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Journal Pre-proof

Non-invasive mechanical ventilation or high-flow oxygen therapy in the COVID-19 pandemic: Dead heat broken

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PII: S2173-5727(22)00306-X

DOI: <https://doi.org/10.1016/j.medine.2022.10.018>

Reference: MEDINE 1804

To appear in: *Medicina Intensiva (English Edition)*

Please cite this article as: { doi: <https://doi.org/>

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es
crp
MEDIN 1804
S0210-5691(22)00226-1
10.1016/j.medin.2022.06.005
unknown 2022

SCIENTIF LETTER

Non-invasive mechanical ventilation or high-flow oxygen therapy during the COVID-19 pandemic: tie undone

Ventilación mecánica no invasiva u oxigenoterapia de alto flujo en la pandemia de COVID-19: el empate se deshizo

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Todos los autores reconocen no presentar conflicto de intereses en la realización del presente trabajo. El presente manuscrito no ha recibido financiación alguna.

To the Editor,

During the recent COVID-19 pandemic, non-invasive respiratory support has played a crucial role¹ in the management of patients with acute hypoxemic respiratory failure.

The best therapeutic option for these patients has always been a matter of discussion.² Compared to traditional CPAP based non-invasive mechanical ventilation or the use of 2 different levels of pressure, oxygen therapy administered through high-flow nasal cannula (HFNC) has been gaining popularity probably due to how easy it is to use, its high tolerability, and the possibility of applying it outside the ICU setting.³ All these qualities made it an attractive therapeutic option within the first difficult days of the pandemic. However, scientific evidence that backed its use was insufficient.⁴ This triggered our former letter where we claimed, at least temporarily, a tie in this match between both non-invasive respiratory supports.

In our own opinion, the evidence generated by the RECOVERY-RS⁵ trial has turned the tide in favor of non-invasive mechanical ventilation (NIMV). In sports terminology «tie has been undone at the overtime».

The RECOVERY-RS trial was conducted from April 6, 2020 through May 3, 2021 in 48 hospitals from the United Kingdom and Jersey. Patients were randomized to receive CPAP (N=380), high-flow nasal oxygen (N=418) or conventional oxygen therapy (N=475). To maximize performance given the harsh conditions of the pandemic, the study design is a little special. The study consists of 2 parallel randomized clinical trials that share the same control group: in NIMV only capable hospitals, patients were randomized to receive CPAP or conventional oxygen therapy. In HFNC only capable hospitals, however, patients were randomized to receive HFNC or conventional oxygen therapy. In hospitals with the 3 ventilation systems available, randomization occurred among the 3 groups. Primary endpoint was a composite of orotracheal intubation or 30-day mortality. In the 1273 patients studied, the need for orotracheal intubation or 30-day mortality was significantly lower with CPAP (137/377=36.3%) compared to conventional oxygen therapy (158/356=44.4%), an absolute difference of -8% (95%CI, -15% to -1%); $P=0.03$. However, the difference between HFNC (184/415=44.3%) and conventional oxygen therapy (166/368=45.1%) was not statistically significant, an absolute difference of -1% (95%CI, -8% to 6%); $P=0.83$. Due to the randomization-generated comparison and assuming interchangeability between both control groups, Bayesian analysis with the beta-binomial model using a non-informative prior distribution confirmed that the chances of CPAC exceeding HFNC are 0.988 (figure 1) with a number needed to treat of 12.4 patients (95%CI 6-52) (figure 2).

To improve the quality of our healthcare we can assess the meaning of these results by applying these findings to our own data. To perform this easy analysis, we conducted consecutive sampling of patients included in the registry of patients with COVID-19 from our ICU—after approval by the local research ethics committee and after obtaining

the patients or their legal representatives' informed consent—from March 2020 through March 2022 with the diagnosis of moderate or severe hypoxemic respiratory failure. In 788 (88.14%) out of a total of 894 patients with SARS-CoV-2 infection confirmed the reason for ICU admission was acute hypoxemic respiratory failure. We decided to use HFNC on 477 of these patients (53.4%) in our ICU as a first-line respiratory support therapy. The 30-day mortality rate of these patients was 7.33%, and the composite endpoint of orotracheal intubation or 30-day mortality appeared in 263 patients (55.13%). *Ceteris paribus*, if we had used CPAP instead of HFNC in these 477 patients, we would have had 40 fewer patients (95% CI = 8 to 79) in whom we would have had to use intubation or who would have died otherwise.

With the knowledge generated by the RECOVERY-RS trial, tie has been definitively undone. The abuse of HFNC and the lack of rigorous management—based on the scientific evidence available—of non-invasive ventilatory support devices will lead HFNC to dying from its own success without any benefits for the patients whatsoever.

Funding

None whatsoever.

Conflicts of interest

None reported.

Conflict of Interest and Authorship Conformation For
Please check the following as appropriate:

- o All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.

- o This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue.

- o The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript

- o The following authors have affiliations with organizations with direct or indirect financial interest in the subject matter discussed in the manuscript:

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² González-Castro A, Fajardo Campoverde A, Medina A, Alapont VMI. Non-invasive mechanical ventilation and high-flow oxygen therapy in the COVID-19 pandemic: the value of a draw. *Med Intensiva (Engl Ed)*. 2021; 45: 320-321. <https://doi:10.1016/j.medin.2020.04.017>

³ Ricard J-D, Roca O, Lemiale V, Corley A, Braunlich J, Jones P, et al. Use of nasal high flow oxygen during acute respiratory failure. *Intensive Care Med* 2020; 46: 2238-2247.

⁴ Crimi C, Pierucci P, Renda T, Pisani L, Carlucci A. High-Flow Nasal Cannula and COVID-19: A Clinical Review. *Respir Care*. 2022; 67: 227-240 <https://doi:10.4187/respcare.09056>

⁵ Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, et al; RECOVERY-RS Collaborators. Effect of Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With Acute Hypoxemic Respiratory Failure and COVID-19: The RECOVERY-RS Randomized Clinical Trial. *JAMA*. 2022; 327: 546-558. <https://doi:10.1001/jama.2022.0028>

Figura 1: Análisis bayesiano con el modelo Beta-Binomial utilizando una distribución a priori no informativa.

Pie de Figura: el análisis bayesiano con el modelo Beta-Binomial utilizando una distribución a priori no informativa nos indica que la probabilidad de que la CPAP sea superior a las CNAF es de 0,988.

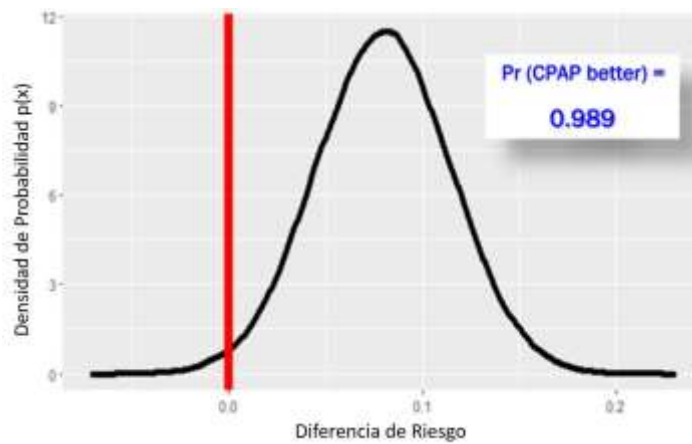


Figura 2: Número necesario de pacientes a tratar (NNT).

Conflict of Interest and Authorship Confirmation Form

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- This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue.
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Figure 1. Bayesian analysis with the beta-binomial model using non-informative prior distribution. Bayesian analysis with the beta-binomial model using non-informative prior distribution tells us that the chances of CPAP exceeding HFNC are 0.988. gr1

Figure 2. Number needed to treat (NNT). gr2

TRADUCCIÓN DE FIGURAS

(Color negro: español · Color azul: inglés)

Figura 1

Diferencia de riesgo

Risk difference

Densidad de probabilidad $p(x)$

Likelihood density function $P(x)$

Figura 2

Número necesario de pacientes a tratar

Number needed to treat

Densidad de probabilidad $p(x)$

Likelihood density function $P(x)$

(95% Cred Int = 6 to 57)

(95% CI, 6 to 57)