COMMENT

Higher PEEP in intubated COVID-19-associated ARDS patients? We are not sure

Andrey I. Yaroshetskiy\(^1,2\)*, Sergey N. Avdeev\(^1\), Anna P. Krasnoshchekova\(^1,2\) and Galia S. Nuralieva\(^1\)

To the editor

We have read with great interest the article published in Critical Care by Somhorst et al. entitled «PEEP-FiO\(_2\) table versus EIT to titrate PEEP in mechanically ventilated patients with COVID-19-related ARDS» [1]. This retrospective observational study aimed to select the «optimum» positive end-expiratory pressure (PEEP) in mechanically ventilated patients with COVID-19-related acute respiratory distress syndrome (ARDS) by electrical impedance tomography (EIT), based on the balance between alveolar collapse and overdistension. The authors got interesting results, showing that non-obese patients with COVID-19-related ARDS had low lung recruitability with «optimum» PEEP close to 10 cmH\(_2\)O, and PEEP levels above the appropriate value in the high PEEP/inspiratory fraction of oxygen (FiO\(_2\)) table in obese patients led to «significant alveolar recruitment and less alveolar overdistension». The authors found «a significant positive correlation between set PEEP and body mass index» that could be the result of PEEP selection according to high chest wall elastance (based on transpulmonary pressure measurement) [2]. The next valuable point mentioned by the authors is that the longer the time course of the disease, the lower would be the lung recruitability which apparently reflected the progression of lung injury in COVID-19 which is characterized by relatively low recruitability [3–5]. Nevertheless, we need to discuss some points concerning the study.

First of all, patients were recruited in the study during the first wave of the pandemic which was characterized by excessive use of invasive mechanical ventilation [6, 7]. The authors did not present intubation criteria and detailed description of patients’ status, such as the prevalence of non-respiratory organ dysfunction, frailty, sepsis, the duration of noninvasive ventilation (NIV) before enrollment, duration of low PaO\(_2\)/FiO\(_2\) and tachypnoea (respiratory distress), and other factors that could lead to early or delayed intubation. Therefore, it is unclear to which subgroup of the population with COVID-19-ARDS the results of the study could be extrapolated.

Second, let’s focus on the oxygenation status as a stratification tool for the selection of the appropriate respiratory support method in ARDS [8]. So, according to Table 1, PaO\(_2\)/FiO\(_2\) in the study by Somhorst et al. was 162 [110–201] mmHg, and the FiO\(_2\) level was around 50% [1]. We can speculate that at least a significant part of these patients could be oxygenated noninvasively—by NIV or high-flow oxygen therapy (HFOT). We have enough data by September 2022, based on RCTs [9, 10], observational studies outside ICU, and a meta-analysis of those studies [11] showing very high efficacy of non-invasive respiratory support in mild, moderate, and even moderate-to-severe hypoxemia in COVID-19-related acute respiratory failure (ARF) reaching 70% overall and more. These studies used moderate PEEP levels (if used at all), without intubation, deep sedation, and neuromuscular blockade and came up with the same outcomes as...
in the present study by Somhorst et al. So, the study did not answer the question of what PEEP value is appropriate for the cohort of invasively ventilated COVID-19-ARDS patients, in whom NIV/HFOT failed.

Third, all patients had slightly decreased compliance and low driving pressure (around 10 cmH₂O) that did not change after the PEEP increase, probably, because of low lung recruitability and non-uniform distribution of the lung injury and atelectasis—(multi)local but not diffuse lung injury [12]. To prove this statement, one might compare EIT data and driving pressure changes during the PEEP trial in obese patients. Re-aeration of the dorsal lung units by higher PEEP levels seen on EIT images without decrease in driving pressure in obese patients apparently confirms non-homogeneous lung collapse predominantly in dependent zones. Unfortunately, lung CT scans that would shed light on the pattern of lung injury and percentage of lung involvement are lacking. Moreover, if lung recruitment was clinically significant after the PEEP increase, we might expect to see an increase in PaO₂/FiO₂ which was not observed.

Fourth, the authors assumed that the EIT method precisely reflects alveolar collapse and overdistension. Costa et al. described the original method of calculating overdistension, postulating that «local tidal volume can be estimated by EIT on a pixel by pixel basis, considering that it correlates very well with local impedance variations», thus local lung compliance could be calculated by dividing the local impedance change to the local driving pressure [13]. This assumption has two potential sources of misinterpretation: First, we cannot measure local driving pressure; second, in hyperinflation, the strain can increase without volume change, i.e., without increase in lung impedance. Accordingly, incorrect interpretation of the EIT’ data can lead to lung overdistension due to inappropriate PEEP.

Lastly, the authors followed the concept of the «optimal» individual PEEP as the combination of minimum collapse and minimum overdistension. This hypothesis never found its confirmation. Moreover, it seems that overdistension could be worse than alveolar collapse [14, 15].

We must say that the results of the study should be interpreted with caution. We can hypothesize that these results can draw the following conclusions: 1) a PEEP trial guided by EIT resulted in moderate PEEP levels in non-obese patients with COVID-19-ARF without regard to the PEEP/FiO₂ table, and PEEP according to BMI in obese patients, which can be higher than «high» PEEP/FiO₂ table levels; 2) these data need confirmation in a large scaled observational studies and RCTs, including NIV. Studies on advanced physiological monitoring (transpulmonary pressure, lung volumes, etc.) in COVID-19-associated ARF during invasive and noninvasive ventilation are urgently needed to confirm or reject this hypothesis.

Abbreviations
ARDS: Acute respiratory distress syndrome; ARF: Acute respiratory failure; BMI: Body mass index; EIT: Electrical impedance tomography; FiO₂: Inspiratory fraction of oxygen; HFOT: High-flow oxygen therapy; ICU: Intensive care unit; NIV: Noninvasive ventilation; PaO₂: Partial pressure of oxygen in arterial blood; PEEP: Positive end-expiratory pressure; RCT: Randomized controlled trial.

Acknowledgements
Not applicable.

Author contributions
AÏY, SNA, APK, and GSN conceived the comment. AÏY and SNA drafted the manuscript. All authors revised the drafted manuscript and read and approved its final version.

Declarations
Ethical approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
AÏY reported personal fees from GE, Philips Respironics, Covidien, Fisher & Paykel, Drager, Triton Electronics, Mindray, Pfizer, BBraun, Gilead outside the submitted work. SNA reported personal fees from Boehringer Ingelheim, Pfizer, Novartis, AstraZeneca, Chiesi outside the submitted work. No other disclosures were reported.

Author details
1Sechenov First Moscow State Medical University (Sechenov University), 8 bld 2, Trubetskaya Str, Moscow, Russia 119991. 2Research Institution for Clinical Surgery Division, Anesthesiology and Critical Care Department, Pirogov Russian National Research Medical University, 1, Ostrovitianova str, Moscow, Russia 117997.

Received: 20 September 2022 Accepted: 17 October 2022

References
1. Somhorst P, van der Zee P, Endeman H, Gommers D. PEEP-FiO₂ table versus EIT to titrate PEEP in mechanically ventilated patients with COVID-19-related ARDS. Crit Care. 2022;26:272. https://doi.org/10.1186/s13054-022-04135-5.
2.Gattinoni L, Chiumello D, Carlesso E, Valenza F. Bench-to-bedside review: chest wall elastance in acute lung injury/acute respiratory distress syndrome patients. Crit Care. 2004;8(5):350–5. https://doi.org/10.1186/ cc2854.
3. Roesthuis H, van den Berg M, van der Hoeven H. Advanced respiratory monitoring in COVID-19 patients: use less PEEP. Crit Care. 2020;24(1):230. https://doi.org/10.1186/s13054-020-02953-z.
4. Ball L, Robba C, Maiello L, Herrmann J, Gerard SE, Xin Y, Battaglini D, Brunetti I, Minetti G, Seidt S, Vena A, Giacobbe DR, Bassetti M, Rocchetti M, Cereda M, Castellan L, Patroniti N, Pelosi P. GECOVID (GENoa COVID-19) group. Computed tomography assessment of PEEP-induced alveolar...
Yaroshetskiy et al. Critical Care (2022) 26:327

Publisher's Note

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART). Investigators, Cavalcanti AB, Suzumura EA, Laranjeira LN, Pasani DM, Damiani LP, Guimarães HP, Romano ER, Regnagli MM, Taniguchi LNT, Teixeira C, PinheirodoOliveira R, Machado FR, Diaz-Quijano FA, Filho MSA, Maia IS, Caser EB, Filho WO, Borges MC, Martins PA, Matsui M, Ospina-Tascón GA, Giancursi TS, Giraldo-Ramírez ND, Vieira SR, Asses MGDP, Hasan MS, Szczeklik W, Rios F, Aramoto MB, Berwanger O, RibeirodeCarvalho CR. Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome: a randomized clinical trial. JAMA. 2017;318(14):1335–45. https://doi.org/10.1001/jama.2017.14171.

2. Ziehl DR, Alladina J, Petri CR, Maley JH, Moskowitz A, Medoff BD, Hibbert KA, Thompson BT, Hardin CC. Respiratory pathophysiology of mechanically ventilated patients with COVID-19: a cohort study. Am J Respir Crit Care Med. 2020;210(12):1560–4. https://doi.org/10.1164/rccm.202004-1163LE.

3. Pandya A, Kaur NA, Sacher D, Corragain O, Salerno D, Desai P, Sehgal S, Gordon M, Gupta R, Marchetti N, Zhao H, Patilakh N, Criner GJ, Temple University, COVID-19 Research Group. Ventilatory mechanics in early vs late intubation in a cohort of coronavirus disease 2019 patients with ARDS: a single center’s experience. Chest. 2021;159(2):653–6. https://doi.org/10.1016/j.chest.2020.08.2084.

4. Ferguson ND, Fan E, Camporota L, Antonelli M, Beale R, Brochard L, Brower R, Esteban A, Gattinoni L, Rhodes A, Slutsky AS, Vincent JL, Rubenfeld GD, Thompson BT, Ranieri VM. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med. 2012;38(10):1573–82. https://doi.org/10.1007/s00134-012-2682-1.

5. Greico DL, Menga LS, Cesarano M, Rosà T, Spadaro S, Tironi A, Cariello N, Attili L, Leoni A, Brunetti AM, Zanini M, Lawton T, Ranieri VM, Bajc M, Foygel A, Filho WR, Teixeira A, Oliveira RR, Machado FR, Diaz-Quijano FA, Filho MSA, Maia IS, Caser EB, Filho WO, Borges MC, Martins PA, Matsui M, Ospina-Tascón GA, Giancursi TS, Giraldo-Ramírez ND, Vieira SR, Asses MGDP, Hasan MS, Szczeklik W, Rios F, Aramoto MB, Berwanger O, RibeirodeCarvalho CR. Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome: a randomized clinical trial. JAMA. 2017;318(14):1335–45. https://doi.org/10.1001/jama.2017.14171.

6. Ziehl DR, Alladina J, Petri CR, Maley JH, Moskowitz A, Medoff BD, Hibbert KA, Thompson BT, Hardin CC. Respiratory pathophysiology of mechanically ventilated patients with COVID-19: a cohort study. Am J Respir Crit Care Med. 2020;210(12):1560–4. https://doi.org/10.1164/rccm.202004-1163LE.

7. Pandya A, Kaur NA, Sacher D, Corragain O, Salerno D, Desai P, Sehgal S, Gordon M, Gupta R, Marchetti N, Zhao H, Patilakh N, Criner GJ, Temple University, COVID-19 Research Group. Ventilatory mechanics in early vs late intubation in a cohort of coronavirus disease 2019 patients with ARDS: a single center’s experience. Chest. 2021;159(2):653–6. https://doi.org/10.1016/j.chest.2020.08.2084.

8. Ferguson ND, Fan E, Camporota L, Antonelli M, Beale R, Brochard L, Brower R, Esteban A, Gattinoni L, Rhodes A, Slutsky AS, Vincent JL, Rubenfeld GD, Thompson BT, Ranieri VM. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. Intensive Care Med. 2012;38(10):1573–82. https://doi.org/10.1007/s00134-012-2682-1.

9. Greico DL, Menga LS, Cesarano M, Rosà T, Spadaro S, Tironi A, Cariello N, Attili L, Leoni A, Brunetti AM, Zanini M, Lawton T, Ranieri VM, Bajc M, Foygel A, Filho WR, Teixeira A, Oliveira RR, Machado FR, Diaz-Quijano FA, Filho MSA, Maia IS, Caser EB, Filho WO, Borges MC, Martins PA, Matsui M, Ospina-Tascón GA, Giancursi TS, Giraldo-Ramírez ND, Vieira SR, Asses MGDP, Hasan MS, Szczeklik W, Rios F, Aramoto MB, Berwanger O, RibeirodeCarvalho CR. Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome: a randomized clinical trial. JAMA. 2017;318(14):1335–45. https://doi.org/10.1001/jama.2017.14171.

10. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, Bradley JM, Dark P, Dave C, De Soyaza A, Dennis AV, Devell A, Fairbairn S, Ghani H, Gorman EA, Green CA, Hart N, Hee SW, Kimbley Z, Madathil S, McGowan N, Messer B, Naisbitt J, Norman C, Pareti D, Parkin EM, Patel J, Regan S, Ross C, Rostron AJ, Saim M, Simonds AK, Skilton E, Stallard N, Steiner M, Vancheeswaran R, Yeung J, McCauley DP, RECOVERY-RS Collaborators. Effect of helmet noninvasive ventilation vs high-flow nasal oxygen on days of free respiratory support in patients with COVID-19 and moderate to severe hypoxic respiratory failure: the HENIVOT randomized clinical trial. JAMA. 2021;325(17):1731–43. https://doi.org/10.1001/jama.2021.4682.

11. Cammarota G, Esposito T, Azzolina D, Cosentini R, Menzella F, Alberti S, Coppadoro A, Bellani G, Forlì G, Grasselli G, Cecconi M, Pesenti A, Vitacca M, Lavoir T, Ranieri VM, Di Domenico SL, Resta O, Gidaro A, Patalivo A, Nardi G, Brusasco C, Tesoro S, Navalesi P, Valsalvi R, de Robertis E. Noninvasive respiratory support outside the intensive care unit for acute respiratory failure related to coronavirus-19 disease: a systematic review and meta-analysis. Crit Care. 2021;25(1):268. https://doi.org/10.1186/s12871-021-03697-0.

12. Vieira SR, Puybasset L, Lu Q, Richercheur J, Chuvel P, Coriat P, Rouby JJ. A scanographic assessment of pulmonary morphology in acute lung injury: Significance of the lower inflection point detected on the lung pressure-volume curve. Am J Respir Crit Care Med. 1999;159(S Pt 1):1612–23. https://doi.org/10.1164/ajcc.199.5.9805112.

13. Costa EL, Borges JB, Melo A, Suarez-Sipmann F, Toufen C Jr, Bohm SH, Amato MB. Bedside estimation of recruitable alveolar collapse and hyperdistension by electrical impedance tomography. Intensive Care Med. 2009;35(6):1132–7. https://doi.org/10.1007/s00134-009-1447-4.

14. Gattinoni L, Quintel M, Marini JJ. Volutrauma and atelectrauma: which is worse? Crit Care. 2018;22(1):264. https://doi.org/10.1186/s13054-018-2199-2.