Mechanically ventilated COVID-19 patients failed to meet the criteria for the Berlin definition of ARDS

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Dear Editor,

Using a consensus process, a panel of experts convened in 2011 have simplified and clarified the definition of acute respiratory distress syndrome (ARDS) and gave birth to the so called, Berlin definition of ARDS [1]. The Berlin definition was developed to achieve a more accurate definition and to better match clinical outcomes to severity of illness categories. It provided validated support for three strata of initial arterial hypoxaemia (PaO2/FiO2 categories of ≤ 100, 101–200, and 201–300 mm Hg), which correlated with mortality (45%, 32%, and 27%, respectively) [1]. Now, in 2020–21, critically ill COVID-19 patients presented typical morphological hallmarks of ARDS with lung edema, inflammation, and alveolar hemorrhage (i.e., diffuse alveolar damage) [2]. They were classified as ARDS, because the lung injury was due to an acute lung infection responsive of bilateral infiltrates on chest imaging and was responsive to arterial hypoxaemia despite mechanical ventilation with positive end-expiratory pressure and without cardiac failure explaining the respiratory failure. More than 3000 articles matched the keywords "COVID-19" and "ARDS" in 2020. However, we questioned whether ventilated COVID-19 patients meet the Berlin definition of ARDS because of long latency periods between symptom onset and respiratory failure (should be 1 week or less in the definition of ARDS). To test this assumption, we reported the time from symptoms onset to hospitalization, ICU admission and initiation of the mechanical ventilation in critically ill patients due to community-acquired SARS-CoV-2 infection.

In this single-center study (prospective recording from 2020-03-14 to 2020-04-12), we included critically ill patients due to community-acquired SARS-CoV-2 infection and receiving mechanical ventilation with partial pressure of arterial oxygen to fraction of inspired oxygen (PaO2/FiO2) of 300 mm Hg or less (with positive end-expiratory pressure of 5 cm H_2O or more), with bilateral infiltrates on chest imaging and without cardiac failure explaining the respiratory failure. We reported patients 'characteristics and latency periods. No nominative, sensitive or personal data of patients have been collected. Our study involved the reuse of already recorded and anonymized data. The study falls within the scope of the French Reference Methodology MR-004, which require neither information nor consent of the included individuals. Results are presented in mean $\pm$ SD.

We studied 191 patients of 64.8 ± 10.4 years old, mostly male (64.9%), with PaO2/FiO2 of 141 ± 57 mm Hg, treated with neuromuscular blockers (98.2%) and prone position (90.9%), and having in ICU mortality of 20.9%. The mean times from symptoms onset to hospitalization, ICU admission and initiation of the mechanical ventilation were, respectively, 7.5 ± 3.3, 8.8 ± 3.3, and 10.5 ± 4.0 days (Fig. 1). Only 21.9% (42/191) of these critically ill and ventilated patients had respiratory failure developed within 1 week of the clinical onset and could actually be classified as ARDS according to the Berlin definition.
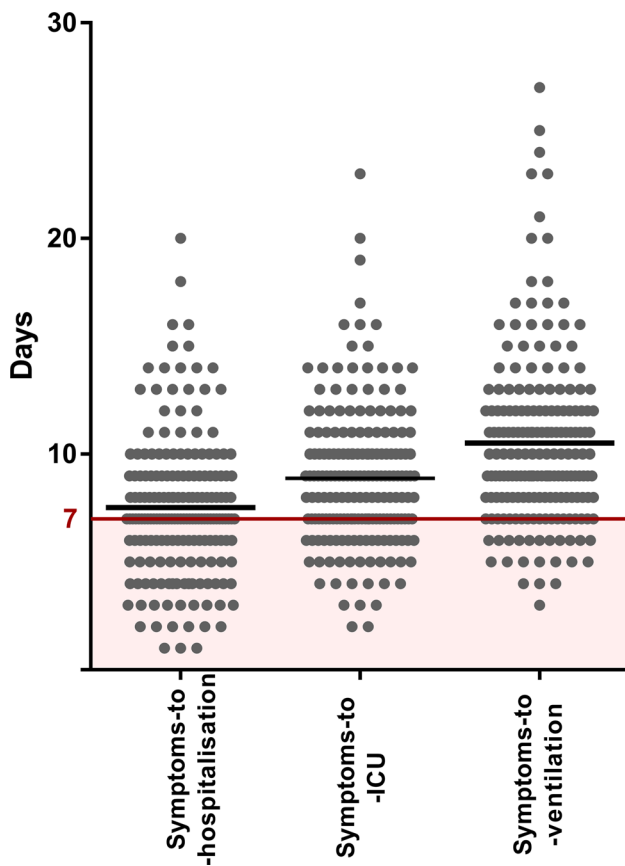
In our experience, the large majority of ventilated COVID-19 patients failed to meet the criteria for the Berlin definition of ARDS, despite severe lung injury and live-threatening condition. Critically ill patients due to SARS-CoV-2 infection cannot be classified as sepsis [3] or as ARDS. The purpose of these observations is not to be picky with the definitions, but to highlight that COVID-19 has been a game changer in our ability to stratify the patients. Definition need to evolve as new information and experience is gained [4]. Considering an expanded definition of ARDS due to the COVID-19 pandemic is a legitimate question that

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In conclusion, we observed that the long latency period between symptom onset and respiratory failure preclude ventilated COVID-19 patients to be stratified as ARDS. We proposed to expand the latency period (up to 14 days) and welcome the feed-back of clinicians caring for critically ill COVID-19 patients.

Declarations

Conflict of interests No competing interests to declare.

Ethics approval and consent to participate No nominative, sensitive or personal data of patients have been collected. Our study involved the reuse of already recorded and anonymized data. The study falls within the scope of the French Reference Methodology MR-004, which require neither information nor consent of the included individuals.

Consent for publication Not applicable.

Fig. 1 Latency periods between symptom onset and respiratory failure of critically ill COVID-19 patients requiring invasive mechanical ventilation. Patients received invasive mechanical ventilation with PaO_2/FiO_2 of 300 mm Hg or less, with bilateral infiltrates on chest imaging and without cardiac failure explaining the respiratory failure. Times from symptom onsets to hospitalization, ICU admission, and initiation of invasive mechanical ventilation are represented by dots (individual value) or black lines (mean value). The 1-week limit for the latency period of the Berlin definition of ARDS is represented by the red line

should be considered. Modifying the latency period for the inciting clinical disorder should be included in this discussion. Given the slower progression of respiratory failure in COVID-19 compared with other causes of ARDS, we propose that a revised definition of ARDS could consider latency longer than 7 days from identification of the ARDS risk factor. As already suggested [4] and in agreement with our results, a latency period (between symptom onset and respiratory failure) up to 14 days seems to be optimal to define COVID-19 ARDS. Whether this longer latency period may apply to all respiratory viral infections including influenza is a more complicated question. In our experience, the time between the onset of symptoms and hospitalization is inferior to one week for viral pneumonia (non-COVID-19; unpublished data from [5]).

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