

LETTER

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Timing of Intubation in Covid-19 ARDS: What “time” really matters?

Vasiliki Tsolaki* and George E. Zakyntinos

To the Editor,

We congratulate Dr. Papoutsi et al. for their study, on the optimal time of intubation in Covid-19 ARDS patients [1]. In their systematic meta-analysis they found that outcomes are not affected from the intubation time (within 24-h of ICU admission or later).

We agree with the authors that “early intubation,” relying solely on the time spent in the Intensive Care Unit (ICU) before intubation, is a rather arbitrary definition and may be misleading. Many important data are lost in this type of analysis, which may affect outcomes. Firstly, ARDS severity in patients receiving early vs late intubation is not reported. Were patients in the two groups of different severity? The authors acknowledge this limitation, but disease severity (as defined by the oxygenation impairment, lung infiltration extent, APACHE II score) and patient heterogeneity, arising from differences in clinical practices, impacts outcomes. Probably, these criteria may be more meaningful than just “time”.

Secondly, ICU admission criteria vary according to resource availability and institution protocols. Thus, hospitalization of non-intubated patients in ICUs is not widely applicable. A substantial proportion of information regarding the optimal intubation time is carried in patients intubated in the wards, and this group has not been included in the analysis. Probably, the time the patients have spent under “distress” during hospitalization, should not be neglected. Therefore, other variables,

besides frank “time”, should be sought to decide when to intubate. In our opinion, the cumulative time with hypoxemia and/or tachypnea are meaningful data to look at. In other words, is Patient-Self Inflicted Lung Injury a matter to care for in Covid-19 ARDS, or should we tolerate hypoxemia and tachypnea to minimize complications from sedation and mechanical ventilation [2, 3]? It would be very informative to know whether early intubation preserves respiratory mechanics.

Optimal intubation time is an issue of great importance, either performed in the ICU or elsewhere, and should be investigated in future, carefully-designed trials. “Silent hypoxia” was one of the initial observations in Covid-19 pathophysiology, present despite extensive pulmonary infiltrates and severe hypoxemia [4]; prone position has been widely adopted in sedated and non-sedated patients, altering oxygenation status and therefore intubation time [5].

The decision to intubate may be an “art of medicine”, yet, in times of such crisis, when doctors from different fields and with different skills, or even young doctors without specialties, are encountered in the decision making, formal thresholds and sound protocols should be introduced.

Authors’ reply

E. Papoutsi, V. G. Giannakoulis, E. Xourgia, C. Routsis, A. Kotanidou and I. I. Siempos

Dear Editor-in-Chief,

We thank Drs Tsolaki and Zakyntinos for their interest in our work [1] and insightful points.

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*Correspondence: vasotsolaki@yahoo.com

Critical Care Department, University Hospital of Larissa, University of Thessaly, Faculty of Medicine, Mezourlo, 41110 Larissa, Greece



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We agree with our colleagues that defining “early” intubation solely based on a time threshold spent in the intensive care unit (ICU) might be arbitrary. We accordingly explored an alternate definition of “early” intubation, using as criterion a prior trial of high flow nasal cannula (HFNC) or non-invasive mechanical ventilation (NIV). This sensitivity analysis aimed to address the notion that patients maintained in spontaneous breathing (HFNC) or receiving partial ventilatory assistance (NIV) may experience high respiratory drive leading to high tidal volume and transpulmonary pressure, which may in turn contribute to development of patient self-inflicted lung injury (P-SILI) [3]. That being said, one should keep in mind that scientific evidence regarding the clinical relevance of P-SILI in humans may not yet be compelling enough to justify early intubation [6].

Also, our colleagues reasonably pointed out that criteria for ICU admission may vary depending on institution protocols and availability of resources. Indeed, availability of resources may substantially influence not only overall outcomes [7] but also the threshold of ICU admission [8]. We attempted to address this issue by performing a subgroup analysis of reports from regions with low disease burden (namely, Germany, Korea and Greece) and we again found that all-cause mortality remained comparable between the two (“early” versus “late” intubation) groups.

Overall, “early” intubation represents a spectrum of definitions. Our meta-analysis explored two (one with and one without a time threshold) and revealed no benefit of early intubation. Therefore, we attempted to convey the message that following a stepwise approach to intubation, by offering the patient a trial of HFNC or NIV, seems reasonable based on the current evidence. Practicing medicine is a cost–benefit balance and it seems that preemptive intubation in critically ill patients with COVID-19 is becoming increasingly difficult to justify.

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Authors' contributions

The authors equally contributed to the concept of the manuscript based on observations on the timing of intubation of COVID-19 ARDS patients. All authors read and approved the final manuscript.

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