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Bridging the gap: Enhancing synchrony in mechanical ventilation

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Abstract

Background
Mechanical ventilation is a life-saving intervention for patients with acute respiratory failure, yet ventilator dyssynchrony a misalignment between patients' effort and ventilator support remains a common challenge in intensive care units (ICUs). Dyssynchrony is associated with prolonged ventilation, diaphragm dysfunction, increased ICU and hospital stays, and higher mortality rates.
Objective
This review aims to provide an in depth analysis of the physiological control of ventilation and its interaction with mechanical ventilators, emphasizing newer technologies and strategies to enhance patient-ventilator synchrony.
Methods
We examine key concepts in mechanical ventilation, including breath initiation (triggering), inspiratory flow patterns, and breath termination (cycling). We discuss the impact of patient-ventilator dyssynchronies, including triggering and cycling abnormalities, and their physiological and clinical implications. Recent advances in ventilator technology and novel monitoring techniques are reviewed for their potential role in optimizing patient-ventilator interactions.
Results
Despite technological advancements, ventilator dyssynchronies remains prevalent, partly due to a lack of clinician education and variability in nomenclature. A recent international quiz assessing knowledge on dyssynchrony revealed an average score of 60%, highlighting the need for improved clinician training. The asynchrony index (AI) is a valuable metric for assessing dyssynchronies, and innovations such as adaptive modes of ventilation newer triggering methods could potentially improve dyssynchronies. Additionally, a novel approach utilizing esophageal pressure or electrical diaphragmatic activity (Edi) for triggering and cycling could enhance synchronization.
Conclusion
Optimizing patient-ventilator interactions is crucial for improving outcomes in mechanically ventilated patients. Education, waveform analysis, and advanced ventilator technologies are key strategies for mitigating this issue. Future research should focus on novel signal-based control mechanisms to enhance ventilator responsiveness and align support with patient effort.

Keywords: Ventilator dyssynchronies, mechanical ventilation, patient-ventilator interaction, respiratory physiology, asynchrony index, esophageal pressure monitoring, AI

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Introduction

Mechanical ventilation is a critical intervention for patients experiencing acute respiratory failure, providing essential support to maintain adequate gas exchange and relieve respiratory distress. Despite technological advancements, ventilator dyssynchronies defined as a mismatch between patient effort and ventilator support remains a common challenge in intensive care units (ICUs). Dyssynchronies can lead to adverse outcomes, including prolonged mechanical ventilation duration, diaphragm dysfunction, extended ICU and hospital stays, [1] reduced likelihood of discharge to home, and increased in-hospital mortality. [2-5]

Over the past decades, mechanical ventilation strategies have evolved to better align with the complex physiology of human respiration. Innovations such as adaptive modes of ventilation and advanced triggering mechanisms have been developed to enhance Patient-Ventilator Interactions (PVI) and synchrony. [6] However, ventilator dyssynchronies continues to occur frequently in ICUs, [7] partly due to a lack of comprehensive understanding of respiratory physiology and the intricate interactions between the patient and the ventilator. Additionally, the significant variability in the nomenclature and definitions of such interactions pose an obstacle in our interpretations. A taxonomy for patient-ventilator interactions and a method to read ventilator waveforms was proposed in 2022 to tackle this issue. [8]

An unpublished recent international quiz assessing knowledge of ventilator dyssynchronies among nearly 200 respondents yielded an average score of 60%, highlighting potential gaps in clinician education regarding patient-ventilator interaction. This knowledge gap is concerning, as dyssynchronies continues to be a frequent occurrence.

The asynchrony index (AI) is a metric used to evaluate the mismatch between a patient's spontaneous breathing efforts and the ventilator's delivered breaths. The index is typically calculated as the percentage of asynchronous breaths relative to the total number of breaths over a given period. [9]

This review aims to provide an in-depth analysis of the physiological control of ventilation and its interaction with mechanical ventilators, with a particular focus on newer technologies. By elucidating these mechanisms, we hope to offer insights that can aid in reducing dyssynchronies and improving patient outcomes.

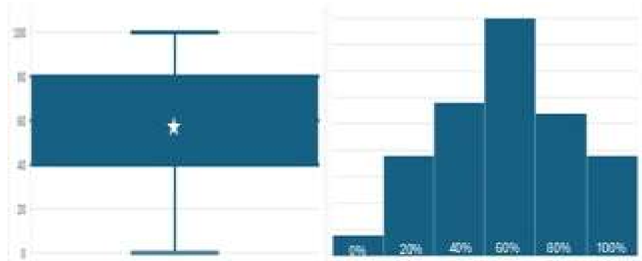


Figure 1: Assessment of clinician knowledge on patient - ventilator dyssynchronies. The box plot (left) illustrates the distribution of quiz scores, showing a median around 60% with considerable variability. The histogram (right) further breaks down score distribution, highlighting peaks and gaps in understanding.

Interaction between mechanical ventilation and respiratory physiology

Initiation of Ventilation (Triggering)

Passive Ventilation: In sedated patients or those lacking spontaneous respiratory effort, the ventilator initiates breaths based on preset parameters (time-triggered ventilation).

- Volume-Controlled Ventilation (VCV): The ventilator delivers a set flow and tidal volume at a predetermined respiratory rate resulting in variable airway pressures depending on respiratory mechanics, set flow, tidal volume, and inspiratory time.
- Pressure-Controlled Ventilation (PCV): The ventilator delivers breaths to achieve a target airway pressure, resulting in variable tidal volumes depending on respiratory mechanics, set pressures, and inspiratory time.

Active Ventilation: In spontaneously breathing patients, the ventilator assists initiated breaths through various triggering mechanisms:

- Flow Triggering: The ventilator detects changes in flow during end-expiration and delivers a breath when the patient generates a specific inspiratory flow rate set by the operator.
- Pressure Triggering: The ventilator detects changes in airway pressure and delivers a breath when the patient generates a specific negative pressure set by the operator.
- Neural Triggering (NAVA): The ventilator leverages diaphragmatic electrical activity (Edi) to estimate respiratory drive, triggering and cycling mechanical assistance. [10]
- Smart Triggering: The ventilator identifies changes in the flow waveform to initiate breaths. [11]

Flow Patterns During Inspiration

The ventilator delivers inspiratory flow in different patterns tailored to the patient's needs. [12]

• Square (Constant) pattern: Delivers a constant flow throughout the inspiratory phase, typically used in volume-controlled ventilation modes. This pattern results in a rapid increase in airway pressure, which is maintained until the set tidal volume is delivered.

• Decelerating pattern: Provides a high initial flow that decreases throughout inspiration, commonly seen in pressure-controlled ventilation modes. This pattern may improve gas distribution and oxygenation by matching the patient's inspiratory demand more closely.

• Sinusoidal pattern: Characterized by a smooth, wave-like flow, resembling natural spontaneous breathing. This pattern is less commonly used in mechanical ventilation but may be observed in certain spontaneous breathing modes.

• Ascending pattern: The accelerating or ascending flow waveform begins with a low initial flow that gradually increases throughout inspiration. However, it has been removed from most modern ventilators due to its detrimental impact on patient work of breathing (WOB) and its association with ventilator asynchronies.

Studies on the impact of flow waveforms on ventilation outcomes have produced conflicting results. Some [13-15] suggest that a decelerating waveform improves oxygenation and lung compliance, while others [16-21] indicate no clear advantage. A recent study [21] suggests that a truncated descending flow waveform minimizes mechanical power, potentially reducing ventilator-induced lung injury (VILI).

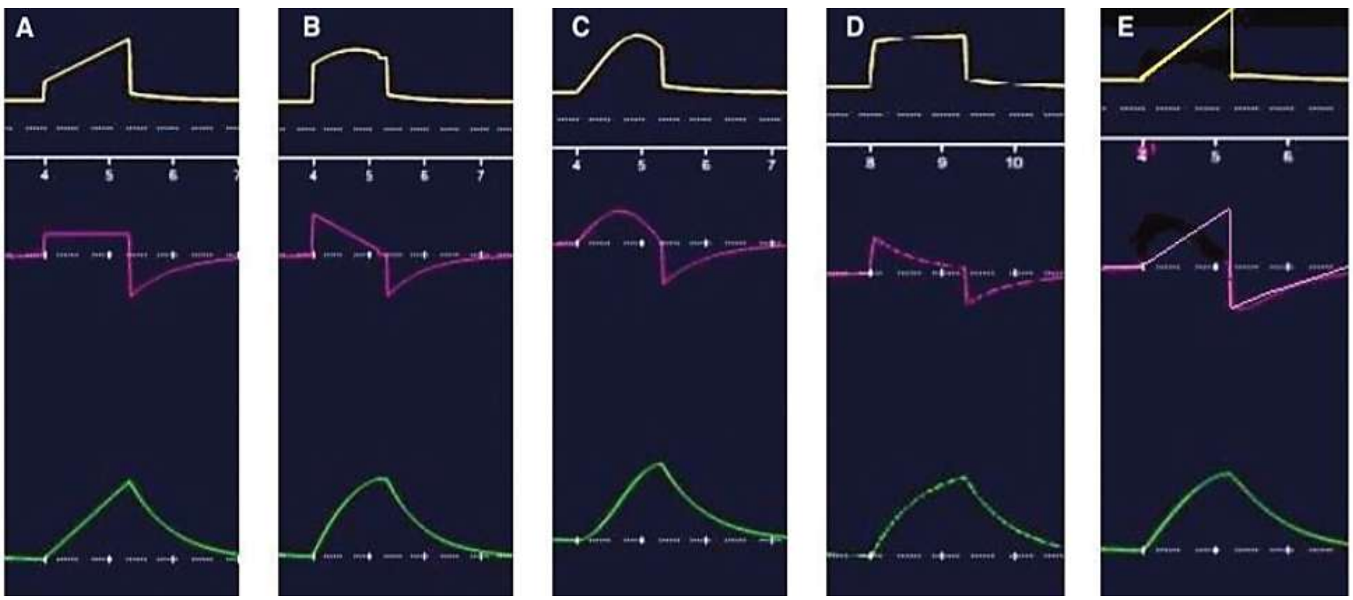


Figure 2: Typical flow waveforms used by different modes of ventilators. Upper yellow curves are the airway pressures in cmH**2**O, middle pink curves are flows in L/min, and lower green curves are tidal volumes in mL (A) Constant or square flow waveform, (B) descending, (C) sinusoidal, (D) decelerating, and (E) ascending. From reference 12.

Flow Patterns During Exhalation

Usually, exhalation is a passive process induced by the elastic recoil of the lungs and chest wall to the set PEEP level in most modes. The depth and the slope of the expiratory flow depends on the expiratory respiratory system mechanics, i.e. the Time Constant **(**τ) which is the product of compliance and resistance. However, sometimes expiratory work could be detected [22] (figure 3). Flow controlled mode is a novel mode of ventilation that uses a controlled constant expiratory flow curve. [23]

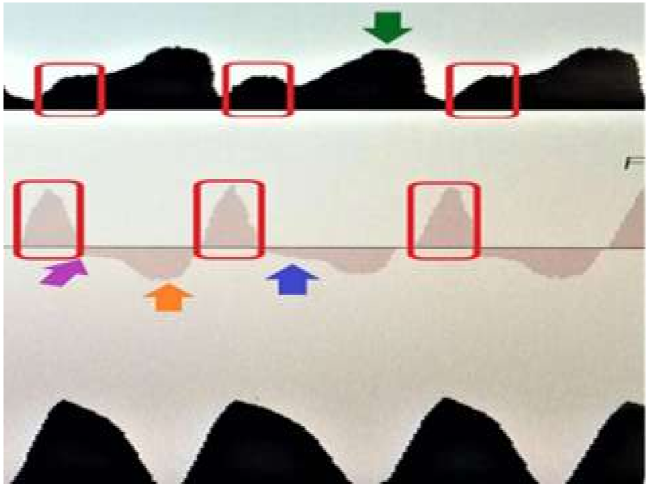


Figure 3: Expiratory work. From top to bottom: pressure-time, flow-time and volume-time curves. We can see a variable inspiratory time characteristic of pressure support ventilation (red rectangle). In expiration time there is expiratory work in which some things happen: a possible early cycling: amputation of the expiratory peak flow (purple arrow), associated to a strong expiratory effort that reverses the expiratory flow from his normal pattern (high at the beginning and less to the end), this effort increases during expiration evidenced by a progressive increase in expiratory flow (blue arrow) and at the end of expiration (orange arrow), there is a strong inspiratory effort that produces a high inspiratory peak flow. This strong expiratory effort causes pressure to rise above set level (green arrow). From reference 22.

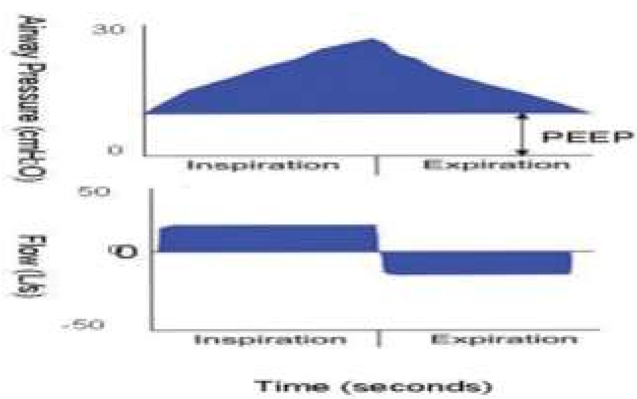


Figure 4: flow-controlled mode. Constant inspiratory and expiratory flow waveforms. From reference 23.

Cessation of Inspiration (Cycling)

The transition from inspiration to expiration is determined by various cycling mechanisms:

- Time-Cycled Ventilation: The ventilator cycles to expiration after a preset inspiratory time, or Inspiratory : Expiratory ratio (I:E) independent of volume or pressure.
- Volume-Cycled Ventilation: The ventilator cycles to expiration after delivering a preset tidal volume, common in VCV. Of note, volume cycle is considered a flow cycle as the ventilator does not control volume but rather the flow and integrate the volume as flow / time.
- Flow-Cycled Ventilation: The ventilator cycles to expiration when inspiratory flow decreases to a predetermined percentage of peak inspiratory flow, commonly used in spontaneous modes like PSV.

Ventilator dyssynchronies related to control of ventilation

Triggering Dyssynchronies

Occurs in 25–38% of mechanically ventilated patients. [2-5,24] Has a higher incidence in COPD [25] due to hyperinflation, where patients must overcome intrinsic PEEP to generate sufficient negative pressure or inspiratory flow to trigger the ventilator. This additional effort is referred to as the threshold load. [26-29]

Other contributing factors include sedation and low respiratory drive, ventilator-related factors, such as the location of the flow or pressure sensor (e.g., within the ventilator itself or near the patient's airway), [30] problems with valve functionality, the type of interface employed (e.g., endotracheal tube versus face mask or helmet), leaks, and elevated resistance introduced by components like heat-and-moisture exchangers (HMEs) or endotracheal tubes, can contribute to triggering issues. [31] Additionally, inappropriately set trigger sensitivities on the ventilator can be a factor.

Diagnosis:

Clinical signs: abdominal movements, suprasternal retraction, which is often specific but not sensitive.

Ventilator waveforms*:* most common method of identifying the patient-ventilator interactions through inspiratory flow-time and pressure-time scalars. Figure 14 gives a brief description of diagnosis and common causes of such dyssynchronies.

Advanced monitoring: Esophageal pressure or electrical activity of the diaphragm monitoring offers high accuracy but rarely used in routine clinical settings

- **Late (Delayed) trigger:** a delay of more than 100 msec between the patients' effort and the breath delivered by the ventilator (Figure 5). [22]
- **Failed (Missed) trigger:** evidence of patients' effort is not followed by a mechanical breath (Figure 6). [31]
- **False (Auto) trigger:** The ventilator erroneously delivers a breath due to flow or pressure artifacts, such as cardiac oscillations, water condensation in circuits or circuit leaks. An expiratory pause maneuver can help in

diagnosis showing no airway drop indicating no patient effort (Figure 7 A-B). [8]

- **Early (Reverse) Triggering:** Reverse triggering is a form of patient-ventilator asynchrony where a patient's inspiratory effort follows a ventilator-initiated breath, rather than preceding it. This phenomenon occurs when the ventilator's passive insufflation stimulates the patient's respiratory center, leading to diaphragmatic muscle contractions or a mismatch between the mechanical and neural timing (Figure 8). [32]

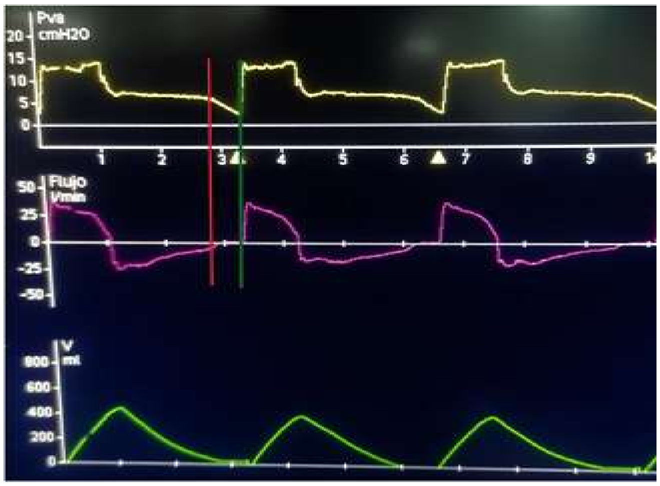


Figure 5: Delayed Triggering or Late Trigger. From top to bottom, the curves represent pressure-time, flow-time, and volume-time. A noticeable time lag of more than 300 milliseconds is observed between the initiation of the patient's effort (red line) and the actual triggering of the breath (green line). The trigger variable was set at a pressure threshold of -4 cmH₂O. From reference 22.

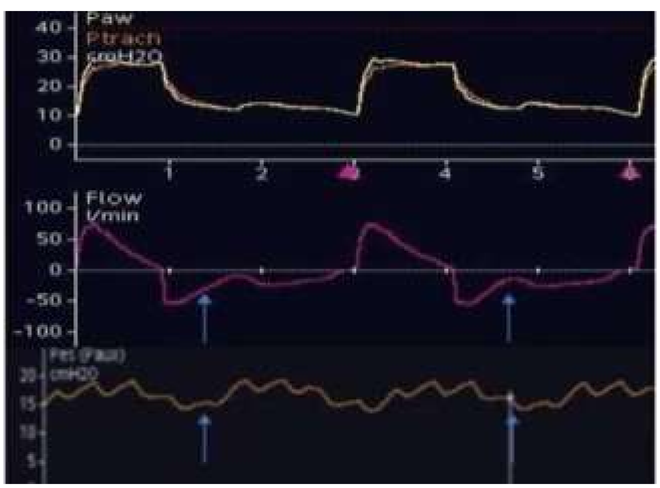


Figure 6: Failed or missed trigger. From top to bottom, the curves represent pressure-time, flow-time, and esophageal pressure-time. Blue arrows point to patient effort with drop on esophageal pressure and alteration of the expiratory flow curve not followed by a mechanical breath. From reference 31.

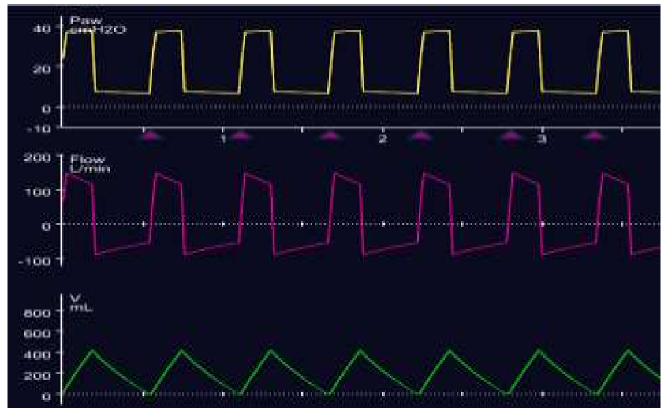


Figure 7A: False (auto) triggering about 100/min caused by heart rate. The pink arrows indicate patient-triggered breath (in this case it is not patient triggered).

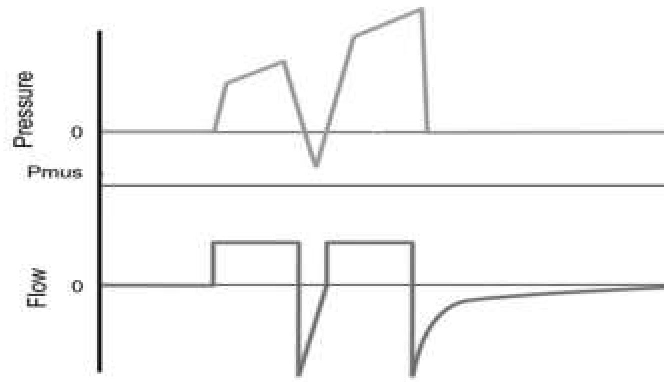


Figure 7B: Schematic drawing False (auto) triggering causing double triggering. From top to bottom, the curves represent pressure-time, Muscle effort (Pmus) and flow-time There is no patient effort indicated by flat Pmus.

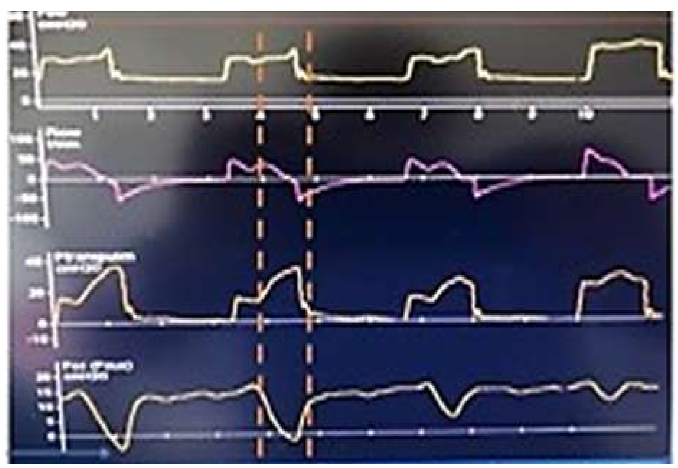


Figure 8: Early or Reverse trigger. From top to bottom, the curves represent pressure-time, flow-time, transpulmonary pressure-time curves, and esophageal pressure-time. The figure shows time triggered breath (no patient effort), followed by patient effort (orange dashed lines) evidenced by the drop of esophageal pressure and alteration of the airway pressure and flow curves. From reference 32.

Cycle Dyssynchronies

- **Early (Premature) Cycling:** Occurs when the ventilator transitions to the expiratory phase before the patient completes their inspiratory effort. Common etiologies include low tidal volume ventilation, patients with a high respiratory drive, short inspiratory time, or high set flow cycling. [8] This may lead to increased work of breathing, patient discomfort, double triggering, which can result in unintentional high tidal volumes and an increased risk of ventilator-induced lung injury (VILI) (Figure 9 A-B).
- **Delayed Cycling:** Delayed cycling occurs when the ventilator's inspiratory phase extends beyond the patient's natural inspiratory effort, leading to a late transition to expiration. This mismatch is common in COPD patients due to factors such as dynamic hyperinflation, increased airway resistance, and altered lung compliance. COPD patients typically have higher lung compliance, those with prolonged inspiratory times and high tidal volumes are more susceptible to delayed cycling. This condition can result in air trapping and the development of auto-PEEP, further increasing the work of breathing and exacerbating respiratory distress. [8]
- **Work Shifting:** Work shifting in mechanical ventilation refers to the unintended transfer of respiratory effort from the ventilator to the patient, often due to inadequate flow or pressure delivery. This occurs when the ventilator fails to meet the patient's inspiratory demand, leading to increased respiratory muscle activity and excessive work of breathing. A common manifestation is insufficient flow asynchrony or "air hunger," seen in volume-controlled ventilation (VCV) as a concavity in the pressure waveform, indicating the patient's effort to draw in more air than the ventilator provides. In severe cases, this can lead to double triggering, increased trans-pulmonary pressure gradients, and potential lung injury. Work shifting is more pronounced in conditions with high respiratory drive, such as agitation, pain, fever, or ARDS, where protective ventilation strategies may impose low tidal volumes and flow rates. Managing work shifting involves optimizing ventilator settings increasing inspiratory flow in VCV, reducing rise time in pressure-controlled modes, or switching to pressure support ventilation (PSV) when possible. Additionally, addressing underlying causes such as pain, anxiety, or fever and ensuring appropriate sedation can help minimize excessive patient effort and improve ventilator synchrony. [33]

Work shifting requires the calculation of the Pmus by an esophageal ballon or other non invasive methods [34] and dividing it by the driving pressure (Pvent).

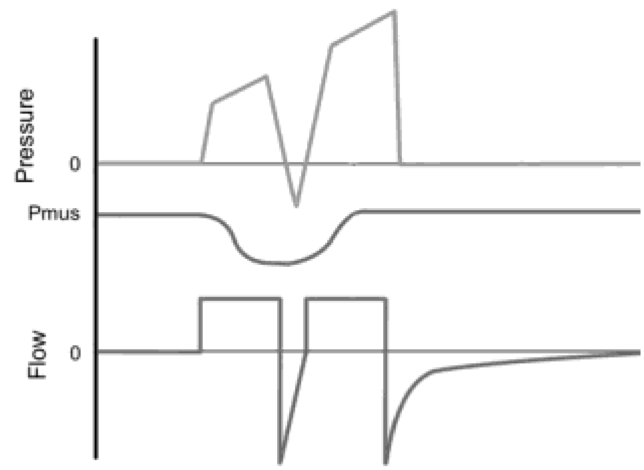


Figure 9A: Early Cycling in Mechanical Ventilation. This waveform illustrates early termination of the ventilator's inspiratory phase before the patient's neural inspiratory effort is complete leading to double trigger. Pmus: patient inspiratory effort

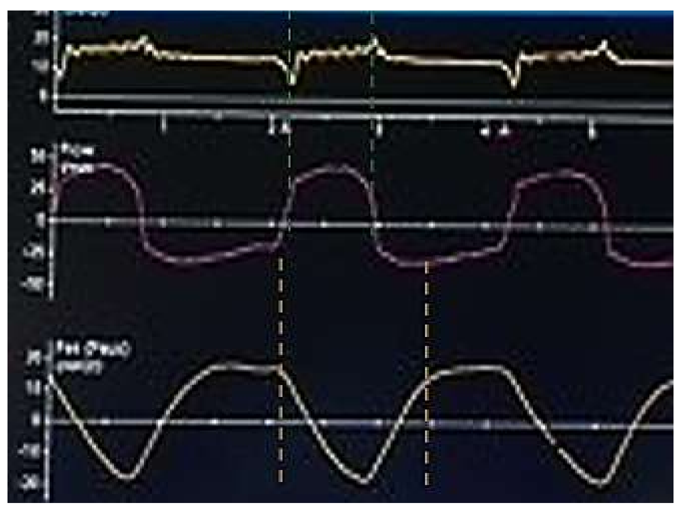


Figure 9B: Early cycling. From top to bottom, the curves represent pressure-time, flow-time, esophageal pressure-time. The green dashed lines show the beginning of the mechanical breath while the dashed yellow lines show the beginning and the end of the patient effort.

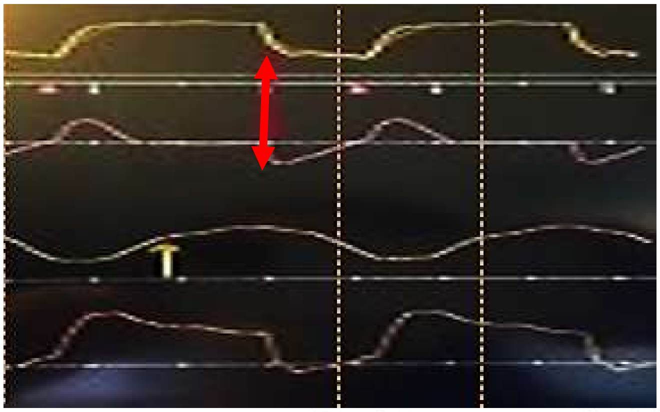


Figure 10: Late or delayed cycling. From top to bottom, the curves represent pressure-time, flow-time, esophageal pressure-time, and transpulmonary pressure-time curves. The yellow arrow points to the end of the patients' effort, and the red double arrow points to the time cycled mandatory breath, the dashed orange lines indicate the beginning and the end of the patients' next breath.

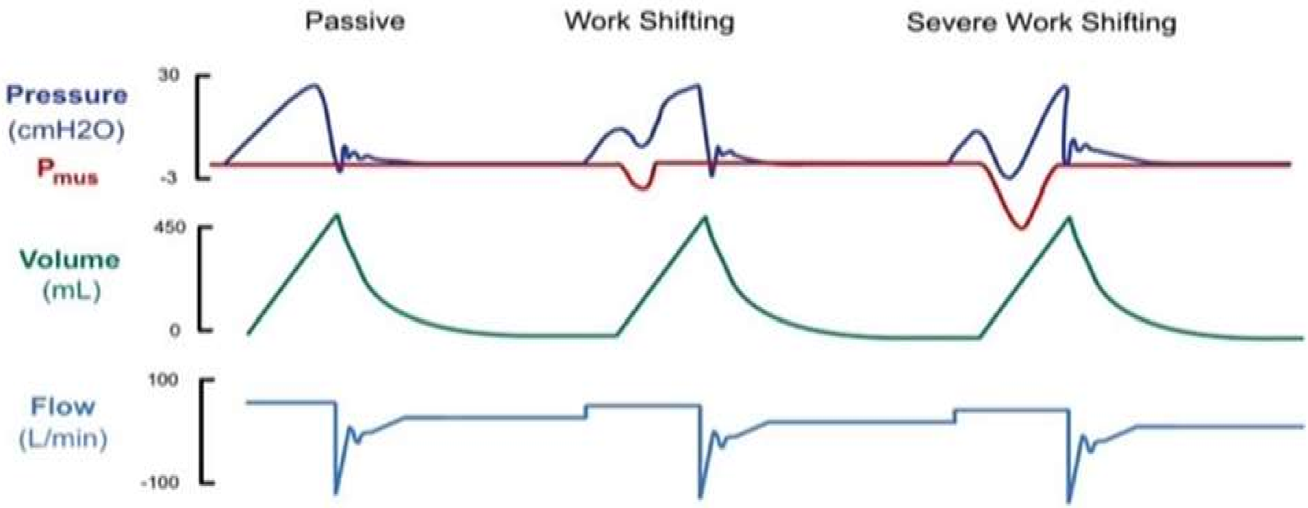


Figure 11: Illustration of Work Shifting in the Volume controlled mode with constant flow: This graph demonstrates the progression from passive ventilation to severe work shifting, highlighting the interaction between airway pressure (blue), patient-generated muscle pressure (red), tidal volume (green), and inspiratory/expiratory flow (blue). In the passive phase, ventilation is fully controlled with no significant patient effort. As work shifting emerges, patient effort increases, reflected by negative Pmus (red) deflections and irregular airway pressure waveforms. In severe work shifting, the patient's inspiratory effort becomes more pronounced, leading to greater negative swings in Pmus, increased respiratory effort, and potential patient-ventilator asynchrony.

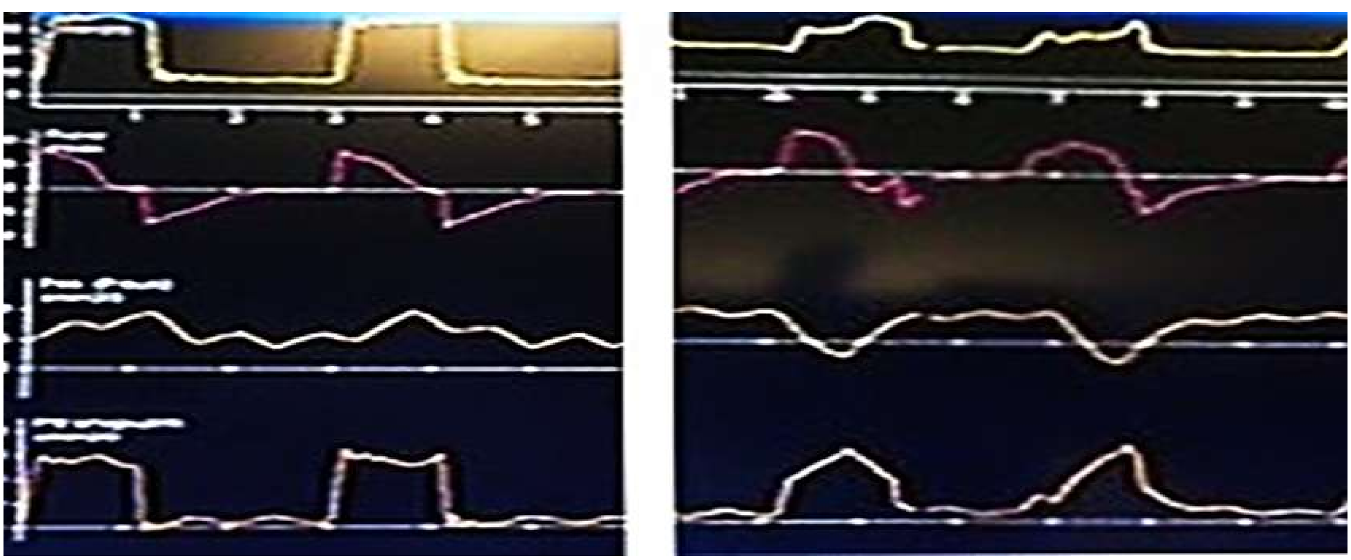


Figure 12: From top to bottom, airway pressure-time, flow-time, esophageal pressure-time, and trans-pulmonary pressure scalers. On the left, a passive patient (notice esophageal pressure is positive during the whole breath, more positive during inspiration. On the right, an active breathing patient with work shifting, notice the negative deflection in the esophageal pressure during inspiration to sub atmospheric pressure with distortion of the airway pressure, flow, transpulmonary pressure curves.

Combating Dyssynchronies

Recognizing the harms that dyssynchronies impose, combating them sounds prudent.

• Recognition and education

Identifying the abnormal PVI is the first step in adjusting the ventilator settings to work harmonically with the patients' effort. Education is an important step to improve clinicians understanding and recognition.

• Ventilator software's (automatically adjust rise time, trigger, cycling)

Many ventilators manufacturers have incorporated automatic software that recognize dyssynchronies and attempt to adjust some of its settings like the rise time, trigger, and cycling criteria to improve them. [35]

• Artificial Intelligence (AI) software with real time analysis. The advances in AI and Machine learning (ML) have made it possible to detect patient-ventilator dyssynchronies in real time. [36] To our knowledge such technology has not been incorporated into current ventilators yet. Figure 13 show an example of AI analysis of patient-ventilator interaction

New Concept: Different signals for Triggering and Cycling

We propose a novel approach to synchronizing ventilation proposes using esophageal balloon or Electrical Diaphragmatic Activity (Edi) signals if available rather than the current traditional ways to guide triggering and cycling, ensuring near-perfect alignment with patient effort. This method could improve synchrony and reduce work shifting, particularly in patients with erratic breathing patterns.

Conclusion

The control of ventilation is a complex physiological process that, when disrupted, leads to patient-ventilator dyssynchronies. Despite advances in ventilator technology, dyssynchronies remains a significant challenge in ICU settings. Understanding respiratory control and its interaction with mechanical ventilation is critical for optimizing ventilator settings, reducing dyssynchrony, and improving patient outcomes. Clinicians must remain vigilant in detecting dyssynchronies, employing individualized strategies such as optimizing triggers, flow patterns, and cycling mechanisms. Ongoing education in ventilator management and research into novel technologies, such as esophageal balloon-guided ventilation, will be essential in advancing patient care and bridging the gap between mechanical support and natural respiratory physiology.

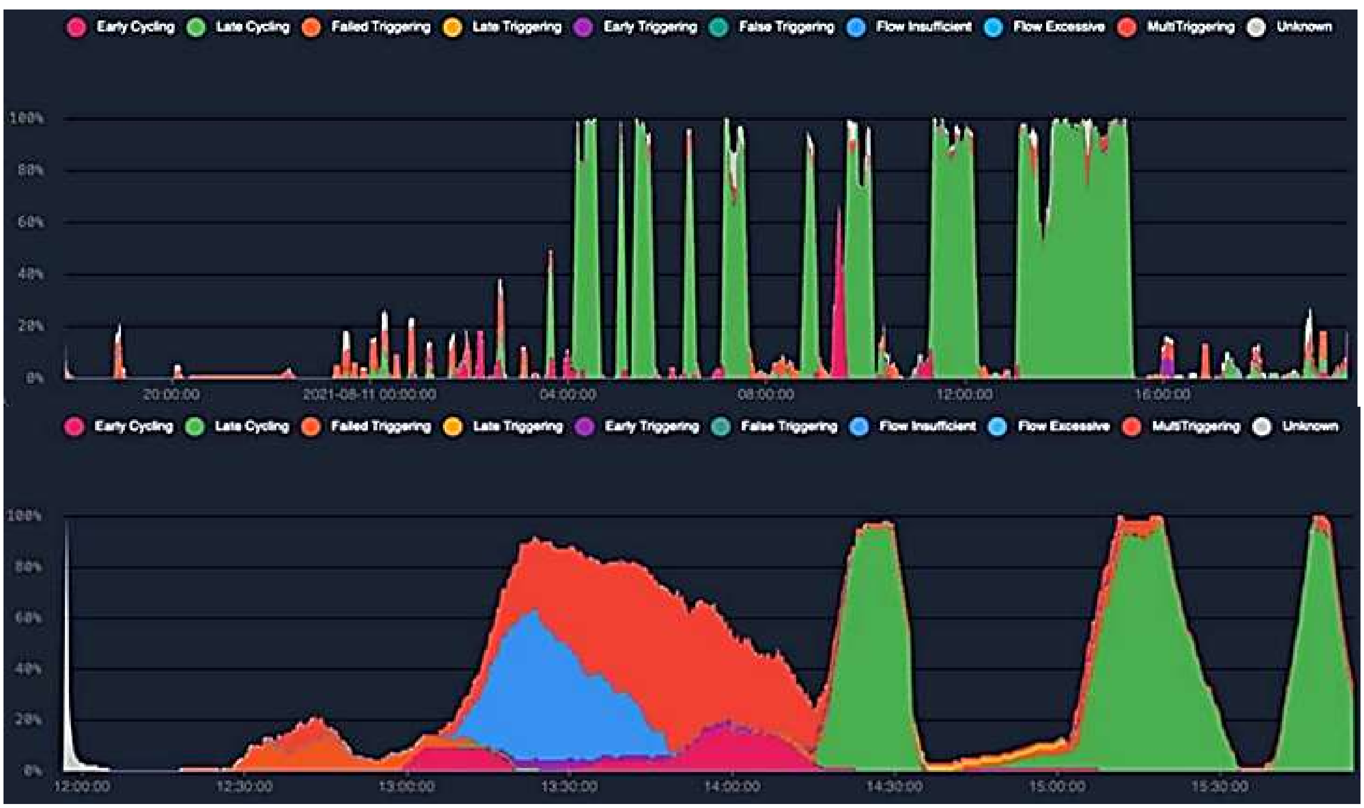
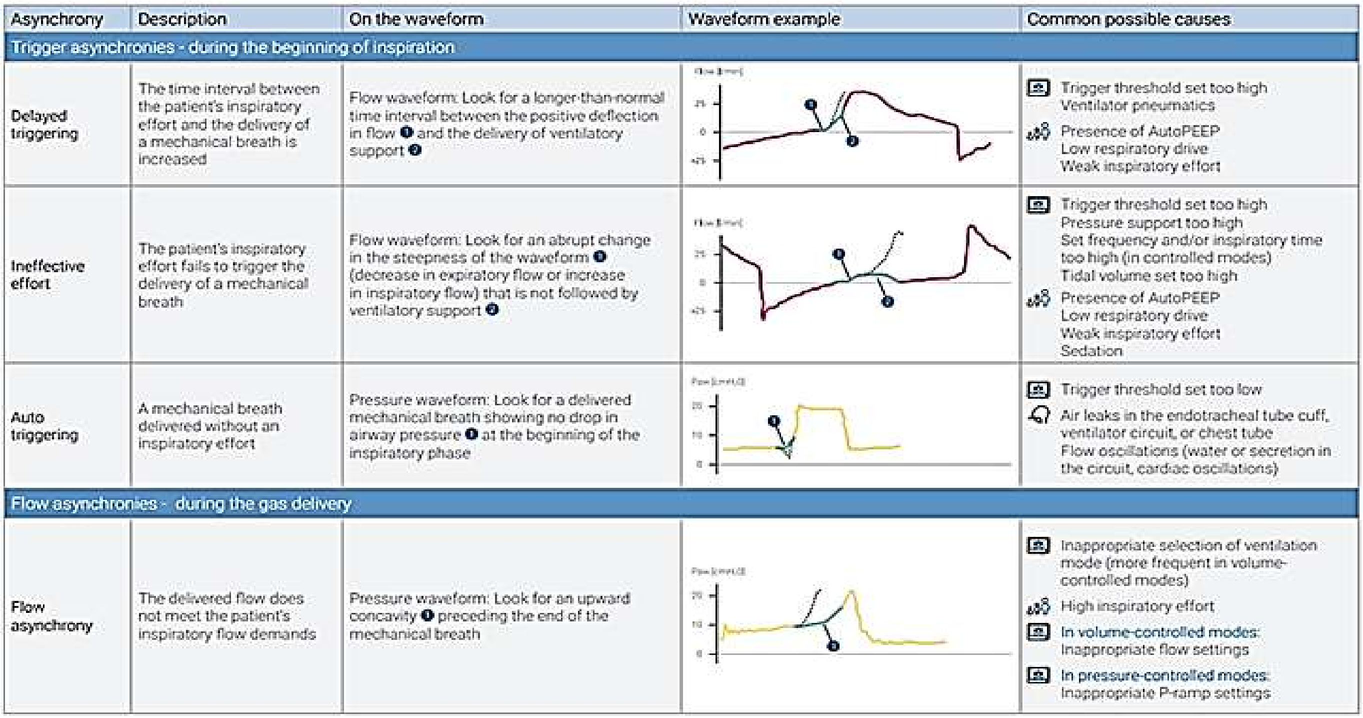
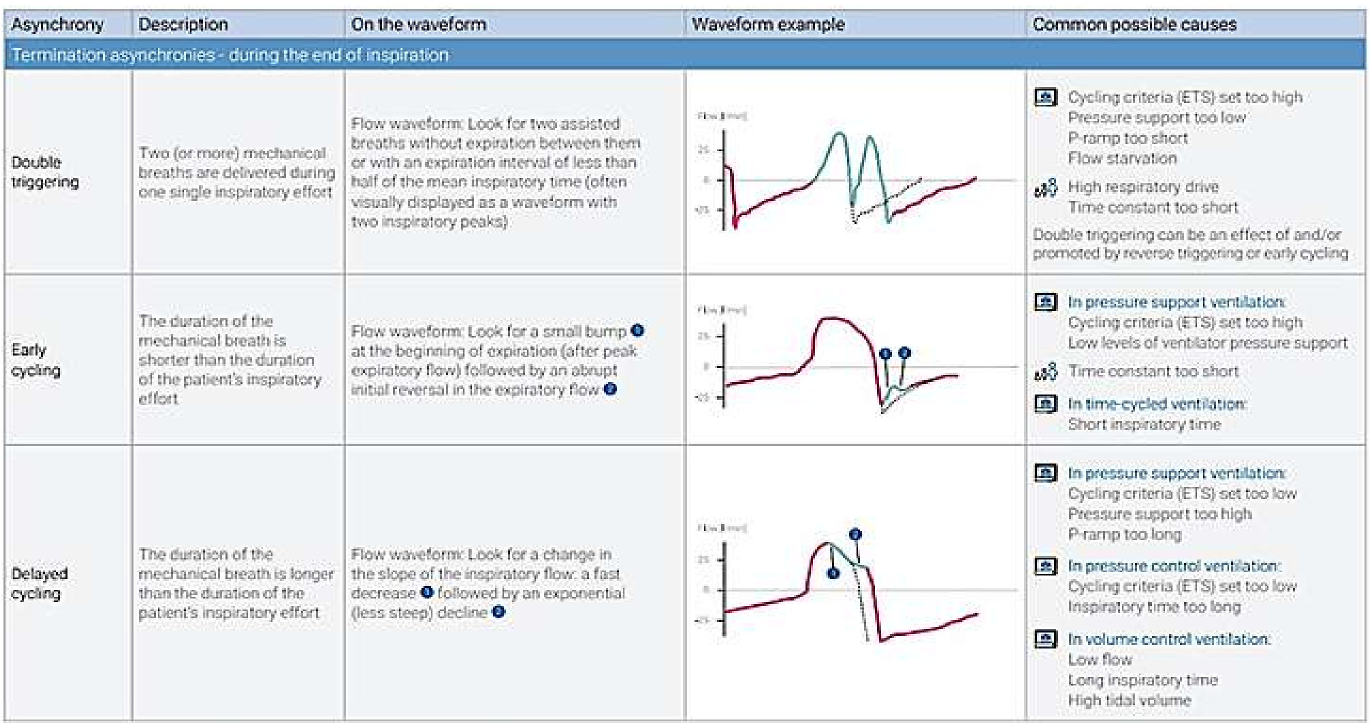


Figure 13: Examples of AI detection of ventilator dyssynchronies. With permission and credit to Deep Breath, Rotterdam, Netherlands.



Asynchrony	Description	On the waveform	Waveform example	Common possible causes
Trigger asynchronies - during the beginning of inspiration				
Delayed triggering	The time interval between the patient's inspiratory effort and the delivery of a mechanical breath is increased	Flow waveform: Look for a longer-than-normal time interval between the positive deflection in flow ❶ and the delivery of ventilatory support ❷		Trigger threshold set too high Ventilator pneumatics Presence of AutoPEEP Low respiratory drive Weak inspiratory effort
Ineffective effort	The patient's inspiratory effort fails to trigger the delivery of a mechanical breath	Flow waveform: Look for an abrupt change in the steepness of the waveform ❶ (decrease in expiratory flow or increase in inspiratory flow) that is not followed by ventilatory support ❷		Trigger threshold set too high Pressure support too high Set frequency and/or inspiratory time too high (in controlled modes) Tidal volume set too high Presence of AutoPEEP Low respiratory drive Weak inspiratory effort Sedation
Auto triggering	A mechanical breath delivered without an inspiratory effort	Pressure waveform: Look for a delivered mechanical breath showing no drop in airway pressure ❶ at the beginning of the inspiratory phase		Trigger threshold set too low Air leaks in the endotracheal tube cuff, ventilator circuit, or chest tube Flow oscillations (water or secretion in the circuit, cardiac oscillations)
Flow asynchronies - during the gas delivery				
Flow asynchrony	The delivered flow does not meet the patient's inspiratory flow demands	Pressure waveform: Look for an upward concavity ❶ preceding the end of the mechanical breath		Inappropriate selection of ventilation mode (more frequent in volume-controlled modes) High inspiratory effort In volume-controlled modes: Inappropriate flow settings In pressure-controlled modes: Inappropriate P-ramp settings



Asynchrony	Description	On the waveform	Waveform example	Common possible causes
Termination asynchronies - during the end of inspiration				
Double triggering	Two (or more) mechanical breaths are delivered during one single inspiratory effort	Flow waveform: Look for two assisted breaths without expiration between them or with an expiration interval of less than half of the mean inspiratory time (often visually displayed as a waveform with two inspiratory peaks)		Cycling criteria (ETS) set too high Pressure support too low P-ramp too short Flow starvation High respiratory drive Time constant too short Double triggering can be an effect of and/or promoted by reverse triggering or early cycling
Early cycling	The duration of the mechanical breath is shorter than the duration of the patient's inspiratory effort	Flow waveform: Look for a small bump ❶ at the beginning of expiration (after peak expiratory flow) followed by an abrupt initial reversal in the expiratory flow ❷		In pressure support ventilation: Cycling criteria (ETS) set too high Low levels of ventilator pressure support Time constant too short In time-cycled ventilation: Short inspiratory time
Delayed cycling	The duration of the mechanical breath is longer than the duration of the patient's inspiratory effort	Flow waveform: Look for a change in the slope of the inspiratory flow: a fast decrease ❶ followed by an exponential (less steep) decline ❷		In pressure support ventilation: Cycling criteria (ETS) set too low Pressure support too high P-ramp too long In pressure control ventilation: Cycling criteria (ETS) set too low Inspiratory time too long In volume control ventilation: Low flow Long inspiratory time High tidal volume

Figures14: Example of ventilator software recognition of dyssynchronies, their recognition, and causes. With permission and credit to Hamilton Medical, Bonaduz, Switzerland. From reference 37

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