

Patient-Ventilator Asynchrony: Etiology and Solutions

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ABSTRACT

Patient-ventilator asynchrony is one of the most cited reasons for giving sedation during mechanical ventilation. Various studies show that 40-50% of increase in sedative dosing is done to curb asynchrony. The acute respiratory distress syndrome (ARDS) network protocol for lung protective ventilation directs the clinician to adjust the ventilator settings or give sedation when there are more than three breaths stacking (double triggers) per minute. This review article discusses the etiology behind patient-ventilator asynchrony and the proposed solutions.

Keywords: Patient-ventilator asynchrony, breath initiation, endexpiratory pressure, neuromuscular blockers

Patient-ventilator asynchrony is one of the most important reasons for patient discomfort. It leads to increased morbidity as well as mortality. It thus becomes essential to understand patient-ventilator interaction and asynchrony for better patient management and outcome.

There are two pumps working during mechanical ventilation. One is mechanical ventilator which is controlled by the physician and another is patient's own respiratory muscle pump which is controlled by the patient. Any mismatch between these two pump leads to patient-ventilator asynchrony. Commonly, the terms used to describe this asynchrony on the ventilator are: "Patient is agitated/restless/fighting the ventilator".

Managing asynchrony is a challenge for the intensivist as it has several significant consequences, which are as follows:

- Increased anxiety and discomfort to the patient
- Increased work of breathing
- Increased requirement for sedation
- Difficult and prolonged weaning

- Prolongation of ventilator days
- Prolonged intensive care unit (ICU) and hospital stay
- Higher incidence of ventilator-associated pneumonia
- Increased need for tracheostomy.

Figure 1 illustrates the vicious cycle post initiation of mechanical ventilation in a patient due to asynchrony that may lead to increased morbidity and mortality.

Figure 2 illustrates that decreasing asynchrony helps in many ways to improve outcome and decrease morbidity.

DEFINITION

When timing of ventilator cycle is not simultaneous with the timing of patient's respiratory cycle, patient-ventilator asynchrony occurs. Any mismatch between neural Ti/Te (Ti - Inspiratory time, Te - Expiratory time) and ventilator Ti/Te or any mismatch between patient's demand and ventilator supply leads to patient-ventilator asynchrony.

When patient's inspiratory effort is not followed by a ventilator breath, it is considered as **ineffective triggering**, this is detected by "a decrease in a pressure of ≥ 0.5 cm along with increase in air flow without triggering an inspiration."

When a single inspiratory effort by the patient is followed by two ventilator breaths, it is called **double triggering**. This is detected by two delivered breaths separated by an expiratory time less than 50% of mean inspiratory time.

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When there is ventilator breath without any inspiratory effort by patient, it is **auto triggering**.

When inspiratory time is less than 50% of mean inspiratory time, it is called **premature cycling**.

When inspiratory time is more than double of mean inspiratory time, it is called **delayed cycling**.

Asynchrony Index

The **asynchrony index** is the total number of asynchronies (including all types of asynchronies) divided by the total triggered as well as ineffectively triggered breaths.

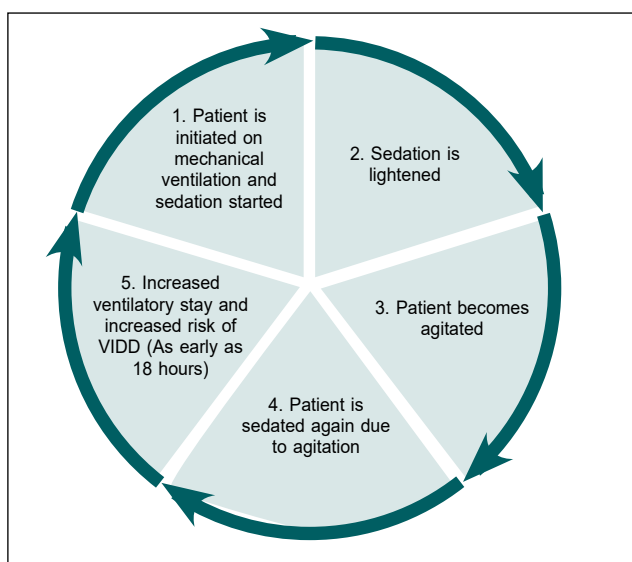


Figure 1. The vicious cycle post initiation of mechanical ventilation in a patient due to asynchrony that leads to increased morbidity and mortality.

VIDD = Ventilator-induced diaphragmatic dysfunction.

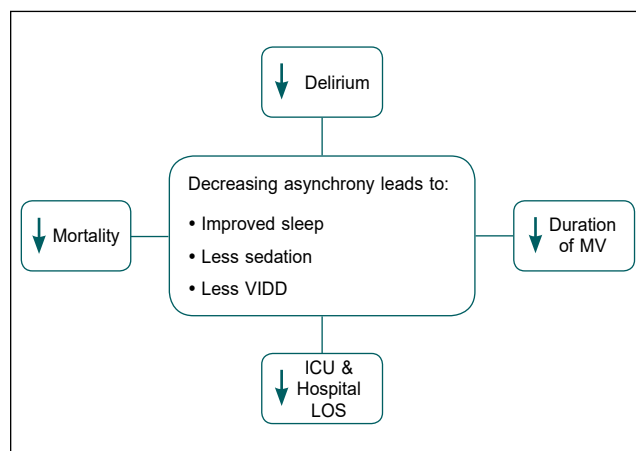


Figure 2. Decreasing asynchrony helps improve outcome and decrease morbidity.

MV = Mechanical ventilation; ICU = Intensive care unit; LOS = Length of stay.

The **ineffective triggering index** is the total number of ineffectively triggered breaths divided by the total triggered and ineffectively triggered breaths.

EPIDEMIOLOGY

Ventilator asynchrony is a common but an under-recognized as well as an undertreated entity. Multiple studies have suggested that 20-30% of patients experience asynchrony in more than 10% of their breaths, among which, ineffective triggering (70-80%) and double triggering are the most common asynchronies. Ineffective triggering is especially more common in patients of chronic obstructive pulmonary disease (COPD), occurring in nearly 80% of them.

Multiple types of asynchrony may be present simultaneously. Studies show that asynchrony index >10% is associated with prolonged ventilator days and prolonged ICU as well as hospital stay (Fig. 3). It also significantly increases weaning time and leads to weaning failure.

Patient-ventilator asynchrony is one of the most cited reasons for giving sedation during mechanical ventilation. Various studies show that 40-50% of increase in sedative dosing is done to curb asynchrony. The acute respiratory distress syndrome (ARDS) network protocol for lung protective ventilation directs the clinician to adjust the ventilator settings or give sedation when there are more than three breaths stacking (double triggers) per minute. While patient agitation and anxiety lead to asynchrony, the reverse is also true. That asynchrony leads to agitation and anxiety which most of the times is inappropriately managed with sedation and neuromuscular blockers. Studies

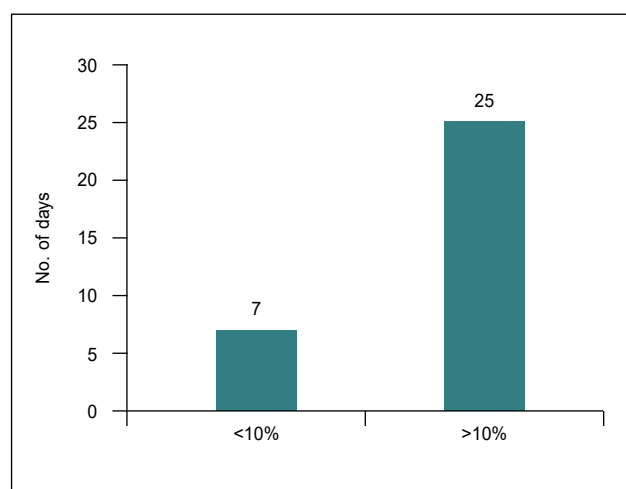


Figure 3. Prolonged ventilator days with asynchrony index >10%.

show that changing ventilator settings in response to patient's breathing pattern is more effective, as well as more rational, than, increasing sedation. Routine use of sedation and neuromuscular blockers should be discouraged for managing asynchrony. They should be used only if asynchrony index >10% after optimizing ventilator settings.

CONTRIBUTING FACTORS

There are various patient-related, disease-related as well as ventilator-related factors which contribute to asynchrony (Table 1).

TYPES AND CLASSIFICATION OF VENTILATOR ASYNCHRONY

Asynchrony can be classified based on trigger, flow and cycling. Trigger asynchrony occurs in trigger phase while flow and cycling asynchrony occur in post trigger phase (Table 2).

GRAPHICAL REPRESENTATION OF COMMONLY OCCURRING ASYNCHRONY

Asynchrony is usually identified clinically (facial expressions, signs of respiratory distress, palpation of chest and abdomen to look for efforts by patients, etc.) and by the simultaneous examination of ventilator waveforms. Esophageal pressure monitoring is used infrequently to identify asynchrony, mainly, being restricted to research settings to estimate pleural pressure.

Commonly occurring asynchrony have been illustrated with graphical examples here (Figs. 4-7).

Table 1. Factors Contributing to Asynchrony

Patient-related/ physiological	Disease-related	Ventilator-related
- Anxiety - Pain - Fever - Delirium	- High resistance (e.g., COPD) - Low compliance (e.g., ARDS) - Auto-PEEP (e.g., COPD) - Decreased/Increased respiratory drive due to central and neuromuscular problems	Inappropriate ventilator settings of trigger, rise time, level of pressure support, cycling, inspiratory flow, respiratory rate, tidal volume, inspiratory time, etc.

COPD = Chronic obstructive pulmonary disease; ARDS = Acute respiratory distress syndrome; PEEP = Positive end-expiratory pressure.

FOUR PHASES OF THE VENTILATORY CYCLE

As shown in Figure 8, breath cycle can be divided into four phases: Breath initiation (Trigger), breath delivery

Table 2. Types of Ventilator Asynchrony

Trigger asynchrony	Flow asynchrony (breath delivery asynchrony)	Cycling/Termination asynchrony
Ineffective trigger/ Delayed trigger	Related to fixed flow	Premature cycling
Double trigger	Related to high flow	Delayed cycling
Auto trigger (<2%)	Related to inadequate flow	
Common asynchrony	Patient breath	Ventilator breath
Ineffective trigger	1	0
Double trigger	1	2
Auto trigger	0	1
Delayed cycling	2	1

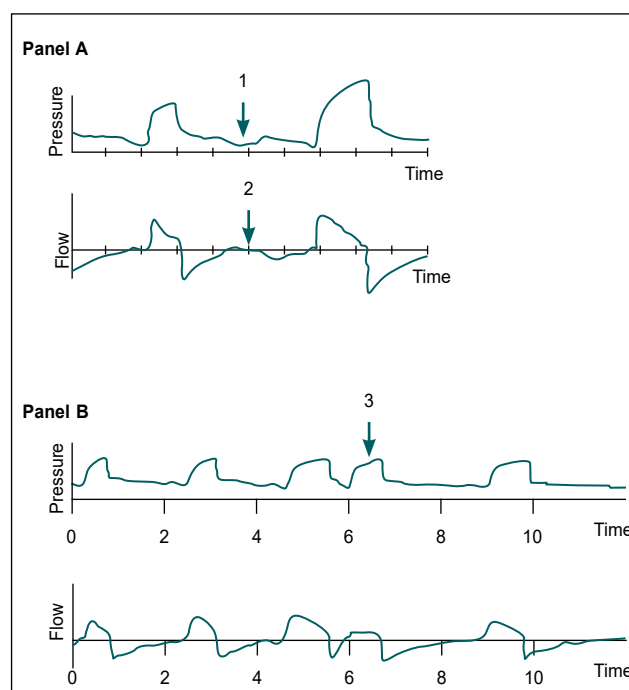


Figure 4. Trigger asynchrony: Panel A is showing ineffective triggering which is shown by a decrease in airway pressure (mark 1) and simultaneous increase in airflow (mark 2). **Panel B** shows double triggering (mark 3).

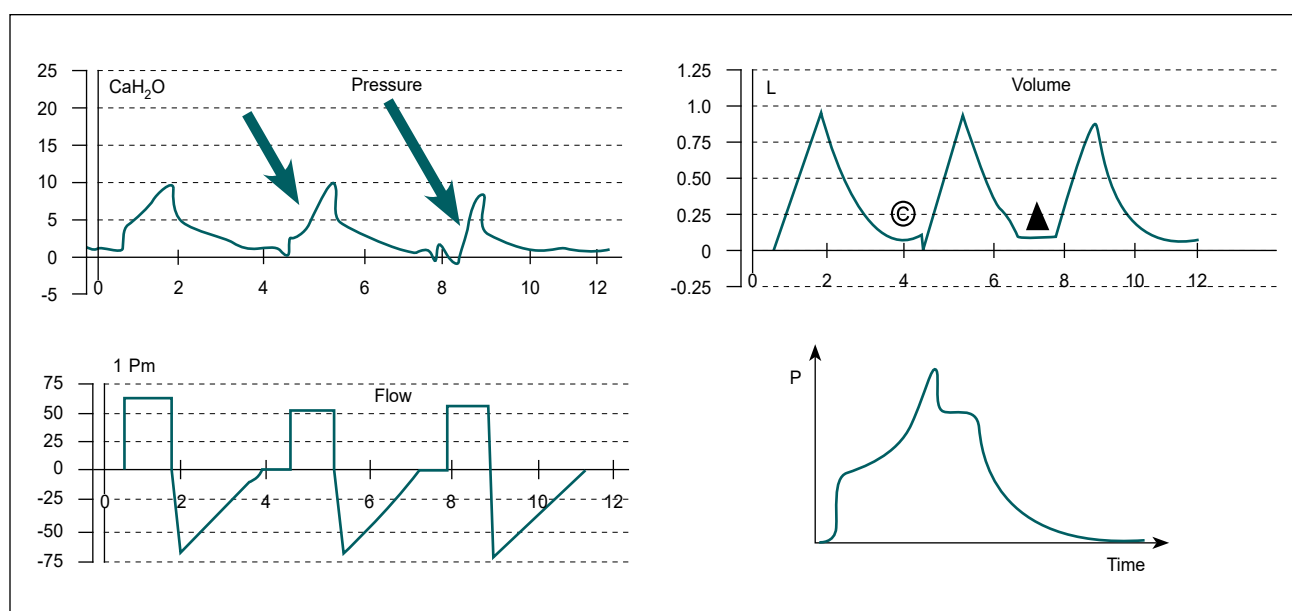


Figure 5. Flow asynchrony: Arrow showing dished out appearance (from convex to concave) due to high flow demand and inadequate flow delivery.

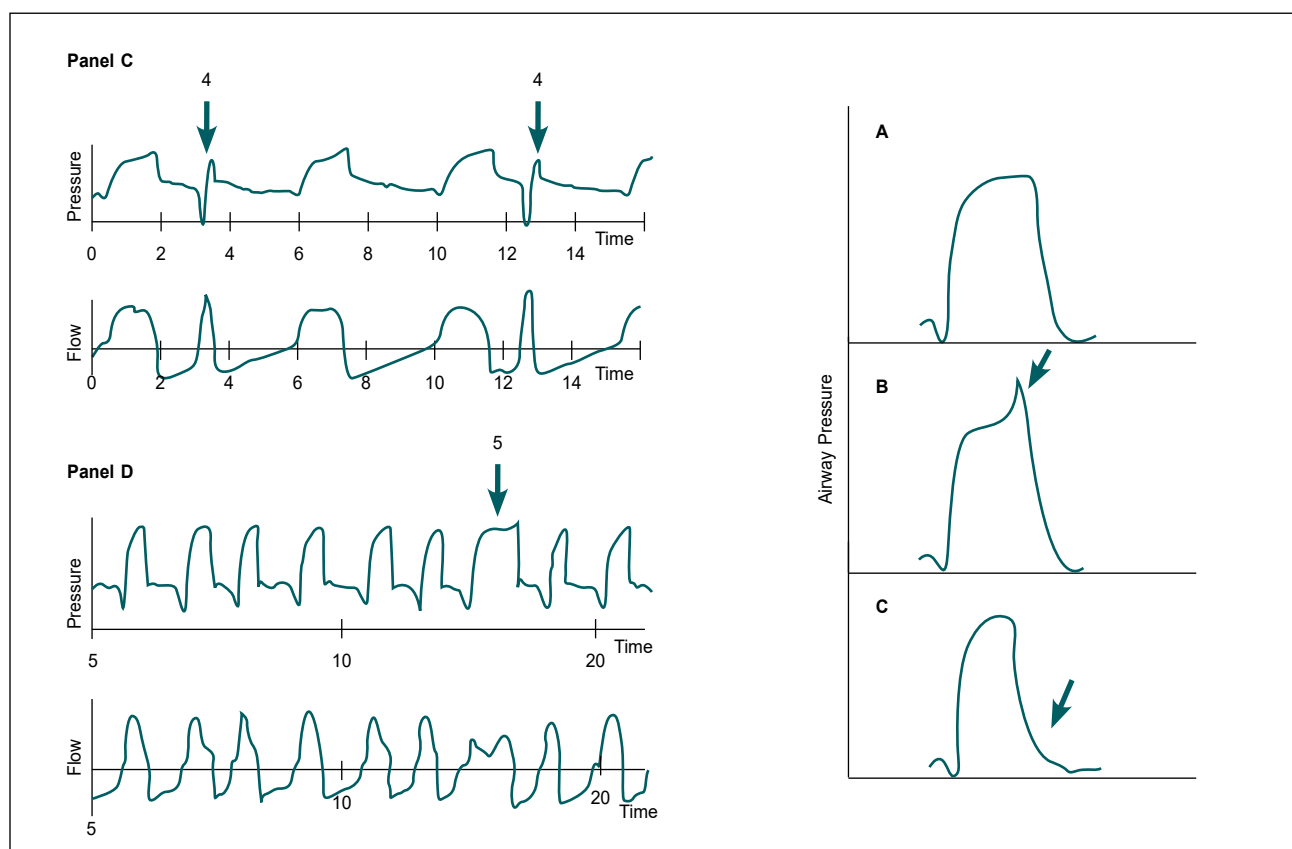


Figure 6. Cycling asynchrony: **Panel C** demonstrates premature cycling (mark 4). **Panel D** demonstrates prolonged cycling (mark 5). Right-sided figure showing pressure-time curves in setting of mismatch with patient and ventilator Ti. **(A)** Normal waveform with matching of neural Ti and ventilator Ti. **(B)** Sudden rise in airway pressure (arrow) indicating that the patient has switched to expiration before completion of mechanical inspiration (Neural Ti < Ventilator Ti). **(C)** Sudden fall in airway pressure (arrow) indicating that patient inspiratory efforts persist after the end of mechanical inspiration (Neural Ti > Ventilator Ti).

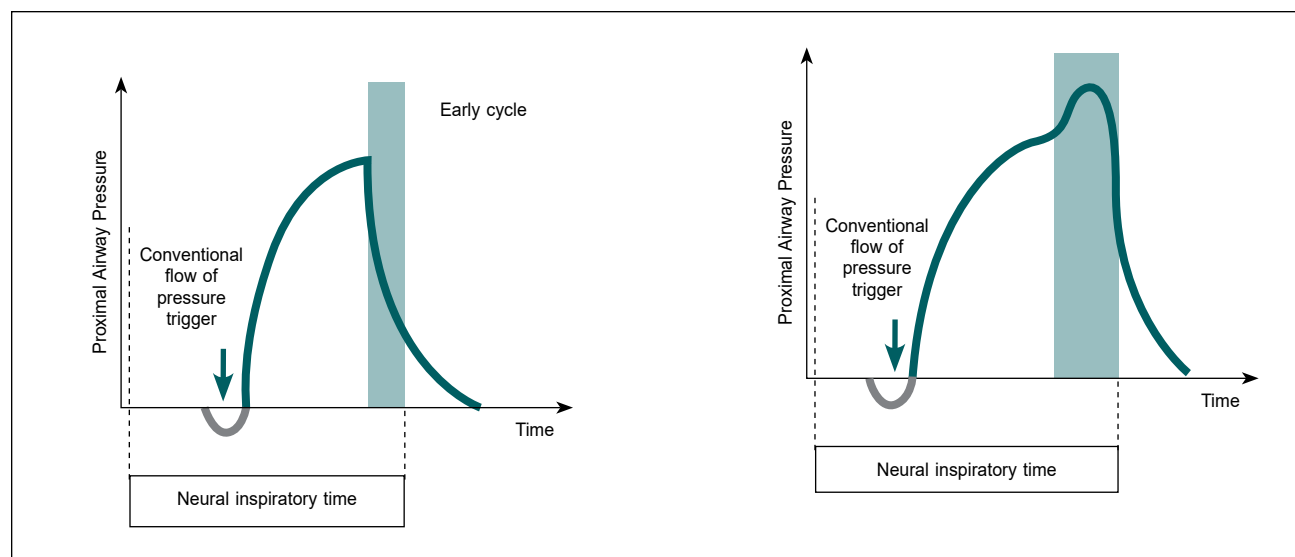


Figure 7. Cycling asynchrony: Figure on the left showing premature cycling while figure on the right showing delayed cycling.

(Flow) which includes rise time and level of pressure support, breath termination (Cycling) and expiration. Problem with any of these phases of respiratory cycle will lead to asynchrony. To minimize patient-ventilator asynchrony, all these phases of breath delivery by ventilator should coincide with patient's breathing pattern.

Triggering

Triggering includes two phases – Trigger phase and post-trigger phase.

Trigger phase is the onset of effort by the patient, to the onset of flow delivery, while the **post-trigger phase** is the onset of flow delivery by the ventilator to the end of inspiration which is significantly longer than the trigger phase.

The main determinants affecting workload associated with triggering are:

- Magnitude of change required to initiate a breath. This can be optimized by increasing trigger sensitivity and appropriate setting of positive end-expiratory pressure (PEEP), particularly, in patients of COPD and bronchial asthma, as air trapping and intrinsic PEEP make it difficult for the patient to trigger inspiration.
- Delay between onset of patient inspiratory effort and the time to ventilator response.

Studies suggest that flow triggering leads to lower work of breathing compared to pressure triggering, but this difference is probably of little clinical significance. Modern

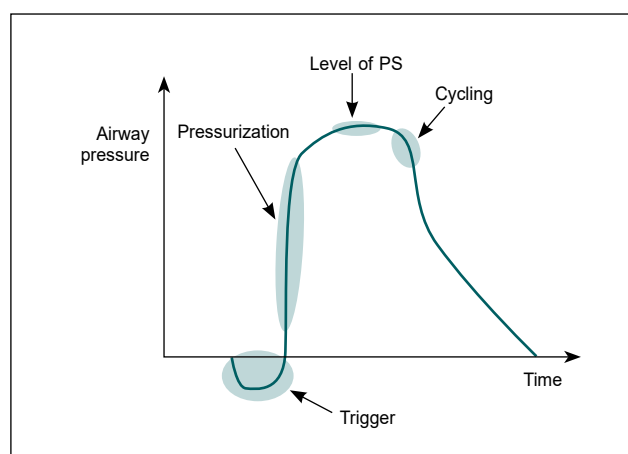


Figure 8. Diagram showing four key phases of pressure support cycle.

ventilators have very sensitive trigger mechanisms, with regards to both the inspiratory effort required to trigger and trigger delay. So triggering adds little to the overall work of breathing. Most difference in work of breathing between pressure and flow trigger is found in the post-trigger phase rather than trigger phase.

Rise-time/Pressurization Slope

During pressure support ventilation (PSV), the slope of pressurization can be adjusted on most modern ventilators. The steeper the slope, the faster the rise of P_{aw} (Airway pressure) to its target value, thus, lower the work of breathing. But, breathing comfort is lowest at both the lowest and highest rise time. Usually, rise time is set between 100 and 200 ms. If a patient exhibits discomfort due to “air hunger”, the rise time can be

hastened to 50 ms. A faster rise time helps increase initial inspiratory flow.

Level of Pressure Support

Figure 9 summarizes the adverse effects of both insufficient as well as excessive pressure support on work of breathing.

Cycling

The transition from inspiration to expiration is known as cycling. Cycling can be time cycled, volume cycled or flow cycled. In PSV, it is flow cycled, where cycling occurs when flow decreases to predetermined fraction of peak inspiratory flow (PIF), defined as expiratory trigger (ET). In most ventilators, ET is 0.25, i.e., 25% of PIF. Higher the ET, lesser the magnitude of delayed cycling and the possibility of improved synchrony, particularly in patients with dynamic hyperinflation and air trapping. The higher ET will cut off inspiration at high flow rates (>25% of PIF) and allow more time for exhalation and minimize air trapping.

The problems that arise from too premature a cycling is that the patient is still in the inspiratory phase, but ventilator has switched to expiration. This can lead to double triggering and increased work of breathing. Thus, when Neural T_i > Ventilator T_i , **premature cycling** occurs and when Neural T_i < Ventilator T_i , **delayed cycling** occurs.

Consequences of delayed cycling

Figure 10 depicts the consequences of delayed cycling. Table 3 summarizes trigger asynchrony.

Reverse Trigger

It can be misidentified as double trigger or auto trigger, but it is different from both and under-recognized form of asynchrony. Various mechanisms for reverse trigger are thoracic or diaphragmatic stretch receptors, spinal reflex, etc. It is reported in deeply sedated patients with ARDS, brain death, etc.

Tables 4 and 5 summarize flow asynchrony and cycling asynchrony, respectively.

NONINVASIVE VENTILATION AND ASYNCHRONY

Noninvasive ventilation (NIV) usually has higher levels of leak causing auto triggering and cycling asynchrony. Asynchrony index is >10% in nearly 40-50% of the patients on NIV. So, asynchrony is of greater concern during NIV.

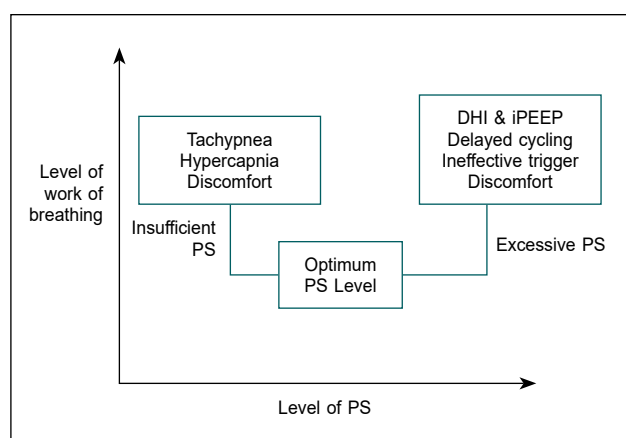


Figure 9. Adverse effects of insufficient as well as excessive pressure support on work of breathing.

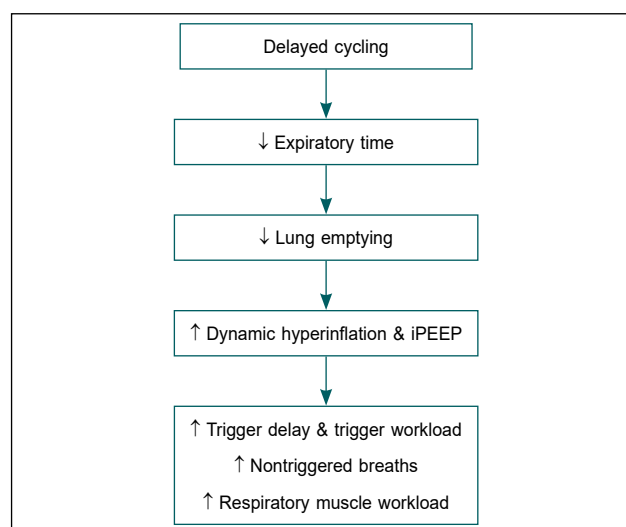


Figure 10. Outcomes of delayed cycling

- Flow cycling during NIV causes more asynchrony than time cycling due to leak (e.g., during pressure assist control).
- Modern ventilators with NIV mode compensate better for leaks (up to 120 L/min) and cause less asynchrony.
- BiPAP machine causes even less asynchrony than mechanical ventilator with NIV modes.

Table 6 represents a technical guide to troubleshooting.

ROLE OF NOVEL MODES OF VENTILATION

Automatic Tube Compensation

Automatic tube compensation (ATC) is not a mode, but, an integration option which can be used in conventional modes in modern ventilators. Endotracheal tube and ventilator tubing may increase

Table 3. Trigger Asynchrony

Type	Causes	Management	Remarks
Trigger asynchrony (Easy to treat)			
Ineffective trigger (Most common)	High (insensitive) trigger threshold	Set appropriate trigger threshold, switch from pressure to flow trigger	- Common in COPD - Marker of severity of diseases as well as increases ventilator days
Delayed trigger	- High auto-PEEP DHI - Decreased respiratory drive (Sedation/neurological cause) - Respiratory muscle weakness - High ET tube resistance	- Increase I:E ratio 1:3 or more, increase flow, decrease MV by decreasing TV & RR, add extrinsic PEEP 50-80% of iPEEP - Stop sedation - Optimize nutrition (Avoid overfeeding and supplement adequate protein) - Correct electrolytes (Potassium, magnesium, phosphate, etc.) - Use ATC (Automatic tube compensation), reduce secretions, kinking of tube, etc.	- Detected by presence of chest/abdominal efforts without flow delivery from ventilator - Ventilator underestimates total RR in this asynchrony, no alarms from ventilator - Flow trigger found to have less WOB, less asynchrony and preferred over pressure trigger - Delayed trigger may be minimized by NAVA (Neurally adjusted ventilatory assist)
Double trigger (Breath stacking, double cycling)	- Small tidal volume, inadequate flow, high respiratory drive - Short inspiratory time, Neural Ti > Ventilator Ti - High flow-cycle threshold - Premature cycling	- Increase ventilator rate/TV to increase minute ventilation or give sedation and decrease air hunger - Shorten rise time - Increase peak flow - Increase Ti - Set appropriate expiratory trigger	- Common in ARDS with protective ventilation - Can occur with cough, sighs - More common with volume targeted ventilation
Auto trigger	- Cardiac oscillation, water in circuit, negative suction through chest drain, etc. - Low (sensitive) trigger threshold - Leak in circuit	- Remove secretions and water condensates from tubing - Set appropriate trigger threshold - Decrease leak	Switching from flow to pressure trigger might help
High work of breathing due to	- Narrow ET tube - High ventilator tubing resistance	- Use ATC - Remove secretion from ET - Increase pressure support level - Remove secretion from ventilator tubing, prevent kinking, etc.	<i>In vivo</i> resistance is higher, so even ATC may underestimate the resistance

work of breathing, which leads to trigger or flow asynchrony. Placement of esophageal balloon and a tracheal catheter is required for accurate detection of same. ATC is supposedly beneficial over PSV in terms of compensating for excess work of breathing due to this. As *in vivo* resistance is usually higher than *in vitro* resistance, ATC may not completely compensate for it.

Proportional Assist Ventilation

Proportional assist ventilation (PAV) is a mode which has been developed to improve synchrony and reduce work of breathing. PAV generates respiratory support as a proportion of the total pressure needed to inflate the respiratory system. In this mode, the total pressure needed to inflate the respiratory system is obtained by

Table 4. Flow Asynchrony

Type	Causes	Management	Remarks
Flow asynchrony (Breath delivery asynchrony) (More common with volume targeted mode than pressure targeted mode)			
Inadequate flow (More common)	• High (slow) rise time in pressure targeted breath • High demand, e.g., Fever, sepsis, pain, anxiety, etc. • Inadequate MV and TV, inadequate flow • Hypoxia and hypercarbia	• Decrease rise time (Faster rise time) • Treat factors causing high demand like pain, fever, sepsis, anxiety, etc. • Increase MV by increasing TV, increase flow • Correct hypoxia and hypercarbia	• Detected by downward deflection (dip) in pressure-time waveform causing deformation of curve from convex to concave (dished out appearance) • Decelerating flow/pressure targeted ventilation is preferred in flow asynchrony
High flow (Less common)	• Low (faster) rise time in pressure targeted breath • High flow in volume targeted breath	• Increase rise time (Slow rise time) • Decrease flow	• Detected by peaking of pressures at the start of inspiration • Causes active exhalation, coughing, etc. • High pressure support may lead to apnea due to fall in $p\text{CO}_2$, especially in CHF.

Table 5. Cycling Asynchrony

Type	Causes	Management	Remarks
Cycling asynchrony (Termination asynchrony) (Difficult to treat) (Common during NIV)			
Premature cycling	• Neural Ti > Ventilator Ti	• Decrease flow rate Or Increase TV to match Neural Ti	• Can be detected by decrease in pressure in pressure-time waveform while increase in airflow in flow-time waveform after termination of ventilator delivered breath • May lead to double triggering and increase work of breathing
Delayed cycling	• Neural Ti < Ventilator Ti • Usually in dynamic hyperinflation • High resistance and low elastic recoil as in COPD	• Decrease ventilator Ti by decreasing pressure support, faster rise time, high flow rate, raising expiratory trigger >25% up to 40-50% • Switch to pressure-support ventilation in patients with variable inspiratory time • Change to time cycled ventilation and match Neural Ti	• Can lead to large TV and less expiratory time, so air-trapping and ineffective triggering in subsequent breaths • Can be detected by tenting at the end of inspiration which shows end of neural inspiration • Can be detected by zero flow state in flow-time waveform in pressure targeted breath

automatic and repeated calculations of resistance and compliance via short end-inspiratory occlusions. That is the reason why leaks impede proper PAV functioning as it underestimates resistance and leads to inadequate ventilatory assist and increased work of breathing.

Neurally-adjusted Ventilatory Assist

Neurally-adjusted ventilatory assist (NAVA) uses diaphragmatic neural activity to trigger gas delivery. Unlike PAV, the trigger mechanism in NAVA is not

Table 6. Technical Guide to NIV Troubleshooting

Problem	Cause	Solution
Ventilator cycling independent of patient effort (Auto trigger)	• Too sensitive trigger • Excessive mask leak	• Adjust trigger sensitivity • Reduce mask leak
Ventilator not triggering despite patient effort (Ineffective trigger)	• Too high trigger sensitivity • Excessive mask leak	• Adjust trigger sensitivity • Reduce mask leak
Inadequate chest expansion despite triggering	Inadequate Tidal volume/pressurization	• Increase IPAP • In neuromuscular disease, keep longer Ti
Chest/Abdominal paradox	Upper airway obstruction	• Avoid neck flexion • Increase EPAP
Premature expiratory effort by patient (Delayed cycling)	Excessive Ti/IPAP	• Adjust Ti • Decrease IPAP

affected by leaks or intrinsic positive end-expiratory pressure (iPEEP).

NAVA improves patient-ventilator synchrony by reducing triggering and cycling delays in comparison to PSV. Despite the theoretical benefit of PAV and NAVA, data till date are not sufficient to claim that either mode is superior to conventional modes such as PSV in terms of major clinical outcomes (i.e., duration of MV, length of ICU stay).

Figure 11 illustrates the way NAVA senses the electrical activity of the diaphragm (Edi), which is the earliest respiratory signal that can be detected while conventional technology is limited to sensing patient effort at final stage of respiratory effort. Figure 12 shows trigger delay between onset of diaphragmatic activity and start of ventilator inspiratory cycle which is common in DHI due to COPD. No ventilator settings can overcome this trigger delay except NAVA which works on sensing electrical activity of diaphragm. Cycling off occurs when EAdi falls to 70% of maximum EAdi.

Other modes

- Volume assured pressure support
- Pressure augmentation
- Automode
- Volume support
- Adaptive support ventilation (ASV)

These are closed loop systems to improve patient ventilator interaction, but at present, major studies show their beneficial efficacy are lacking.

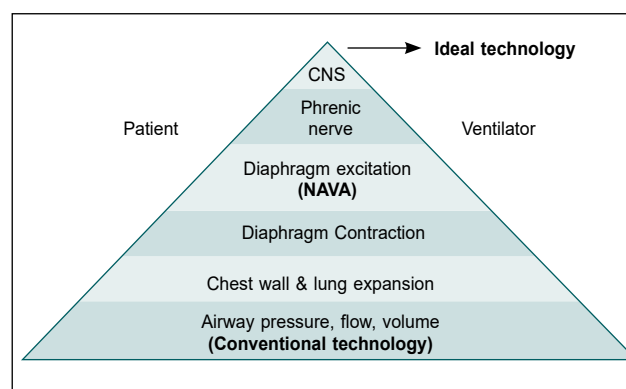


Figure 11. NAVA senses the electrical activity of the diaphragm (Edi).

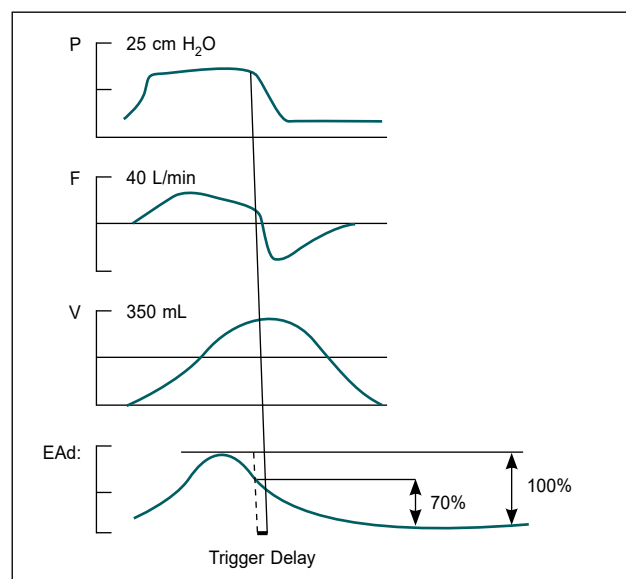


Figure 12. Trigger delay: Trigger delay between onset of diaphragmatic activity and start of ventilator inspiratory cycle which is common in DHI due to COPD.

Approach to Patient Ventilator Asynchrony: Summary

Sedation, analgesia and paralysis	• Give optimum sedation and analgesia during mechanical ventilation, give sedation free interval daily, optimize ventilator settings before increasing sedation. • Treat pain, fever and other treatable factors before increasing sedation. • Use neuromuscular blockers only during intubation, up to 48 hours of intubation in ARDS, routine use after 48 hours not recommended.
Respiratory rate	• Match respiratory rate of ventilator with patient's respiratory rate. • Keep high respiratory rate during low tidal volume ventilation to maintain minute ventilation.
Trigger sensitivity	Optimize trigger sensitivity for each patient while initiating mechanical ventilation and weaning.
PEEP	• Titrate optimum PEEP for each patient. • Use 50-75% of iPEEP as ePEEP to counter auto-PEEP.
Inspiratory flow	Increase flow when high demand, decelerating flow when flow asynchrony.
Inspiratory time	Match neural Ti with Ventilator Ti. Shorter Ti when high flow demand, auto-PEEP, expiratory flow limitation, etc.
Cycling	Use high cycling cut-off when expiratory flow limitation to minimize dynamic hyperinflation (i.e., increase from 25% to up to 50%).
Rise time	Faster rise time when high flow demand; Set as per patient's demand (Usual range – 50-200 ms).
Mode	Pressure targeted mode preferred over volume targeted mode when flow asynchrony is there.

KEY POINTS

- An uncomfortable patient should be evaluated for asynchrony, apart from physical and psychological causes of distress. Asynchrony index >10% or any asynchrony causing patient discomfort is considered significant and should be treated.
- Excessive ventilator support leads to ineffective triggering while insufficient ventilator support leads to increased work of breathing.
- Do not forget to set trigger sensitivity. Always look at the patient as well as ventilator graphics before and after changing any ventilator settings and stay there for a while. Intensivist should look at the ventilator waveforms to assess status of lungs as well as of patient in same way as a cardiologist looks at the ECG for the heart.
- Use modes which you are familiar with. Don't use newer modes, just because they are there and the manufacturer claims certain advantages. Basic modes are sufficient for most situations. It is you and your monitoring which will improve synchrony and outcome, not any mode by itself.
- It should be noted that every patient is different and the same ventilator settings are not suitable for all patients. Clinicians must optimize ventilator settings at the bedside for each patient individually to improve the synchrony between patient and ventilator. Stay and watch the patient for some time after each change of settings.
- Heavy sedation or neuromuscular blockade is not the answer to all ventilator alarms and it should be used as a last resort to improve patient-ventilator interaction.
- Appropriate treatment of contributing factors to asynchrony (e.g., fever, pain, anxiety, iPEEP, bronchospasm, decreased drive due to sedation, electrolyte abnormalities, malnutrition leading to muscle weakness, etc.) is essential to improve asynchrony. Just changing ventilator settings is not going to be of any use.
- Normal arterial blood gas (ABG) analysis doesn't mean optimum ventilator settings; patient can have increased work of breathing despite normal ABG values.
- Mechanical ventilation does not guarantee decreased work of breathing. Many studies have found lower airway pressures during assisted breath, as compared to controlled breaths, which shows continuous inspiratory muscle contraction during mechanical inflation which increases work of breathing.
- Multiple studies demonstrate that pressure targeted ventilation improves flow asynchrony as compared

to volume targeted ventilation. Use pressure targeted/decelerating flow pattern ventilation whenever flow asynchrony is the main problem.

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It is Premature to Change Authorized COVID-19 Vaccines Dosing, Schedules: FDA

The idea of modifying the authorized dosing or schedules of COVID-19 vaccines was premature and was not supported by the available data, stated the US FDA.

The agency said that it had been following discussions and news reports about decreasing the number of doses, increasing the length of time between the doses, reducing the dose in half, or mixing and matching vaccines in a bid to vaccinate more people. While the questions were reasonable to consider, the agency stated that changing the FDA-authorized dosing or schedules of these vaccines at this time is premature and has no robust evidence available. In the absence of appropriate data supporting the changes in vaccine administration, there is a significant risk of placing public health at risk... (*Reuters*)

Covaxin to be Tested on Children as Young as 2 Years

After becoming the first COVID-19 vaccine in the world to be tested on children as young as 12 years, Covaxin is now going to be tested on children as young as 2 years, stated Bharat Biotech chairman and managing director Dr Krishna Ella.

A clinical trial is now being planned on children aged 2-15 years. A proposal will soon be submitted to the subject expert committee. Ella emphasized that Covaxin is an inactivated virus vaccine based on a tried and tested vero cell platform that has been used for several vaccines. Covaxin was the first among the COVID-19 vaccines to initiate testing on children (in September). Covaxin Phase II trials were conducted on 380 volunteers in September 2020 that included participants aged 12-65 years. The Pfizer vaccine started testing on 12-year-olds in October while Moderna started enrolling participants aged 12 years and above in December... (*ET Healthworld – TNN*)

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- 💧 Nutritional & Iron deficiency
- 💧 Lack of Appetite
- 💧 Chronic Gastrointestinal Blood Loss
- 💧 Chronic Kidney Disease

