Published in final edited form as:

Anesth Analg. 2018 February ; 126(2): 725–726. doi:10.1213/ANE.0000000000002556.

Intratidal analysis of intraoperative respiratory system mechanics: keep it simple.

Robert Huhle, M.Sc.¹, Davide D'Antini, M.D.², Jacob Herrmann, M.Sc.³, Pasquale Raimondo, M.D.², Lucia Mirabella, M.D.², Sabine N.T. Hemmes, M.D., Ph.D.⁴, Marcus J. Schultz, M.D., Ph.D.⁴, Paolo Pelosi, M.D., F.E.R.S.⁵, David W. Kaczka, M.D. Ph.D.⁶, Gilda Cinnella, M.D.², Marcelo Gama de Abreu, M.D., M.Sc., Ph.D., D.E.S.A.^{1, #}, European Society of Anaesthesiology and the PROtective VEntilation Network

¹Department of Anaesthesiology and Intensive Care Medicine, Pulmonary Engineering Group, University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany; ²Department of Anaesthesia and Intensive Care, University of Foggia, Italy; ³Departments of Anesthesia and Biomedical Engineering, University of Iowa, Iowa City, IA, USA; ⁴Department of Intensive Care & Laboratory for Experimental Intensive Care and Anesthesiology (L E I C A), Academic Medical Center at the University of Amsterdam, Amsterdam, Netherlands; ⁵Department of Surgical Sciences and Integrated Diagnostics, IRCCS AOU San Martino IST, University of Genoa, Genoa, Italy ⁶Departments of Anesthesia, Biomedical Engineering, and Radiology, University of Iowa, Iowa City, IA, USA.

Dear Editor,

We thank Dr. Spaeth and colleagues for their interest in our study¹, which was conducted in a subpopulation of the PROVHILO trial².

The authors expressed concern that our linear regression model assumes a “strictly constant resistance,” and compare its limitations to those of the stress index technique. The stress index assumes that during *constant* inspiratory flow, the pressure-time profile behaves according to a power law, with negligible dynamic contributions of resistance to transient pressure fluctuations. However, our linear regression analysis of the respiratory system assumes that dissipative pressure losses are not constant, but rather proportional to the measured flow. Such a model is therefore able to characterize minor fluctuations during constant-flow inflation, whereas the stress index cannot. Furthermore, our linear regression technique does not fit a quadratic polynomial to *total* (i.e., resistive and elastic) pressure as a function of volume, but rather only to the *elastic* pressure. In other words, pressure losses due to resistive and elastic phenomena are estimated separately and simultaneously. Thus the

[#]Address for correspondence and reprints: Marcelo Gama de Abreu, MD, MSc, PhD, DESA, Department of Anaesthesiology and Intensive Care Medicine, Pulmonary Engineering Group, University Hospital Carl Gustav Carus, Technische Universität Dresden, Fetscherstr. 74, 01307 Dresden, Germany, Tel +49 351 458 18070 Fax +49 351 458 4336, mgabreu@uniklinikum-dresden.de.

Authors' contributions:

All authors contributed to drafting the manuscript, approved its final version and are accountable for all its aspects.

Declaration of interests

Dr. Kaczka and Mr. Herrmann are co-founders and shareholders of OscillaVent, Inc.

model used for our regression technique can be used to assess nonlinear elastic behaviour during *any* modality of controlled ventilation, which does not apply to the stress index³.

Dr. Spaeth and colleagues also express concern over non-negligible effects of nonlinear resistance in the presence of minor deviations from constant inspiratory flow due to nonlinear flow-dependent resistive properties of endotracheal tubes. We assumed that a linear resistance model (LRM) would sufficiently account for 1st-order effects of minor flow fluctuations during constant-flow inflation, and thus the nonlinear elastic components of the respiratory system model alone account for nonlinearity in the resulting elastic pressure-volume relationship. To test possible differences, we applied an extended nonlinear resistance model (NLRM), incorporating a flow-dependent component of resistance, as shown in Eq. 1:

$$P_{aw}(t) = R_1 \cdot \dot{V} + R_2 \cdot |\dot{V}| \cdot \dot{V} + E_1 \cdot V + E_2 \cdot V^2 + P_0 \quad \text{Eq. 1}$$

where P_{aw} is the airway pressure determined at the endotracheal tube, t is time, R_1 and R_2 are the linear and nonlinear components of resistance, respectively, V is volume, E_1 and E_2 are the linear and nonlinear components of elastance, respectively, with P_0 representing P_{aw} at end-expiration. The root-mean square error after model fitting according to Eq. 1 was reduced in NLRM compared to LRM ($RMSE = RMSE_{NLRM} - RMSE_{LRM} = -0.0174$ $[-0.038 \dots -0.007]$ Median[1st...3rd quartile]). However, % E_2 calculated as % $E_2 = E_2 \cdot V / (E_1 + E_2 \cdot V)$ with the parameters extracted from Eq. 1 were highly correlated with the results from our publication¹ (Figure 1). Therefore, accounting for the nonlinear component of resistance does not impact on the conclusions of our study.

The authors of the letter recommended the so-called gliding-SLICE method⁴, which is susceptible to minor fluctuations, artefacts, and signal noise in pressures and/or flows. Furthermore, we did not aim to evaluate the extent to which intra-tidal recruitment and/or overdistension occur within a breath, but rather which of these nonlinear phenomena dominates the mechanical characteristics of the breath. Therefore, it is appropriate to use an approach which robustly characterizes the overall degree of elastic pressure-volume nonlinearity by considering the entire inspiratory phase, using a relatively simple regression model.

Funding

The PROVHILO trial was partially funded by the Clinical Trial Network of the European Society of Anaesthesiology. Authors were funded by their respective departments.

References

1. D'Antini D, Huhle R, Herrmann J, Sulemanji DS, Oto J, Raimondo P, Mirabella L, Hemmes SNT, Schultz MJ, Pelosi P, Kaczka DW, Vidal Melo MF, de Abreu M Gama, Cinnella G, European Society of Anaesthesiology and the PROtective VEntilation Network. Respiratory System Mechanics During Low Versus High Positive End-Expiratory Pressure in Open Abdominal Surgery: A Substudy of PROVHILO Randomized Controlled Trial. *Anesth Analg* 2017.

2. The PROVE network investigators. High versus low positive end-expiratory pressure during general anaesthesia for open abdominal surgery (PROVHILO trial): a multicentre randomised controlled trial. *The Lancet* 2014;384:495–503. Available at: <http://linkinghub.elsevier.com/retrieve/pii/S0140673614604165>. Accessed January 4, 2016.
3. Carvalho AR, Spieth PM, Pelosi P, Vidal Melo MF, Koch T, Jandre FC, Giannella-Neto A, de Abreu MG. Ability of dynamic airway pressure curve profile and elastance for positive end-expiratory pressure titration. *Intensive Care Med* 2008;34:2291–9. [PubMed: 18825365]
4. Schumann S, Burcza B, Haberthür C, Lichtwarck-Aschoff M, Guttman J. Estimating intratidal nonlinearity of respiratory system mechanics: a model study using the enhanced gliding-SLICE method. *Physiol Meas* 2009;30:1341 Available at: <http://iopscience.iop.org/0967-3334/30/12/004>. Accessed September 25, 2013. [PubMed: 19864706]

Figure 1 -
Relationship between $\%E_2$ calculated from linear resistance model (LRM) and nonlinear resistance model (NLRM).