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Ventilator associated or induced lung injury. Does the name matter? Point and counterpoint

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Abstract

The terminology used to describe lung injuries in patients receiving mechanical ventilation has significant implications for clinical practice, research, and communication among healthcare professionals. This point-counterpoint discussion paper explores the debate over the appropriate term to use: "ventilator-associated lung injury" (VALI) or "ventilator-induced lung injury" (VILI).

The first author argues in favor of the term "ventilator-associated lung injury" from epistemology, philosophy, epidemiology and statistics, seems to correctly substantiate the relationship between lung injury as a consequence of inadequate mechanical ventilator programming. According to this perspective, "associated" more accurately reflects the complex interplay of these elements, which together contribute to the development of lung injury in ventilated patients.

The second author advocates for the term "ventilator-induced lung injury," underscoring the direct causative role of mechanical ventilation in the development of lung injuries. This perspective highlights the specific pathological changes that result directly from mechanical ventilation strategies. According to this prospective "induced" is considered a more precise term, attributing the injury directly to the intervention of mechanical ventilation.

Through this exchange, the authors provide a comprehensive analysis of the clinical and scientific implications of each term, ultimately seeking to guide consensus in the field regarding the most accurate and useful terminology.

Keywords: VALI, VILI

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Point: Ventilation Associated Lung Injury (VALI) A statistical argument

Introduction

Evidence-based medicine has been a steadily growing maelstrom over the last few years. Different statistical strategies are employed to generate the best evidence currently available. However, in recent times a dilemma has arisen regarding the appropriate term to relate lung damage that occurs when critically ill patients are connected to mechanical ventilators, irrespective of etiology. Induced versus associated damage - that is the dilemma.

Statistical logic

Inductive (or inferential) reasoning is based on the generalization of a concept from a minor premise. In the so-called 'non-demonstrative argument', the truth of the premises does not necessarily entail the truth of the conclusion. [1] Aristotle himself pointed out that the various inductive arguments are not conclusive, i.e., non-demonstrative. Karl Popper [2] claimed that induction is untenable and should be excluded from any reasoning that claims to be rational. [3] In this view, inductive arguments need to replace conclusions with assertions of probability. Statistical inference presupposes the existence of mutually exclusive hypotheses that can be gradually eliminated over a finite number of experiments until the most plausible one remains, thus falling into a vicious circle.

According to probability theory, the epistemological definition of induction [4] is a complex issue, in the context of avoiding the consequence that the probability of any universal statement asserting something about the world is zero, whatever the observational evidence. The solution, according to Popper's classical falsificationist method, [5] is to use the falsifiability condition as a demarcation criterion for scientific knowledge (deduction). In short, in analytical induction, precision is sacrificed in order to gain correspondence with reality, and knowledge of a phenomenon achieves a minimum of generalization that could serve as a basis for further study, whereas in falsificationism, statements are discarded in order to reduce ignorance about a phenomenon so that the phenomenon can be said with certainty not to be and the constant categories or characteristics remain potentially falsifiable but temporarily true of that phenomenon. Statistics is the tool that helps us to estimate the probability of error in such a refutation. [6]

Association between two variables

In epidemiology, measures of association are indicators that quantify the strength or magnitude with which a given health event (presumed outcome) is related to a given factor (presumed cause). [7] Measures of association are based on comparing incidences: the incidence of disease in those individuals exposed to the factor under study (or incidence among those exposed) with the incidence of disease in those individuals not exposed to the factor under study (or incidence among those not exposed). This is known as relative risk. [8]

Under certain circumstances, these measures of association allow causal inferences to be made especially by means of a statistical function. The most robust measures of association are calculated using incidence, as it allows us to establish beyond doubt that the effect (event or disease) appears after exposure to the factor. [9]

From a statistical point of view, the probability that the observed effect or a larger one has occurred by chance, assuming that the effect did not exist, can be assessed by hypothesis testing. This probability is known as statistical significance and is represented by the well-known p-value. However, this level of significance does not inform neither the magnitude of the effect nor its clinical relevance.

VALI, the evidence

There is much recent, high-quality evidence to support the argument for the term 'ventilator-associated lung injury' between mechanical ventilation and lung parenchyma over 'induced injury'. However, the term VALI has already been used long ago, when the International Consensus Conference on Critical Care Medicine emphatically promulgated the term 'ventilator-associated lung injury'. [10]

Randomized experimental studies suggest that low tidal volume ventilation probably attenuates VALI by limiting mechanical damage to the lung, while hypercapnia attenuates VALI by limiting pro-inflammatory and biochemical mechanisms of injury. In combination, they generate a potential synergistic effect for the prevention of VALI. [11]

Pathophysiological studies, published by respected and recognized authors in the field of critical respiratory medicine, make use of the term VALI. [12] An interesting review by Rocco and colleagues [13] supports the association between the genesis of

VALI through specific mechanotransduction mechanisms and individual threshold values. Observational studies in humans demonstrated an association between e-cigarettes and VALI. [14] A randomized clinical trial demonstrated that VALI was associated with an interaction between individual proinflammatory profile and ventilator-imposed mechanical load. [15] Larger studies, such as the systematic review with meta-analysis of randomized clinical trials by Sarkar and colleagues, [16] demonstrated that impedance tomography-guided PEEP titration was associated with lower mortality and incidence of VALI in ARDS patients.

Conclusions

The term ‘ventilator associated lung injury’ or VALI, from epistemology, philosophy, epidemiology and statistics, seems to correctly substantiate the relationship between lung injury as a consequence of inadequate mechanical ventilator programming. Different authors worldwide, through solid experimental and clinical studies, have shown their preference for the use of the term VALI over VILI. There is still a long way to go.

Counterpoint: Ventilator Induced Lung Injury (VILI)

Introduction

Mechanical ventilation is a life-saving intervention used in critical care to support patients with respiratory failure. However, the use of ventilators is not without risks. One significant complication is lung injury related to the mechanical ventilation itself. The mechanisms by which the ventilator is implicated in creating or worsening lung injuries are numeral and complex. [17]

The true incidence of lung injury during mechanical ventilation is still unknown owing to many factors:
- The difficulty to distinguish between lung injury caused by the ventilator versus the natural progression of the disease state. [18]
- Lack of diagnostic radiological or biomarkers. [19,20]
- Other diseases that can occur during mechanical ventilation like ventilator associated pneumonia (VAP) [21] or transfusion related acute lung injury. [22]

This has led the CDC to infer an empiric new definition of Ventilator associated events (VAE) based on criteria of worsening oxygenation or the need for increased PEEP. [23]

There is an ongoing debate about the terminology used to describe this complication, specifically whether it should be termed "ventilator-induced lung injury" (VILI) or "ventilator-associated lung injury" (VALI). We make the argument of why "ventilator-induced lung injury" is the more accurate term.

Ventilator-Induced Lung Injury (VILI)
VILI refers to lung damage directly caused by the mechanical forces and pressures exerted by the ventilator on the lung tissues. The term "induced" emphasizes a direct causal relationship between the use of the ventilator and the resultant lung injury. This highlights the mechanical aspects of ventilation as the primary source of the damage.

Ventilator-Associated Lung Injury (VALI)
VALI implies a looser association where the lung injury occurs in the presence of mechanical ventilation but does not necessarily pinpoint the ventilator as the direct cause.
The term "associated" suggests a correlation rather than causation, which can be misleading in understanding the specific role of mechanical ventilation in causing lung damage.

Pathophysiology of VILI

- Barotrauma: Excessive airway pressures can lead to alveolar overdistension and rupture with consequent pneumomediastinum, subcutaneous emphysema, and pneumothorax. [24]
- Volutrauma: High tidal volumes can cause overinflation of the lung units, resulting in cellular injury and inflammatory responses. [25]
- Atelectrauma: Repeated opening and closing of alveoli during the ventilation cycle can cause shear stress and subsequent lung injury. [26]
- Biotrauma: Mechanical ventilation can trigger an inflammatory response in the lungs, leading to further tissue damage. [19]
- Ergotrauma: the energy delivered from the ventilator into the lungs can contribute to lung injury and has been summarized into the mechanical power concept. [27]
- Rheotrauma: the effect of gas flow can play an effect on lung injury through shear stress injury. [28]
- Patient-Ventilator dyssynchrony: can cause large tidal volumes and trans-pulmonary pressure that can further propagate lung injury. [29]
- Trans-pulmonary pressure: the positive pleural pressure induced by positive pressure ventilation can increase the lung stress at end of inspiration and worsening atelectasis at end of expiration. [18]
- Ventilator induced diaphragmatic dysfunction (VIDD): characterized by a reduction in the diaphragm's ability to generate force, as well as structural damage and atrophy of diaphragm muscle fibers. VIDD can also lead to diaphragm contractile dysfunction and weaning failure. [30]
- Ventilator induced hemodynamic effects: positive pressure ventilation alters the normal heart-lung

interaction and can have deleterious effects on hemodynamics and the right ventricle especially in the cases of auto-PEEP and pulmonary hypertension. [31,32]

These mechanisms clearly indicate that the injury is a direct result of the mechanical forces applied by the ventilator, supporting the use of the term "induced."

It is also fair to note the crucial role of clinicians setting and adjusting the ventilators. We clinicians are responsible for the effects of the ventilator on the critically ill so in essence, VILI can be also expressed as Clinicians induced lung injury. Automated or intelligent modes requiring less clinician manipulation have shown promise in reducing VILI. [33]

Clinical and Research Perspectives

Precision in Communication: In clinical practice and research, precise terminology is crucial. "Induced" leaves no ambiguity about the causative role of the ventilator, aiding in clearer communication among healthcare professionals and researchers.

In theory, the distinction matters because it can influence how clinicians approach prevention and treatment. If the injury is deemed "ventilator-induced," the focus might be on adjusting ventilator settings. If it's considered "ventilator-associated," the approach might also include managing underlying conditions or preventing secondary complications

Focus on diagnosis and prevention: Understanding that the lung injury is induced by the ventilator underscores the importance of optimizing ventilator settings to minimize harm. It promotes a more proactive approach to preventing VILI through diagnostic strategies [34] and lung-protective ventilation concepts. [35]

Conclusions

Two equally convincing yet conflicting conclusions I can think of:

- Terminology matters: The term "ventilator-induced lung injury" is more accurate and informative than "ventilator-associated lung injury." It clearly identifies the ventilator as the direct cause of lung damage, guiding better clinical practices and research focus. Accurate terminology is essential for effective communication, understanding, and prevention of this significant complication in the critical care settings.

- Terminology doesn't matter: In the end, while the distinction between "ventilator-induced" and "ventilator-associated" lung injury has conceptual importance, its practical impact on day-to-day clinical decisions is often limited. The debates highlight the complexity of mechanical ventilation and the need for careful, individualized patient management. However, whether a clinician calls it VILI or VALI, the focus remains on protecting the lungs and optimizing ventilation settings to improve patient outcomes.

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