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Letter to Editor

Fundamental Misconceptions in the Interpretation of the Origin of Ventilator-Induced Lung Injury

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Conceptual errors underlie much of today's interpretation of mechanical ventilation and the rationale of Lung-Protective Strategies (LPS). In LPS Tidal Volume (TV) must be minimized, even when ventilation remains far below vital capacity. This view treats "stretch" as intrinsically injurious. Yet the mechanical consequences of any given volume change depend critically on the pressure environment in which that volume change occurs.

During spontaneous breathing or Negative Pressure Ventilation (NPV), inspiration is driven by a fall in Pleural Pressure (P_{pl}). The lung is drawn away from the chest wall and expands under external physiological "pulling" forces. During Positive Pressure Ventilation (PPV) in a closed thorax, the same volume is achieved by raising airway pressure (P_{aw}). This inevitably raises P_{pl} and intrathoracic Pressure (P_{th}, the mean of P_{pl} and P_{aw}), so the lung changes volume while being pressed against the chest wall and while tissue is compressed by surrounding pressures (P_{th}) (Fig.1).

Clinical practice implicitly acknowledges this distinction. During PPV we restrict TV to "protect" the lung, yet after extubation we encourage deep spontaneous breaths to counteract atelectasis. Apparently we realize that PPV promotes collapse whereas strong negative P_{pl} reverses it, but we still accept the claim that PPV and NPV are physiologically equivalent with respect to ventilator-induced lung injury (VILI).
Two influential concepts have fueled this misconception.

First, Dreyfuss' volutrauma [1]. In his seminal rat experiments, summarized under the provocative title "barotrauma = volutrauma", lung injury occurred when animals were ventilated above their vital capacity. Dreyfuss' experiments also showed that injury could be avoided when lung expansion was prevented by external pressure. Thus, injury was not caused by volume per se, but by the pressure conditions that allowed excessive expansion to occur: barotrauma after all. Nevertheless, the volutrauma concept became the conceptual foundation for limiting TV in clinical ventilation and for the central premise of LPS: that smaller TVs are inherently safer, while the role of P_{pl} and P_{th} was largely neglected.

Second, Loring's widely cited assertion that PPV and NPV are equivalent because both can generate the same volume by the same transpulmonary pressure [2,3]. This argument traces back to Comroe's observations in the era of open-thorax surgery, when lungs were passively inflated without an intact chest wall [4]. While appropriate in that setting, it does not describe ventilation in a closed thorax. NPV generates transpulmonary pressure by lowering P_{pl}. PPV can generate the same transpulmonary gradient only by elevating P_{aw} and unavoidably, elevating P_{pl} and P_{th}. Equal transpulmonary pressure therefore

does not imply equivalence of P_{pl} behavior, lung-chest wall interaction or compressive loading of lung tissue.

Additional confusion stems from experimental studies that purported to compare PPV and NPV in excised animal lungs [5]. By removing the thoracic cage they eliminate the pleural space, the very structure that creates the physiological distinction between PPV and NPV *in-vivo*. Without a chest wall, the lung behaves approximately as a single compliant structure; PPV and NPV will then, by definition, produce similar transpulmonary pressures for a given volume. Such preparations therefore cannot test the mechanics of ventilation in the intact chest and their findings cannot support a clinical claim of equivalence between PPV and NPV.

A simple thought experiment illustrates the point. Consider a relaxed supine subject at functional residual capacity with $P_{pl} \approx -5$ mbar. Place a weight on the abdomen: lung volume falls and P_{pl} rises. The original volume can be restored either by raising P_{aw} (PPV) or by lowering the surrounding pressure around thorax and abdomen (NPV). The first strategy further elevates P_{pl}; the second removes the load from the diaphragm and restores both volume and the original, negative P_{pl}. Identical volumes are achieved under fundamentally different P_{pl} conditions.

In ARDS this is not subtle: P_{pl} may become markedly positive while PEEP is also positive, shifting the P_{th} milieu from sub-atmospheric to strongly super-atmospheric. The lung must then change volume while being compressed and pressed against the chest wall.

Klassen, et al., provided direct experimental support for this distinction using porcine lungs with a small visceral pleural leak: for the same TV, PPV required substantially higher driving pressure than NPV, while air leakage from the peripheral lung was several-fold greater during NPV, indicating more effective ventilation of the subpleural regions [6]. These results were confirmed by Eckert in similar experiments investigating staple-line position during lung resection surgery [7].

Taken together, the prevailing equivalence claim rests on a category error: it either generalizes volutrauma beyond its mechanistic context or "compares" PPV and NPV in models where the pleural space has been removed. Because NPV is the only form of mechanical assistance that preserves the physiological mechanism of inspiration (a fall in P_{pl} with atmospheric P_{aw}), it deserves renewed consideration in modern respiratory care.

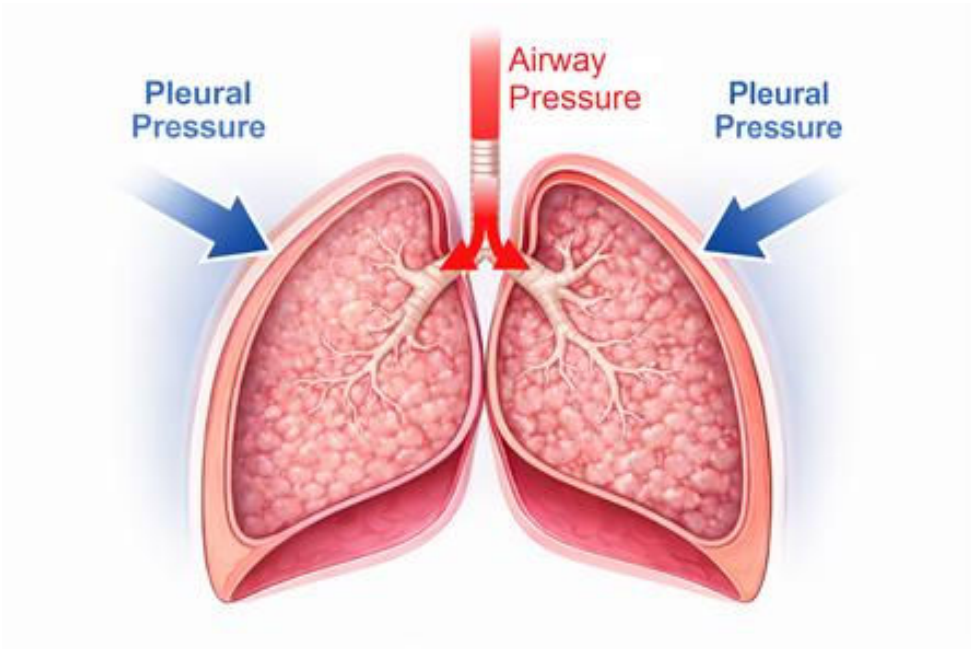

Figure 1: Lung parenchyma sandwiched between P_{aw} and P_{pl}, illustrating that lung tissue stress depends on the surrounding pressure environment, not on volume alone.

Keywords: Mechanical Ventilation; Pleural Pressure; Intra-Thoracic Pressure; Lung Protective Strategies; VILI

Conflict of Interest

Apart from their university/hospital affiliations, both authors (JvE and JPM) are members of the Exovent Developing Group, which is a UK registered charity (no. 1189967:10 Queen St Pl, London EC4R 1BE, UK.) https://exovent.org None of the authors is receiving any honoraria from this charity. On behalf of all authors, the corresponding author states that there is no conflict of interest. JPM reports payments or honoraria from Medec international outside the submitted work. JPM is a member of a Belgium registered charity ESPCOP vzw (no. 1030137921: Beukenpark 19 9930 Lievegem, BE). https://espcop.eu and co-founder of MT4L. https://mt4l.com, a company developing not related airway products.

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Informed Consent Statement

Not applicable.

Authors' Contributions

All authors have contributed equally to this work and have reviewed and approved the final manuscript for publication.

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