Great Britain Journals Press

London Journal of Medical and Health Research
General Section

RESEARCH FINGERPRINT

IDENTIFIER
LJMHR-226753

PEER REVIEW
Double Blind

SIMILARITY CHECK
Perplexity AI and iThenticate

ACCESS
Open Access

LANGUAGE
English

PRINT ISSN
2515-5784

ONLINE ISSN
2515-5792

EDITION

ABBREVIATION
LJMHR

VOLUME
26

ISSUE
4

YEAR
2026

KEY DATES

RECEIVED
2026-04-03

ACCEPTED
2026-04-13

CATALOGING

CROSSMARK DOI
10.34257/226753UK

MESH CLASS
D001237, D011175, D001281, D011187

ICD CLASS
J98.1

UDC CLASS
612.2

Article Record

The Paradox of Airway Closure: From Protection to Pathology

CORRESPONDENCE

AUTHORS & AFFILIATIONS

Jan van Egmond ¶‖*

PhD, Clinical Physicist
ORCID 0000-0001-9561-5777

Jan Mulier §‡

ζ PhD, Anaesthesiologist
ORCID 0000-0001-6664-8270

¶ Anaesthesiology, Radboud University Medical Centre, Nijmegen, The Netherlands Department. (OA)

‖ Donders Institute for Brain, Cognition and Behaviour. Donders Centre for Cognition, Radboud University, Nijmegen, The Netherlands.

§ Faculty of Medicine and Health Sciences, Basic and applied medical sciences, Ghent University, Ghent, Belgium (OA)

‡ Department of Anesthesiology and Pain clinic, Ghent University Hospital, Ghent, Belgium

ABSTRACT

Airway closure, first recognized by Laennec and later quantified in studies by Dollfuss, Hedenstierna and Hughes, represents a physiological phenomenon with far-reaching clinical consequences. While often overlooked in critical care, its role in promoting atelectasis, impaired gas exchange, and ventilator-induced lung injury is well established. The present narrative review revisits the fundamental physiology of airway closure, its exacerbation in anaesthesia and obesity, and its near-universality in mechanically ventilated ARDS patients. A reinterpretation of pleural pressure data from landmark studies, suggests that airway closure may be far more prevalent than currently appreciated. Strategies such as optimal PEEP and avoidance of high oxygen fractions are discussed, with emphasis on the urgent need for better integration of airway closure physiology into clinical practice. This article re-examines how positive airway pressure in combination with elevated intrathoracic pressure — the inevitable companion of positive pressure ventilation — underlies many of the adverse effects attributed to modern mechanical ventilation. By contrast, negative pressure ventilation, long abandoned, may offer physiological advantages worth reconsidering. The question we must now ask is: could a return to negative extra-thoracic pressure — or a hybrid model — prevent the very complications we have come to accept as inevitable?

Index Terms: Mechanical Ventilation • Positive Pressure Ventilation • Negative Pressure Ventilation • Airway Resistance • Airway Closure • Atelectasis • Ventilator Induced Lung Injury • Pleural Pressure • Intra-thoracic pressure

FUNDING
No external funding was declared for this work.

CONFLICTS
The authors declare no conflict of interest.

AI USAGE
No generative AI was used for analysis or results.

HOW TO CITE
van Egmond et al. (2026). The Paradox of Airway Closure: From Protection to Pathology. London Journal of Medical and Health Research, 26(4), 31-38. DOI: 10.34257/226753UK

ACCESS ONLINE

METADATA CONTINUATION

AUTHOR CONTACT QR LEDGER

Jan van Egmond¶‖II*

Jan Mulier§‡ζ

ARCHIVAL RECORD

LJMHR · Vol 26 · Issue 4 · 2026

Article ID LJMHR-226753 · DOI 10.34257/226753UK

Print ISSN 2515-5784 · Online ISSN 2515-5792

CROSSREF DOI 10.34257/226753UK

NARRATIVE REVIEW

The Paradox of Airway Closure: From Protection to Pathology

Jan van Egmond[¶‖∐*] iD **and Jan Mulier**[§‡ζ] iD

QUALIFICATIONS / ROLES

∐ PhD, Clinical Physicist
ζ PhD, Anaesthesiologist

AFFILIATIONS

¶ Anaesthesiology, Radboud University Medical Centre, Nijmegen, The Netherlands Department. (**OA**)
‖ Donders Institute for Brain, Cognition and Behaviour. Donders Centre for Cognition, Radboud University, Nijmegen, The Netherlands. (**OA**)
§ Faculty of Medicine and Health Sciences, Basic and applied medical sciences, Ghent University, Ghent, Belgium (**OA**)
‡ Department of Anesthesiology and Pain clinic, Ghent University Hospital, Ghent, Belgium (**OA**)

Abstract

Airway closure, first recognized by Laennec and later quantified in studies by Dollfuss, Hedenstierna and Hughes, represents a physiological phenomenon with far-reaching clinical consequences. While often overlooked in critical care, its role in promoting atelectasis, impaired gas exchange, and ventilator-induced lung injury is well established. The present narrative review revisits the fundamental physiology of airway closure, its exacerbation in anaesthesia and obesity, and its near-universality in mechanically ventilated ARDS patients. A reinterpretation of pleural pressure data from landmark studies, suggests that airway closure may be far more prevalent than currently appreciated. Strategies such as optimal PEEP and avoidance of high oxygen fractions are discussed, with emphasis on the urgent need for better integration of airway closure physiology into clinical practice. This article re-examines how positive airway pressure in combination with elevated intrathoracic pressure — the inevitable companion of positive pressure ventilation — underlies many of the adverse effects attributed to modern mechanical ventilation. By contrast, negative pressure ventilation, long abandoned, may offer physiological advantages worth reconsidering. The question we must now ask is: could a return to negative extra-thoracic pressure — or a hybrid model — prevent the very complications we have come to accept as inevitable?

Keywords: *Mechanical Ventilation, Positive Pressure Ventilation, Negative Pressure Ventilation, Airway Resistance, Airway Closure, Atelectasis, Ventilator Induced Lung Injury, Pleural Pressure, Intra-thoracic pressure*

Correspondence: Jan van Egmond (e-mail: jan.vanegmond.kf@gmail.com)

1 Introduction

Despite decades of technical progress in mechanical ventilation, an important mechanical consequence of positive pressure ventilation (PPV) remains insufficiently appreciated: the rise in pleural pressure (P_{pl}) and intrathoracic pressure (P_{it}) that inevitably accompanies the application of positive airway pressure (P_{aw}) within a thorax that does not actively expand. This increase in surrounding tissue pressure may compress the lung parenchyma and the small peripheral airways, particularly in dependent regions or in lungs with reduced compliance.

The present article is not intended as a comprehensive review of airway closure or ventilator-induced lung injury (VILI). Rather, it focuses on a specific mechanical interpretation: that airway closure, atelectasis, hyperinflation, and related complications during PPV are closely linked to lung tissue compression caused by elevated pleural and intrathoracic pressure. This perspective differs from the common emphasis on transpulmonary pressure alone, suggesting that reductions in transpulmonary pressure by themselves are insufficient to explain or prevent atelectasis during positive-pressure ventilation.

The transition from negative pressure ventilation (NPV) to PPV in the mid-20th century was driven largely by practical advantages—airway access, emergency applicability, and ease of use—rather than by controlled physiological comparison. As a result, the mechanical differences between inflating the lung by raising P_{aw} and inflating it by lowering P_{pl} may have remained underappreciated. The present review reconsiders airway closure in that light.

TRIBUTE TO PROFESSOR HEDENSTIERNA

The ideas presented in this paper have been profoundly influenced by the pioneering work of Göran Hedenstierna, whose studies from the 1970s onward laid much of the foundation for our current understanding of airway closure, atelectasis, and the effects of oxygen and pressure on lung mechanics.

Those who met Göran (JPM) may recall his persistent warning against the routine use of high oxygen concentrations during PPV. He repeatedly emphasized the relationship between inspired oxygen fraction and the development of atelectasis. At the time, however, few of us fully understood the mechanism he proposed, and clinical practice changed little—we continued to increase the oxygen concentration to 100% before intubation and before terminating PPV and proceeding to extubation.

When I (JvE) revisited his 1976 paper on airway closure [1], I realized how far ahead of his time he had been. He recognized that airway closure is not merely a pathological phenomenon, but a physiological mechanism that protects the lung at low volumes. His meticulous experiments demonstrated how anaesthesia, PPV, and high oxygen concentrations disturb this delicate balance and thereby promote atelectasis.

"This concept is increasingly reflected in contemporary lung-protective strategies, which recommend avoiding unnecessarily high inspired oxygen fractions. During maintenance, weaning, and immediately prior to extubation, FiO_2 may often be limited to approximately 0.4 whenever clinically feasible, whereas higher FiO_2 values, up to approximately 0.8, may be appropriate during induction and airway management [2]."

In addition, positive pressure ventilation differs fundamentally from spontaneous breathing and NPV in its hemodynamic effects. The increase in intrathoracic pressure reduces venous return and cardiac preload, may impair cardiac output, and can transiently affect organ perfusion, for example by reducing urine output. At the same time, it decreases left ventricular afterload while increasing right ventricular afterload through elevated pulmonary vascular resistance.

In May 2021, I wrote to Professor Hedenstierna to share my reflections on the contemporary implications of his work, unaware that my letter would reach him only weeks before his passing. I am convinced that, had our paths crossed earlier, we would have found substantial common ground.

This paper therefore stands, in part, as a continuation of his line of reasoning—exploring how P_{pl}, P_{it}, and airway closure interact to shape both ventilation and perfusion. His scientific legacy remains a source of insight for those who seek to understand and preserve the lung's intrinsic physiology rather than override it.

2 Mechanical Framework

The lung parenchyma is mechanically interposed between the pleural space and the conducting airways (Figure 1). P_{pl} acts on the external surface of the lung, whereas P_{aw} is transmitted through the bronchial tree into the alveolar space. Both therefore contribute to the pressure environment surrounding the small intraparenchymal airways, particularly the terminal and respiratory bronchioles—highly compliant, collapsible structures of submillimeter diameter that supply individual acini.

For this reason, lung tissue compression cannot be understood from transpulmonary pressure alone. Transpulmonary pressure (P_{tp}), defined as alveolar pressure (P_{alv}) minus P_{pl} (in contrast to the very commonly used definition: $P_L = P_{aw}$ minus P_{pl}. The two definitions are only equivalent in the absence of airway closure.), describes distending pressure across the lung, but does not by itself describe the absolute pressure acting on the parenchyma. A useful approximation of the compressive load on the parenchyma is the mean of P_{aw} and P_{pl}:

$$P_{it} \approx (P_{aw} + P_{pl})/2. \tag{1}$$

When P_{aw} and P_{pl} rise simultaneously, P_{tp} may remain unchanged while the absolute pressure surrounding the parenchyma increases. Under such conditions, small compliant airways embedded in lung tissue may narrow or close, especially in gravity-dependent regions, where the weight of the overlying lung tissue increases local compressive forces, an effect that may be further enhanced in the presence of edema. This distinction helps explain why PPV and NPV cannot be considered mechanically equivalent even at similar P_{tp}'s.

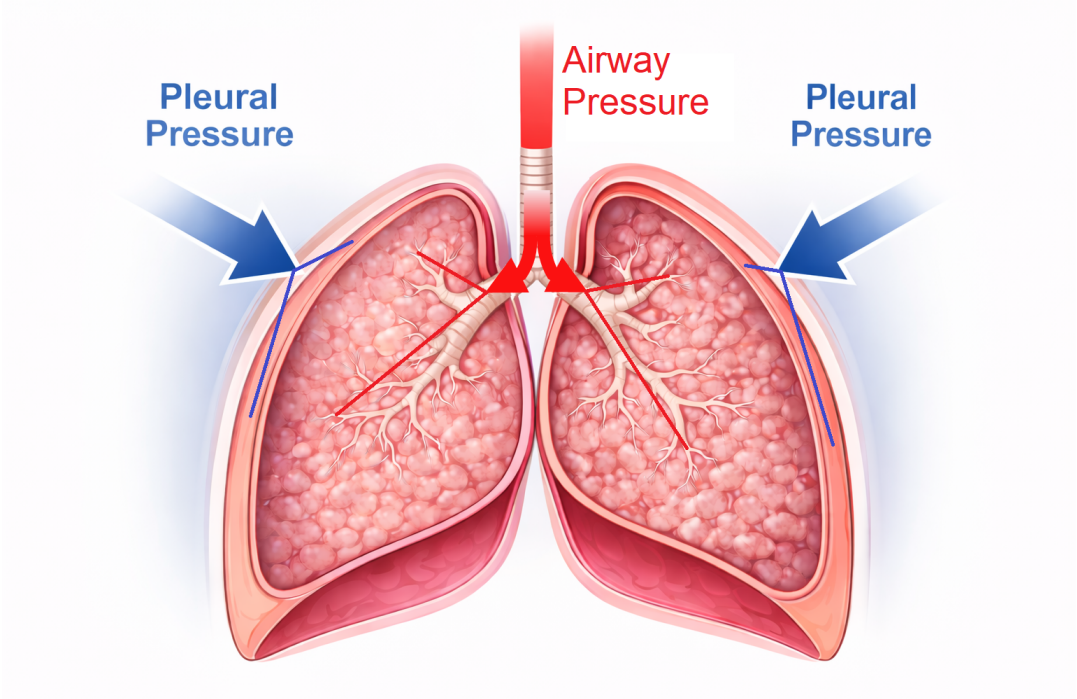

Figure 1. Pressures acting on the lung parenchyma during positive and negative pressure ventilation, the parenchyma is sandwiched between pleural space and the main airways. During positive pressure ventilation, airway pressure is elevated above atmospheric pressure and pleural pressure rises in parallel. During negative pressure ventilation, pleural pressure is reduced below atmospheric pressure (i.e., becomes more negative), while airway pressure remains at atmospheric level. Airway pressure is transmitted throughout the bronchial tree into the alveolar space and therefore contributes directly to the mechanical compression experienced by the lung tissue.

3 Physiological Airway Closure

Airway closure is a well-established physiological phenomenon. In patients with small airway disease, peripheral airway closure becomes evident during forced expiration, as demonstrated by expiratory CT imaging, in which air trapping and mosaic attenuation are recognized as indirect markers of small-airway closure [3]. Milic-Emili, in his 2007 review [4], recalled that René Laennec had already described "trapped air" in the excised lung around 1820. Dollfuss et al. [5] demonstrated that expiration below functional residual capacity (FRC) initiates airway closure, and Hughes et al. [6] confirmed this in the excised dog lung. According to these classical observations, closure of the feeding airway occurs when local trans-airway pressure falls below a threshold of about 2–2.5 cmH_2O.

This mechanism protects the alveolus against complete collapse: the small airway closes before the alveolar unit itself is fully compressed. In the healthy spontaneously breathing subject, such closure is common and usually transient and reversible. Excluded units are readily reintegrated during the next inspiration or spontaneous sigh, preserving ventilation–perfusion matching and lung volume stability.

Because P_{pl} becomes less negative toward the dependent regions of the lung, closure begins in the dependent lung and progresses upward as P_{it} rises or lung volume falls. This gravitational dependence is reflected in the classic concepts of closing volume and closing capacity [7].

This gravitational sequence is also directly reflected in the lower, leftward limb of the pressure–volume relationship. As lung volume decreases below FRC, progressively more dependent airways reach their closing threshold, resulting in a gradual loss of ventilated units over a pressure range that corresponds to the vertical P_{pl} gradient. The residual volume thus represents the lung volume at which airway closure has extended throughout the lung. At still lower pressures, this volume remains trapped (as noticed by Laennec), since the closed airways prevent further emptying.

COMPRESSIVE LOAD DURING INSPIRATION: WHY PPV MAY TURN PHYSIOLOGY INTO PATHOLOGY

Figure 2. illustrates the simulated compressive load on lung parenchyma by PPV and NPV, both applied with an identical driving pressure of 10 cmH_2O and zero end-expiratory pressure. Although resulting volume changes may be (they are not! See below under "Experimental support from isolated lungs") comparable, the underlying pressure environment differs fundamentally.

The simulation shown in Figure **??** is based on a simplified lumped-parameter model of the respiratory system, consisting of a single-compartment lung enclosed within a compliant chest wall. Both lung and chest wall compliances were assumed to be linear and equal (150 mL/cmH_2O), with a functional residual capacity (FRC) of 2.4 L and a pleural pressure of -6 cmH_2O at FRC.

The model was not intended to represent regional heterogeneity or complex lung mechanics, but rather to illustrate the effect of different pressure application modes on the mechanical environment of the lung. In particular, the simulation highlights how airway pressure contributes to parenchymal compression during PPV, whereas NPV alters the surrounding pressure without increasing airway pressure.

In the absence of PEEP or negative end-expiratory pressure (NEEP), expiratory curves for PPV and NPV are nearly superimposed. However, when PEEP or NEEP is introduced, the curves diverge, reflecting differences in the pressure environment during both inflation and deflation.

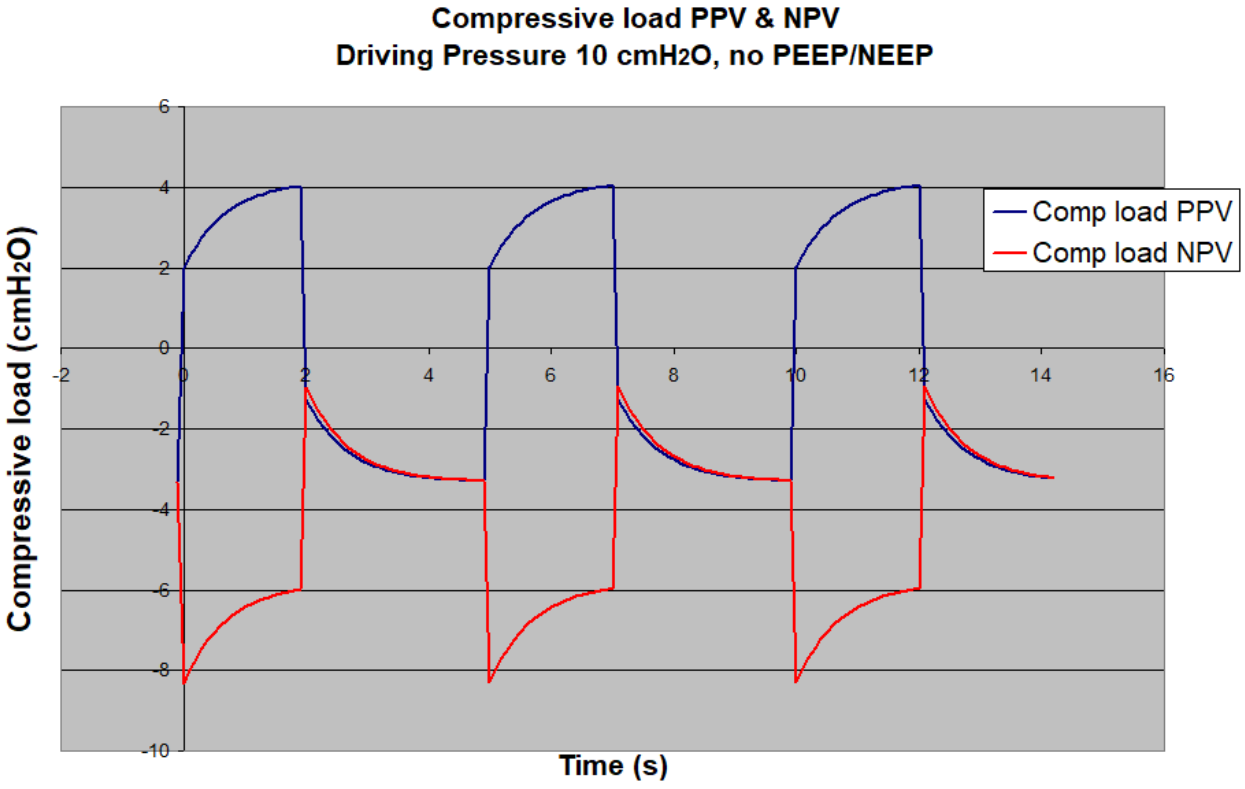

Figure 2. Compressive load on parenchyma during mechanical ventilation. The load is depicted during both NPV and PPV, with a driving pressure of 10 cmH_2O (≈ 10 mbar). Here no PEEP (NEEP for NPV) is applied, that is why the expiration curves are identical (the slight differences are due to the simulation process: $\Delta t \to 0$ would make them coincide perfectly). PEEP will shift the curve upward for PPV and downward for NPV and make this equivalence disappear.

Compressive load is approximated as the mean P_{it}, here defined as $(P_{aw} + P_{pl})/2$. During inspiration with NPV, P_{pl} becomes more negative, reducing this mean pressure and thereby decreasing tissue compression. In contrast, during PPV, P_{aw} rises above atmospheric pressure and P_{pl} increases accordingly, resulting in an increase in compressive load during inspiration.

This difference has major consequences for small peripheral airways. Under physiological conditions, airway closure during expiration is typically transient and reversible. However, under PPV—particularly in dependent regions—closed airways may fail to reopen during the subsequent inspiration, because the rise in P_{aw} is accompanied by an increase in surrounding tissue pressure.

Airway hysteresis, partly related to surface tension and adhesive forces at the airway walls, ongoing gas absorption, and the absence of sufficiently negative P_{pl} interact to stabilize airway closure. Hysteresis implies that reopening requires higher distending pressures than those present at end-expiration, while ongoing gas absorption further reduces the volume of isolated acini, particularly at high inspired oxygen fractions. In the absence of sufficiently negative P_{pl} to relieve surrounding tissue compression, these regions may remain closed despite apparently adequate transpulmonary pressure. Thus, a normally protective physiological mechanism may evolve into a pathological state characterized by persistent exclusion of peripheral lung units, impaired recruitment, and progressive atelectasis.

From a clinical perspective, this has important implications for the interpretation of P_{es} measurements. In routine practice, transpulmonary pressure is estimated as P_{aw} - P_{es}, assuming that P_{aw} is transmitted to the alveoli. However, this assumption no longer holds once peripheral airway closure occurs e.g. during expiration. At the moment of closure, alveolar pressure in the affected units equals the P_{aw} at which flow ceases locally, after which these units become mechanically uncoupled from the airway opening. Subsequent decreases in P_{aw} are therefore not transmitted to these regions. As a result, a transpulmonary pressure calculated from P_{aw} and P_{es} may not reflect the local mechanical conditions within closed or excluded lung units. Airway opening pressure (AOP), typically assessed during inspiration, provides information on reopening but does not capture the alveolar pressure at which closure occurred during expiration.

This mechanism helps explain why airway closure is frequently observed in anaesthetized and mechanically ventilated patients, particularly in conditions associated with elevated P_{pl}, such as obesity, ARDS, reduced chest wall compliance, pneumoperitoneum, and Trendelenburg positioning.

It should be emphasized that this expression represents a global or mean approximation of the pressure acting on the lung parenchyma. While P_{aw} is relatively uniform throughout the lung at a given moment, P_{pl} exhibits substantial regional variation, primarily due to gravitational effects and the weight of overlying lung tissue. This results in a vertical gradient of parenchymal compression, with higher compressive forces in dependent regions and lower values in non-dependent regions.

This spatial heterogeneity is further amplified in the presence of lung injury, edema, or regional stiffening, where local mechanical conditions may deviate markedly from the mean estimate. Consequently, the compressive load on the parenchyma is not uniform, but greatest in dependent regions, where airway closure is also most likely to occur.

In this context, the approximation $P_{it} \approx (P_{aw} + P_{pl})/2$ should be interpreted as a conceptual framework rather than an exact local descriptor of pressure transmission. This limitation does not diminish the relevance of the concept itself, but rather highlights that its clinical implications are most pronounced in dependent lung regions, where pleural pressure, and thus parenchymal compression, is highest.

4 Experimental Support from Isolated Lungs

Direct mechanical support for this concept comes from isolated-lung experiments comparing PPV and NPV. Klassen et al. [8] and Eckert et al. [9] ventilated excised lungs either by applying positive pressure at the airway opening or by applying negative pressure externally around the lung.

Klassen et al. [8] showed that, for a given tidal volume, PPV required approximately twice the driving pressure needed during NPV. This already suggested greater internal flow limitation during PPV. Even more striking was their observation that a small peripheral defect at the lung surface leaked almost five times more during NPV than during PPV at comparable tidal volumes. Eckert et al. [9] reported concordant findings.

The interpretation is straightforward. During NPV, peripheral regions remain ventilated and in communication with the airway tree, allowing gas to reach and escape through the peripheral defect. During PPV, by contrast, the much smaller leakage indicates that the distal lung is poorly ventilated or functionally excluded. These experiments therefore provide direct evidence that PPV promotes peripheral airway narrowing or closure, whereas NPV preserves distal airway patency.

5 Clinical Analogue: Delayed Pneumothorax

A similar phenomenon appears to occur clinically in delayed pneumothorax during PPV. In a recent case report [10], a pneumothorax remained occult during ongoing PPV and became apparent only after the patient resumed spontaneous breathing.

This behaviour mirrors the isolated-lung findings. During PPV, elevated P_{aw} and P_{pl} increase parenchymal compression, so that a pleural defect in a poorly ventilated peripheral region may not communicate effectively with the central airways. Air leak into the pleural space then remains limited, and pneumothorax may not become clinically evident. When spontaneous breathing resumes, P_{pl} becomes more negative, peripheral airways reopen, and the distal defect again communicates with the airway tree. The pneumothorax then declares itself.

Thus, delayed pneumothorax can be understood as an in vivo counterpart of the reduced peripheral leak observed during PPV in isolated lungs [8,9].

LESSONS FROM COPD: AVOIDANCE OF COMPRESSIVE LOADING

The mechanical consequences of elevated P_{it} are well illustrated in patients with chronic obstructive pulmonary disease (COPD). These patients characteristically avoid forceful expiration, as increased P_{pl} leads to airway narrowing and premature closure of small airways. Instead, they adopt a breathing pattern with prolonged, low-flow expiration and often operate at an increased end-expiratory lung volume.

By elevating FRC, COPD patients maintain airway patency and reduce airway resistance, thereby minimizing the compressive effects of P_{it} on peripheral airways. This adaptive strategy reflects an intuitive avoidance of the very mechanism that may be imposed during PPV.

In this context, PPV—by increasing P_{pl} and P_{it} during inspiration—may counteract these protective adaptations, promoting airway closure and increasing resistance, particularly in already vulnerable lung regions [11].

6 PEEP: Stabilization and Compression

The effects of positive end-expiratory pressure (PEEP) require careful interpretation. PEEP is often described as "recruiting" the lung, but its action is mechanically dual.

On the one hand, PEEP raises P_{aw} and thereby raises P_{it}, which increases compressive loading of the parenchyma, especially in dependent regions. On the other hand, the resulting increase in lung volume enlarges airway caliber and may stabilize small airways against collapse. Because airway resistance decreases strongly with airway radius, this volume effect can be substantial.

The apparent benefit of PEEP may therefore reflect geometric expansion and airway stabilization rather than true relief of tissue compression. The net effect depends on the balance between increased absolute pressure and increased lung volume. This duality may help explain why PEEP sometimes improves oxygenation and compliance while not necessarily reversing the underlying compressive mechanism.

6.1 Flow Dependence of Airway Closure

Airway closure is influenced not only by static pressure levels but also by the temporal pattern of pressure application. Because different lung regions have different time constants, rapid inspiration preferentially fills units with short time constants, typically more central or less compressed regions.

During fast inspiration, proximal units fill early and raise pleural and parenchymal pressure before more distal regions have had time to fill. This early rise in P_{it} may further compress peripheral airways, making the distal lung progressively less accessible during the same breath. In contrast, a more gradual flow profile allows distal regions more time to fill before compressive forces increase.

This concept offers a plausible mechanical explanation for the benefits reported with flow-controlled strategies. Flow-controlled expiration (FLEX) [12] reduces rapid pressure decline during expiration and may thereby limit derecruitment. Likewise, regulated inspiratory and expiratory flow, as used in devices such as the EVONE ventilator [13], may promote more homogeneous distribution of ventilation by avoiding abrupt pressure changes.

7 Clinical Evidence: Obesity, ARDS, and AOP

Clinical observations also support a major role of elevated P_{pl} in airway closure. In supine obesity, increased abdominal pressure displaces the diaphragm cranially and raises P_{pl}. Behazin et al. [14] described complete airway closure under such conditions, with inspiratory flow appearing only after P_{aw} exceeded the AOP.

AOP is a useful physiological marker, but it should not be interpreted too simplistically. The measured AOP most likely represents the pressure at which the first previously closed regions reconnect with the central airways, not the pressure at which the entire lung has reopened. Because P_{pl} varies substantially from non-dependent to dependent lung, reopening must be expected to proceed gradually over a pressure range.

Thus, the presence of an AOP confirms airway closure, but the absence of a clearly measurable AOP does not exclude it. If PEEP is already close to or above the opening pressure of the least dependent regions, flow may appear immediately during inspiration as P_{aw} rises, even though much of the lung was initially functionally closed. This distinction is important in obesity and ARDS, [15,16] where elevated P_{pl} may cause widespread airway closure without a dramatic or easily recognized AOP.

PLEURAL PRESSURE, THORACIC VOLUME, AIRWAY CLOSURE AND THE "BABY LUNG" IN ARDS

As emphasized by Grasso [17], the reduced compliance of the respiratory system in ARDS may arise from either the lung or the chest wall. Distinguishing between these requires knowledge of P_{pl}, which can be estimated from oesophageal pressure measurements. Several studies have applied this approach to guide ventilator settings, notably those by Talmor [18], Beitler [19], and Kassis [20]. Selected data from these studies are summarized in Table 1.

Two observations emerge consistently from these data.

First, the calculated compliance of the thoracic wall remains within a near-normal range. C_{TW} can be estimated from tidal volume (TV) and the difference between end-inspiratory and end-expiratory P_{pl} ($EIPpl$ and $EEPpl$, respectively):

$$C_{TW} \approx TV/(EIPpl - EEPpl) \tag{2}$$

Across the reported datasets, this yields values on the order of 120 $ml.cmH_2O^{-1}$, suggesting that the thoracic wall itself is not markedly stiff.

Second, $EEPpl$ is markedly elevated, typically around +15 to +18 cmH_2O. If one assumes a normal reference P_{pl} of approximately −6 cmH_2O at FRC, this implies an increase in thoracic volume of roughly:

$$\Delta V \approx (EEPpl + 6) \times C_{TW} \tag{3}$$

which corresponds to an increase of several litres above FRC. Thus, the thorax appears to operate at substantially elevated volumes even at end-expiration.

These observations have important implications for airway patency. To maintain an alveolus open at such elevated P_{pl}, P_{alv} must exceed P_{pl} by a sufficient margin. If one assumes that a pressure difference on the order of a few cmH_2O (≈ 2–3 cmH_2O) is required to maintain airway patency, then P_{alv} in such regions must lie well above P_{pl}.

However, the P_{aw} available at end-expiration is limited by the applied PEEP. When the pressure required to keep peripheral units open exceeds this P_{aw}, those regions can no longer remain in communication with the airway tree and must therefore be functionally closed.

This reasoning suggests that, under the conditions reported in Table 1, a substantial fraction of the lung is likely to be excluded from ventilation at end-expiration. The concept of the "baby lung" [21] in ARDS is consistent with this interpretation: only a relatively small portion of the lung remains aerated and ventilated, while the remainder is functionally closed or fluid-filled.

An important consequence is that, during a low-flow inflation manoeuvre, the measured AOP may not be clearly discernible if PEEP is already close to or above the opening pressure of the least dependent lung regions. In that situation, the absence of a clearly defined AOP does not exclude substantial airway closure, because flow may begin immediately while a large part of the lung remains functionally closed.

Additional studies reporting elevated P_{pl} during mechanical ventilation, including observations in COVID-19 patients [22], support this overall picture of a lung compressed within a high-pressure thoracic environment. Under these conditions, airway closure, gas trapping, and redistribution of ventilation toward a limited "baby lung" appear as natural mechanical consequences [23] rather than isolated phenomena.

In addition, if expiratory flow limitation is present, incomplete emptying may further increase end-expiratory lung volume and P_{pl}, reinforcing airway closure and contributing to the characteristic combination of hyperinflation and a reduced "baby lung".

Table 1. Pleural pressure (P_{es}) measurements in mechanically ventilated ARDS patients. Data extracted from the studies of Talmor [18], Beitler [19] and Kassis [20]. Cited variables are tidal volume, *TV*, End-Expiratory and End-Inspiratory pleural pressures, *EEPpl* and *EIPpl* and plateau pressure. The thorax wall compliance (C_{TW}) and the extra volume above FRC (Extra V>FRC) were calculated form the provided data.

Author	Series	N	*TV* (ml)	*EEPpl* (mbar)	*EIPpl* (mbar)	PEEP (mbar)	Plateau (mbar)	C_{TW} (ml/mbar)	Extra V > FRC (ml)
Talmor	P_{es} guided (base)	30	484	17.2	21.2	14.0	29	121	2807
	Conventional (base)	30	491	16.9	20.7	15.0	29	129	2959
	P_{es} guided (72 h)	30	472	18.4	21.7	18.0	28	143	3490
	Conventional (72 h)	30	418	14.3	17.9	12.0	25	116	2357
Beitler	P_{es} guided	102	396	16.0	19.0	14.0	28	132	2905
	Emperical PEEP	98	362	15.0	18.0	12.5	27	121	2531
Kassis	Day 1	40	360	13.7	16.1	13.5	25	150	2955
	Day 3	38	390	13.0	15.9	13.0	24	134	2546

From a clinical perspective, it may be useful to consider whether the reduction in ventilated lung volume is predominantly driven by inflammatory consolidation or by pressure-dependent airway closure. Bedside physiological markers such as the stress index and the recruitment-to-inflation (R/I) ratio may provide indirect insights into this distinction. The stress index, derived from the shape of the airway pressure–time curve during constant-flow inspiration, may suggest intratidal recruitment when compliance increases during inflation. The R/I ratio estimates the proportion of volume gain with higher PEEP that is attributable to recruitment rather than further inflation of already open units.

For example, a high recruitability, reflected by an elevated R/I ratio, may indicate that non-aerated regions can be reopened, whereas a low recruitability may be consistent with consolidated tissue or regions that remain closed due to persistent compressive forces. However, this distinction remains imperfect, as airway closure and inflammation frequently coexist and interact.

This underscores the importance of considering the mechanical environment, particularly pleural pressure, when interpreting the "baby lung" concept at the bedside.

8 Improvement by Reduction of Pleural Pressure

Experimental and clinical observations support the importance of P_{pl} in determining lung mechanics and injury. In a porcine model, Yoshida et al. [24] demonstrated that continuous negative abdominal pressure significantly reduced the severity of VILI. By lowering P_{pl}, this intervention reduced the compressive load on the lung and improved aeration of dependent regions.

More recently, Xiong and colleagues [25] applied negative pressure around the abdomen to limit and resolve postoperative atelectasis, further supporting the physiological rationale of external decompression of the thorax.

These findings are consistent with the broader physiological principle that reduction of P_{pl} facilitates airway patency and lung expansion. Interventions that decrease P_{it}—such as negative pressure applied externally or preservation of spontaneous inspiratory effort—tend to counteract airway closure and promote recruitment.

Spontaneous breathing during assisted ventilation illustrates this mechanism, as does Neurally Adjusted Ventilatory Assist [26]. Inspiratory muscle activity lowers P_{pl} and may partially offset the rise in P_{pl} induced by the ventilator. In this way, part of the required pressure is generated by the diaphragm rather than imposed via the airway, limiting increases in compressive load within the thorax.

Prone positioning provides a clinically well-established example of the beneficial effects of reducing P_{pl}. When applied correctly—i.e., with the abdomen allowed to hang freely—abdominal pressure on the diaphragm is reduced, permitting caudal displacement of the diaphragm and lowering P_{pl}, particularly in dependent lung regions. This reduction in compressive load promotes more homogeneous ventilation and facilitates recruitment.

The physiological and clinical benefits of prone positioning in ARDS, including improved oxygenation and reduced mortality, have been demonstrated in the PROSEVA trial by Guérin et al. [27]. While these effects are commonly attributed to improved ventilation–perfusion matching and redistribution of lung densities, the associated reduction in P_{pl} may, at least in part, represent a key underlying mechanism contributing to the improved homogeneity of ventilation observed during prone positioning.

Together, these observations support the concept that reducing P_{pl} is not merely a theoretical consideration but a practical means of improving lung function and mitigating injury.

9 Absorption Atelectasis and Pulmonary Edema

Once a lung unit has become isolated by airway closure, gas absorption may convert functional exclusion into persistent atelectasis. Oxygen is gradually absorbed into the pulmonary capillary blood, reducing alveolar gas volume and lowering P_{alv}. If insufficient poorly soluble gas remains, the alveolus may collapse completely. This is the mechanism of absorption atelectasis emphasized by Hedenstierna [28] and others and explains why high inspired oxygen fractions may aggravate collapse in poorly ventilated lungs.

The subsequent fate of such a collapsing unit is governed not only by gas dynamics but also by fluid balance across the alveolo-capillary barrier. This balance is described by the Starling equation:

$$J = K[(P_1 - P_2) - \sigma(\pi_1 - \pi_2)] \tag{4}$$

where P denotes hydrostatic pressure, π oncotic pressure (largely determined by plasma proteins such as albumin), K the filtration coefficient, and σ the reflection coefficient.

Under normal conditions, hydrostatic and oncotic forces are balanced, resulting in minimal net fluid flux. However, a decrease in P_{alv} due to gas absorption alters the local hydrostatic gradient across the alveolar wall. This shift favours movement of fluid from the interstitium into the alveolar space.

As a result, the gas volume lost by absorption may be replaced by liquid, stabilizing the collapsed state. In this way, airway closure not only initiates atelectasis, but may also promote its persistence through fluid accumulation [29].

10 Implications for Ventilation Strategy

These considerations suggest that lung-protective ventilation should not focus exclusively on tidal volume reduction [30]. An equally important goal may be limitation of excessive P_{pl} and P_{it}.

PEEP should be interpreted as a compromise between airway stabilization and tissue compression. AOP should be used as an indicator of closure, but its absence not as proof of full reopening. Flow-controlled ventilation deserves attention because gradual pressure change may reduce peripheral exclusion.

Preservation of spontaneous inspiratory effort, when well synchronized with ventilator support, may also be beneficial because diaphragmatic activity can partly substitute for ventilator-generated pressure and thereby limit the rise in P_{pl}. By contrast, vigorous inspiratory effort against a closed system may generate very negative P_{alv}'s and promote edema.

Finally, NPV and related decompressive approaches merit renewed consideration. By lowering P_{pl} rather than raising P_{aw}, NPV expands the lung while reducing parenchymal compression and promoting peripheral airway patency. Historical observations, experimental data, and recent clinical applications of extra-thoracic or abdominal negative pressure all support the physiological rationale for revisiting this principle with modern monitoring techniques.

11 Conclusions

Airway closure during mechanical ventilation should not be regarded merely as an incidental or late phenomenon. It is a predictable mechanical consequence of elevated absolute pressure around the parenchyma, especially in dependent regions and in lungs with reduced compliance or increased chest wall load.

The distinction between P_{tp} and absolute P_{it} is therefore crucial. During PPV, the rise in P_{aw} is accompanied by a rise in P_{pl}, so that inflation occurs under conditions of increased parenchymal compression. This environment promotes peripheral airway closure, impaired recruitment, gas trapping, absorption atelectasis, and possibly pulmonary edema. In contrast, spontaneous breathing and NPV expand the lung while lowering the surrounding pressure.

Recognizing airway closure as a consequence of lung tissue compression may help reinterpret several familiar clinical phenomena, including AOP, PEEP responsiveness, delayed pneumothorax, hyperinflation, and the "baby lung". It also suggests that future lung-protective strategies should pay greater attention not only to volume, but to the absolute pressure environment within which that volume is delivered.

Importantly, airway closure should not be viewed solely as a pathological phenomenon. Under physiological conditions, it likely serves a protective role by limiting ventilation of regions where effective gas exchange is not beneficial and by preventing excessive local stress. The paradox arises when this inherently protective mechanism is exposed to an altered mechanical environment. During positive pressure ventilation, elevated intrathoracic pressure transforms airway closure from a regulated, adaptive process into a widespread and persistent phenomenon, contributing to gas trapping, impaired recruitment, and lung injury. In this context, what is normally protective becomes pathological.

ABBREVIATIONS

The following abbreviations are used in this manuscript:

ARDS Adult Respiratory Distress Syndrome

PEEP Positive End Expiratory Pressure

COPD Chronic Obstructive Pulmonary Disease

FRC Functional Residual Capacity

TV Tidal Volume

NPV Negative Pressure Ventilation

PPV Positive Pressure Ventilation

P_{alv} Alveolar pressure

P_{tp} Transpulmonary pressure ($= P_{alv} - P_{pl}$) opposite to $P_L = P_{aw} - P_{pl}$

P_{aw} Airway pressure

P_{pl} Pleural pressure

P_{it} Intrathoracic pressure $= (P_{aw} + P_{pl})/2$

C_{lungs} Compliance of the lungs

C_{TW} Compliance of the thorax wall

EEPpl End-Expiratory pleural pressure

EIPpl End-Inspiratory pleural pressure

REFERENCES

[1] Hedenstierna G, McCarthy G, Bergström M: Airway closure during mechanical ventilation. Anesthesiology 1976; 2:114-23. doi: 10.1097/00000542-197602000-00003.

[2] Young CC, Harris EM, Vacchiano C, Bodnar S, Bukowy B, Elliott RRD, Migliarese J, Ragains C, Trethewey B, Woodward A, Gama de Abreu M, Girard M, Futier E, Mulier JP, Pelosi P, Sprung J. Lung-protective ventilation for the surgical patient: international expert panel-based consensus recommendations. Br J Anaesth. 2019 Dec;123(6):898-913. doi: 10.1016/j.bja.2019.08.017.

[3] Ghosh S. Computed tomography findings in bronchial asthma: quantification of air trapping and correlation with pulmonary function tests. Acta Radiologica. 2023;64(4):1418-1421. doi:10.1177/02841851221135233.

[4] Milic-Emili JM, Torchio R, D'Angelo E: Closing volume: a reappraisal (1967–2007). Eur J Appl Phys 2007; 99:567–83. doi: 10.1007/s00421-006-0389-0.

[5] Dollfuss RE, Milic-Emili JM, Bates DV: Regional Ventilation of the Lung, Studied with Boluses of ^{133}Xenon. Resp Phys 1967; 2:234-46. DOI:10.1016/0034-5687(67)90057-6.

[6] Hughes JMB, Rosenzweig DY, Kivitz PB. Site of airway closure in excised dog lungs: Histologic demonstration. J Appl Phys 1970; 29: 340–344. doi: 10.1152/jappl.1970.29.3.340.

[7] https://derangedphysiology.com/main/cicm-primary-exam/required-reading/respiratory-system/Chapter%20055/clinical-significance-and-measurement-closing-capacity.

[8] Klassen C, Eckert CE, Wong J, Guyette JP, Harris JL, Thompson S, et al. Ex-vivo modeling of perioperative air leaks in porcine lungs. IEEE Trans Biomed Eng. 2018;65:2827-36.

[9] Eckert CE, Harris JL, Wong JB, Thompson S, Kassis ES, Tsuboi M, et al. Preclinical quantification of air leaks in a physiologic lung model: Effects of ventilation modality and staple design. Med Devices (Auckl). 2018;11:433-42.

[10] Mulier JP, van Egmond, J, Beckers Perletti L, van Peteghem C, Desender L, Debaerdemaeker L. Delayed Detection of Iatrogenic Pneumothorax After Port Catheter Insertion Under Positive Pressure Ventilation: a Case report. A&A Practice. 2026;20:e02186. DOI: 10.1213/XAA.0000000000002186

[11] Van Egmond J, Mulier JP. Why Do We Ignore Negative Pressure Ventilation in COPD? CHEST Critical Care. 2026. DOI: 10.1016/j.chstcc.2026.100266.

[12] Borgmann S, Schmidt J, Goebel U, et al. Dorsal recruitment with flow-controlled expiration (FLEX): an experimental study in mechanically ventilated lung-healthy and lung-injured pigs. Crit Care 2018;22:245.

[13] Barnes T, Enk D. Ventilation for low dissipated energy achieved using flow control during both inspiration and expiration. Trends in Anaesthesia and Critical Care 2019;24:5-12.

[14] Behazin N, Jones SB, Cohen RI, and Loring SH. Respiratory restriction and elevated pleural and esophageal pressures in morbid obesity. J Appl Physiol (2010) 108: 212–18. doi: 10.1152/japplphysiol.91356.2008.

[15] Cheng W, Jiang J, Long Y, Yuan S, Sun Y, Zhao Z, He H. Phenotypes of esophageal pressure response to the change of positive end-expiratory pressure in patients with moderate acute respiratory distress syndrome. J Thorac Dis 2024;16(2):979-988. https://dx.doi.org/10.21037/jtd-23-771.

[16] Van Egmond J, Mulier J. Airway closure during mechanical ventilation of acute respiratory distress syndrome patients. J Thorac Dis 2024. doi: 10.21037/jtd-24-636.

[17] Grasso S, Stripoli T. Editorial: Transpulmonary Pressure–based Mechanical Ventilation in Acute Respiratory Distress Syndrome. Am J Resp Crit Care Med 2018; 197: 977-8. doi: 10.1164/rccm.201801-0132ED.

[18] Talmor D, Sarge T, Malhotra A, O'Donnell CR, Ritz R, Lisbon A, Novack V, Loring SH: Mechanical Ventilation Guided by Esophageal Pressure in Acute Lung Injury. N Engl J Med 2008; 359:2095-104. doi: 10.1056/NEJMoa0708638.

[19] Beitler JR, Talmor D. Strategies to adjust positive end-expiratory pressure in patients with ARDS. 2019 JAMA; 322(6): 580–582. Doi:10.1001/jama.2019.7888.

[20] Kassis EB, Loring SH, Talmor D. Should we titrate peep based on end-expiratory transpulmonary pressure?—yes. Ann Transl Med 2018;6(19):390. Doi: 10.21037/atm.2018.06.35.

[21] Gattinoni L, Pesenti A. The concept of "baby lung". Intensive Care Med. 2005; 31(6):776-84. doi: 10.1007/s00134-005-2627-z.

[22] Gibot S, Conrad M, Courte G, Cravoisy A: Positive End-Expiratory Pressure Setting in COVID-19-Related Acute Respiratory Distress Syndrome: Comparison Between Electrical Impedance Tomography, PEEP/FiO_2 Tables, and Transpulmonary Pressure. Front Med 2021; 8:720920. doi: 10.3389/fmed.2021.720920.

[23] Van Egmond J, Kristensen MS, Mulier JP. The emergence of the "baby lung": a mechanical consequence of positive pressure ventilation and reduced pulmonary compliance. J Thorac Dis 2025. https://dx.doi.org/10.21037/jtd-2025-1693.

[24] Yoshida T, Engelberts D, Otulakowski G, Katira B, Post M, Ferguson ND, Brochard L, Amato MBP, Kavanagh BP. Continuous Negative Abdominal Pressure Reduces Ventilator-induced Lung Injury in a Porcine Model. Anesthesiology 2018; 129:163-72. doi: 10.1097/ALN.0000000000002236.

[25] Xiong S, Xiao J, Hong L, Shen X, Tao H, Jin R, Xu Q, Su L, Zhan C. Negative extra-abdominal pressure (NEXAP)-based lung recruitment maneuver versus standard lung recruitment maneuver in the treatment of postoperative atelectasis after cardiac surgery: A single-center randomized controlled trial. J Crit Care 2025. doi: 10.1016/j.jcrc.2025.155124.

[26] Conseil M, Jaber S, Galia F, Molinari N, Chanques G, De Jong A and Capdevila M. Neurally adjusted ventilatory assist in critical care patients with and without obesity: a prospective randomized crossover study. Annals of Intensive Care (2025) 15:128. https://doi.org/10.1186/s13613-025-01552-x.

[27] Guérin C et al. for the PROSEVA Study Group. Prone Positioning in Severe Acute Respiratory Distress Syndrome. N Engl J Med 2013;368:2159-68. DOI: 10.1056/NEJMoa1214103.

[28] Rothen HU, Sporre B, Engberg G, Wegenius G, Reber A, Hedenstierna G. Prevention of atelectasis during general anaesthesia. Lancet 1995; 345: 1387-1391. Doi: 10.1016/S0140-6736(95)92595-3.

[29] Van Egmond J, Booij LHDJ, Mulier JP. The role of pleural pressure on fluid dynamics and responsiveness. Intensive Care Med (2025). Doi: 10.1007/s00134-025-07820-5.

[30] The 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;342:1301-8. doi: 10.1056/NEJM200005043421801.