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EDITORIAL

Pulmonary air leak in COVID-19: time to learn from our mistakes

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Since the late 90s, pulmonary air leak, including pneumothorax and pneumomediastinum, has been considered an uncommon complication of invasive mechanical ventilation, occurring in < 10% of patients with acute respiratory distress syndrome (ARDS) [1]. However, soon after the novel coronavirus disease 2019 (COVID-19) appeared, many of us began to see it more frequently than before [2]. Several questions arose. Did this finding depend on the very high prevalence of ARDS during the pandemic? Did it reflect a specific trait of COVID-19? Was it our responsibility?

Knox et al. [3] aimed to address the first two questions in this issue of Intensive Care Medicine. They reviewed the chest imaging reports of 2211 patients with ARDS due to COVID-19 and 5522 with ARDS of different origin and found that the incidence of pneumothorax or pneumomediastinum in the two groups was similar, 24% and 22.5%. However, following adjustment for confounders, it was higher in the former than in the latter group (odds ratio 1.31, 95%-confidence interval 1.13–1.52).

The overall incidence of a pulmonary air leak (22.9%) was very high. This result is partly explained by the decision to include subjects with trauma, any pneumothorax or pneumomediastinum regardless of its volume or need for drainage, cases due to invasive procedures, and by considering the entire hospital stay. Even so, we are still surprised to read that approximately one-fourth of the patients had an air leak.

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Unfortunately, the authors did not address the third question. While answering, it is crucial not to blame ourselves but to cure the next patients with COVID-19 better.

In the following sections, we will briefly describe the pathogenesis of alveolar rupture, focus on mechanisms that may explain the findings of Knox et al. [3], and conclude with the most important lessons we have recently learned on this topic.

Alveolar rupture usually results from a large alveolar deformation generated by a high transpulmonary pressure that is the pressure gradient across the alveolar wall. The maximal transpulmonary pressure reached during ventilation can be reasonably measured as the difference between the end-inspiratory plateau airway pressure (inside the alveoli) and the corresponding esophageal pressure (a surrogate of the pleural pressure outside of the alveoli). The safe upper limit of transpulmonary pressure for healthy human alveoli is probably 20–25 cmH_2O [4].

Alveolar rupture can then be due to a large increase in airway pressure generated by the ventilator (as during invasive controlled ventilation), a large decrease in pleural pressure generated by the patient (as during spontaneous breathing), or a combination of the two (as during invasive assisted ventilation or non-invasive ventilation) [4].

Ventilator-induced lung injury (VILI)

In the study by Knox et al. [3], 400 patients developed a pneumothorax or pneumomediastinum after receiving invasive mechanical ventilation with a plateau pressure up to 34 (30–40) cmH_2O and positive end-expiratory pressure (PEEP) up to 16 (14–20) cmH_2O. The driving (plateau minus PEEP) airway pressure probably exceeded 15 cmH_2O in many of them. Similar ventilatory settings increase the risk of alveolar rupture during ARDS

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Table 1 Mistakes we made and lessons learned while curing patients with COVID-19

Mistakes we made	Lessons we learned
Treating moderate-to-severe hypoxemia with very high PEEP as we used to do in patients with ARDS of other origins	In many patients with COVID-19, the morphological and functional lung response to a higher PEEP is less positive than expected. Hyperinflation can exceed recruitment [13]. Now we rarely use PEEP > 10–12 cmH_2O. If alveolar collapse remains an issue, we prefer prone positioning to increase PEEP further [14]
Tolerating end-inspiratory plateau pressure as high as 30–32 cmH_2O as we used to do in patients with ARDS of other origins	During COVID-19, several factors increase the risk of air leak, including lung inhomogeneities and tissue "frailty". Chest wall compliance is frequently normal, so pleural pressure increases by only a few cmH_2O. Therefore, the transpulmonary pressure is only a few cmH_2O lower than the alveolar pressure. Being cautious, we now consider 26 cmH_2O as a safer upper limit. Obese patients may be an exception
Delaying ICU admission and intubation in patients with signs of respiratory distress (also because of shortage of resources)	Strong inspiratory efforts largely increase transpulmonary pressure. Invasive mechanical ventilation with individually tailored tidal volume and airway pressure can be the safest option for patients with severe respiratory distress
Underestimating the risks of spontaneous breathing in patients assisted by a ventilator	Recognizing and mitigating vigorous inspiratory efforts and frequent asynchronies can be extremely difficult. In case of doubt, esophageal pressure swings [4] (or central venous pressure swings as a surrogate [15]) should be measured, and controlled ventilation started or resumed

Herein we list some mistakes we made and some lessons we learned during the first waves of the pandemic. The way we treat patients with COVID-19 has changed accordingly. We acknowledge that the changes we describe are based on our direct experience, the experience of our colleagues, and pathophysiological reasoning but not high-quality clinical trials (as they are not available yet)

ARDS, acute respiratory distress syndrome; *COVID-19*, coronavirus disease 2019; *ICU*, intensive care unit; *PEEP*, positive end-expiratory pressure

unrelated to COVID-19 [5, 6] and possibly even during COVID-19.

Large tidal volumes, high respiratory rates, and high inspiratory flows could have contributed to an air leak by increasing the total amount of energy delivered to the alveoli over time (the so-called mechanical power [7]). However, these variables were not reported in the study.

Patient-self-inflicted lung injury (P-SILI)

One hundred thirty one patients developed a pneumothorax or pneumomediastinum without receiving invasive mechanical ventilation. Eighty-one were treated with non-invasive ventilation, and the others with low or high-flow oxygen for a few days (on average, the air leak was diagnosed 7 days [3–13] after hospital admission). In these patients, the alveolar rupture was probably caused by repeated vigorous inspiratory efforts with large decreases in pleural pressure and increases in transpulmonary pressure [4]. Just as invasive assisted ventilation, non-invasive ventilation could have been particularly risky. In fact, with these two modes, the alveolar and pleural pressure change in opposite directions, driven by the ventilator's and the patient's activity, and the transpulmonary pressure can easily become too high. Poor patient-ventilator interaction up to the extreme where patients "fight" against the ventilator, favored by an elevated respiratory drive [8], severe cough due to non-vented circuits, and poor management of hyperactive delirium [9], may have all contributed to rising this risk.

Lung inhomogeneities

Early COVID-19 frequently presents with large areas of poorly aerated lung tissue or ground glass opacities, where inhomogeneities can act as "stress risers": aerated alveoli adjacent to collapsed ones are exposed to excessive tension even when the overall lung inflation is not that large due to local pressure multiplication [10].

Decreased tissue resistance to inflation

During COVID-19, pneumocyte necrosis and emphysematous changes are common, especially in sub-pleural regions. With time, lung lesions can progress toward fibrosis and parenchymal destruction. Pulmonary embolism with multiple infarcts may be an additional insult [11]. The resulting tissue frailty can predispose to alveolar rupture independently from exposure to very high transpulmonary pressure [12].

Iatrogenic procedures

Finally, pulmonary air leak may have resulted from invasive procedures such as central line insertion, especially if performed by inexperienced personnel or with limited access to ultrasound guidance, as possible during a pandemic.

In Table 1, we summarize the most important lessons we learned during the pandemic, which are indirectly supported by the findings of Knox et al. [3]. Translating

them to the bedside will hopefully make pulmonary air leaks uncommon even in patients with COVID-19.

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Declarations

Conflicts of interest
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