Intensive Care Med
https://doi.org/10.1007/s00134-019-05559-4

LETTER

High-fidelity computational simulation to refine strategies for lung-protective ventilation in paediatric acute respiratory distress syndrome

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Dear Editor,

Mechanical ventilation in paediatric acute respiratory distress syndrome (PARDS) is less studied than in adults, with guidelines for ventilation adapted from adult ARDS. However, PARDS has a distinct epidemiology, and adult ARDS guidelines may not be appropriate in children. As an example, clinical trials suggest that lower tidal volumes (V_T) reduce mortality in adult ARDS [1]. Recent research has highlighted the potential of lung-protective strategies based on limiting driving pressure (ΔP) and mechanical power to reduce ventilator induced lung injury (VILI) [2, 3]. No trials have tested protective ventilation in PARDS, and observational studies are unclear [4]. Concerns about hypercapnia or increased dead space in paediatrics contribute to the hesitancy to lower V_T. There is an urgent need for studies that can provide additional evidence regarding how lung-protective ventilation could be implemented in PARDS. We hypothesized that analysis of a large PARDS data set using a computational simulator would allow us to (a) determine the scope (in terms of lowering V_T, ΔP, and mechanical power) for safely implementing more protective ventilation; and (b) develop, test, and directly compare strategies for achieving this.

Using a prospective cohort of PARDS from the Children's Hospital of Philadelphia with detailed data collection (see Supplement), we developed and tested four lung-protective strategies for reducing either V_T (strategies 1–3) or ΔP (strategy 4). Strategy 1 reduced V_T maintaining constant minute ventilation, strategy 2 reduced V_T maintaining alveolar ventilation with a fixed ratio of inspiratory time to total cycle time, strategy 3 reduced V_T maintaining alveolar ventilation with fixed inspiratory flow, and strategy 4 simultaneously reduced V_T and ΔP. The simulations continued incrementally reducing V_T until safety constraints (hypoxemia, hypercarbia, peak pressure > 35 cmH_2O, respiratory rate [RR] > 40 breaths/min) were violated.

The simulator accurately reproduced patient data (Figs. S2 and S3) in the development cohort. Similar V_T reductions were achieved using strategies 1–3 (15%, 12%, and 14%; Figs. 1, S4, S5), with the number of patients being ventilated using $V_T > 10$ mL/kg falling to zero. Strategy 1 produced no significant change in mechanical power (+1%; $p = 0.2$, signed-rank test) but both strategies 2 and 3 resulted in increases (+22% and +19%; both $p < 0.05$). Strategy 4 reduced ΔP by 6% for all 30 patients in the cohort, and by 17% for the 13 patients on which this strategy could be applied without violating constraints. Strategy 4 was the only approach that produced a significant reduction in mechanical power (−8%; $p < 0.05$). Similar trends were seen in test cohort 1 (ages 1–2 years) and 2 (initial $V_T > 10$ mL/kg), with test cohort 2 showing the greatest potential for lung-protective ventilation (Figs. 1, S7, S8).

Our data suggests that PARDS patients are routinely over-ventilated and there is scope for achieving protective ventilation without compromising gas exchange.

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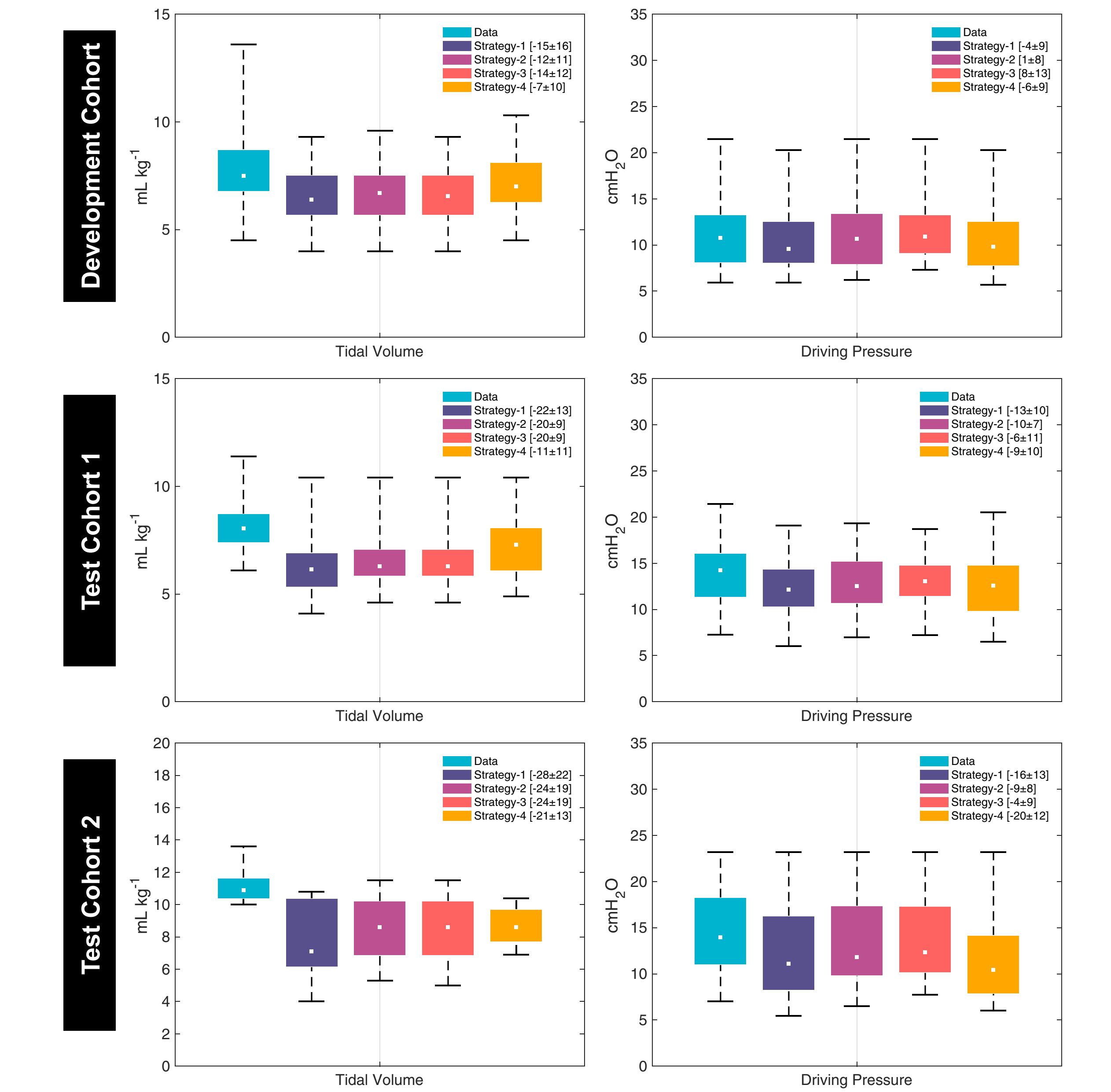

Fig. 1 Box plots show data as median (white dot), interquartile range (boxes), and full range (whiskers) of all patient data before and after implementation of different strategies. Numbers in brackets refer to percentage average change from baseline (mean ± SD). Panels compare the amount of tidal volume (left panels) and driving pressure (right panels) changes in the development cohort, and in the two test cohorts. Test cohort 2 (initial tidal volume > 10 mL/kg) showed the greatest scope for potential reduction in tidal volumes and driving pressure

Such interventions could be readily implemented at the bedside by clinicians directly, or automatically via closed-loop control algorithms. Our results support the design of randomized trials to better delineate the role of lung-protective ventilation in PARDS.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-019-05559-4) contains supplementary material, which is available to authorized users.

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Funding

DGB and JGH acknowledge funding from the UK Engineering and Physical Sciences Research Council (Grant No. EP/P023444/1). NY acknowledges funding from the NIH (Grant No. NIH K23 HL-136688).

Compliance with ethical standards

Conflicts of interest
The authors declare that they have no conflicts of interests.

Ethical approval
The study was reviewed by the CHOP Institutional Review Board, and requirement for informed consent was waived.

Publisher's Note

Accepted: 2 February 2019
Published online: 14 February 2019

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