Journal Club

Chadi Barakat

2020-05-11

UNIVERSITY OF ICELAND
FACULTY OF INDUSTRIAL ENGINEERING, MECHANICAL ENGINEERING AND COMPUTER SCIENCE
JÜLICH Forschungszentrum | JÜLICH SUPERCOMPUTING CENTRE
Joint Research Center for Computational Biomedicine | RWTH AACHEN UNIVERSITY

RESEARCH

Open Access

What links ventilator driving pressure with survival in the acute respiratory distress syndrome? A computational study

Anup Das[1], Luigi Camporota[2], Jonathan G. Hardman[3] and Declan G. Bates[1*]

Abstract

Background: Recent analyses of patient data in acute respiratory distress syndrome (ARDS) showed that a lower ventilator driving pressure was associated with reduced relative risk of mortality. These findings await full validation in prospective clinical trials.

Methods: To investigate the association between driving pressures and ventilator induced lung injury (VILI), we calibrated a high fidelity computational simulator of cardiopulmonary pathophysiology against a clinical dataset, capturing the responses to changes in mechanical ventilation of 25 adult ARDS patients. Each of these in silico patients was subjected to the same range of values of driving pressure and positive end expiratory pressure (PEEP) used in the previous analyses of clinical trial data. The resulting effects on several physiological variables and proposed indices of VILI were computed and compared with data relating ventilator settings with relative risk of death.

Results: Three VILI indices: dynamic strain, mechanical power and tidal recruitment, showed a strong correlation with the reported relative risk of death across all ranges of driving pressures and PEEP. Other variables, such as alveolar pressure, oxygen delivery and lung compliance, correlated poorly with the data on relative risk of death.

Conclusions: Our results suggest a credible mechanistic explanation for the proposed association between driving pressure and relative risk of death. While dynamic strain and tidal recruitment are difficult to measure routinely in patients, the easily computed VILI indicator known as mechanical power also showed a strong correlation with mortality risk, highlighting its potential usefulness in designing more protective ventilation strategies for this patient group.

Keywords: Mechanical ventilation, Driving pressure, Dynamic strain, Mechanical power, Tidal recruitment, Acute respiratory distress syndrome

Introduction

- The paper is a part of ongoing research on ARDS and cardiopulmonary physiological simulation, and builds on a lot of previous work.
- Published in *Respiratory Research* in 2019 (vol. 20, no. 29).
- The authors implement their physiological simulator to find correlation between driving pressure (among other parameters) and Ventilator-Induced Lung Injury (VILI)

Materials

- Cardiopulmonary physiological simulator (Warwick model)
- Data from 25 patients described in related research by Borges *et al*. Analysing the Horowitz Quotient of these patients classified them as follows:
  - 13 Severe ARDS
  - 7 Moderate ARDS
  - 6 Mild ARDS
- Ventilator settings from another related study by Amato *et al*.

Methods

- Run a simulation of the 25 patients from Borges *et al*. in order to verify accuracy of the model.
- Calculate VILI indices: respiratory system compliance (C_{rs}), intra-tidal recruitment, mechanical power, mean alveolar pressure, and strain on the lungs (static and dynamic).

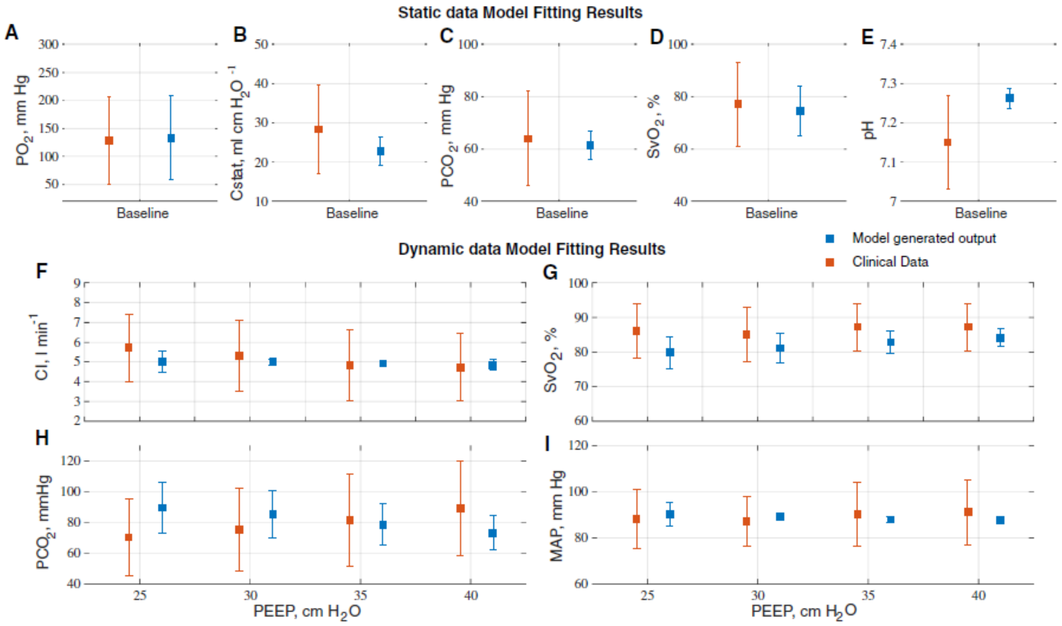

Fig. 1 Results of fitting patient data to model to acquire virtual ARDS subjects. Subplots **a-e** show the results of fitting the model to static data and **f-i** show the results of fitting the model to dynamic data. All error bars show the mean and 1 standard deviation of clinical data (Borges 2006) in red and corresponding model outputs in blue. PO_2 - partial pressure of oxygen in arterial blood, Cstat - static Compliance, PCO_2 - partial pressure of carbon dioxide in arterial blood (mm Hg), SvO_2 - oxygen Saturation in mixed venous blood, pH - pH of arterial blood, CI - cardiac Index (ml min^{-1} m^{-2}), MAP - mean arterial pressure (mm Hg)

Results

- The researchers found positive correlation between high Driving Pressure (ΔP) and the VILI indices **dynamic lung strain**, **mechanical power**, and **tidal recruitment**.
- High values of Peak End-Expiratory Pressure (PEEP) with constant ΔP were correlated with minor changes in VILI indices above.
- High PEEP with low ΔP caused reduction in the VILI indices.
- Finally, the three indices above were strongly positively correlated with mortality risk.

Discussion

- Proved accuracy and applicability of their model.
- Highlighted the importance of Dynamic Strain, Tidal Recruitment and Mechanical Power as indicators of mortality risk in ARDS patients.

Model Parameter	Increasing DP constant PEEP		Constant DP Increasing PEEP		Reducing DP Increasing PEEP		Average
	r	p	r	p	r	p	r
Dynamic Strain	0.985	0.002	0.534	0.353	0.989	0.001	0.836
Tidal Recruitment	0.960	0.010	0.879	0.049	0.992	0.001	0.944
Mechanical Power	0.987	0.002	0.451	0.446	0.969	0.007	0.802
Mean Alveolar Pressure	0.956	0.011	0.495	0.397	-0.981	0.003	0.157
Dynamic Compliance	0.959	0.010	0.612	0.273	-0.948	0.014	0.208
Oxygen Delivery	0.886	0.045	0.721	0.170	-0.556	0.331	0.350
Cardiac Output	0.178	0.775	0.087	0.890	-0.036	0.954	0.076
PF ratio	0.984	0.002	0.507	0.383	-0.974	0.005	0.172
Static Strain	0.981	0.003	0.392	0.514	-0.989	0.001	0.128
VD/VT	-0.935	0.020	-0.705	0.184	-0.880	0.049	-0.840

The table reports the Pearson linear correlation coefficient (r) between the simulated outputs and mortality data reported in 12, with corresponding p value using the students t distribution. Shaded areas highlight parameters with strong positive and significant correlations with mortality data ($r > 0.85$, $p < 0.05$). Table ordered in descending order for average r. PF ratio is the ratio of arterial oxygen tension to fraction of O_2 in inspired air. VD/VT is the physiological deadspace fraction

- Confirmed experimentally that reducing driving pressures and increasing PEEP improves results for these indices.

Further Takeaways

- The authors mentioned that indices like dynamic strain are good markers for lung injury but not feasible at the bedside, unlike mechanical power which can be derived by simply inserting values into an equation.
- They acknowledge limitations of their work due to the limited information in their source material, but also in the simulation aspect of their physiological model.

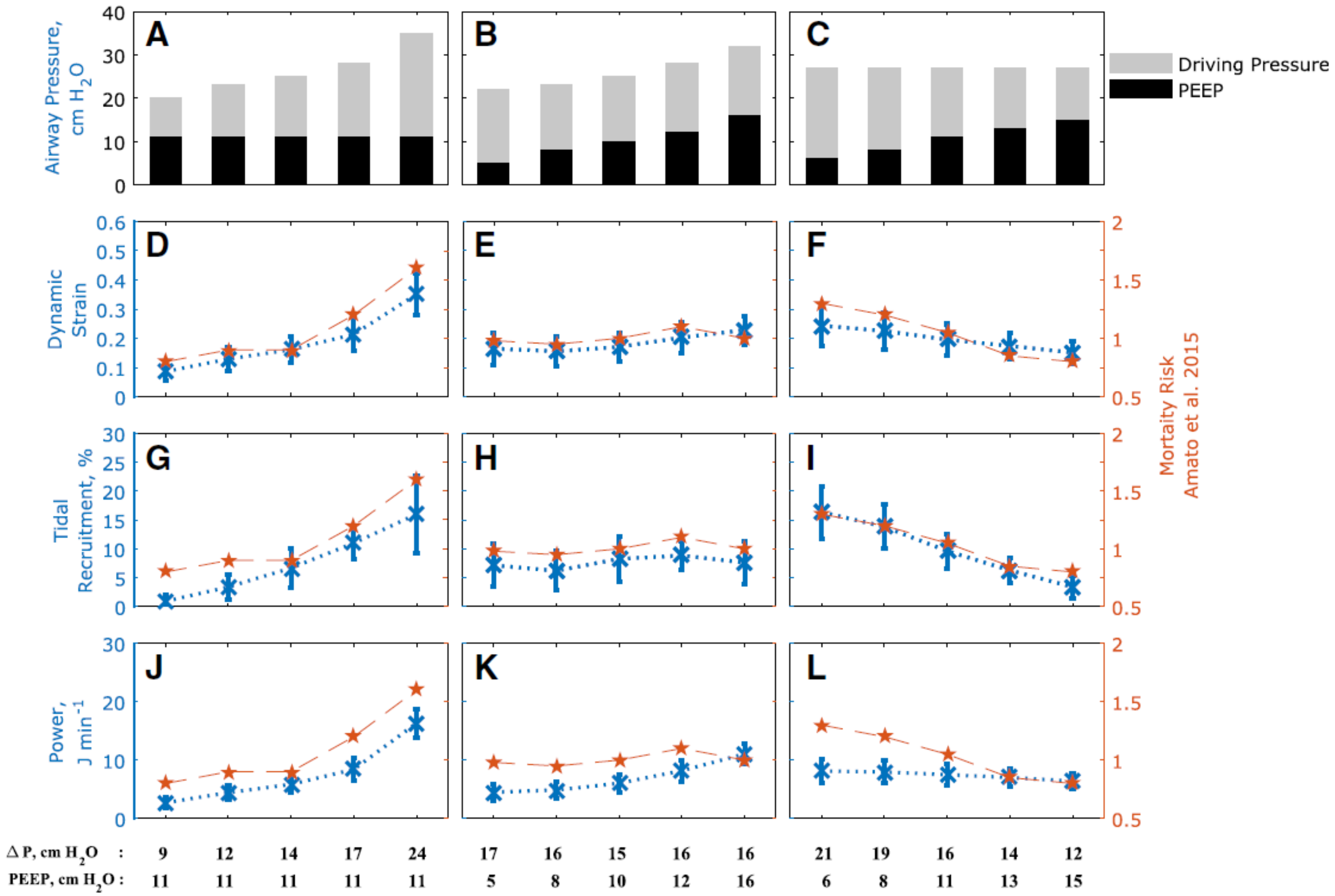

Fig. 2 Results of changing driving pressure and PEEP (**a-c**) on dynamic strain (**d-f**), intra-tidal recruitment (**g-i**) and mechanical power (**j-l**). Subplots **d**–**i** also indicate the mortality risk rates (red) published in Amato et al. (12) for the same changes in airway pressure and PEEP (**a-c** and listed at the foot of the figure) shown here. Blue crosses show mean values in the population and the error bars represent 1 standard deviation

Thank you