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.

Journal of Critical Care xxx (xxxx) xxx

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

Authors response: Feasibility of non- invasive respiratory drive and breathing pattern evaluation using CPAP in COVID-19 patients

Dear Editor,

We thank Antonio Esquinas and co-authors for critically discussing the results of our study "Feasibility of non- invasive respiratory drive and breathing pattern evaluation using CPAP in COVID-19 patients", recently published in the *Journal of Critical Care* [1]. We would like to take the opportunity to respond to the authors' concerns and to clarify some methodological points of our study.

First, regarding the amount of positive end-expiratory pressure (PEEP) applied with high-flow nasal cannula (HFNC) and its equivalence with continuous positive airway pressure (CPAP). Although HFNC demonstrated a true PEEP-like effect with an increase in end-expiratory lung volume (EELV) [2], it is true that this effect is very limited and is not equivalent to conventional CPAP. Furthermore, a direct comparison of CPAP and HFNC is difficult because the airway pressure level during HFNC is highly variable between patients and during the respiratory cycle [3]. In the most optimal conditions, HFNC can provide up to 3 cmH_2O of end-expiratory tracheal pressure (5 cmH2O with closed mouth) [3,4]. PEEP level is much higher, around 10–11 cmH_2O, when CPAP is used during acute hypoxemic respiratory failure (AHRF), especially during the COVID-19 pandemic [5]. In our study, we deliberately chose a lower CPAP pressure level. Indeed, our objective was not to assess the effect of PEEP on the respiratory drive. CPAP was rather an instrument in determining physiologic parameters, in conditions as close as possible to HFNC's. The effect of PEEP on respiratory drive was explored in the experimental work of Morais et al., cited by the authors [6]. This study showed that PEEP-induced lung recruitment in spontaneously breathing animals decreased the intensity of inspiratory effort, and decreased both localized pulmonary stretch and subsequent self-induced lung injury. In some of our patients, CPAP may indeed have induced a lung recruitment (despite low pressure levels and a short application), which could have lowered respiratory drive and effort. Some evaluation of EELV, as it can be done with electrical impedance tomography, might have address this potential bias.

Second, the authors noted the hypocapnia observed in our patients and questioned its interaction with respiratory drive. During AHRF, the relation between $PaCO_2$ and minute ventilation (Ve) changes, with an uncoupling of the so-called "ventilation curve" (Ve change induced by a $PaCO_2$ change) and the "brain curve" (i.e. the neural respiratory drive for a given $PaCO_2$) [7]. This results in a higher sensitivity to CO_2 and explains why patients with AHRF are generally hypocapnic. Thus, decreased $PaCO_2$ and increased P0.1 are both related to increased respiratory drive.

Finally, the reliability of respiratory drive parameters is questionable with a non-invasive interface such as a face mask, and the air leaks it generates. These leaks are likely to underestimate the true P0.1 value. In spite of this limitation, in all of our patients P0.1 was much higher than the normal values, indicating a high respiratory drive, which was expected in them. However, CPAP-assisted measurement of P0.1 is probably decreasing the signal-to-noise ratio of this parameter (validated in invasive mechanical ventilation), and we agree with the authors' final comment that further clinical trials are warranted to validate the accuracy of P0.1 in this setting.

Declaration of Competing Interest

The authors declare that they have no competing interest.

References

[1] Dargent A, Hombreux A, Roccia H, Argaud L, Cour M, Guérin C. Feasibility of non-invasive respiratory drive and breathing pattern evaluation using CPAP in COVID-19 patients. J Crit Care. 2022;69:154020. https://doi.org/10.1016/j.jcrc.2022.154020.
[2] Corley A, Caruana LR, Barnett AG, Tronstad O, Fraser JF. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. Brit J Anaesth. 2011;107:998–1004. https://doi.org/10.1093/bja/aer265.
[3] Parke R, McGuinness S, Eccleston M. Nasal high-flow therapy delivers low level positive airway pressure. Brit J Anaesth. 2009;103:886–90. https://doi.org/10.1093/bja/aep280.
[4] Groves N, Tobin A. High flow nasal oxygen generates positive airway pressure in adult volunteers. Aust Crit Care. 2007;20:126–31. https://doi.org/10.1016/j.aucc.2007.08.001.
[5] Aliberti S, Radovanovic D, Billi F, Sotgiu G, Costanzo M, Pilocane T, et al. Helmet CPAP treatment in patients with COVID-19 pneumonia: a multicenter, cohort study. Eur Respir J. 2020;56:2001935. https://doi.org/10.1183/13993003.01935-2020.
[6] Morais CCA, Koyama Y, Yoshida T, Plens GM, Gomes S, Lima CAS, et al. High positive end-expiratory pressure renders spontaneous effort noninjurious. Am J Resp Crit Care. 2018;197:1285–96. https://doi.org/10.1164/rccm.201706-1244oc.
[7] Spinelli E, Mauri T, Beitler JR, Pesenti A, Brodie D. Respiratory drive in the acute respiratory distress syndrome: pathophysiology, monitoring, and therapeutic interventions. Intensive Care Med. 2020;46:606–18. https://doi.org/10.1007/s00134-020-05942-6.

Auguste Dargent, MD, PhD
Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437 Lyon, France
APCSe VetAgro Sup UPSP 2016.A101, Marcy l'Etoile, France
*Corresponding author at: Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437 Lyon, France.
E-mail address: auguste.dargent@chu-lyon.fr

Alexandra Hombreux, MD
Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437 Lyon, France

Hugo Roccia, MD
Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437 Lyon, France

https://doi.org/10.1016/j.jcrc.2022.154073

Please cite this article as: A. Dargent, A. Hombreux, H. Roccia, et al., Authors response: Feasibility of non- invasive respiratory drive and breathing pattern evaluation us..., Journal of Critical Care, https://doi.org/10.1016/j.jcrc.2022.154073

Laurent Argaud, MD, PhD
Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437 Lyon, France
Université de Lyon, Université Claude Bernard Lyon 1, Faculté de médecine Lyon-Est, F-69373 Lyon, France

Martin Cour, MD, PhD
Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437 Lyon, France
Université de Lyon, Université Claude Bernard Lyon 1, Faculté de médecine Lyon-Est, F-69373 Lyon, France

Claude Guérin, MD, PhD
Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437 Lyon, France
Université de Lyon, Université Claude Bernard Lyon 1, Faculté de médecine Lyon-Est, F-69373 Lyon, France

Available online xxxx