ramr
American Review of Respiratory Medicine
Revista Americana de Medicina Respiratoria

REVIEW ARTICLE

ISSN 1852-236X

Patient Self-Inflicted Lung Injury: Pathophysiology, Monitoring of Respiratory Effort, and Individualized Ventilatory Strategy

Lesión pulmonar autoinfligida por el paciente: fisiopatología, monitorización del esfuerzo respiratorio y estrategia ventilatoria individualizada

Tomás Salomón[1], Facundo Fanego[1], Martin Ignacio Mastandrea[1, 3], Bárbara Daglio[1, 2], Matias Bertozzi[3, 4]

[1] Complejo Médico de la Policía Federal Argentina Churruca-Visca, Autonomous CIty of Buenos Aires, Argentina
[2] Hospital General de Agudos Carlos G. Durand, Autonomous CIty ofBuenos Aires, Argentina
[3] Hospital General de Agudos Donación Francisco Santojanni, Autonomous CIty of Buenos Aires, Argentina
[4] Sanatorio Anchorena de San Martín, Buenos Aires, Province of Argentina

Received: 06/23/2026
Aceptado: 09/03/2026

Correspondence
Tomás Salomón. E-mail:
tomassalomon96@gmail.com

ABSTRACT

Patient Self-Inflicted Lung Injury: Pathophysiology, Monitoring of Respiratory Effort, and Individualized Ventilatory Strategy: A Narrative Review

Patient self-inflicted lung injury (P-SILI) is a particularly relevant phenomenon in patients with acute respiratory failure (ARF) undergoing invasive mechanical ventilation (IMV). In this context, excessive spontaneous respiratory effort may generate or worsen pre-existing lung injury through mechanisms that operate even when programmed ventilatory parameters remain within an apparently protective range.

Throughout the literature, multiple variables have been proposed for monitoring respiratory effort and pulmonary mechanics. Direct methods, such as esophageal pressure and diaphragmatic electrical activity, allow more accurate quantification of patient effort, whereas indirect methods, such as P0.1 or diaphragmatic ultrasound, estimate its magnitude through surrogate variables. Although there is no consensus regarding the best monitoring strategy, understanding the importance of its assessment is crucial to avoid errors in the individualization of ventilatory support.

This narrative review develops the concept of P-SILI by addressing its historical evolution, its pathophysiological basis, and the impact of different ventilatory modes on its prevention or exacerbation. In addition, it examines the association between respiratory effort variables and relevant clinical outcomes—mortality, length of stay in the intensive care unit (ICU), and duration of mechanical ventilation (MV)—in patients with acute respiratory failure undergoing IMV. Finally, it provides an integrative synthesis aimed at supporting a practical approach to individualized monitoring and ventilatory adjustment.

Key words: mechanical Ventilation | ventilator-Induced Lung Injury | work of Breathing | monitoring | physiologic | respiratory distress syndrome

Rev Am Med Resp 2026;26:109-121. https://doi.org/10.56538/ramr.NEIW7159

https://creativecommons.org/licenses/by-nc-sa/4.0/

©Revista Argentina de Medicina Respiratoria

RESUMEN

La lesión pulmonar inducida por el paciente es un fenómeno particularmente relevante en pacientes con falla respiratoria aguda bajo ventilación mecánica invasiva. En este contexto, el esfuerzo respiratorio espontáneo excesivo puede generar o agravar el daño pulmonar preexistente mediante mecanismos que operan incluso cuando los parámetros ventilatorios programados se encuentran dentro de un rango aparentemente protectores. A lo largo de la bibliografía, se han propuesto múltiples variables para el monitoreo del esfuerzo respiratorio y la mecánica pulmonar. Los métodos directos, como la presión esofágica y la actividad eléctrica del diafragma, permiten cuantificar con mayor precisión el esfuerzo del paciente, mientras que los métodos indirectos como P0.1 o la ecografía diafragmática aproximan su magnitud a partir de variables subrogadas. Si bien no existe un consenso sobre cuál es la mejor estrategia de monitorización, comprender la importancia de su valoración es crucial para evitar errores en la individualización del soporte ventilatorio. Esta revisión narrativa desarrolla el concepto de lesión pulmonar inducida por el paciente abordando su evolución histórica, sus bases fisiopatológicas, el impacto de los distintos modos ventilatorios en su prevención o exacerbación. Además, examina la asociación entre las variables de esfuerzo respiratorio y los diferentes desenlaces clínicos relevantes —mortalidad, días de estancia en unidad de cuidados intensivos, días de ventilación mecánica — en pacientes con falla respiratoria aguda bajo ventilación mecánica invasiva. También aporta una síntesis integradora para un enfoque práctico de monitorización y ajuste ventilatorio individualizado.

Palabras clave: ventilación mecánica | lesión pulmonar inducida por ventilación mecánica | trabajo respiratorio | monitoreo fisiológico | síndrome de dificultad respiratoria

IINTRODUCTION

Prevention of ventilator-induced lung injury (VILI) has been one of the cornerstones of mechanical ventilation for more than 3 decades.[1] This challenge becomes particularly relevant during partial ventilatory support, when the patient's respiratory effort substantially determines the resulting pressures and volumes.[2,3]

The distinction between controlled MV and spontaneous breathing (SB) should not be reduced to a simple opposition between "artificial" and "physiological" breathing. Although SB provides important physiological benefits, it may aggravate a pre-existing lung injury when respiratory drive (RD) and the resulting effort are unevenly distributed. The lung parenchyma does not distinguish between the sources of applied mechanical energy; rather, the risk of injury is determined by the magnitude of the resulting transpulmonary pressure (ΔP_L) and its regional distribution. Thus, vigorous respiratory efforts may generate mechanical loads comparable to or even greater than those produced by injurious mechanical ventilation, even when the set ventilator parameters appear to be safe.[4]

In this context, the concept of P-SILI was introduced, referring to lung injury resulting from injurious spontaneous breathing patterns in patients with ARF, even in the presence of apparently protective ventilator settings.[2]

Key mechanisms include regional increases in ΔP_L, the pendelluft phenomenon (PP), and heterogeneous redistribution of ventilation.[5,6] The concept of P-SILI, in itself, does not determine the optimal timing of intubation or the use of partial ventilatory support; rather, it represents one physiological consideration within a comprehensive clinical assessment.[7-10] This dilemma has highlighted the need for a personalized physiological approach within the framework of precision medicine.

This narrative review describes the historical evolution of P-SILI, its pathophysiological mechanisms, and the impact of ventilatory modes on its prevention or exacerbation. As a secondary

objective, we examine the association between respiratory effort variables and clinical outcomes –including mortality, duration of MV, and ICU length of stay– in patients with ARF.

2. HISTORICAL EVOLUTION

The concept of P-SILI was articulated in 2017 by Brochard et al, although its foundations date back several decades.[2] In 1988, Mascheroni et al demonstrated in a sheep model that sustained spontaneous hyperventilation could cause pulmonary edema and severe histologic lung injury in the absence of MV, providing some of the earliest evidence that SB itself could contribute to lung injury.11 By the early 2000s, concerns had emerged that ventilator-derived variables might not fully reflect the actual mechanical load (ML) imposed on the alveoli in the presence of spontaneous inspiratory effort.[12]

A major turning point occurred in the early 2010s, when Yoshida et al demonstrated that vigorous inspiratory effort could markedly increase ΔP_L and worsen lung injury despite the use of protective tidal volumes (≤ 6–8 mL/kg predicted body weight [PBW]) and a plateau pressure ≤ 30 cmH_2O.5 They also characterized the pendelluft phenomenon, whereby diaphragmatic contraction causes an early regional redistribution of gas toward dependent regions, resulting in localized overdistension without an increase in global tidal volume.6 However, Antonelli et al emphasized that the effects of SB depend on the severity of the underlying lung injury: in milder forms, spontaneous breathing may promote alveolar recruitment and preserve diaphragmatic function, whereas in moderate-to-severe acute respiratory distress syndrome (ARDS), the potential for mechanical stress may predominate.[13]

In 2017, Brochard et al integrated these findings under the term P-SILI, describing a lung injury that is generated or aggravated by excessive respiratory effort through increases in lung stress (pressure applied to the pulmonary parenchyma) and strain, particularly in previously injured lungs.[2]

The COVID-19 pandemic represented a second major turning point. The high respiratory drive observed in patients with SARS-CoV-2–associated ARDS, including those receiving noninvasive respiratory support, renewed interest in the potential contribution of P-SILI and in the optimal timing of intubation. This period further emphasized the possibility that patient-generated inspiratory forces may contribute substantially to lung stress beyond that attributable to the invasive ventilatory support.[14]

For the purposes of this review, P-SILI is defined as exposure of a patient with acute lung injury to sustained or excessive respiratory effort that increases global and regional lung stress and strain, potentially aggravating the lung injury even in the presence of apparently protective ventilator settings. *(Figure 1)*

3. PHYSIOLOGICAL BASIS AND MECHANISMS OF PATIENT SELF-INFLICTED LUNG INJURY

The pathophysiological mechanisms underlying P-SILI can be grouped into three main, closely interrelated pathways:

3.1 Increased Lung Stress and Strain: Global and Regional Overdistension

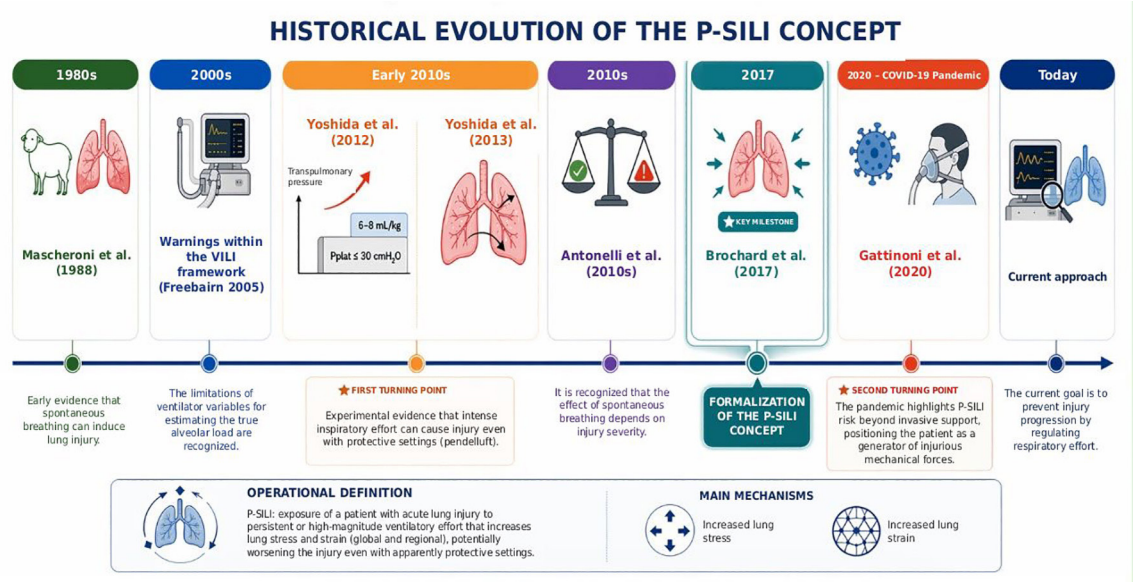
Tidal volume can be generated by positive pressure applied at the airway or by negative pressure generated by the inspiratory muscles. In both cases, parenchymal deformation depends on the ΔP_L (ΔP_L = Paw – Ppl). In lungs with high elastance and a reduced aerated lung volume ("baby lung"), vigorous inspiratory efforts (ΔPes < –10 cm H_2O) can activate inflammatory pathways, even with moderate tidal volumes.[5] Mechanical injury should not be viewed as the consequence of an isolated effort, but rather as the result of repetitive ML of a vulnerable lung, in which the same energy is concentrated over a smaller volume of aerated tissue, thereby promoting tissue stress and strain.[4]

During SB, reductions in pleural pressure increase ΔP_L and tidal volume, promoting both global and regional overdistension.[15] Lung heterogeneity plays a central role in this process: the coexistence of aerated regions with collapsed or fluid-filled areas results in an uneven regional distribution of ΔP_L, such that some regions are exposed to mechanical loads greater than those predicted from global measurements.[16]

3.2 Regional Heterogeneity of Lung Stress: The Pendelluft Phenomenon

In 2013, Yoshida et al demonstrated through electrical impedance tomography (EIT) that the negative pleural pressure generated by diaphrag-

Figure 1. Historical evolution of the P-SILI concept.



Note: The images included in this document are my own work. Assistance from the BioRender® and ChatGPT® platforms was used.

matic contraction is not uniformly distributed throughout injured lungs.[6] These changes are more pronounced in dependent regions and induce intrapulmonary gas movement towards non-dependent regions before the ventilator delivers inspiratory flow –the pendelluft phenomenon– resulting in occult regional overdistension that is not reflected in global tidal volume or airway pressures.

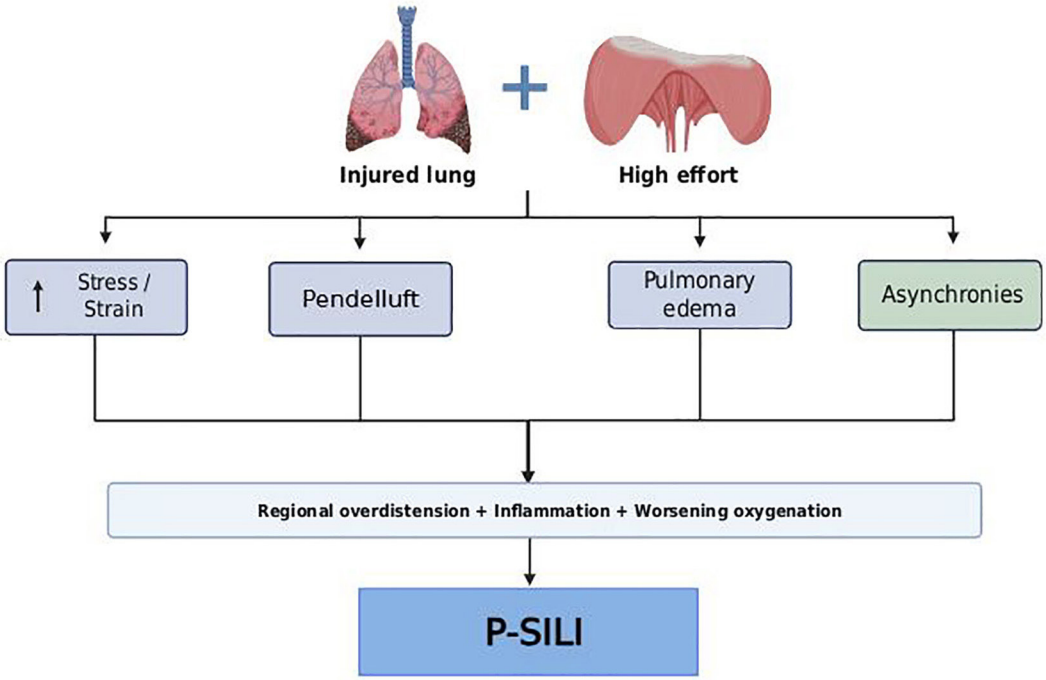
Subsequent studies in patients with difficult weaning correlated the presence of pendelluft (>20–25% of tidal volume) with longer duration of mechanical ventilation and 28-day mortality.[6,17] The magnitude and frequency of pendelluft have also been associated with increased levels of inflammatory biomarkers related to lung injury, supporting its potential biological relevance as a mechanism of injury. Its absent correlation with global variables such as ΔPes, ΔP_L and tidal volume further underscores its predominantly regional nature.[18]

3.3 Progression of Pulmonary Edema Due To Increased Vascular Transmural Pressure

When the effort is intense and mechanical support is low, alveolar pressure may fall below the set level of positive end-expiratory pressure (PEEP). Brochard et al proposed that, in a lung with increased alveolar-capillary permeability, this reduction increases vascular transmural pressure and promotes fluid extravasation into the interstitium and alveolus.[2] Repessé et al further described how large negative pleural pressure swings increase left ventricular afterload and venous return, thereby promoting pulmonary edema.[19] This may establish a self-reinforcing cycle: increased respiratory drive → increased respiratory effort → more edema → impaired oxygenation → further increase in respiratory drive.

Patient–ventilator asynchronies may further contribute to this process. Double triggering (DT) was the asynchrony associated with the greatest increases in tidal volume, dynamic transpulmonary driving pressure (ΔP_L,dyn), and transpulmonary mechanical energy, representing a potential mechanism through which P-SILI may be promoted by repeated increases in lung stress and strain in a vulnerable lung.[20] Experimental studies have shown that the consequences of DT may differ according to the ventilation mode, with greater risk of overdistension during volume-controlled ventilation and greater potential for atelectrauma during pressure-controlled ventilation.[21] Thus, patient–ventilator asynchronies provide a link between the pathophysiology of P-SILI and the ventilatory mode, as their occurrence and consequences depend both on patient effort and on how each mode delivers inspiratory flow, terminates inspiration, and modulates patient–ventilator interaction. *(Figure 2)*

Figure 2. Pathophysiological mechanisms involved in patient self-inflicted lung injury. References: P-SILI: patient self-inflicted lung injury.



4. Impact of Ventilatory Modes on Patient Self-Inflicted Lung Injury

Ventilatory modes differentially modulate the interaction between patient respiratory effort and the ML delivered to the lung. An increase in respiratory muscle effort (Pmus) tends to increase tidal volume and ΔP_L in an approximately linear fashion; however, this relationship is not uniform and can be substantially modified by the ventilatory mode and the mechanical properties of the respiratory system.[22]

4.1 Controlled Modes: VC-CMV and PC-CMV

In controlled ventilatory modes, the ventilator provides the full work of breathing when the patient is deeply sedated or pharmacologically paralyzed. In the absence of spontaneous effort, the risk of P-SILI is minimal, as the lung receives only programmed mechanical energy.[1] This scenario changes substantially when the patient regains spontaneous respiratory activity.

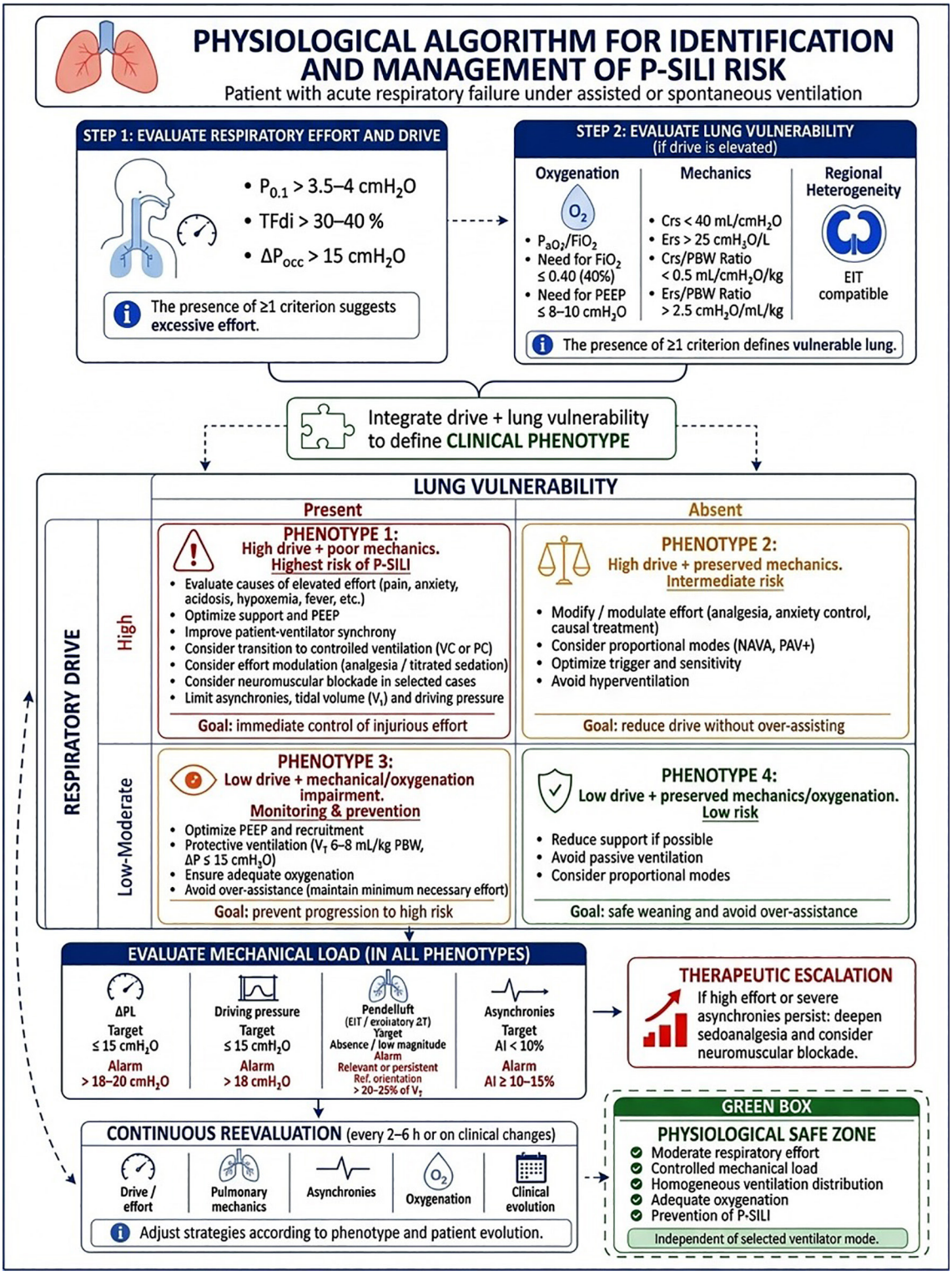
In volume-controlled continuous mandatory ventilation (VC-CMV), tidal volume is set independently of the patient's effort. When a vigorous effort occurs during the inspiratory phase, negative pleural pressure is superimposed on positive airway pressure, increasing ΔP_L beyond the expected value.[6] Paradoxically, the tidal volume remains constant –a defining characteristic of the mode– which can mask a dangerously elevated transpulmonary load.

In pressure-controlled continuous mandatory ventilation (PC-CMV), the pressure is set, whereas the resulting tidal volume depends on respiratory system impedance and spontaneous effort. Vigorous effort can generate a larger than expected tidal volume, increasing the ΔP_L and the risk of overdistension.[2] An apparently protective inspiratory pressure may prove insufficient if the tidal volume and the resulting total pressures are not monitored.

In both modes, the critical variable is not the mode itself, but the control of the RD through adjustment of analgesia and sedation, ensuring that the tidal volume does not exceed 6-8 mL/kg of PBW.[24] The most dangerous asynchrony is DT: a very high RD with neurological inspiratory times exceeding those that were programmed can trigger a second breath during the expiratory phase, doubling the effective tidal volume and the transpulmonary mechanical energy.[24]

Variables to monitor: Resulting tidal volume (≤ 6-8 mL/kg PBW), P0.1 or ΔPocc (pressure deflection during an expiratory occlusion) as a proxy

Figure 3. Algorithm for the management of patients at potential risk of P-SILI.



for drive, DT frequency on flow curves, ΔP_L,dyn and ΔPes.

4.2 Spontaneous Modes with Fixed Support: PC-CSV

Pressure support ventilation (PSV) delivers a preset pressure level with each patient effort, maintaining it until inspiratory flow falls below a cycling threshold.

The ventilator setting that most significantly impacts the risk of P-SILI is the level of pressure support. Insufficient pressure support leads to excessive respiratory muscle effort with a disproportionate drop in pleural pressure, increasing ΔP_L and promoting pendelluft and pulmonary edema secondary to increased vascular transmural pressure.[3,5] Conversely, excessive pressure support can cause overdistension, elevated tidal volumes, and overassist-induced diaphragmatic atrophy.[25]

Inspiratory cycling represents another variable with direct clinical implications. A very low threshold prolongs inspiratory time beyond neural effort, generating overassist and increasing tidal volume. A very high threshold terminates inspiration prematurely, promoting DT and post-cycling effort.[26] Trigger sensitivity also plays a role: an insensitive trigger imposes a high threshold to initiate the breath, increasing pre-assist inspiratory work.[27]

Finally, PEEP modulates risk in PC-CSV through its effects on elastic loading and diaphragmatic geometry. In patients with auto-PEEP, an appropriate extrinsic PEEP reduces the effective triggering threshold and triggering effort, whereas an inadequate level can increase total effort and, in lungs with low compliance (static or dynamic), amplify regional ΔP_L.[28]

Parameters to adjust in PC-CSV: pressure support level (targets: P0.1 < 3,5 cmH_2O, ΔPocc < 15 cmH_2O, TFdi 15-30%, ΔPes −5 a −10 cmH_2O), cycling threshold (to avoid DT and overassist), trigger sensitivity (most sensitive setting without inducing auto-triggering), and individualized PEEP basing on respiratory mechanics and patient effort.

4.3 Proportional Modes: PAV+ and NAVA

Proportional modes represent a qualitatively different approach: assistance is scaled in proportion to patient effort on a breath-by-breath basis. In PAV+, pressure is proportional to volume and flow generated by muscular effort, compensating for the elastic and resistive properties of the respiratory system.[29] In NAVA, assistance is scaled directly to the electrical activity of the diaphragm (EAdi), captured via a nasogastric catheter with integrated electrodes.[30]

The primary ventilator setting in PAV+ is the proportional gain, expressed as percentage support (% assist). Higher percentage support results in greater amplification of patient muscular effort. This is precisely the critical point: if the gain is set too high in a patient with elevated RD, the mode amplifies this excessive effort, increasing tidal volume and ΔP_L beyond safe limits.[29,31] The mode faithfully "accompanies" the patient, which is beneficial when drive is appropriate, but potentially injurious when pathologically elevated.

In NAVA, the equivalent setting is the NAVA level ($cmH_2O/\mu V$). Titrating this setting requires an understanding of the patient's baseline EAdi level: high gain settings in the presence of elevated EAdi can translate into disproportionate pressures and volumes. The main advantage of NAVA is its ability to respect neural cycling –the ventilator cycles off when EAdi ceases rather than by flow criteria– virtually eliminating overassist and underassist secondary to cycling desynchrony.[32]

In both proportional modes, the set PEEP level remains relevant as a modulator of elastic load, recruitment, and triggering effort. The key difference with regard to PC-CSV is that in PAV+ and NAVA, the interaction between PEEP and patient effort is more evident in real time because assistance scales dynamically on a breath-by-breath basis.[31,33]

Critical condition in proportional modes: in the presence of excessively high respiratory drive (P0.1 > 3.5 - cmH_2O, ΔPocc > 15 cmH_2O), proportional gain does not protect the lung. In such cases, reducing the gain or transitioning to a controlled mode is preferable to maintaining proportional support.

4.4 PEEP Titration

PEEP represents a cross-cutting variable across all ventilatory modes, with effects that vary depending on the patient and their underlying pathology. In patients with ARDS and high recruitment potential, PEEP application can mitigate the risk of P-SILI by reducing ΔP_L, decreasing alveolar collapse, and homogenizing ventilation

distribution—resulting in reduced regional overdistension and pendelluft.[34,35] Additionally, PEEP can improve lung compliance (static or dynamic, depending on the monitoring method) and optimize diaphragmatic geometry, enabling ventilatory effort to generate more effective ventilation with lower muscle work.[36,37] The benefits of PEEP depend not on its absolute level, but on its impact on lung mechanics: when its optimization is associated with a reduction in respiratory effort and ΔP_L, the probability of achieving lung-protective ventilation targets increases.[38-40]

However, elevated PEEP levels can cause overdistension, making monitoring crucial. Individualized titration strategies using EIT and ΔP_L attenuate dynamic lung stress and the work of breathing, improving mechanics without increasing the risk of overdistension.[34] Together, these mechanisms contribute to mitigating the pathophysiological drivers of P-SILI.

In different clinical contexts –such as low recruitment potential, preserved mechanics, or a non-homogeneous pathology– the response to PEEP can be heterogeneous, limiting the extrapolation of its benefits and emphasizing the need for an individualized approach with physiological interpretation of its impact on lung mechanics and respiratory effort.

5. MONITORING RESPIRATORY EFFORT: A STEPWISE, PRACTICAL APPROACH

Once the ventilatory strategy has been selected, structured monitoring of respiratory effort and ML is essential for early detection of P-SILI risk and individualized treatment management. A stepwise approach based on available ICU resources is proposed:

5.1 Level 1: Parameters Available in Any ICU

Airway occlusion pressure at 100 ms (P0.1) represents the most robust ventilator-derived parameter for noninvasive estimation of RD. It is measured during the initial 100 ms of an inspiratory effort against an occluded airway.[33,41] Its primary limitation is that it may underestimate true respiratory drive in the presence of an elevated respiratory system impedance.

Expiratory occlusion pressure (Pocc), obtained via a manual, random occlusion at end-expiration, serves as a complementary tool to estimate Pmus and ΔP_L,dyn using validated correction factors.[42,43]

5.2 Level 2: Bedside Available Tools

Ultrasound enables advanced, noninvasive functional assessment. Diaphragmatic thickening fraction (TFdi) is the ultrasound parameter with the most robust evidence base. Values above 30% to 40% during assisted ventilation suggest excessive muscular effort, whereas values below 15% to 20% indicate over-assistance or risk of disuse atrophy.[25,37] Umbrello et al demonstrated that during assisted ventilation, TFdi correlates significantly with inspiratory effort indices –specifically the esophageal and diaphragmatic pressure–time products (PTPes and PTPdi, respectively)– whereas diaphragmatic excursion demonstrated no correlation with any of these metrics.[44]

5.3 Level 3: Advanced Monitoring

Esophageal pressure swing (ΔPes), measured using an esophageal balloon positioned in the lower third of the esophagus, represents the reference standard for accurate quantification of respiratory effort. An inspiratory deflection > 10 cmH_2O indicates elevated effort, whereas values > 15 cmH_2O are associated with a significant risk of P-SILI.45 It also enables estimation of transpulmonary pressure, for which the threshold for overdistension lung injury ranges between 20 and 25 cmH^2O. Its primary limitation is the need for specific training to ensure correct placement and interpretation.[46]

The EAdi, available on ventilators equipped with the NAVA module, provides continuous monitoring of central respiratory drive and fine detection of asynchronies not evident on conventional waveforms.[47]

Finally, the EIT offers real-time, noninvasive monitoring of regional ventilation distribution, with particular utility for detecting the pendelluft phenomenon. A high frequency of pendelluft has been associated with elevated inflammatory biomarkers, prolonged duration of IMV, and worse outcomes.[6,18] Because its expression depends on patient effort, pulmonary heterogeneity, and ventilator settings, no single cutoff point applies across all clinical scenarios.

Combining appropriate ventilatory mode selection with stepwise, contextualized monitoring of respiratory effort is the most effective strategy to minimize the risk of P-SILI. The following section

analyzes the clinical implications of these findings and proposes practical recommendations for bedside implementation.

6. IDENTIFICATION OF PATIENTS AT RISK FOR P-SILI

Identifying patients at risk for P-SILI is as fundamental as the monitoring variables previously described. Their identification rests on two primary pillars: parameters linked to respiratory mechanics –specifically elastance (Ers) or static compliance (Crs)– and oxygenation indices.

Regarding respiratory mechanics, patients with worse mechanics have been shown to be at higher risk for elevated ΔP during spontaneous breathing, as well as poorer clinical outcomes when exposed to high respiratory effort.[10,48] Lower Crs levels result in greater effort required to generate tidal volume gains.[49] The literature is variable regarding the cutoff points for these measurements, which may be expressed as absolute values or values indexed to predicted body weight (Crs/PBW or Ers/PBW).[50]

Oxygenation levels represent another key component; patients with moderate-to-severe ARDS and PaO_2/FiO_2 levels below 150 demonstrate worse outcomes than those with higher oxygenation levels.[51]

For practical purposes in this review, candidate cutoff points are provided to guide decision-making and stratify the risk of lung injury. Suggested values include: 40 mL/CmH2O of Crs and 25 CmH_2O/L of Ers and a Crs/PBW of 0.5 mL/cmH_2O/kg or 2.5 cmH_2O/ml/kg for Ers/PBW. Regarding oxygenation indices, a value of PaO_2/FiO_2 of ≤ 150 is adopted as the cutoff point to define higher severity and, consequently, greater lung vulnerability to the mechanical burden generated by patient effort.[10,22,50,52]

7. DOES MAINTAINING RESPIRATORY EFFORT AND LUNG MECHANICAL LOAD VARIABLES WITHIN OPTIMAL RANGES REDUCE MORTALITY, SHORTEN THE DURATION OF MECHANICAL VENTILATION, AND DECREASE ICU LENGTH OF STAY?

Available evidence demonstrates a consistent association between elevated respiratory effort and worse clinical outcomes. Both excessively low and high levels of respiratory drive and effort are linked to adverse outcomes; however, this relationship is non-linear and appears particularly dependent on the severity of hypoxemia and the duration of exposure to high stress levels (Table 2).

In summary, maintaining P-SILI-related monitoring variables within optimal ranges is associated with reduced mortality, a higher number of ventilator-free days, and shorter ICU length of stay. Total ML delivered to the lung (ΔP_L,dyn and Δpstat) appears to be a more robust predictor than tidal volume or respiratory effort alone. These findings underscore the need for individualized monitoring and ventilator strategies aimed at maintaining effort and ML within a "safe zone" to improve clinical outcomes in patients with ARF.[54-56]

8. CLINICAL INTEGRATION: A PHYSIOLOGICAL ALGORITHM FOR P-SILI RISK IDENTIFICATION AND MANAGEMENT

The inherent complexity of evaluating respiratory effort in critically ill patients demands a structured operational framework that integrates physiology with real-time clinical decision-making. The proposed algorithm organizes clinical interventions around two sequential questions: Is respiratory drive elevated? and, if so, is the lung vulnerable to the mechanical load generated by this effort?

Assessment of respiratory drive serves as the mandatory first step. The presence of one or more criteria –P0.1 > 3.5-4 cmH_2O, TFdi > 30-40% or ΔPocc > 15 cmH_2O– points toward excessive respiratory effort. Although high drive alone does not define final risk, it dictates subsequent evaluation. When respiratory drive is low or moderate and respiratory mechanics is preserved, the patient falls into a low-risk category where proportional modes are appropriate, prioritizing the preservation of diaphragmatic function and avoiding over-assistance.

Upon confirmation of elevated respiratory drive, lung vulnerability—defined by PaO_2/FiO_2 ≤ 150, Crs < 40 mL/cmH_2O or regional heterogeneity evidenced by EIT– determines stratification into four phenotypes with distinct therapeutic implications. Phenotype 1, with high respiratory drive and poor mechanics, represents the highest-risk scenario requiring immediate intervention: reduction of respiratory drive through analgesia and sedation with or without neuromuscular

Table 1. Ventilatory modes and their relationship to P-SILI

Mode type	Ventilator mode	Set variables	Risk mechanism	Condition of highest risk	P-SILI Risk
Mandatory	VC-CMV	Vt, RR, Ti:Te, PEEP, trigger	Fixed Vt + spontaneous effort → uncontrolled ΔP_L. Double triggering doubles effective Vt	High drive with insufficient sedation and set Ti < neurological Ti	**High** (if spontaneous effort is present)
	PC-CMV	Inspiratory pressure, RR, Ti, PEEP, trigger	Fixed pressure + effort → unpredictable resultant Vt and increased ΔP_L	High drive with set pressure that does not limit the resultant Vt	**High** (if spontaneous effort is present)
Spontaneous	PC-CSV	PS level, cycling threshold, PEEP, trigger	Insufficient PS → excessive ΔPes. High PS → high Vt, overdistension. Early cycling → Double triggering	High drive with inadequate PS (low or high levels)	**Moderate** (Dependent on settings and effort)
Proportional	PAV+	Proportional gain (% assist), PEEP	High gain amplified by excessive effort → uncontrolled Vt and ΔP_L	High drive with high gain	**Moderate** (dependent on high drive and gain)
	NAVA	NAVA gain (cmH2O/mV), PEEP	High gain in context of high EAdi amplifies injurious effort	High EAdi with disproportionate NAVA gain	**Low - moderate** (better neural coupling; persistent risk with high drive)

Table 2. Association between respiratory effort, mechanical load, and clinical outcomes

Clinical study	Primary variable	Population	Main finding	Clinical implication
Ter Haar et al. 2025	P0.1	COVID-ARDS in transition to PSV	P0.1 > 3,5 cmH_2O → ↑ UCI mortality, ↓ Ventilator-free days y ↑ ICU length of stay	Early prognostic marker
Le Marec et al. 2024	P0.1	Patients on mechanical ventilation for any reason	P0.1 > 3,5 cmH_2O → ↓ survivance at day 90 y ↓ weaning probabily	Independent risk factor for mortality
Parrilla-Gómez et al. 2025	Time spent in high effort	Moderate-to-severe ARDS	Non-survivors spend more time in the high range (12% vs 3%) and have greater exposure to ΔP_L,dyn	The duration of effort matters more than the point value
Grassi et al. (ICEBERG) 2025	ΔP_L,dyn y ΔPstat	Hypoxemic respiratory failure	Higher mechanical load → ↑ UCI mortality (ΔP_L,dyn 19 vs 16 cmH_2O)	Total load is more predictive than VT or isolated effort alone
Dianti et al. 2025	P0.1, Pocc y ΔP_L,dyn	Patients on mechanical ventilation for any reason	U-shaped relationship: intermediate values (P0.1 2–5 cmH_2O; Pocc –10 to –20 cmH_2O) are the most favorable	There is a 'safe zone' of effort
Chi et al. 2022 / Liu et al. 2024	Pendelluft (EIT)	HRF y difficult weaning	Presence of pendelluft → ↑ UCI length of stay, ↓ Ventilator-free days y ↑ mortality	Regional marker of poor prognosis

blockade, transition to controlled ventilation, and strict limitation of tidal volume and driving pressure. Phenotype 2, with high respiratory drive and preserved mechanics, allows a more cautious strategy centered on PEEP optimization, correction of triggers amplifying respiratory drive (hypoxemia, acidosis, pain, anxiety), and use of pressure support ventilation (PSV) under strict surveillance for asynchronies and occult tidal volume. Phenotype 3, with low respiratory drive and impaired mechanics, requires close monitoring to prevent the development of excessive effort while maintaining safe ventilatory parameters. Phenotype 4, with low respiratory drive and preserved mechanics,

presents lower risk and a higher likelihood of a safe transition to spontaneous breathing.

Regardless of the phenotype, continuous assessment of ML (ΔP_L, driving pressure, pendelluft, and asynchronies) must be conducted during any clinical status change. When respiratory effort cannot be controlled with initial interventions, therapeutic escalation is mandatory: deepening analgesia and sedation and considering neuromuscular blockade, particularly in the presence of severe asynchronies or persistent high effort with documented risk of P-SILI.

The central message of the algorithm is to maintain the patient within a physiologically safe zone –defined by moderate respiratory effort, controlled mechanical load, and homogeneous ventilatory distribution– regardless of the selected ventilatory mode. The integration of physiological principles, monitoring, and individualized management determines effective prevention of patient-self-inflicted lung injury.

9. CONCLUSION

P-SILI represents a complex pathophysiological entity whose prevention does not depend on the ventilatory mode, but rather on the systematic integration of respiratory drive, lung mechanics, and the resulting mechanical load. Available evidence indicates that maintaining effort and ΔP_L within physiologically safe ranges is associated with better clinical outcomes, although this relationship is non-linear and depends on individual lung vulnerability. A stepwise monitoring approach, adapted to the resources of each Unit, serves as the primary tool to identify risks early and guide individualized management. Within this framework, precision medicine applied to mechanical ventilation emerges as the paradigm that best addresses the complexity of acute respiratory failure.

Conflict of interest

Authors have no conflicts of interest to declare

REFERENCES

1. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med. 2013;369:2126-36. https://doi.org/10.1056/NEJMra1208707
2. Brochard L, Slutsky A, Pesenti A. Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. Am J Respir Crit Care Med. 2017;195:438-42. https://doi.org/10.1164/rccm.201605-1081 °CP
3. Yoshida T, Fujino Y, Amato MB, Kavanagh BP. Fifty years of research in ARDS. Spontaneous breathing during mechanical ventilation. Risks, mechanisms, and management. Am J Respir Crit Care Med. 2017;195:985-92. https://doi.org/10.1164/rccm.201604-0748 °CP
4. Gattinoni L. Ventilation-induced lung injury exists in spontaneously breathing patients with acute respiratory failure: We are not sure. Intensive Care Med. 2017;43:256-8. https://doi.org/10.1007/s00134-016-4483-4
5. Yoshida T, Uchiyama A, Matsuura N, Mashimo T, Fujino Y. Spontaneous breathing during lung-protective ventilation in an experimental acute lung injury model: high transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury: High transpulmonary pressure associated with strong spontaneous breathing effort may worsen lung injury. Crit Care Med. 2012;40:1578-85. https://doi.org/10.1097/CCM.0b013e3182451c40
6. Yoshida T, Torsani V, Gomes S, et al. Spontaneous effort causes occult pendelluft during mechanical ventilation. Am J Respir Crit Care Med. 2013;188:1420-7. https://doi.org/10.1164/rccm.201303-0539OC
7. Ter Haar EAMD, Renes MH, Zijlstra HW, et al. Association of P0.1 with duration of ventilation and mortality in patients with COVID-19 ARDS. CHEST Crit Care. 2025;3:100112. https://doi.org/10.1016/j.chstcc.2024.100112
8. Baedorf-Kassis E, Murn M, Dzierba AL, et al. Respiratory drive heterogeneity associated with systemic inflammation and vascular permeability in acute respiratory distress syndrome. Crit Care. 2024;28:136. https://doi.org/10.1186/s13054-024-04920-4
9. Le Marec J, Hajage D, Decavèle M, et al. High airway occlusion pressure is associated with dyspnea and increased mortality in critically ill mechanically ventilated patients. Am J Respir Crit Care Med. 2024;210:201-10. https://doi.org/10.1164/rccm.202308-1358OC
10. Parrilla-Gómez FJ, Castellví-Font A, Boutonnet V, et al. Association of breathing effort with survival in patients with acute respiratory distress syndrome. Crit Care Med. 2025;53:e1982-94. https://doi.org/10.1097/CCM.0000000000006797
11. Mascheroni D, Kolobow T, Fumagalli R, Moretti MP, Chen V, Buckhold D. Acute respiratory failure following pharmacologically induced hyperventilation: an experimental animal study. Intensive Care Med. 1988;15:8-14. https://doi.org/10.1007/bf00255628
12. Freebairn R. Spontaneous breathing during mechanical ventilation in ARDS. Critical Care and Shock Journal. 2005;8:61-5. https://criticalcareshock.com/2005/08/3201/

13. Antonelli M. Ventilation-induced lung injury exists in spontaneously breathing patients with acute respiratory failure: No. Intensive Care Med. 2017;43:253-5. https://doi.org/10.1007/s00134-016-4488-z
14. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 does not lead to a «typical» acute respiratory distress syndrome. Am J Respir Crit Care Med. 2020;201:1299-300. https://doi.org/10.1164/rccm.202003-0817LE
15. Liu W, Chi Y, Zhao Y, He H, Long Y, Zhao Z. Occurrence of pendelluft during ventilator weaning with T piece correlated with increased mortality in difficult-to-wean patients. J Intensive Care. 2024;12:23. https://doi.org/10.1186/s40560-024-00737-z
16. Cressoni M, Cadringher P, Chiurazzi C, et al. Lung inhomogeneity in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med. 2014;189:149-58. https://doi.org/10.1164/rccm.201308-1567OC
17. Carteaux G, Parfait M, Combet M, Haudebourg A-F, Tuffet S, Mekontso Dessap A. Patient-self inflicted lung injury: A practical review. J Clin Med. 2021;10:2738. https://doi.org/10.3390/jcm10122738
18. Cornejo RA, Arellano DH, Ruiz-Rudolph P, et al. Inflammatory biomarkers and pendelluft magnitude in ards patients transitioning from controlled to partial support ventilation. Sci Rep. 2022;12:20233. https://doi.org/10.1038/s41598-022-24412-1
19. Repessé X, Vieillard-Baron A, Geri G. Value of measuring esophageal pressure to evaluate heart-lung interactions-applications for invasive hemodynamic monitoring. Ann Transl Med. 2018;6:351. https://doi.org/10.21037/atm.2018.05.04
20. Sottile PD, Smith B, Stroh JN, Albers DJ, Moss M. Flow-limited and reverse-triggered ventilator dyssynchrony are associated with increased tidal and dynamic transpulmonary pressure. Crit Care Med. 2024;52:743-51. https://doi.org/10.1097/CCM.0000000000006180
21. Norisue Y, Usami S, Ito Y, et al. Lung injury promoted by strong inspiratory efforts and breath stacking: impact of ventilation mode. Intensive Care Med Exp. 2025;13:110. https://doi.org/10.1186/s40635-025-00821-0
22. Telias I, Madorno M, Pham T, et al. Physiological consequences of breathing effort according to the mode of ventilation during acute hypoxemic respiratory failure. Am J Respir Crit Care Med. 2025;212:487-99. https://doi.org/10.1164/rccm.202411-2155OC
23. Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, et al. 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. https://doi.org/10.1056/NEJm²00005043421801
24. Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive Care Med. 2006;32:1515-22. https://doi.org/10.1007/s00134-006-0301-8
25. Goligher EC, Dres M, Fan E, et al. Mechanical ventilation-induced diaphragm atrophy strongly impacts clinical outcomes. Am J Respir Crit Care Med. 2018;197:204-13. https://doi.org/10.1164/rccm.201703-0536OC
26. Blanch L, Villagra A, Sales B, et al. Asynchronies during mechanical ventilation are associated with mortality. Intensive Care Med. 2015;41:633-41. https://doi.org/10.1007/s00134-015-3692-6
27. Carteaux G, Lyazidi A, Córdoba-Izquierdo A, et al. Patient-ventilator asynchrony during noninvasive ventilation: a bench and clinical study. Chest. 2012;142:367-76. https://doi.org/10.1378/chest.11-2279
28. Talmor D, Sarge T, Malhotra A, et al. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med. 2008;359:2095-104. https://doi.org/10.1056/NEJMoa0708638
29. Akoumianaki E, Lyazidi A, Rey N, et al. Mechanical ventilation-induced reverse-triggered breaths: a frequently unrecognized form of neuromechanical coupling. Chest. 2013;143:927-38. https://doi.org/10.1378/chest.12-1817
30. Demoule A, Clavel M, Rolland-Debord C, et al. Neurally adjusted ventilatory assist as an alternative to pressure support ventilation in adults: a French multicentre randomized trial. Intensive Care Med. 2016;42:1723-32. https://doi.org/10.1007/s00134-016-4447-8
31. Carteaux G, Córdoba-Izquierdo A, Lyazidi A, Heunks L, Thille AW, Brochard L. Comparison between neurally adjusted ventilatory assist and pressure support ventilation levels in terms of respiratory effort. Crit Care Med. 2016;44:503-11. https://doi.org/10.1097/CCM.0000000000001418
32. Sinderby C, Navalesi P, Beck J, et al. Neural control of mechanical ventilation in respiratory failure. Nat Med. 1999;5:1433-36. https://doi.org/10.1038/71012
33. Telias I, Damiani F, Brochard L. The airway occlusion pressure P0.1 to monitor respiratory drive during mechanical ventilation: increasing awareness of a not-so-new problem. Intensive Care Med. 2018;44:1532-35. https://doi.org/10.1007/s00134-018-5045-8
34. Mauri T, Grieco DL, Spinelli E, et al. Personalized positive end-expiratory pressure in spontaneously breathing patients with acute respiratory distress syndrome by simultaneous electrical impedance tomography and transpulmonary pressure monitoring: a randomized crossover trial. Intensive Care Med. 2024;50:2125-37. https://doi.org/10.1007/s00134-024-07695-y
35. Yoshida T, Roldan R, Beraldo MA, et al. Spontaneous effort during mechanical ventilation: Maximal injury with less positive end-expiratory pressure: Maximal injury with less positive end-expiratory pressure. Crit Care Med. 2016;44:e678-88. https://doi.org/10.1097/CCM.0000000000001649

36. Jansen D, Jonkman AH, Vries HJ de, et al. Positive end-expiratory pressure affects geometry and function of the human diaphragm. J Appl Physiol. 2021;131:1328-39. https://doi.org/10.1152/japplphysiol.00184.2021
37. Goligher EC, Dres M, Patel BK, et al. Lung- and diaphragm-protective ventilation. Am J Respir Crit Care Med. 2020;202:950-61. https://doi.org/10.1164/rccm.202003-0655 °CP
38. Pérez J, Accoce M, Dorado JH, et al. Failure of first transition to pressure support ventilation after spontaneous awakening trials in hypoxemic respiratory failure: Influence of COVID-19. Crit Care Explor. 2023;5:e0968. https://doi.org/10.1097/CCE.0000000000000968
39. Pérez J, Dorado JH, Navarro E, Morais CC, Accoce M. Mechanisms of lung and diaphragmatic protection by high PEEP in obese COVID-19 ARDS: role of the body mass index. Crit Care. 2022;26:182. https://doi.org/10.1186/s13054-022-04051-8
40. Dianti J, Fard S, Wong J, et al. Strategies for lung- and diaphragm-protective ventilation in acute hypoxemic respiratory failure: a physiological trial. Crit Care. 2022;26:259. https://doi.org/10.1186/s13054-022-04123-9
41. Telias I, Junhasavasdikul D, Rittayamai N, et al. Airway occlusion pressure as an estimate of respiratory drive and inspiratory effort during assisted ventilation. Am J Respir Crit Care Med. 2020;201:1086-98. https://doi.org/10.1164/rccm.201907-1425OC
42. Bertoni M, Telias I, Urner M, et al. A novel non-invasive method to detect excessively high respiratory effort and dynamic transpulmonary driving pressure during mechanical ventilation. Crit Care. 2019;23:346. https://doi.org/10.1186/s13054-019-2617-0
43. Dianti J, Bertoni M, Goligher EC. Monitoring patient-ventilator interaction by an end-expiratory occlusion maneuver. Intensive Care Med. 2020;46(12):2338-41. https://doi.org/10.1007/s00134-020-06167-3
44. Umbrello M, Formenti P, Longhi D, et al. Diaphragm ultrasound as indicator of respiratory effort in critically ill patients undergoing assisted mechanical ventilation: a pilot clinical study. Crit Care. 2015;19:161. https://doi.org/10.1186/s13054-015-0894-9
45. Bertoni M, Spadaro S, Goligher EC. Monitoring patient respiratory effort during mechanical ventilation: Lung and diaphragm-protectiv ventilation. En: Annual Update in Intensive Care and Emergency Medicine. Cham: Springer International Publishing; 2020. p. 21-35.
46. Grieco DL, Chen L, Brochard L. Transpulmonary pressure: importance and limits. Ann Transl Med. 2017;5:285. https://doi.org/10.21037/atm.2017.07.22
47. Bellani G, Mauri T, Coppadoro A, et al. Estimation of patient's inspiratory effort from the electrical activity of the diaphragm. Crit Care Med. 2013;41:1483-91. https://doi.org/10.1097/CCM.0b013e31827caba0
48. Vaporidi K, Psarologakis C, Proklou A, et al. Driving pressure during proportional assist ventilation: an observational study. Ann Intensive Care. 2019;9:1. https://doi.org/10.1186/s13613-018-0477-4
49. Yoshida T, Uchiyama A, Fujino Y. The role of spontaneous effort during mechanical ventilation: normal lung versus injured lung. J Intensive Care. 2015;3:18. https://doi.org/10.1186/s40560-015-0083-6
50. Goligher EC, Costa EL, 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;203:1378-85. https://doi.org/10.1164/rccm.202009-3536OC
51. Dianti J, Lovblom LE, Iftikhar MA, et al. Association of respiratory drive and effort with mortality and time to discharge in patients on mechanical ventilation in Canada: a longitudinal, prospective, registry-based cohort study. Lancet Respir Med. 2025;13:1087-95. https://doi.org/10.1016/S2213-2600(25)00297-8
52. Zalucky AA, Dianti J, Neyton LPA, Sinha P, Liu KD, Matthay MA, et al. Elastance may determine the neuromuscular blockade effect on mortality in acute respiratory distress syndrome. Am J Respir Crit Care Med. 2025;211:966-74. https://doi.org/10.1164/rccm.202406-1231OC
53. Grassi A, Bianchi I, Teggia Droghi M, et al. Increased Driving Pressure During Assisted Ventilation for Hypoxemic Respiratory Failure Is Associated with Lower ICU Survival: The ICEBERG Study. Am J Respir Crit Care Med. 2025;211:2169-79. https://doi.org/10.1164/rccm.202411-2146OC.
54. Grassi A, Bianchi I, Teggia Droghi M, et al. Increased driving pressure during assisted ventilation for hypoxemic respiratory failure is associated with lower ICU survival: The ICEBERG study. Am J Respir Crit Care Med. 2025;211:2169-79. https://doi.org/10.1164/rccm.202411-2146OC
55. Chi Y, Zhao Z, Frerichs I, Long Y, He H. Prevalence and prognosis of respiratory pendelluft phenomenon in mechanically ventilated ICU patients with acute respiratory failure: a retrospective cohort study. Ann Intensive Care. 2022;12:22.
56. Liu W, Chi Y, Zhao Y, He H, Long Y, Zhao Z. Occurrence of pendelluft during ventilator weaning with T piece correlated with increased mortality in difficult-to-wean patients. J Intensive Care. 2024;12:23.