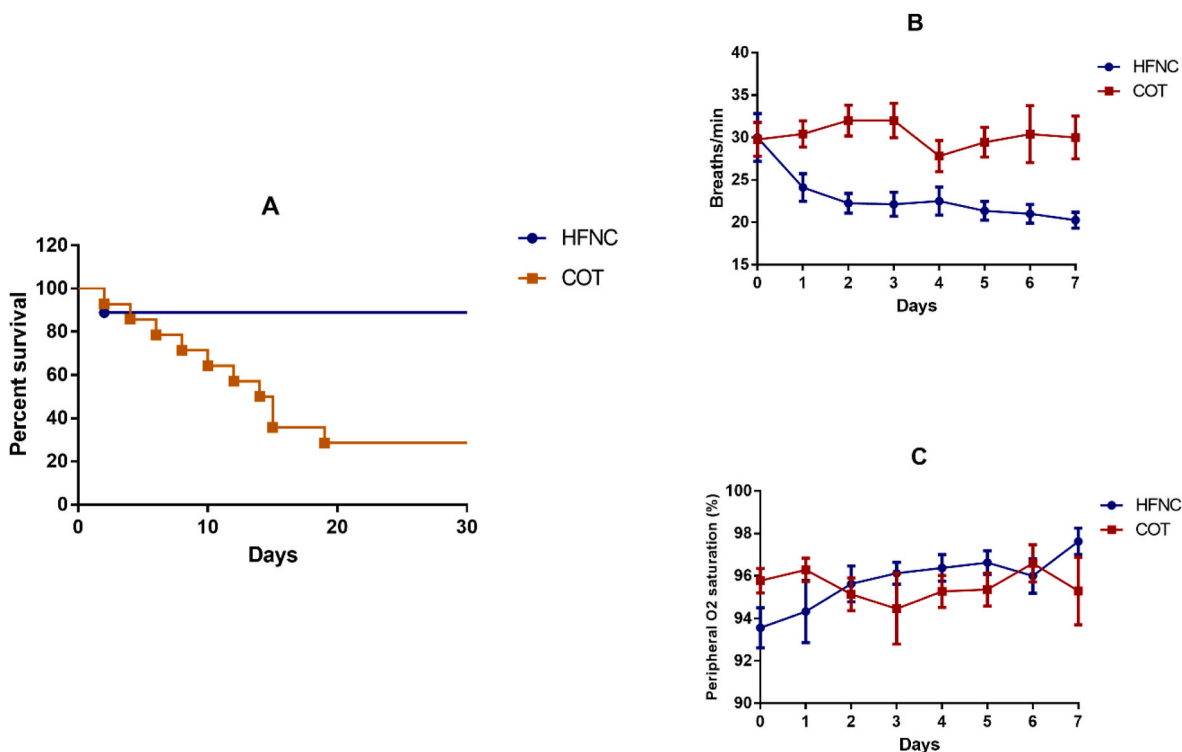


Fig. 1. Shows the Kaplan Meier survival curve (A), the maximum breathing frequency (B) and peripheral O<sub>2</sub> saturation (C) during the course of the disease. Day 0 is the moment before inclusion and before start of HFNC treatment. HFNC: high flow nasal cannula, COT: conventional oxygen therapy.

COVID-19 population. A DNI order is not a reason for withdrawal from this apparently successful treatment. We have evaluated the effect of HFNC versus COT in COVID-19 patients with respiratory failure, whom were not eligible for ETI due to comorbidities, frailty or a DNI order. An explanation for the higher survival rate in the HFNC group may be the decrease in breathing frequency and thus reduction of respiratory distress. As such, patients on HFNC were able to maintain oral food intake without interrupting oxygen treatment, as opposed to those receiving COT. Interrupting oxygen supply may lead to accelerated starvation and exhaustion. Therefore, we assume that patients on HFNC experienced a higher degree of comfort and consequently a greater survival, which is in line with HFNC treatment in non-COVID-19 settings [9]. Comfort during HFNC treatment is not only of importance in the curative setting, but could also improve end-of-life comfort in the palliative setting [10].

In conclusion, HFNC seems a promising rescue treatment for older, non-ICU candidates with COVID-19 and respiratory failure in the ward. Bearing in mind the limitations and the small sample size, we still demonstrated a higher survival rate and reduction in maximum breathing frequency in the HFNC group. Therefore, we recommend offering HFNC to hospitalized older patients, and encourage further investigations to validate these findings.

#### Declaration of competing interest

None.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmed.2021.106666>.

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