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LETTER

Driving pressure and adjunctive therapies in pulmonary sequelae of COVID-19 patients under invasive ventilation

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Dear Editor,

A non-negligible proportion of critical patients affected by coronavirus disease 2019 (COVID-19) and with acute respiratory distress syndrome (ARDS) need invasive mechanical ventilation (IMV) [1]. This population is most at risk of developing respiratory sequelae after hospital discharge, most commonly represented as impairment of carbon monoxide diffusing capacity (D_{LCO}) [2]. Predictive factors of lung diffusing capacity (D_{LCO}) impairment after IMV due to COVID-19 are unknown.

This is a multicentre, prospective observational study in 51 Spanish intensive care units (ICUs). A total of 861 consecutive COVID-19 patients (confirmed by polymerase chain reaction) who underwent IMV from March 2020 to July 2021 and survived were included. At hospital admission, we collected sociodemographic, anthropometric, comorbidity, and lifestyle data. Moreover, in-hospital clinical and biological parameters, ventilatory parameters, and adjunctive therapies at three IMV time points (day one, three and the last day), and lung function and computed tomography findings at follow-up were assessed. Material and methods as well as statistical analysis are shown in electronic supplementary material (ESM).

The median (p_{25}–p_{75}) time from discharge to follow-up was 3.5 (2.7–4.7) months. The median age was 61 (53–67) years, and 26.9% were women. The mean (SD) percentage of predicted D_{LCO} at follow-up was 70.3% (18%), with 27.5% of patients with a D_{LCO} < 60% (see ESM). The evolution of ventilatory parameters according to D_{LCO} groups is described in the supplemental material. Predictive factors for D_{LCO} < 60% were (1) length of IMV [OR: 1.95 (1.65–2.31, p < 0.001)], (2) age [OR: 1.32 (1.11–1.58, p = 0.002)], (3) initial driving pressure (DP at day one of intubation) [OR: 1.23 (1.02–1.47, p = 0.033)], (4) time from symptoms to intubation [OR: 1.15 (0.99–1.35, p = 0.075)], (5) prone positioning (PP) [OR: 0.69 (0.46–1.02, p = 0.062)], and (6) lung recruitment maneuvres (LRMs) [OR: 0.42 (0.30–0.60, p < 0.001)] (Fig. 1). A clinical scoring tool, named CIBERESICU SCORE, was developed considering these predictors (https://trrm.shinyapps.io/CIBERESUCIscore/).

Mechanical ventilation leads to increased mechanical stress and potential lung damage, increasing the risk of ventilator-induced lung injury (VILI) [3]. Relatedly, our results showed that ventilatory parameters and adjunctive therapies that are associated to the protective ventilation such as DP [4], PP, and LRMs [5] were not only associated with mortality but also the development of pulmonary sequelae in surviving severe COVID-19 patients who received IMV.

This study has some limitations. First, there were a large number of patients missing follow-up data, including D_{LCO} measurement, and these patients were excluded from our analysis. However, there were no clinical differences at

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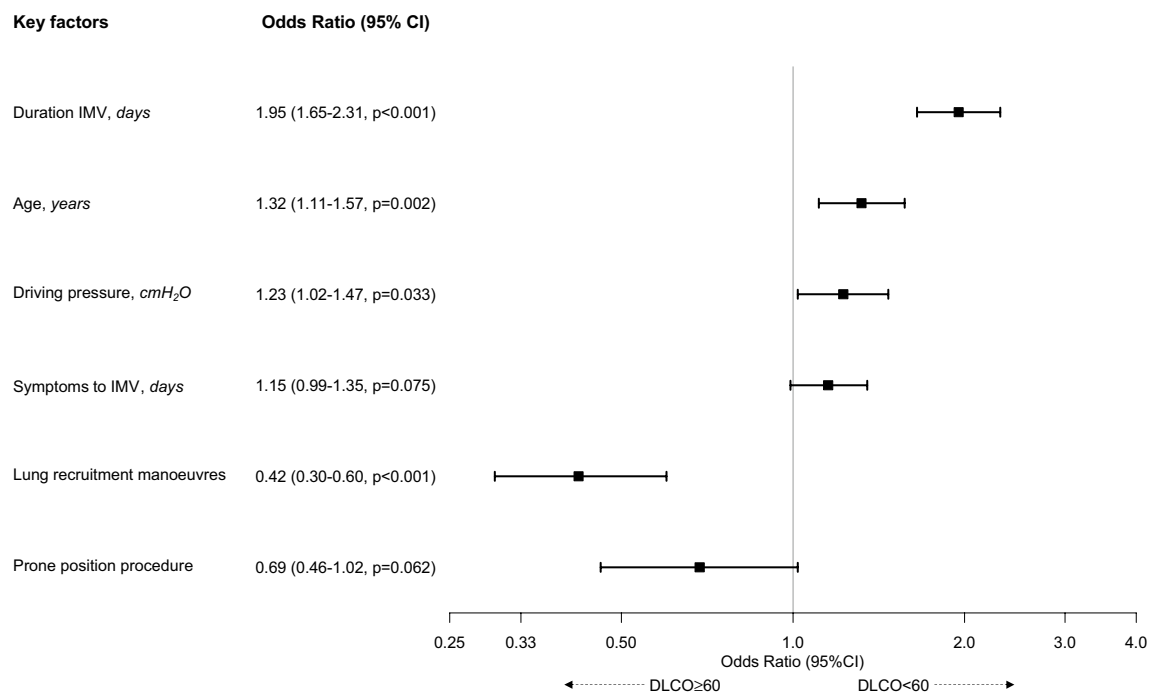

Fig. 1 Factors associated with D_{LCO} impairment included in final multivariate model. ORs (95% CIs) are shown as 1-SD changes for continuous predictors. D_{LCO} diffusing capacity for carbon monoxide

baseline or in disease severity between them (supplemental material). Second, this was a short-term follow-up study and probably a proportion of patients will improve D_{LCO} after this first follow-up. However, our score can guide decision making by both policy makers and specialist care professional when planning and designing care and follow-up plans for critical COVID-19 after hospital discharge. Third, the study included almost all the variants of COVID-19; however, the most recent variant, omicron, was not included due to the recruitment period. Along the same lines, the management of this type of patient has changed throughout the pandemic and the proportion of vaccinated patients in our cohort is very low (0.92%). In addition, we do not have information on symptoms and quality of life to assess the impact of this functional impairment. Further studies are needed to validate our results and our clinical score including new COVID-19 variants and vaccinated patients.

In conclusion, in this large cohort of intubated COVID-19 patients, we identified parameters related to IMV, such as time to intubation, length of IMV, DP, LMRs and PP, directly implicated in an altered D_{LCO} after hospital discharge. For the first time, a scoring tool considering all of these parameters plus age is available for use in daily clinical practice to identify high-risk patients and perform more efficient follow-up. Clinicians could use this score and its bedside parameters to guide decision making to plan proper and efficient follow-up of these patients after hospital discharge.

Supplementary Information
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Conceptualization (JG, IDB, FB), data curation (IDB), formal analysis (IDB), funding acquisition (AT, FB), investigation (all), methodology (JG, IDB, AM, AT, FB), project administration (AT, FB), supervision (AT, FB), writing—original draft (JG, IDB), and writing—review and editing (all). All authors provided final approval of the version submitted for publication.

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Declarations

Conflicts of interest

The authors declare no conflicts of interest.

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