Patient-Ventilator Interactions

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KEYWORDS

• Patient-ventilator interactions • Ventilator dys-synchrony • Interactive ventilator modes
• Proportional assist ventilation • Neutrally adjusted ventilatory assist

KEY POINTS

- Ventilator muscle fatigue is a reversible loss of the ability to generate force or velocity of contraction in response to increased imposed elastic and resistive loads.
- A goal of mechanical ventilation is to provide safe and effective ventilatory support without imposing additional loads from patient-ventilator dys-synchrony.
- Interactive breaths require that patient effort and the ventilator response be synchronous during all 3 phases of breath delivery lest dys-synchronies occur.
- The proper delivery of assisted or supported breaths considers all 3 phases of breath delivery and uses clinical data, ventilator graphics, and at times a trial-and-error approach to optimize patient-ventilator interactions.
- Two new modes of ventilation, proportional assist and neutrally adjusted ventilatory assist, are specifically designed to optimize patient-ventilator interactions.

INTRODUCTION

Mechanical ventilator support can be controlled entirely by the ventilator, as in the controlled mechanical ventilation of a passive patient, or can interact with patient's respiratory muscle efforts, as in assisted or supported ventilation of an actively breathing patient.[1] Controlled mechanical ventilation provides the benefit of a guaranteed minute ventilation with a predetermined ventilatory pattern but often at the cost of heavy sedation or even neuromuscular blockade to silence dys-synchronous ventilatory muscle activity. Unfortunately, silencing of these muscles contributes to a state of respiratory muscle weakness, also known as ventilator-induced diaphragm dysfunction, characterized by loss of their force generating capacity and earlier onset of fatigue.[2,3] Further, excessive sedation accompanying mechanical ventilation lengthens duration of mechanical ventilation, intensive care unit (ICU) stay, hospitalization, and possibly predisposes to delirium.[3–5]

Assisted or supported ventilation, if synchronous with the patient's ventilatory muscle efforts, shares the work of breathing, facilitates muscle recovery from respiratory fatigue or failure, and avoids excessive sedation.[6–8] For this ideal shared relationship to occur, synchrony must exist between the flow and pressure delivery of the ventilator and the patient's effort during all 3 phases of breath delivery: initiation, flow delivery, and termination. Failure to synchronize breath delivery with patient effort results in a counterproductive situation because additional loads are imposed on the ventilatory muscles. This phenomenon is described as patient-ventilator dys-synchrony (PVD). Subsequently, patient distress and discomfort are

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increased along with the need for additional sedation. This article first reviews ventilatory muscle physiology with particular focus on imposed loads in the setting of fatigue and respiratory failure. It then focuses on the various ways patient effort and ventilator flow delivery interact with basic and advanced features during patient-triggered breaths with a focus on synchronous interactions. Finally, it introduces 2 newer modes of mechanical ventilation: proportional assist ventilation (PAV) and neurally adjusted ventilatory assist (NAVA), both of which are intended to optimize this relationship.

VENTILATORY MUSCLES: NORMAL PHYSIOLOGY, FATIGUE, AND FAILURE

Ventilatory muscles are designed for a lifetime of continuous work. Physiologic and pathophysiologic demands must be overcome or respiratory failure and even death may ensue. The diaphragm, a musculotendinous sheet of skeletal muscle separating the thoracic and abdominal cavities is the most significant and well-studied of ventilatory muscles. Lung inflation occurs when a sufficient force is generated largely by the diaphragm to overcome the elastic and resistive loads imposed by the respiratory system and deliver gas to the alveoli.[9] The total pressure (P_{tot}) generated by the ventilatory muscles (P_{mus}), the mechanical ventilator (P_v), or both, must overcome the loads of respiratory system elastic recoil (P_{el}) and airway resistance (P_{res}) for a given flow (V') and volume change (ΔV). This can be expressed by the equation of motion in which C_{rs} is respiratory system compliance and R is airway resistance.[1,9]

$$P_{tot} = P_{el} + P_{res}$$

$$P_{tot} = (\Delta V/C_{rs}) + (R \times V')$$

Ventilatory muscle fatigue is a reversible loss of the ability to generate force or velocity of contraction in response to these loads.[10,11] Fatigue and failure are ultimately determined by an imbalance in muscle capabilities against the loads imposed. In critically ill patients, these capabilities are often significantly impaired by limitations in energy supply, oxygen extraction, metabolic derangements, inefficient weak muscles, and intrinsic positive end-expiratory pressure (PEEP), all further predisposing to fatigue.[11–14]

Increase in ventilatory muscle demands result primarily from the increased mechanical loads of abnormal respiratory mechanics (pressure loads) and increased ventilation needs (volume loads).[11,13,15] Mechanical loads can be described as the single values of work, the integral of pressure over change in volume, or pressure-time product (PTP), the integral of pressure over inspiratory time.[15] PTP with its reliance on pressure loads better correlates with muscle energetics, fatigue potential, and oxygen consumption. Thus, it is increasingly favored to measure the energy demands of ventilatory muscles. Further efforts have expanded on the PTP with a value known as the pressure time index (PTI) assessing pressure load (P_i) as a fraction of maximal pressure (Pi_{max}) generating capabilities along with the fraction of the total ventilatory duty cycle (T_{tot}) devoted to muscle contraction or inspiratory time (T_i). This is an even more reliable measure of energy expenditure and predictor of muscle fatigue.[16–18]

$$PTI = (P_i/Pi_{max})\ (T_i/T_{tot})$$

PTI values generally exceed 0.05 at rest and are rarely greater than 0.1 even with strenuous exercise. Values greater than 0.15 for the diaphragm predict a finite period before fatigue develops.[16]

All components of the PTI can change unfavorably in the setting of acute respiratory failure leading to ventilatory muscle fatigue and failure.[1] In patients challenged with high resistive loads, such as chronic obstructive pulmonary disease (COPD), asthma, or large airway obstructions; or with high elastic loads, such as interstitial lung disease, cardiogenic pulmonary edema, or acute respiratory distress syndrome (ARDS), the required ventilatory pressures (Pi) can be life-threatening. Additionally, pressure loads imposed from ventilator dys-synchrony may contribute to the Pi, impeding respiratory muscle recovery. A low Pi_{max} typical of neuromuscular disease, malnutrition, or shock further reduces ventilatory muscles reserves in the setting of a critical illness. High minute ventilation requirements typical of acute respiratory failure often increase tidal volume (Vt) and shorten the total ventilator cycle time (increase breathing rate) increasing T_i/T_{tot}. Central adaptive but potentially counterproductive mechanisms may influence this pattern, triggering the onset of rapid shallow breathing, which reduces P_i at the cost of increasing the ratio of physiologic dead space and possibly worsening hypercapnia.[19]

Optimal ventilator management minimizes ventilator-induced loads during mechanical ventilation while supporting recovery from the inciting unfavorable demands. The following sections focus on the role and management of ventilator-induced loads, their importance, and novel approaches to optimization.

INTERACTIVE VENTILATOR MODES AND PATIENT-VENTILATOR DYS-SYNCHRONY

Interactive breaths are described as assisted or supported. An assisted breath is patient-triggered and time or volume-cycled, whereas a

supported breath is patient-triggered and flow cycled. Assisted and supported breaths interact with patient efforts through all 3 phases of breath delivery: initiation (trigger), gas delivery (target), and termination (cycling).[7] Delivered breaths and patient demands must match during all 3 phases to be synchronous. If not, PVD occurs, resulting in additional imposed mechanical loads.

Breath Triggering

Assisted or supported breaths are initiated or triggered by patient effort. Patient effort is sensed by either a drop in circuit pressure (pressure trigger) or circuit bias flow (flow trigger) initiating breath delivery.[20] Triggers must be sensitive enough to recognize patient effort so as to not impose an additional load but not too sensitive to predispose to autotriggering. Importantly, a triggering delay from onset of patient effort to delivery of breath is often unavoidable due to inherent valve system sensitivity or responsiveness (**Fig. 1**).

Despite improvements in triggering technology over the past 2 decades, triggering dyssynchronies continue to occur and are manifest as either delayed or missed triggers, or else as extra or double triggers. Delayed or missed triggers may be a consequence of inappropriate trigger sensitivity settings. A sensitive triggering threshold is desirable to reduce unnecessary threshold muscle loading in all mechanically ventilated patients but may be especially important in critically ill patients in whom neuromuscular weakness, impaired ventilatory drive, and fatigue often complicate triggering and recovery. However, an overly sensitive trigger may lead to autotriggering in which even tube condensation, small circuit leaks, and cardiac oscillations trigger breaths. The result could be hyperventilation, breath stacking, and intrinsic PEEP.[20,21] Intrinsic PEEP may also be due to high minute ventilation, increased expiratory flow limitation, or increased expiratory flow resistance.

Missed or delayed triggers can also be a consequence of intrinsic PEEP. This occurs because the patient's ventilatory muscles must first overcome the load from positive end expiratory pressure remaining in the alveoli before any circuit pressure or flow change can occur and a breath triggered.[22]

At the bedside, triggering missed or delayed triggers clinically appear as a patient effort with chest wall rise and/or abdominal motion followed by absent or delayed breath delivery. This is best appreciated by placing a hand on the patient's chest and observing the ventilator's response to effort. Graphically, in more obvious cases negative airway pressure deflections with delayed or absent delivery of positive pressure may be seen. This information can actually be used to quantify the

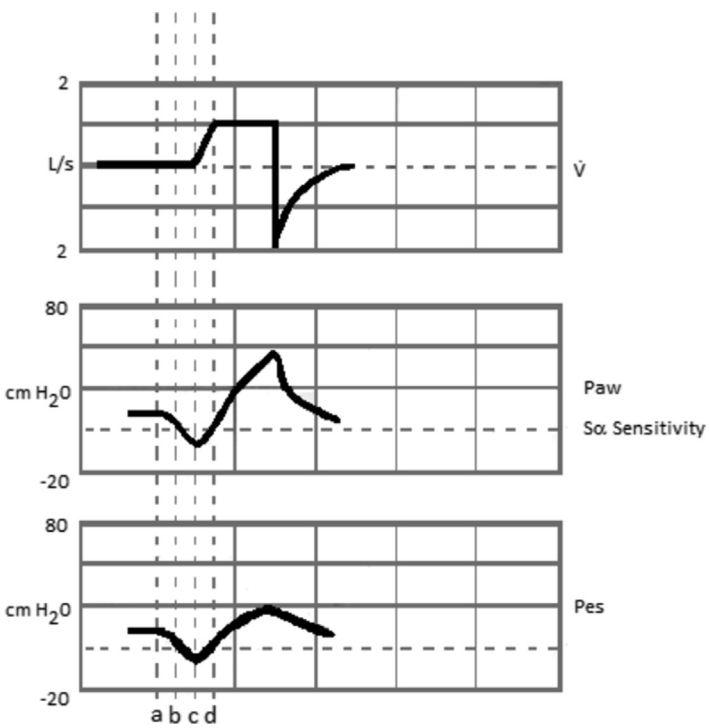

Fig. 1. Airway flow ($\dot{V}$), airway pressure (P_{AW}), and esophageal pressure (P_{es}) tracings over time. Point a represents onset of patient effort. Point b represents recognition of this effort by the ventilator. Point c marks the beginning of flow delivery. Point d marks the attainment of target flow. The pressure decline from a to b represents trigger sensitivity, whereas the duration from point b to point d is considered the responsiveness of the system.

work or PTP triggering dys-synchrony.[20,23,24] Another underappreciated finding can be a reduction or reversal of expiratory flow without breath delivery. Unfortunately, indicators of important trigger dys-synchrony are often absent from ventilator graphics due to small but significant efforts undetectable to the machine. These missed efforts require either physical examination or even more sensitive methods, such as a diaphragmatic electromyography (EMG) or esophageal pressure manometry to detect.[25]

Another form of trigger dys-synchrony is double triggering. As previously noted, this can be an artifact from excessively sensitive trigger sensors. However, there are 2 other situations in which double triggering can occur. One is when mechanical breath cycling occurs before patient effort has ceased and the persistent effort triggers an additional breath (see later discussion). Another cause of double triggering is reverse triggering. This is a poorly understood phenomenon that occurs when a machine-triggered breath elicits a reflex in the patient's ventilator control center that initiates an inspiratory effort that either results in a prolongation of the original breath or the triggering of a second breath.

Trigger dys-synchronies with delayed or absent breath delivery are the most common form of patient ventilator dys-synchrony, equaling as much as 88% of dys-synchronous breaths.[8] Further, in a prospective study of 62 subjects undergoing assisted mechanical ventilation for acute respiratory failure, Thille and colleagues[26] reported that 85% of all trigger dys-synchronies were wasted efforts. Trigger dys-synchronies are increasingly frequent with intrinsic PEEP development, less sensitive inspiratory triggers, and a higher arterial blood pH.[8,21]

Flow Delivery

Following breath initiation, gas is delivered by the ventilator in a given flow pattern that must be synchronous with the demands of the ventilatory muscles.[27] If flow is synchronous with that contraction pattern, the inspiratory muscle PTP resembles the physiologic sine wave pattern; however, if not, dys-synchrony with additional demanding imposed loads occurs.

Clinically, flow dys-synchrony presents with significant patient discomfort because efforts are not met with the desired flow (flow starvation). Graphically, this is appreciated by the airway pressure-time waveform being sucked down during breath delivery.[1] An estimate of this imposed loading can be calculated by comparing the difference between the area under the curve of the pressure-time tracings of the assisted or supported to a controlled breath.[28,29]

At no point is this dys-synchrony likely more apparent than in the setting of acute respiratory failure when inspiratory flow demands are high and can vary from breath to breath. In this scenario, unmet flow demands increase inspiratory effort, patient discomfort, and excess sedation needs. As may be expected, flow dys-synchrony seems more common with ventilator modes that deliver a fixed flow (flow-targeted) breath rather than variable flow delivery (pressure-targeted breaths).[30–32]

Breath Cycling

Mechanical ventilators cycle or terminate delivered flow to end inspiration based on multiple criteria, including attainment of a set T_i (pressure assist breath), delivery of set Vt (volume assist breath) or decline in inspiratory flow to a set threshold (pressure support breath). The end of mechanical T_i must coincide with the end of the patient's neural T_i or a cycling dys-synchronies occur.[33]

If the ventilator breath is longer than the patient's neural inspiratory time, the patient may actually fight the ventilator, recruiting expiratory muscles in an attempt to force expiration. Graphically, a sudden increase in the airway pressure-time waveform above plateau pressure may be noted near the end of inspiration.[33–35] This may be increasingly common in patients with obstructive airways disease receiving pressure support.[36,37] In this scenario, obstructed airways mean that delivered inspiratory flow decreases very slowly with mechanical T_i potentially exceeding neural T_i due to the flow cycling mechanism. This leads to further dys-synchrony as intrinsic PEEP accumulates and the potential for trigger dys-synchrony increased.

If neural T_i lasts longer than mechanical T_i, then premature cycling occurs. Clinically, the inspiratory muscles continue to contract uncomfortably into mechanical expiratory time against the sudden elastic recoil of the chest wall. This persistent effort can also trigger a second breath, often identified as double-triggering or breath stacking by the clinician.

STRATEGIES TO IMPROVE PATIENT-VENTILATOR INTERACTIONS

The goal of ventilator management in actively breathing patients is safe and effective support while assuring patient-ventilator synchrony to avoid additional imposed loads. In most cases, the patient's ventilatory drive should deliver a

pattern of ventilation that provides adequate gas exchange with minimal load to the ventilator muscles and synchrony with this should be the goal. However, if the ventilatory drive seems inappropriate then a search for reversible causes should be performed first and treated. For example, if the ventilatory drive is inappropriately excessive due to dyspnea, pain, or anxiety, these conditions may need to be managed first before synchrony can be achieved. Additionally, dys-synchrony in 1 phase of breath delivery may lead to dys-synchrony in another (eg, delayed cycling leading to trigger dys-synchrony). As synchrony improves in 1 phase of breath delivery, patient dyspnea, anxiety, and ventilatory drive may decrease to a more optimal synchrony level. Ultimately, the proper delivery of assisted or supported breaths must focus on all 3 phases of interactive breath delivery.

Optimizing Triggering

The clinician should choose the trigger sensor, flow, or pressure that is most sensitive and responsive to patient effort without predisposing to autotriggering. Additionally, sources of autotriggering, such as small circuit leads or condensation in the circuit, should be corrected. Of note, ventilators may have both types of effort sensors (pressure and flow triggers) present and respond to whichever trigger sensor is activated first.

There are several clinical strategies to deal with intrinsic PEEP. Initial efforts should aim to treat the causes of intrinsic PEEP by reducing minute ventilation, lengthening the expiratory time, and improving airway mechanics. The triggering load from intrinsic PEEP can also be reduced by the careful use of applied circuit PEEP. This will narrow the gradient between circuit and intrinsic PEEP and lessen the imposed load.[22,24] This can be guided by the use of an esophageal balloon or careful bedside application of PEEP by the clinician. When an esophageal balloon is used, pressure tracings allow measurement of intrinsic PEEP and 70% to 80% of the gradient can be provided as circuit PEEP.[38,39] If an esophageal balloon is not available, circuit PEEP can be empirically titrated and the patient's response followed. If the application of PEEP is helpful, delayed or absent breaths will decrease and the patient will appear more comfortable. An important sign to look for is the amount of pressure required for the Vt. The clinician must be careful that applied PEEP is less than intrinsic PEEP as excessive applied PEEP will drive the end inspiratory pressure up in flow-targeted, volume-cycled ventilation.

Optimizing Flow Delivery

Key to any discussion regarding optimizing flow delivery is to first distinguish flow-targeted, volume-cycled breaths versus pressure-targeted breaths with variable flow. Flow-targeted, volume-cycled breaths are currently the most common breath type used in modern ICUs.[40] The clinician controls the flow magnitude or pattern, inspiratory time, and thus the Vt delivered. Unfortunately, the fixed flow delivery pattern prevents any interaction with the patient's variable ventilatory drive and flow dys-synchronies can occur.

When using flow-targeted, volume-cycled breaths, the Vt, flow rates, and shape of flow can be adjusted for patient comfort.[41] In the ARDS Network trial showing benefits to the use of low Vts versus larger ones, flow-targeted, volume-cycled breaths were used and Vts from could be adjusted 4 to 8 mL/kg ideal body weight for comfort. Of note, there was no increased need of sedation for the low Vt group compared with those receiving the larger Vts strategy.[42,43] The magnitude of flow may also be increased in the setting of increased demands and the shape of the flow can be adjusted (sinusoidal vs square vs decelerating) to enhance synchrony.[44,45] When properly titrated, comparable comfort may be achieved when comparing variable flow, pressure-targeted breaths with flow-targeted, volume-cycled breaths.[46]

Assisted or supported ventilation with variable flow and pressure-targeted breaths reduces this dys-synchrony because the ventilator delivers whatever flow is needed to attain the set pressure target. This feature may be more comfortable to the patient (**Fig. 2**).[30,32] Pressure-targeted breaths have several additional features that can be used to optimize synchrony. Manipulation of the initial flow through a feature known as rise time adjustment increases or decreases the rate of rise of inspiratory pressure toward the set target. This may be particularly helpful in patients with forceful inspiration from acute respiratory failure when a rapid pressurization pattern may synchronize better.[47,48] Another available feature that may optimize synchrony is the ability to calculate endotracheal tube resistance and subsequent adjustment of the ventilator circuit pressure profile to produce a more favorable pressure profile. Observational studies have suggested that this, as well as rise time adjustment may reduce imposed loads but no studies have shown that these features alter clinical outcomes.[47–49]

The clinical goals with pressure-targeted breaths are the same as flow-targeted,

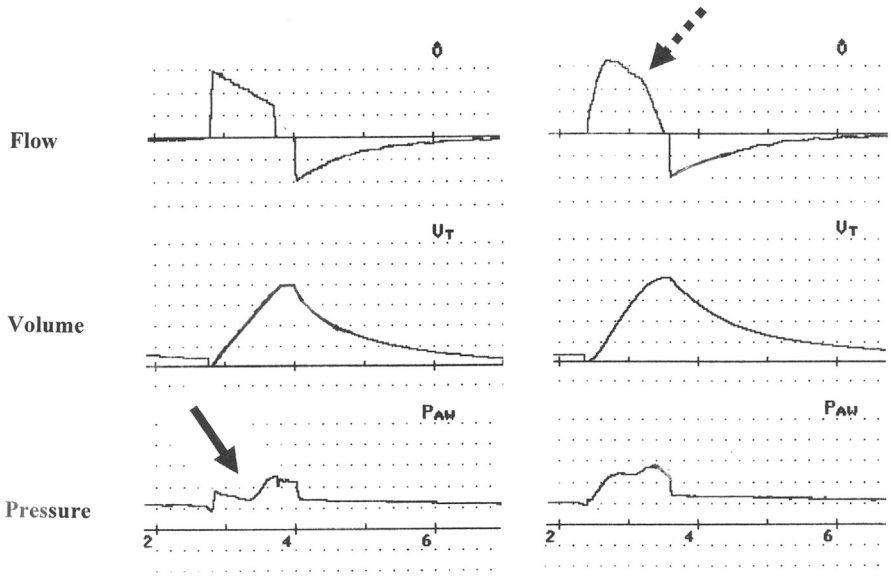

Fig. 2. Flow, volume, and P_{AW} over time. On the left, a flow-targeted breath is delivered with inadequate flow for patient demand. Dys-synchrony is manifest by the downward coved airway pressure profile (*solid arrow*) with the patient sucking down the graphic. On the left, a pressure-targeted breath delivers a similar tidal volume (Vt); however, synchrony is eliminated due to variable flow (*dashed arrow*). (*Data from* Collett PW, Perry C, Engel LA. Pressure-time product, flow, and oxygen cost of resistive breathing in humans. J Appl Physiol (1985) 1985;58(4):1263–72.)

volume-cycled breaths: provide proper muscle unloading along with safe and effective Vts (4–8 mL/kg ideal body weight) while minimizing dys-synchrony.[1] A concern with pressure targeting is that Vt control is less certain. Inadequate pressure settings can overload muscles and not achieve these goals. At the other extreme, excessive pressure settings cause overdistention and/or air trapping, potentially harming the patient with worsening ventilator-induced lung injury and dys-synchrony. Newer hybrid modes allow the clinician to set a target Vt and then the ventilator automatically adjusts or regulates the pressure to maintain that volume. Although this may sound like an ideal scenario, abrupt changes in effort, such as from anxiety, pain, or dyspnea, may create high Vts, which will lead the ventilator to inappropriately lower inspiratory pressure.[50,51]

Optimizing Cycling

Breath cycling should synchronize mechanical T_i and neural T_i, assuring patient comfort and avoiding excessive inspiratory times that result in excessive Vts, air trapping, and premature breath terminations. Cycling adjustments are generally applied in a trial-and-error approach. With flow targeting, the breath duration can be adjusted by the set inspiratory time or the addition of an inspiratory pause. With pressure targeting, the set inspiratory time is directly adjusted with pressure-assisted breaths or flow cycling criteria with pressure support breaths. A higher percentage of peak flow cycling in pressure support will shorten a breath, whereas a lower percentage of peak flow cycling criteria results in a longer breath.[34,52,53]

IMPACT OF PATIENT-VENTILATOR DYS-SYNCHRONY

Although determining the true frequency of PVD is difficult, it is likely ubiquitous.[21,25,26,54,55] If any patient is observed long enough, dys-synchrony will almost certainly be observed but it is more common in patients with significant underlying disease, such as COPD or ARDS. A median of 2.1 asynchronous breaths per minute have been observed in critically ill patients with 24% of these patients having greater than 10% of efforts wasted on dys-synchrony.[26]

Although the role of PVD in imposing additional loads, worsening respiratory mechanics, and increasing patient discomfort with need for additional sedation are well described, its relation to other adverse outcomes, such as mortality and hospital length of stay, remains less

clear.[8,56] de Wit and colleagues[55] demonstrated a relationship between dys-synchrony in the first day of mechanical ventilation and longer duration of mechanical ventilation, decreased 28-day ventilator-free survival and longer ICU and hospital stays but no differences in ICU or hospital mortality in an observational study of 60 subjects. Further supporting the impact of dys-synchrony, Thille and colleagues[26] showed that asynchrony indices (breaths with trigger dys-synchronies or total breaths) above 10% were associated with longer duration of mechanical ventilation and a trend toward increased mortality. These relationships remain of uncertain significance because it is particularly difficult to distinguish if dys-synchrony is causative of worse outcomes or only a common link to a poor prognosis.

PROPORTIONAL ASSIST VENTILATION AND NEURALLY ADJUSTED VENTILATORY ASSIST

PAV and NAVA are 2 new modes of ventilation designed specifically to optimize patient-ventilator interactions. They do this by responding instantaneously to the patient's inspiratory demand to reduce patient effort to a preset degree. PAV accomplishes this by using nearly instantaneous respiratory resistance or compliance measurements to guide its response, whereas NAVA directly measures the electrical activity of the diaphragm and applies support based on its level of excitation.[57,58] PAV and NAVA differ from conventional modes in that if the patient demands more support, they receive it, as opposed to fixed settings (Fig. 3).[59]

Although viewed as a new mode of ventilation, the concept of PAV was first described back in 1992.[57] PAV amplifies the patient's own inspiratory effort by increasing or decreasing airway pressure and flow in conjunction with patient effort. The software algorithm underlying the technology continuously and automatically adjusts the pressure and flow based on patient flow demand throughout the inspiratory cycle to maintain the set degree of support. The basic theory of operation for PAV is based on the equation of motion:

$$P_{tot} = (\Delta V/C_{rs}) + (R \times V')$$

In patients that are interacting with the ventilator $P_{tot} = P_{mus} + P_v$ in which P_{mus} is patient-generated muscular pressure and P_v is the pressure generated by the ventilator. In spontaneously breathing patients, the pressure generated by the inspiratory muscles (P_{mus}) is used to overcome the compliance and resistance of the respiratory system. In mechanically ventilated patients, the P_{tot} applied to the respiratory system equals the P_{mus} from the patient and supplied airway pressure (P_v). The algorithm then converts this information to the work of breathing (WOB) for each breath. The clinician is required to set the percentage of the WOB that the ventilator will assume; the patient contributes the rest. For instance, if 60% WOB is dialed in on the ventilator, then 60% of the WOB for that breath will be supported. The patient is then required to assume the other 40%. An increased inspiratory effort by the patient (increasing the total WOB for the breath) results in increased support from the ventilator to keep its contribution to the breath at 60%. The reverse, however, is true. If the patient generates smaller inspiratory efforts, the support from the ventilator will decrease (but still be at 60% of the total WOB for that particular breath). This differs from pressure support ventilation (PSV) in that changes in inspiratory effort are met with the same pressure throughout the breath (Fig. 4). Triggering of the breath to inspiration in PAV is accomplished in the same manner as conventional ventilation. Cycling to exhalation in PAV occurs when the flow diminishes to the set threshold (eg, when flow reaches 3 L per minute) as opposed to a flow decay percentage threshold, as is the case in PSV. Because there is a close link between P_v and P_{mus} (because P_{mus} drives P_v), the end of the mechanical inflation coincides much more closely with the neural end of inspiration.

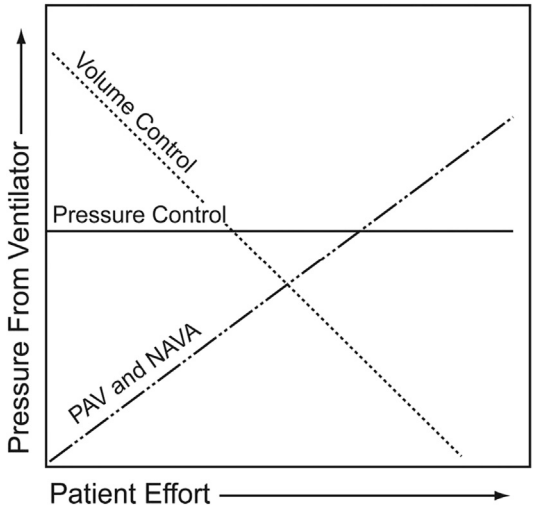

Fig. 3. Ventilator response to patient effort in conventional modes and PAV and NAVA. (*From* Kacmarek RM. Proportional assist ventilation and neurally adjusted ventilatory assist. Respir Care 2011; 56(2):140–8. [discussion: 142]; with permission.)

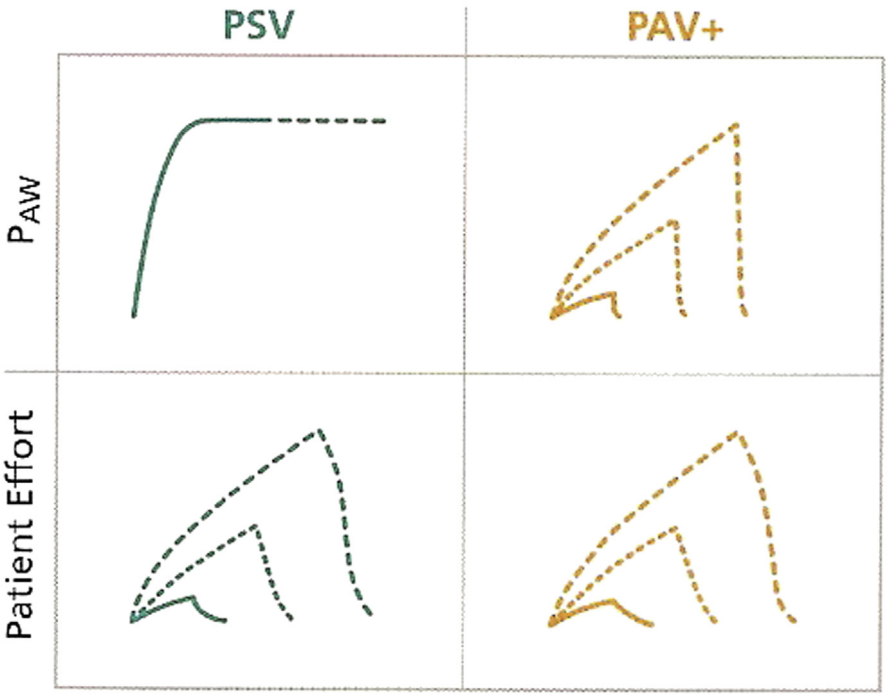

Fig. 4. The response of PSV and PAV with load-adjustable gain factors (PAV+) to different levels of patient effort.

PAV has been compared with PSV in several studies. With PSV, setting the pressure level too high can result in longer inspiratory time (often past the cessation of patient effort) and higher Vt.[38,60] PAV may have advantages here in that the patient is better able to modulate their breath and control their Vt. Passam and colleagues[61] examined 9 hypercapnic COPD subjects on both PAV and PSV at 4 different support levels each. They found an increased number of missed breaths with increasing support in PSV. There was no increase in the number of missed efforts at any of the PAV levels. The reason for these findings was that the higher the pressure level in PSV, the longer the inspiratory time, which created inadequate time for expiration and the development of intrinsic PEEP. Ranieri and colleagues[62] compared PAV to PSV in a hypercapnic-induced state in 12 subjects. They compared PSV levels of 10 and 20 cm H_2O to PAV support levels of 80% and 40%. The results were that PAV preserved minute ventilation by changes in Vt modulated through patient effort as opposed to an increased respiratory rate in PSV. Being able to modulate the Vt resulted in less WOB and less patient discomfort with PAV. Grasso and colleagues[63] compared comfort levels between PSV and PAV in 10 subjects with increased mechanical loads produced by thoracic and abdominal binding. They found that only PAV was able to maintain Vt and minute ventilation. Subjects receiving PSV had higher respiratory rates and were more uncomfortable. Likewise, Kondili and colleagues[64] found similar results in 10 subjects with increased workloads (sandbags on the anterior surface of the chest wall and abdomen). PAV resulted in less Vt reduction and respiratory rate change than PSV and PAV resulted in more efficient respiratory load compensation. Mitrouska and colleagues[65] examined the response of 3 different modes (volume assist control, PSV, and PAV) to a hypercapnic challenge in 7 healthy subjects. They found that PAV produced the best adaptation to the hypercapnic conditions with the most comfort. So, in terms of Vt modulation during increased loads, it does seem that PAV offers a benefit in terms of better patient control as well as increased comfort.

There are several studies comparing patient-ventilator synchrony between PAV and PSV. Xirouchaki and colleagues[66] examined the performance of PAV versus PSV in 208 critically ill subjects. In this study, PAV resulted in a lower failure rate during spontaneous breathing (11.1% compared with 22% in PSV, $P = .04$) and a lower incidence of subject ventilator dys-synchrony (5.6% vs 29% in PSV, $P<.001$). Costa and colleagues[67] compared PSV to PAV in terms of the Asynchrony Index (AI). In this crossover study of 11 subjects, 5 out of the 11 had an AI greater than 10% in PSV, whereas the AI was nil with PAV. A recent study

looked at the use of PAV during sleep to reduce the number of sleep disruptions due to PVD. The investigator did, indeed, find that there were fewer subject-ventilator asynchronies and a better quality of sleep in PAV.[68] Another recent study looked at the number of ventilator interventions and sedation use in PAV compared with PSV. These investigators concluded that the use of PAV resulted in less sedation use and a lower number of ventilator manipulations, suggesting that the ventilator was more responsive to the subjects' varying needs.[69]

The current data suggest that PAV can adjust better to changing lung mechanics and that it does provide better patient-ventilator synchrony. However, PAV is not without its drawbacks. The patient must have an adequate drive to breath. Weak efforts will only elicit a weak response in PAV and inconsistent efforts may not produce enough support to overcome the respiratory load. Also, PAV, like other forms of conventional ventilation, cannot compensate for nor overcome the effects of intrinsic PEEP.

NAVA accomplishes the same goal as PAV but through a different mechanism. NAVA uses diaphragm EMG signals to detect patient triggers as well as guide inspiratory gas delivery. A specifically designed nasogastric tube equipped with a series of EMG electrodes located near its distal end captures the electrical activity of the diaphragm and passes the information back to the ventilator, which maintains respiratory support (pressure and flow) that is proportional to the signal strength. Because the ventilator and the diaphragm work with the same signal, mechanical coupling between the diaphragm and the ventilator is practically instantaneous. As EMG activity increases, the applied pressure increases and, as the diaphragm relaxes, airway pressure decreases. The clinician sets the applied pressure for each microvolt of EMG activity and, as with PAV, the effort is proportionally distributed between the ventilator and the patient. The level of support varies from 1 cycle to the next and is directly proportional to the EMG activity.

NAVA is designed to optimize synchrony in all 3 phases of the breath: triggering, flow or pressure response, and cycling to exhalation. At the onset of the breath, gas delivery begins when the diaphragm is stimulated as opposed to the traditional methods of breath initiation detection (changes in circuit flow or a drop in circuit pressure). Interestingly, from the triggering perspective, severe air trapping or large system leaks do not compromise patient triggering in NAVA. This makes it appealing for the COPD population. NAVA may also have a unique place in the neonatal population and in noninvasive ventilation (NIV). The use of uncuffed endotracheal tubes in neonates and NIV in general carry with them the potential for leaks in the system. Because NAVA is supplying support based solely on diaphragm excitement, the delivered support is not affected as could be the case with traditional modes. Flow and pressure response, like PAV, are proportional to the inspiratory demand. From this perspective, the intrabreath response will essentially apply support based solely on demand as opposed to fixed flows and/or pressures. As for cycling to exhalation, both NAVA and PAV end the breath when patient demand essentially is gone (PAV with flow and NAVA with diaphragmatic signal) as opposed to the fixed time, volume delivery, or percentage flow decay used in traditional modes of ventilation.

There are several recent studies comparing NAVA to traditional modes of ventilation in terms of patient-ventilator synchrony. Colombo and colleagues[70] compared NAVA and PSV with 3 different levels of support each. They found that, at the lowest levels of support, there was minimal variation in respiratory pattern between the modes. However, at the higher levels there was more air trapping and cycling dys-synchrony in the PSV group. The PSV group had an AI of 36% but the AI in NAVA was 0. Spahija and colleagues[71] reported similar findings in 12 COPD subjects. This group used 2 different levels of support in each mode: the lowest tolerated in PSV and 7 cm H_2O above that, and NAVA settings at the same average peak pressures. They found that the AI was 23% in the PSV group, whereas it was only 7% in the NAVA group. The investigators attributed these findings to air trapping and cycling dys-synchrony. Terzi and colleagues[72] compared NAVA and PSV in 11 subjects with ARDS in 4 levels of assistance: 100%, 120%, 140%, and 160%. As would be expected, the Vt in PSV rose with each increased level of assistance, whereas the Vt remained stable in the NAVA group. Also, the AI rose in PSV with each increase in level of assistance. In NAVA, the AI remained well below 10%. The investigators concluded that, in ARDS, NAVA holds promise in limiting the risk of over-assistance and improves patient-ventilator synchrony and patient-ventilator interaction. A recent study by Yonis and colleagues[73] examined the use of NAVA versus PSV for an extended period of time (23 hours). In terms of subject-ventilator synchrony, their results mirrored those presented earlier. An interesting finding in this study was that double triggering was more frequent in NAVA. The investigators postulated that this

could be due to the presence of some EMG signals with a biphasic appearance causing 2 successive cycles. Although it did not seem to increase the work of breathing, it is unknown if this contributed to patient discomfort.

With NIV, several studies show NAVA reduces the inspiratory trigger delay, harmonizes the patient's offend-inspiration with the cycling off of the ventilator, and reduces the asynchronies that occur between the patient and the ventilator.[74–77] Evidence in the neonatal arena has shown similar outcomes as in the adult studies.[77–79] In a study by Beck and colleagues,[77] the investigators also found that there were no differences in triggering and cycling synchrony in invasive compared with NIV with NAVA.

Evidence indicates that both PAV and NAVA improve neuromechanical coupling and improve patient-ventilator synchrony compared with PSV and other conventional modes of ventilation. They also help patients establish a ventilatory pattern more consistent with their inspiratory demands. Unfortunately, there no good randomized trials looking at outcome benefits such as mortality and ventilator duration.

SUMMARY

For patients treated with mechanical ventilation, the goal is to provide safe and effective ventilatory support without imposing additional loads from the ventilator, also known as dys-synchrony. Dys-synchrony imposes additional mechanical pressure loads on ventilator muscles that may result in further fatigue and the need for sedation to treat patient discomfort. Assisted or supported breaths may improve patient-ventilator synchrony but must interact with patient demands during all 3 phases of breath delivery: trigger, target, and cycle. The proper delivery of these breaths considers all 3 phases and uses clinical data, ventilator graphics, and at times a trial-and-error approach to optimize patient-ventilator interactions. Newer modes, such as PAV and NAVA, are designed specifically to optimize patient-ventilator interactions but await good clinical outcome data before routine use.

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