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Esophageal pressure guided closed-loop ventilation: A theoretical framework toward precision mechanical ventilation

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Abstract

Background
Esophageal balloon manometry is a surrogate for pleural pressure and has been in clinical use for decades. The main advantages for its use are to partition the total lung and chest wall mechanics, thus providing transpulmonary inspiratory, expiratory, and driving pressure monitoring as the true stress delivered to the lung, and the capability to measure the transpulmonary mechanical power as the true energy delivered to inflate the lungs. Thus, it can provide more insight into lung and diaphragmatic protective ventilation than total airway pressure alone. Its capability as the gold standard to measure patient effort, muscle pressure, and to diagnose patient-ventilator interactions and dyssynchronies adds further value to its usage.

Proposed Framework
As the paradigm shifts toward personalized lung and diaphragm-protective ventilation, alongside increased recognition of ventilator-induced and patient self-inflicted lung injury (VILI and P-SILI respectively), using esophageal balloon manometry seems to be the ultimate tool to achieve these goals. In this paper, we introduce an automated theoretical closed-loop ventilation mode that is based on adjusting the inspiratory and expiratory transpulmonary pressures to a safe zone to provide true individualized lung and diaphragmatic protective ventilation, while simultaneously adjusting the triggering, maintaining, and cycling of breaths according to the patient's neural time and effort, potentially detecting and eliminating dyssynchronies.

Clinical Implications
This adaptive mode aims to optimize the balance between lung recruitment, overdistension, and respiratory muscle unloading, addressing VILI, P-SILI, ventilator induced diaphragm dysfunction (VIDD) and dyssynchronies.

Conclusion
The theoretical esophageal pressure guided closed-loop ventilation based on continuous input and feedback from the esophageal balloon represents a physiologically attractive framework toward individualized lung and diaphragm protective ventilation can conceptually lead to safer personalized ventilation, significantly lessen dyssynchronies, and potentially improve mortality outcomes in acute respiratory failure. However, this concept remains theoretical and unvalidated. Future studies are required before claims regarding feasibility, safety and outcome benefits can be made.

Keywords: Esophageal balloon manometry, Transpulmonary pressures, dyssynchronies, closed-loop ventilation.

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Introduction

Esophageal balloon manometry has become an important bedside monitoring tool in advanced mechanical ventilation because it provides an estimate of pleural pressure (Ppl) and allows calculation of trans-pulmonary pressure (airway pressure Paw – Pleural pressure Ppl). This helps to partition total respiratory mechanics into lung and chest wall mechanics, [1] estimate inspiratory effort (muscle pressure (Pmus), work of breathing (WOB), and pressure-time product (PTP). [2,3] Adjusting inspiratory pressures and PEEP according to trans-pulmonary pressures have shown promise in reducing ventilator-induced lung injury (VILI), patient self-inflicted lung injury (P-SILI), and ventilator-induced diaphragm dysfunction (VIDD). [4,5]

Patient-ventilator dyssynchrony (PVD) is a common and potentially deleterious complication during mechanical ventilation, associated with increased work of breathing, patient discomfort, prolonged mechanical ventilation, and ventilator-induced lung injury (VILI). Patient-Ventilator Interactions (PVI) remain a fundamental issue during mechanical ventilation when the ventilatory support intensity and timing doesn’t match the patients’ neural drive, effort, or timing. [6-8]

Despite decades of refinement in pneumatic triggering and cycling algorithms, patient-ventilator dyssynchrony (PVD) remains a ubiquitous clinical challenge. Incidence varies widely in the literature, affecting up to 30%-40% of ventilated patients in some reports, [9] while others shown that they can be detected in 96-100% of mechanically ventilated patients at some point during their ventilation course. [10] These dyssynchronous events are not merely technical glitches; they are independently associated with increased sedation, neuromuscular blockade requirements, prolonged stay on mechanical ventilation and increased mortality.

Dyssynchronies can occur during inspiration (related to the initiation of the breath or triggering), during the breath (work shifting), at the switch between inspiration and expiration (cycling), and can also occur during the expiratory phase. [8,11] While conventional monitoring relies on airway pressure and flow waveforms, these methods often fail to accurately detect complex dyssynchronies.

Esophageal manometry, utilizing an esophageal balloon catheter, provides a reliable surrogate for pleural pressure, enabling the direct unmasking of patients’ inspiratory effort and timing, and provide key insights into the mechanisms underlying patient-ventilator dyssynchrony and its clinical consequences. [12] Despite all the benefits of the catheter, its clinical use, especially in ARDS remains very low. [13]

This manuscript presents a hypothetical esophageal pressure-guided adaptive ventilation framework rather than a validated mechanical ventilation mode. The proposed framework is designed to support individualized lung- and diaphragm-protective ventilation strategies by integrating esophageal pressure-derived variables into ventilator control. It may improve detection and elimination of selected dyssynchronies to mitigate risks of VILI, P-SILI, and VIDD. The proposed targets and algorithmic responses should be interpreted as hypotheses requiring future validation studies rather than established clinical recommendations. The manuscript also discusses the technical limitations, implementation challenges and proposing future directions for algorithmic conflict resolution.

Potential role in lung protective ventilation

The transpulmonary driving pressure (Paw - Ppl) has shown to be major determinants of lung stress and major contributors in VILI. [14] Inspiratory transpulmonary pressure below 15-20 cmH_2O and trans-pulmonary driving pressure below 10-12 cmH_2O were shown to reduce the incidence of VILI and mortality. [15-17]

Setting PEEP according to the end-expiratory transpulmonary pressures at approximately 0 ± 2 cmH_2O delivers a more physiologic and personalized way of setting PEEP to prevent atelectasis, repeated opening and closing of alveoli and thus atelectrauma and have shown to improve oxygenation and possible mortality in ARDS as demonstrated in the EPVent trials and subsequent reanalyses. [18-21]

Like total mechanical power, transpulmonary mechanical power is surfacing as an important parameter for mortality in mechanical ventilation however, a definitive safe value has not been estimated yet. [22,23]

“The proposed framework would enable the ventilator to continuously adjust the delivered inspiratory pressure and PEEP to achieve the predefined physiological targets while remaining within the established safety window.”

Potential role in PVI, dyssynchronies and Diaphragm-Protective Ventilation

Clinician expertise and education remain an essential part in the detection and management of dyssynchronies. However, dyssynchronies might be difficult to recognize from the traditional pressure and flow-time curves. [12] Additionally, dyssynchronies could be sporadic making a continuous analysis, scrutiny and adjustments difficult at the bedside. [24] Interdependence of dyssynchronies is a challenge, changing a setting to fix one problem might create another. Other difficulties include the lack of standardization of the definitions of different dyssynchronies along the lack of a "gold standard" in determining the nature of the PVI. [8]

The esophageal balloon is considered the gold standard in measuring the patients' inspiratory efforts like the muscle pressure (Pmus), work of breathing (WOB), and pressure-time product (PTP). [2,3] It is also considered the gold standard in identifying and classification of PVI and dyssynchronies as it delineates in detail the start, the duration and the depth of the inspiratory effort. [5]

Some other modes have shown promise in reducing dyssynchronies like Proportional Assist Ventilation (PAV), [25] Neurally Adjusted Ventilatory Support (NAVA), [26] Adaptive Support Ventilation modes (ASV), [27] each have their advantages and pitfalls (Appendix 1 is a detailed description and comparison of those modes).

Some ventilator manufacturers have integrated automatic synchrony software algorithms that can detect and correct some dyssynchronies in real time. Most studies were done using IntelliSync+ (Hamilton Medical, Bonaduz, Switzerland) during PSV have shown improvement especially in trigger delay compared to cycle delay. [28-30]

The following section discusses selected dyssynchronies and how the proposed framework may detect or eliminate them. Figures of each dyssynchrony are in appendix 2.

Triggering phase

Trigger dyssynchronies occur when the initiation of the mechanical breath does not align with the onset of the patient's neural inspiration. Common types include missed, delayed, double, and reverse triggering. [8,11] Traditional triggering includes flow and pressure thresholds.

Missed and delayed triggering

The most common causes include airway trapping (auto-PEEP), muscle weakness and oversedation where the threshold for such triggers fail to respond to patients' effort (Figures 1 and 2 in appendix 2). [8,31]

"Having the breaths triggered by the negative deflection of the esophageal balloon with immediate delivery of the breath will reduce such dyssynchronies even in the presence of auto-PEEP."

Double trigger

Double triggering occurs when a strong, sustained patient inspiratory effort outlasts the ventilator's set inspiratory time, triggering a second consecutive breath before complete exhalation. [32,33] This results in "breath stacking," delivering a tidal volume that can be twice the intended amount, significantly increasing the risk of increasing inspiratory transpulmonary pressure, stress, strain, volutrauma and VILI (Figure 3 in appendix 2).

"Continuous dynamic adjustments of the inspiratory time and the magnitude of assisted pressure to precisely meet spontaneous respiratory timing and drive. Theoretically, this may reduce the incidence of double triggering and *mitigate the potential risk of VILI"*

Reverse triggering and Early triggering

Reverse triggering is a form of neuromechanical coupling with different phenotypes, [34] this phenomenon can be classified based on the presence of an intrinsic respiratory pattern (entrainment) or its absence. A passive ventilator-initiated breath triggers a reflexive contraction of the patient's diaphragm. If this reflexive effort is strong and outlasts the machine's inspiratory phase, it can also lead to breath stacking and double triggering (Figure 4 in appendix 2). [32-35]

Early trigger occurs when a machine-triggered inspiration precedes the patient trigger effort. The key finding is the start of inspiratory flow followed by evidence of inspiratory pressure generated by the respiratory muscles (Pmus), which may or may not trigger another breath. Patient effort may occur any time during inspiration or early during expiration. [8,11,35]

The esophageal balloon might be able to differentiate between both types of dyssynchronies and phenotypes, however it might be difficult to determine if the inspiratory effort is just a reflex like in reverse triggering or entrainment as in early trigger.

"The proposed mode based on triggering and cycling using the esophageal balloon can unmask entrainment. However, to prevent the ventilator from simply increasing the respiratory rate to match the entrained reflex, the algorithm must recognize the entrainment pattern and temporarily lower the mandatory rate to unmask the patient's true intrinsic neural drive.

Auto trigger

When the ventilator erroneously delivers a breath due to flow or pressure artifacts, such as cardiac oscillations, water condensation in circuits or circuit leaks without patient effort [8,11] (Figure 5 in appendix 2).

"Triggering based on the esophageal balloon may eliminate flow-artifact dyssynchronies, provided the algorithm includes robust filtering for cardiac oscillations within the esophageal pressure signal."

Work shifting

Is the unintended transfer of respiratory effort from the ventilator to the patient, often due to inadequate flow or pressure delivery (air hunger). This occurs when the ventilator fails to meet the patient's inspiratory demand, leading to increased respiratory muscle activity and excessive work of breathing. [36] The Patient-Ventilator Breath Contribution (PVBC), or work shifting index, represents the work done by the patient relative to the total work.

The esophageal balloon is the gold standard of measuring the patients' muscle effort (Pmus), calculated as:

$$(E_{CW} \times V_T) - \Delta P_{ES}$$

Where E_{CW} is the chest wall elastance, VT is the tidal volume, ΔP_{ES} is the change in esophageal pressure during active breathing.

To obtain the chest wall elastance accurately, passive conditions are required when no effort is produced by the patient. [37] As an alternative, the simple delta swing in the esophageal pressure during active breathing has been used as an estimate of the Pmus (Pmus ≈ ΔPES). [38] Other ways to obtain the dynamic chest wall elastance have been described without the need for passive situations or holding maneuvers. [39] A less accurate way of estimating the chest wall elastance is through the Pes-Volume loop as the line between the inspiratory and the expiratory phase especially if there is no strong respiratory activity and at the end of exhalation (near the passive chest recoil) with no expiratory muscle activity. [2] This method can be influenced by the respiratory muscle activities too (Figure 6 Appendix 2).

A more robust method for the ventilator to calculate the Pmus continuously will be through the least square fitting method of the equation of motion. [40] It requires the microprocessor to dynamically estimate resistance and elastance which are already in use in new generation mechanical ventilators.

Furthermore, the paradigm of "Diaphragm-Protective Ventilation" (or mitigating myotrauma) emphasizes the need to maintain patient effort within a safe physiological range. It is widely recommended to keep Pmus between 3 and 15 cmH_2O to avoid disuse atrophy with overassistance or load-induced injury with underassistance. [41-43]

"The proposed adaptive mode that sets the applied airway pressure (with set limits to the airway and trans-pulmonary driving pressures) to maintain a certain relationship between the patient effort and the ventilator pressure depending on the state of the respiratory failure would be an ideal. For an example during the initial phase where the main concern is resting the respiratory muscles would require less patient effort, while in the weaning phase a more patient effort would be required."

Cycling dyssynchronies

The ventilator cycles the breaths based on inspiratory set flow criteria (like in VCV or PSV), or inspiratory time (like in PCV modes). Cycling dyssynchronies occur when there is a mismatch between the patients' inspiratory effort duration and the cycling criteria of the ventilator that can lead into early or delayed cycling [8,11] (Figure 7-8).

"*An esophageal balloon guided variable cycling criterion terminating the breath exactly when the patient inspiratory effort ceases based on the esophageal pressure signal indicates the end of neural inspiration would therefore eliminate such dyssynchronies. This can be adjusted in cases of auto-PEEP in severe obstructive cases where inspiratory time might need to be automaticallyshortened"*

Major Pitfalls and difficulties and algorithmic conflict resolution

Despite its physiologic appeal, esophageal manometry remains underutilized in most intensive care units [4,13] because the technique is technically demanding, interpretation is nuanced, and several artifacts may lead to misleading conclusions. Understanding and overcoming those pitfalls are essential before incorporating esophageal pressure measurements into clinical decision-making.

Among the most common difficulties are incorrect balloon position or displacement, disconnection from the ventilator, incorrect balloon filling volumes, esophageal and cardiac artifacts, patients' positioning, and poor reproducibility between operators. Furthermore, there is ongoing debate regarding the use of absolute esophageal pressure values versus delta (change in) pressure. [4,5,9]

Apart from clinical expertise, recalibration and manual trouble shooting, for a mode to be dependent on the esophageal ballon, reliable reproducible waveforms are needed. Some suggestions include:

- Automated calibration: smart catheters for automatic balloon calibration, air volume adjustments, real-time artifact correction, continuous quality indicators and position verification algorithms
- AI Integration: Integration with artificial intelligence and machine learning might make all the above process seamless, quick, and reliable
- Failsafe: A safe back up to a regular conventional mode or manual override will be important safeguard for any malfunction or loss of signal. An alarm or visual notification for clinicians about returning to backup mode would be important.

Algorithmic Conflict Resolution

A theoretical closed-loop system must have a hierarchy of safety limits to resolve conflicting physiological goals. For example, if adjusting PEEP to achieve an end-expiratory transpulmonary pressure of 0 cmH_2O results in an end-inspiratory transpulmonary pressure exceeding 20 cmH_2O, the algorithm must prioritize safety. Typically, limiting transpulmonary driving pressure to < 12 cmH_2O must take precedence over perfect end-expiratory recruitment to prevent VILI.

Proposed Closed-Loop Architecture

The proposed closed-loop architecture would consist of three integrated control layers operating in parallel within a single ventilator microprocessor.

- The first layer, the Lung Protection Controller, continuously acquires the esophageal pressure signal alongside airway pressure and flow, calculates end-inspiratory transpulmonary pressure, end-expiratory transpulmonary pressure, and transpulmonary driving pressure in real-time, and automatically adjusts the applied airway pressure and PEEP to maintain these values within predefined safety thresholds.
- The second layer, the Synchrony Controller, utilizes the raw esophageal pressure waveform after digital filtering to remove cardiac oscillations and motion artifacts to trigger breaths at the onset of the patient's neural inspiratory effort and to cycle breaths precisely at its termination, thereby replacing conventional pneumatic triggering and cycling algorithms.
- The third layer, the Diaphragm Protection Controller, continuously estimates muscle pressure (Pmus) and modulates the magnitude of pressure support to maintain patient effort within the safe physiological range of 3 to 15 cmH_2O.

An overarching conflict resolution hierarchy governs the interaction between these three layers: transpulmonary driving pressure limits always take precedence over recruitment targets, and airway pressure safety ceilings override Pmus optimization goals. A failsafe module continuously monitors signal quality indices and automatically reverts the ventilator to a conventional backup mode with clinician notification if the esophageal pressure signal becomes unreliable.

Validation Roadmap

Clinical translation of this closed-loop architecture would require a phased validation strategy. The first phase should involve computational modeling and bench testing using high-fidelity lung simulators programmed with various respiratory mechanics profiles including normal lungs, ARDS with low compliance, obstructive physiology with auto-PEEP, and obese patients with high chest wall elastance to verify that the algorithm responds appropriately across the full spectrum of clinical scenarios and maintains all parameters within safety limits under both stable and rapidly changing conditions. The second phase would consist of a prospective, physiological study in mechanically ventilated ICU patients already instrumented with esophageal balloon catheters, comparing the algorithm's automated recommendations against expert clinician decisions in an advisory only way to assess agreement, response time, and safety. The third phase would be a randomized controlled crossover trial comparing the closed-loop mode against conventional clinician directed ventilation, with primary endpoints of time spent within lung protective transpulmonary pressure targets, asynchrony index, and Pmus within the safe range, and secondary endpoints including duration of mechanical ventilation, sedation requirements, and ICU mortality.

Table 1 and figure 8 summarize how the algorithm would automatically adjust the ventilator settings to stay within the protective safe limits while safeguarding against dyssynchronies. All adjustments feed into a continuous re-assessment loop, enabling breath by breath optimization of lung protection and patient-ventilator synchrony.

Table 1: Summarizes how the automated mode can adjust to maintain safe lung protective ventilation and to reduce dyssynchronies.

Physiologic Parameter	Proposed Ventilator Action	Proposed physiological Target / Safe Limit
Inspiratory Transpulmonary pressure	Adjust airway pressure	$P_{TP\ Insp}$ below 20-25 cmH_2O
Expiratory Transpulmonary pressure	Adjust PEEP	$P_{TP\ Exp}$ between 0 ± 2 cmH_2O
Transpulmonary driving pressure	Adjust airway pressure and PEEP $P_{TP\ Insp-Exp}$	$P_{TP\ \Delta P}$ between 10-12 cmH_2O Paw $\Delta P < 15$ cmH_2O
Transpulmonary mechanical power	Adjust P_{TP}, respiratory rate, tidal volumes for a safe trans-pulmonary mechanical power	Unknown yet
Breath Triggering	Trigger based on P_{ES} deflection	Trigger at -1 to -2 cmH_2O
Breath duration (Inspiratory time)	Adjust the Insp time from the beginning till the end of the patients' neural breath time or P_{mus} duration	Variable
Breath cycling	Cycling at the end of P_{mus} duration (as above)	Variable
Airway pressure	Adjust the airway pressure to maintain certain work shifting index depending on the phase of respiratory failure from 100% to maintain no patients' effort to lesser % during recovery or weaning	keep P_{mus} between 3-15 cmH2O Paw $\Delta P < 15$ cmH2O

P_{AW}: airway pressure, P_{TP}: Trans-pulmonary pressure, P_{es}: esophageal pressure, P_{PL}: Pleural pressure, Pmus: muscle pressure

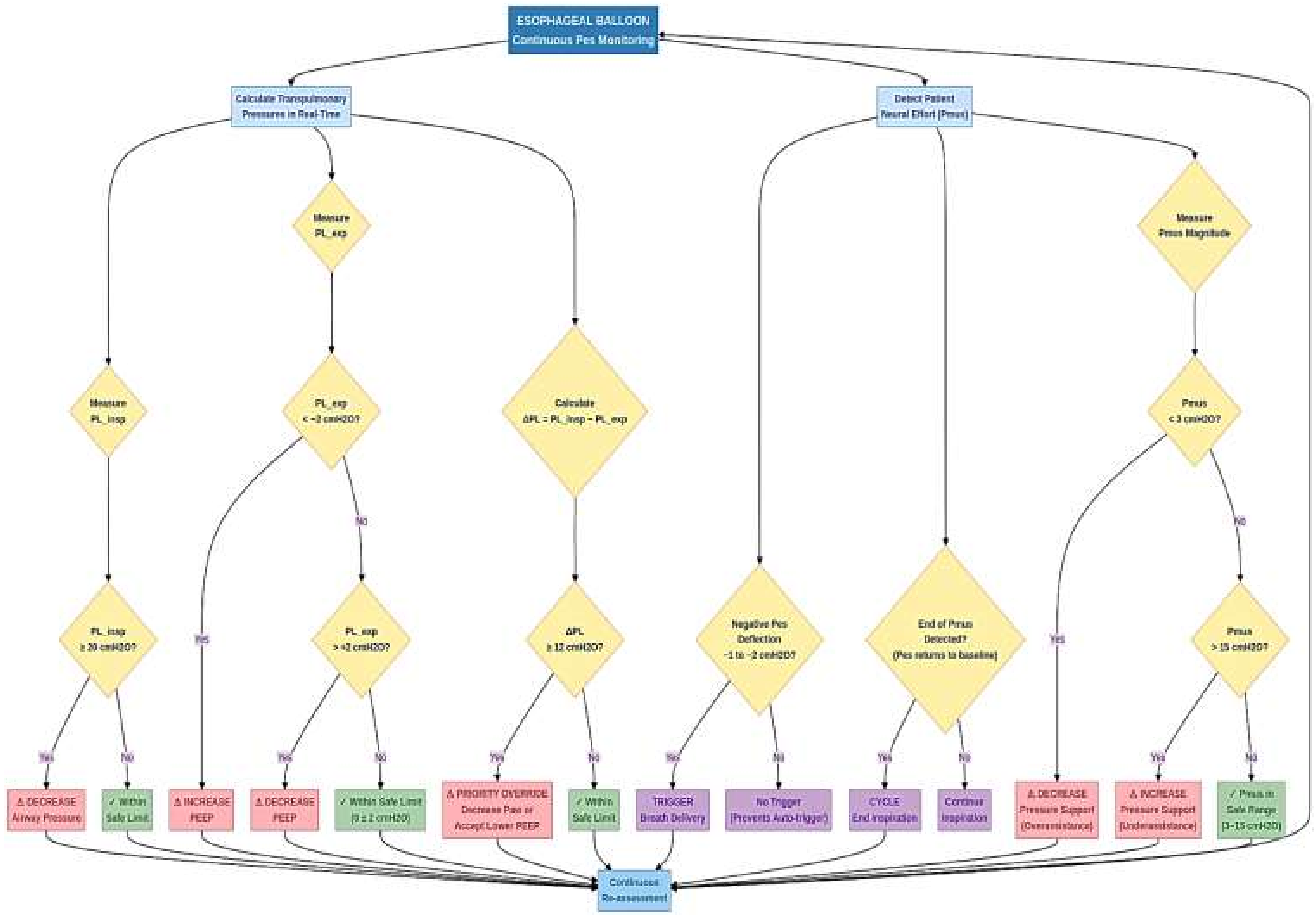

Figure 8: Closed-loop algorithm for esophageal pressure-driven automated ventilator adjustments.

The flowchart illustrates the two parallel decision pathways originating from continuous esophageal pressure (Pes) monitoring. The left pathway calculates transpulmonary pressures in real-time (end-inspiratory PL, end-expiratory PL, and transpulmonary driving pressure ΔPL) and automatically adjusts airway pressure and PEEP to maintain values within safe limits (PL_insp < 20 cmH_2O, PL_exp 0 ± 2 cmH_2O, ΔPL < 12 cmH_2O). A priority override ensures that driving pressure limits take precedence over recruitment targets when goals conflict. The right pathway detects patient neural effort (Pmus) to guide breath triggering (initiated at ΔPes −1 to −2 cmH_2O), cycling (terminated when Pes returns to baseline), and pressure support titration (maintaining Pmus between 3 and 15 cmH_2O for diaphragm-protective ventilation).

All adjustments feed into a continuous re-assessment loop, enabling breath by breath optimization of lung protection and patient-ventilator synchrony.

Paw: airway pressure; PEEP: positive end-expiratory pressure; PL: transpulmonary pressure; Pes: esophageal pressure; Pmus: muscle pressure; ΔPL: transpulmonary driving pressure.

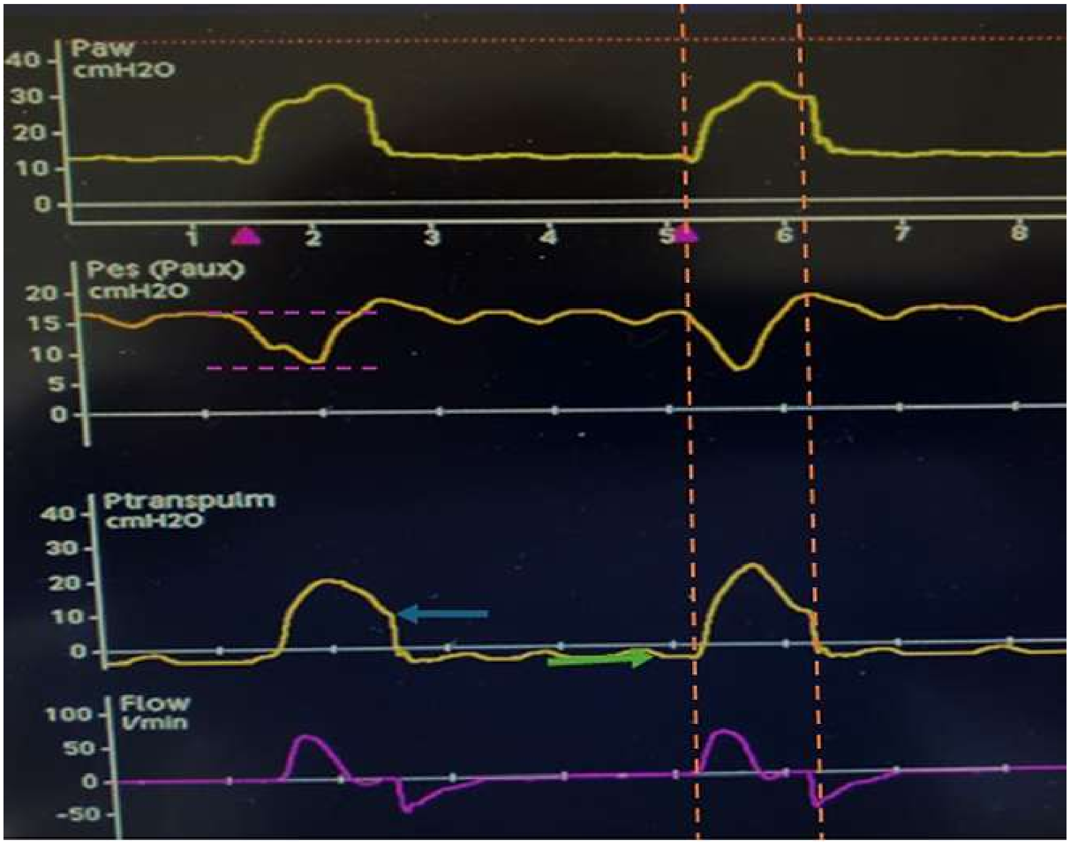

Figure 9: Summary of good patient-ventilator interaction and trans-pulmonary pressure goals.
From top, airway pressure-time, esophageal pressure – time, trans-pulmonary pressure – time, flow time curves. The horizontal purple dashed lines in the esophageal pressure shows Pmus about 10 cmH_2O, the blue arrow in the trans-pulmonary pressure curve shows end inspiratory pressure about 10 cmH_2O, and the green arrow shows end expiratory pressure about -2 cmH_2O (no holding maneuvers done but there are no inspiratory or expiratory flow respectively). The vertical dashed orange lines show a good match in the triggering phase (start of the patients' effort indicated by the negative deflection of the esophageal pressure), the cycling phase (exhalation starts at the end of the patient effort as indicated by the return of the esophageal pressure)

Conclusion

Esophageal pressure monitoring provides a physiologically informative variables which is essential to achieve individualized lung and diaphragm-protective ventilation with potential impact to improve recognition and mitigation of selected dyssynchronies.

The proposed framework of esophageal pressure-guided closed-loop ventilation mode could guide the development of algorithms designed to implement individualized lung and diaphragm-protective ventilation, detect and eliminated different types of dyssynchronies. The framework is still theoretical requiring prospective validation before clinical feasibility, safety and outcome benefits can be claimed.

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