CHEST

The Significance of Sizes

Which Matters Most?

Luigi Pisani, MD, PhD
Bari, Italy
Marcus J. Schultz, MD, PhD
Amsterdam, The Netherlands

In this issue of *CHEST*, Samanta et al[1] present their investigation into the adoption of protective ventilation in a diverse and well-sized patient population. Their analysis of data from over 12,000 patients sheds light on the insufficient utilization of low tidal volume ventilation (LTVV) in critically ill, invasively ventilated patients in North America and the United Kingdom. Notably, among the patients in their cohort, those exposed to excessively high tidal volume (V_T) experienced the highest mortality rates. This study offers valuable real-world evidence on LTVV implementation, derived from an extensive analysis of electronic medical records (EMRs), providing a solid foundation for our comprehension of this subject matter.

Although the adoption of LTVV has seen improvement over the years, a significant portion of patients still receive ventilation with excessive V_T,[2,3] as confirmed by Samanta et al.[1] Patients in North America seem to exhibit greater protection against the use of excessive V_T when compared with their counterparts in the United Kingdom. Additionally, Samanta et al[1] highlight that shorter patients and those with obesity are at a higher risk of not receiving LTVV, aligning with findings from previous studies.[2]

FOR RELATED ARTICLE, SEE PAGE 333

AFFILIATIONS: From the Department of Precision-Regenerative Medicine and Jonic Area (DiMePRe-J) (L. P.), Section of Anesthesiology and Intensive Care Medicine, University of Bari "Aldo Moro"; the Nuffield Department of Medicine (L. P., M. J. S.), Center for Tropical Medicine and Global Health, Oxford, England; the Mahidol–Oxford Tropical Medicine Research Unit (MORU) (L. P., M. J. S.), Mahidol University, Bangkok, Thailand; the Department of Intensive Care (M. J. S.), Amsterdam University Medical Centers; and the Department of Anesthesia (M. J. S.), General Intensive Care and Pain Management, Division of Cardiothoracic and Vascular Anesthesia & Critical Care Medicine, University of Vienna, Vienna, Austria.

CORRESPONDENCE TO: Luigi Pisani, MD, PhD; email: luigipisani@gmail.com

DOI: https://doi.org/10.1016/j.chest.2023.11.002

Nevertheless, whether we might be applying excessive rigor in this regard is worth considering. What precisely defines a "low V_T," or, to be more precise, what constitutes an appropriate V_T? There are various ways to interpret the results of the pivotal Respiratory Management in Acute Lung Injury/ARDS (ARMA) trial,[4] which forms the cornerstone for the evidence of benefit of LTVV. First, this study's findings can be seen as endorsing the "utilization of low V_T," but at the same time, they equally support the "avoidance of high V_T." Second, the ARMA trial focused on patients with ARDS, and its findings may not be generalizable to patients without this condition.[5] Moreover, we should contextualize ARMA historically. At the time of ARMA, many, if not all, ARDS patients were "passive," because patients frequently were kept deeply sedated and were often paralyzed. The practice of muscle paralysis and sedation has evolved since then, with the more frequent and earlier use of spontaneous ventilation modalities. We are well aware of the challenges associated with titrating V_T in patients who have control over their breathing.

Moreover, additional considerations have arisen since the ARMA trial. We have refined the concept that V_T should invariably be "low." First, we've gained insights into the significance of a low driving pressure (ΔP) which may be equally critical. What should clinicians do when they are faced with a "high V_T" but a low ΔP? Second, the adoption of LTVV can lead to a compensatory increase in respiratory rate to maintain minute ventilation. This heightened respiratory rate carries potential risks because it escalates the mechanical power of ventilation,[6] potentially translating into more mortality and morbidity.[7] And finally, the interplay between these key elements of lung protection could be crucial, because a combination of low V_T with high respiratory rate could be beneficial in a patient with stiff lungs but harmful in patients with less stiff lungs.[6]

EMRs may not consistently gather all of this information, and data collection may occur at varying time points. When using routinely collected patient data such as those from medical records, it is imperative to

exercise caution when reporting aggregate measures of repeated data, bearing in mind that specific variables or parameters within these data sets must be interpreted in a time-sensitive matter. Incorporating calculated parameters in EMRs, such as the previously mentioned ΔP and mechanical power of ventilation, can undoubtedly assist in this regard and facilitate personalized protective ventilation at the bedside. However, integrating and analyzing all data comprehensively to determine whether a more effective implementation of LTVV, or conversely, its absence, results in improved lung protection or, conversely, diminished lung protection, is imperative.

As with other observational studies, this analysis, while confirming associations, falls short of demonstrating causation. We might realize a specific condition prompts the use of a high V_T and that such conditions are also associated with outcomes. Obesity, short stature, and being a woman are not, of course, among them. However, other conditions are conceivable, such as sepsis, with increased CO_2 production, or kidney injury, leading to metabolic acidosis. This is one well-known pitfall of EMR-based studies. EMRs often lack high-quality data on potential confounders, thus limiting assessments of complex interactions.

A recent perspective suggests that EMRs failed to make the lives of health care workers easier.[8] However, they have made health care workers more accountable for processes of care such as ventilation management. Large studies from Brazil found how organizational factors such as better nurse staffing, nurse autonomy, and use of structured checklists are linked to adherence to processes of care such as low tidal ventilation.[9] We also know protective ventilation is feasible in resource-limited settings, because middle-income countries show equal capabilities of LTVV compared with high-income countries.[3,10] This is where EMR-based studies could help: EMRs allow for extensive longitudinal follow-up and recording of variations in time––in both higher- and lower-income settings.[11] For instance, beyond poor absolute implementation, the study by Samanta et al[1] found little variation in V_T over the course of individual ventilation episodes. This at least suggests that LTVV may not be implemented that well, although we cannot be sure of that.

Next to EMRs, there are quality clinical databases or ICU registries that allow comparative effectiveness research, which is directly linked to the implementation issue raised by Salluh et al.[12] A recent well-designed registry-based study demonstrated how a lung-protective ventilation intervention, dynamic pressure limitation, can be synergic to traditional LTVV in protecting the lung and improving survival in the ICU.[13] Interoperability of data between EMRs and ICU registries is rapidly increasing, opening to new and robust implementation research possibilities.

EMRs allow for vigilance over lung-protective ventilation while concepts and intervention targets evolve. Implementation and quality improvement research may not seem attractive, but we must keep leveraging pragmatic data sources to assess whether we are changing our daily practice.

Financial/Nonfinancial Disclosures

L. P. and M. J. S. are partly funded by Wellcome.

References

1. Samanta RJ, Ercole A, Harris S, Summers C. Low tidal volume ventilation is poorly implemented for patients in North American and United Kingdom ICUs using electronic health records. *Chest*. 2024;165(2):333-347.
2. Swart P, Deliberato RO, Johnson AEW, et al. Impact of sex on use of low tidal volume ventilation in invasively ventilated ICU patients: a mediation analysis using two observational cohorts. *PLoS ONE*. 2021;16:e0253933.
3. Pisani L, Algera AG, Neto AS, et al. Geoeconomic variations in epidemiology, ventilation management, and outcomes in invasively ventilated intensive care unit patients without acute respiratory distress syndrome: a pooled analysis of four observational studies. *Lancet Glob Health*. 2022;10:e227-e235.
4. Brower RG, Matthay MA, Morris A. et al.; Acute Respiratory Distress Syndrome Network, Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1301-1308.
5. Simonis FD, Serpa Neto A, Braber A, et al. Writing Group for the PReVENT Investigators, Effect of a low vs intermediate tidal volume strategy on ventilator-free days in intensive care unit patients without ARDS: a randomized clinical trial. *JAMA*. 2018;320(18):1872-1880.
6. Goligher EC, Costa ELV, Yarnell CJ, et al. Effect of lowering Vt on mortality in acute respiratory distress syndrome varies with respiratory system elastance. *Am J Respir Crit Care Med*. 2021;203:1378-1385.
7. Serpa Neto A, Deliberato RO, Johnson AEW, et al. Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts. *Intensive Care Med*. 2018;44:1914-1922.
8. Hswen Y, Voelker R. Electronic health records failed to make clinicians' lives easier: will AI technology succeed? [Published online ahead of print October 4, 2023]. *JAMA*. https://doi.org/10.1001/jama.2023.19138
9. Midega TD, Bozza FA, Machado FR, et al. Organizational factors associated with adherence to low tidal volume ventilation: a secondary analysis of the CHECKLIST-ICU database. *Ann Intensive Care*. 2020;10:68.
10. Pisani L, Algera AG, Serpa Neto A, et al. Epidemiological characteristics, ventilator management, and clinical outcome in patients receiving invasive ventilation in intensive care units from 10 Asian middle-income countries (PRoVENT-iMiC): an international,

multicenter, prospective study. *Am J Trop Med Hyg*. 2021;104(3):1022-1033.

11. Woldemariam MT, Jimma W. Adoption of electronic health record systems to enhance the quality of healthcare in low-income countries: a systematic review. *BMJ Health Care Inform*. 2023;30:e100704.

12. Salluh JIF, Quintairos A, Dongelmans DA, et al. National ICU registries as enablers of clinical research and quality improvement. *Crit Care Med*. 2024;52(1):125-135.

13. Urner M, Jüni P, Rojas-Saunero LP, et al. Limiting dynamic driving pressure in patients requiring mechanical ventilation. *Crit Care Med*. 2023;51:861-871.