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LETTER

Effects of increasing PEEP on lung stress and strain in children with and without ARDS

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Dear Editor,

The ratio of tidal volume to functional residual capacity (FRC), defined as "volumetric" strain, causes physical lung deformation. The corresponding change in transpulmonary pressure at end inspiration, defined as stress, is directly applied to the alveolus [1]. Both stress and strain may cause global or local lung deformation and microscopic or macroscopic tissue damage, representing significant determinants of ventilator-induced lung injury [1]. A modified nitrogen washout/washin technique, measuring end-expiratory lung volume (EELV), correlated well with computed tomography and was proposed as a valuable tool to optimize ventilator settings, improving lung protective ventilation [2]. The aim of this study was to evaluate the effect of positive end-expiratory pressure (PEEP) on EELV, compliance of the respiratory system (Crs), and stress/strain in children with acute respiratory distress syndrome (ARDS), and compare it with children "at risk of ARDS" and those with no lung injury using the modified nitrogen washout/washin technique (see electronic supplementary material). To monitor the effects of the disease evolution on the PEEP-induced increases in lung stress/strain, measurements were repeated at pre-determined time points. We hypothesized that PEEP escalation increases EELV, Crs, strain, and stress in mechanically ventilated children, potentially influenced by disease severity and timing.

A total of 700 measurements were recorded in 25 mechanically ventilated critically ill children (ARDS, $n=8$; at risk of ARDS, $n=5$; without lung injury, $n=12$). ARDS patients had higher oxygenation index (OI > 4) and $PaCO_2$, lower PaO_2/FiO_2, PaO_2, and prolonged length of stay ($p<0.01$). EELV repeatedly increased in response to increasing PEEP levels over the different time points in each of the three ARDS groups, remaining lower in the ARDS compared to the at-risk group ($p<0.05$) (Supplemental-Figure 1a). The Crs only showed weak increasing trends in ARDS at 6 and 18 h in response to the PEEP escalation, being lower compared to the at-risk group ($p<0.05$) (Supplemental-Figure. 1b). Escalated increases of PEEP from 4 to 10 cmH_2O increased static and global-stress and static strain higher and earlier in the non-ARDS groups compared to the ARDS ($p<0.05$), but within safe limits (static strain < 1, dynamic strain < 0.5, and static stress < 20 cmH_20) (Fig. 1). PEEP escalation did not affect dynamic strain at any time-point.

Similarly to our results, previous reports have shown that strain and stress are higher in ARDS compared to non-ARDS patients and that Crs is not affected by changes in PEEP [3]. Using the nitrogen washout/washin technique, we demonstrated that although PEEP escalation from 4 to 10 cmH_2O increases strain and stress, their levels remain below reported harmful levels [1]. PEEP-induced differences of increase in strain and stress between ARDS and non-ARDS patients might be explained by group differences in the degree of inhomogeneity. In ARDS, the ratio between lung and total elastance varies widely, while the ventilatable parenchyma is strongly reduced in size [4]. It has been assumed that the inhomogeneous areas act as local stress multipliers doubling the stress compared to that present in other parts of the same lung. Accordingly, compared to non-ARDS, PEEP might need to be doubled in ARDS to produce the same degree of strain/stress increases [5].

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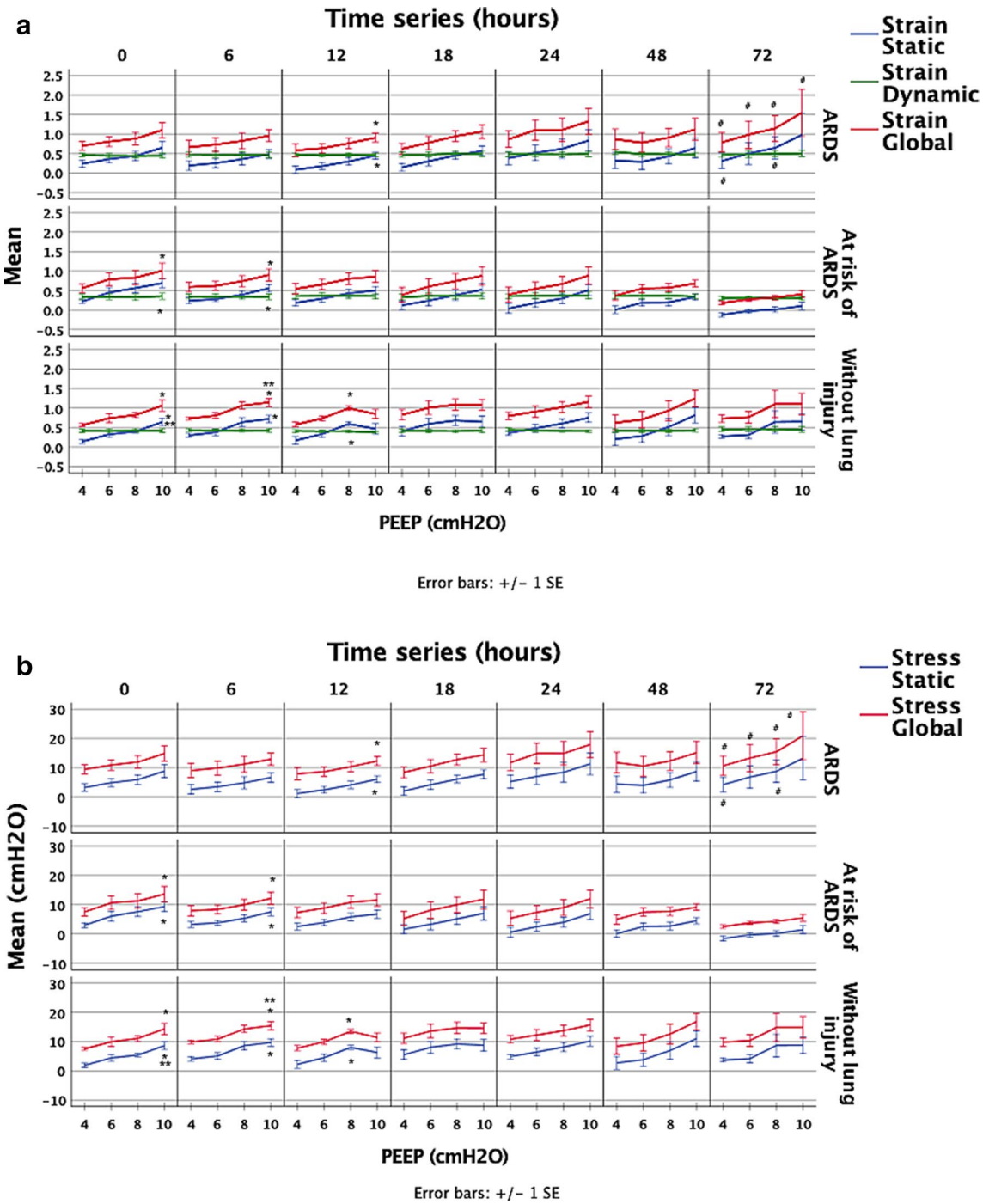

Fig. 1 Escalated increases of PEEP from 4 to 10 cmH_2O increased **a** static and global strain and **b** static stress earlier in the non-ARDS groups (first 6 h) compared to the ARDS group (12 h). By 72 h, ARDS patients attained higher strain and stress levels compared to controls; PEEP escalated increases did not exert any effect on dynamic strain at any time-point. *PEEP 10 vs. 4 mmHg, $p < 0.05$; **PEEP 10 vs. 6 mmHg, $p < 0.05$; #ARDS vs. at risk of ARDS, $p < 0.05$; *ARDS* acute respiratory distress syndrome, *PEEP* positive end-expiratory pressure

Electronic supplementary material
The online version of this article (https://doi.org/10.1007/s00134-019-05667-1) contains supplementary material, which is available to authorized users.

Author contributions
SI, EG, and GB contributed to the conception and design of the research; SI and EG contributed to the acquisition and analysis of the data; PB, PB, and TT contributed to the acquisition of the data; SI, EG, and GB contributed to the interpretation of the data; SI and GB drafted the manuscript; SI, MM, PB, and GB critically revised the manuscript. All authors agree to be fully accountable for ensuring the integrity and accuracy of the work and read and approved the final manuscript.

Compliance with ethical standards

Conflicts of interest
The author declares that they have no conflict of interest.

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