

Critical Care Perspective

Patient–Ventilator Interaction

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One of the most frequent reasons for instituting mechanical ventilation is to decrease a patient's work of breathing. To achieve this goal, neuromuscular blockade was initially used to eliminate a patient's respiratory efforts, resulting in controlled ventilation. Neuromuscular blocking agents, however, predispose to numerous hazards, and, today, some means of assisted ventilation is usually employed. Surprisingly, we do not know the ideal level of respiratory muscle unloading during mechanical ventilation. To consider this issue, we need a means of measuring a patient's respiratory effort. Inspiratory pressure–time product (PTP), which quantifies swings in intrathoracic pressure, is closely related to oxygen cost of breathing and has several advantages over measurements of mechanical work of breathing (1). In 17 patients failing a trial of weaning from mechanical ventilation, their average PTP was 388 cm H₂O · s/min (2); the average value in healthy subjects is 94 cm H₂O · s/min. With carefully selected settings, a patient's inspiratory PTP can be reduced into the normal range with assisted ventilation (3). For the most effective unloading of the inspiratory muscles, the ventilator should cycle in synchrony with the activity of a patient's own respiratory rhythm. The interplay between these two pumps is complex, and problems can arise at several points in the respiratory cycle: the onset of ventilator triggering, the rest of inspiration after triggering, the switch from inspiration to expiration, and the end of expiration.

TRIGGERING OF THE VENTILATOR

Ventilators provide positive pressure assistance whenever a patient's inspiratory effort decreases pressure in the ventilator circuit by 1 to 2 cm H₂O. The latter value, selected by clinicians, is termed the set sensitivity (4). Patients reach the set sensitivity by activating their inspiratory muscles, but they cannot switch off respiratory motor output at the point of triggering (5). As a result, considerable effort is commonly expended over the period of mechanical inflation that follows the trigger phase. The level of patient effort during this post-trigger phase is closely related to a patient's respiratory drive at the point of triggering ($r = 0.78$) (3). As such, measures that decrease respiratory drive may enhance respiratory muscle rest during mechanical ventilation. If sedatives are used for

this purpose, however, the dosage and method of administration need to be carefully selected (6).

If respiratory drive at the point of triggering is important, one might intuitively expect that effort during the remainder of inspiration would determine patient effort during the remainder of inspiration. Such an association was suggested by Giuliani and coworkers (7). Leung and coworkers (3) applied graded levels of pressure support in 11 critically ill patients and achieved a fourfold reduction in overall patient effort but observed no change in patient effort during the time of triggering. The constancy of effort during the trigger phase was probably due to different factors becoming operational as the level of ventilator assistance was varied (Figure 1). When patients were receiving a low level of pressure support, their respiratory drive was high and the time to trigger the machine was short; as a result, they generated large swings in intrathoracic pressure over a short time. When patients received a high level of pressure support, their respiratory drive was lower but more time was needed to trigger the machine; as a result, they generated much smaller swings in intrathoracic pressure, but over a longer time. Thus, increases in the level of ventilator assistance do not substantially decrease patient effort during the time of triggering.

Opening a demand valve during pressure triggering can impose substantial effort (4). In an attempt to overcome this problem, flow triggering was introduced. With this approach, the ventilator is triggered when a patient's effort creates a difference between the inspiratory and expiratory base flow in the circuit. Aslanian and coworkers (8) found that the time required for triggering was 43% less with flow triggering than with pressure triggering, and effort during the time of triggering was decreased by 62%. Patient effort during the post-triggering phase, however, was equivalent for pressure and flow triggering. As a result, the overall effect on total patient effort was small, and the clinical benefit of flow triggering appears to be much less than commonly stated.

INEFFECTIVE TRIGGERING

The increased use of bedside displays of pressure and flow tracings has led to a growing awareness of the frequency with which patients fail to trigger a ventilator (3, 9, 10). When receiving high levels of pressure support or assist-control ventilation, a quarter to a third of a patient's inspiratory efforts may fail to trigger the machine (3). The number of ineffective triggering attempts increases in direct proportion to the level of ventilator assistance (3).

In a study of factors contributing to ineffective triggering, a decrease in the magnitude of inspiratory effort at a given level of assistance was not the cause—indeed, effort was 38% higher during nontriggering attempts than during the triggering phase of attempts that successfully opened the inspiratory valve (3). Significant differences, however, were noted in the characteristics of the breaths before the triggering and non-triggering attempts. Breathes before non-triggering attempts had

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a higher tidal volume than did the breaths before triggering attempts, 486 ± 19 and 444 ± 16 ml, respectively, and a shorter expiratory time, 1.02 ± 0.04 and 1.24 ± 0.03 s, respectively. An abbreviated expiratory time does not allow the lung to return to its relaxation volume, leading to an increase in elastic recoil pressure. Indeed, intrinsic positive end-expiratory pressure (PEEP_i) was higher at the onset of nontriggering attempts than at triggering attempts: 4.22 ± 0.26 and 3.25 ± 0.23 cm H₂O, respectively. Thus, nontriggering results from premature inspiratory efforts that are not sufficient to overcome the increased elastic recoil associated with dynamic hyperinflation (3).

An elevated PEEP_i may result from an increase in elastic recoil pressure or expiratory muscle activity. The relative contributions of these two factors to ineffective triggering were investigated in healthy subjects receiving pressure support and in whom airflow limitation was induced with a Starling resistor (11). PEEP_i was more than 30% higher at the onset of nontriggering attempts than before triggering attempts—similar to the situation in critically ill patients (3). The magnitude of expiratory effort, quantified as the expiratory increase in gastric pressure, did not differ before triggering and nontriggering attempts. In contrast, elastic recoil, estimated as gross PEEP_i minus the increase in gastric pressure, was higher before nontriggering attempts than before triggering attempts: for example, 14.1 and 4.9 cm H₂O, respectively, at pressure support of 20 cm H₂O. That nontriggering was caused by the elastic recoil fraction of PEEP_i, not that resulting from expiratory effort, suggests that external PEEP might be clinically useful in reducing ineffective triggering.

Although the magnitude of expiratory effort does not appear to influence the success of triggering attempts, the time that expiratory efforts commence in relation to the cycling of the ventilator is an important factor. Investigators have quantified the relationship between the onset of expiratory muscle activity, measured with a wire electrode in the subject's transversus abdominis, and the termination of mechanical inflation by the ventilator (11). This relationship was quantified in terms of phase angle: expiratory muscle activity commencing before the termination of mechanical inflation produces a negative phase angle, and activity commencing after the end of inflation gives a positive phase angle. The phase angle between neural and mechanical events was more negative before nontriggering attempts than before triggering attempts: for example, -50° and -19° , respectively, at pressure support of 20 cm H₂O (11). The more negative phase angle means that mechanical inflation continued for a longer time into neural expiration in the breaths preceding nontriggering attempts. Continuation of me-

chanical inflation into neural expiration counters expiratory flow, and also decreases the time available for unopposed exhalation. Consequently, elastic recoil increases. In turn, a greater inspiratory effort will be needed to achieve effective triggering. In this way, the time that a patient commences an expiratory effort (in relation to cycling-off of mechanical inflation) partly determines the success of the ensuing inspiratory effort in triggering the ventilator. Algorithms that achieve better coordination between the end of mechanical inflation and the onset of a patient's expiration should lessen this form of patient-ventilator asynchrony, although such algorithms have yet to be rigorously evaluated in patients (12).

SETTING OF INSPIRATORY FLOW

When a patient is first connected to a ventilator, inspiratory flow is set at some default value, such as 60 L/min. Many critically ill patients have an elevated respiratory drive and the initial setting of flow may be insufficient to meet flow demands. As a result, patients will struggle against their own respiratory impedance and that of the ventilator, with consequent increase in the work of breathing. To minimize this likelihood, clinicians commonly employ a much higher flow, e.g., 80 to 100 L/min. Recent studies, however, suggest that a high flow setting may be counterproductive in this situation.

In healthy subjects, Puddy and Younes (13) found that an increase in inspiratory flow from 30 to 90 L/min caused respiratory frequency to increase from 8.8 to 14.1 breaths/min. The increase in frequency was nearly complete within the first two breaths and did not change thereafter despite the development of respiratory alkalosis. This flow-associated tachypnea has been shown to be independent of breathing route, temperature of inspired gas, and delivered volume; it also persists after anesthesia of the airway, denervation of receptors in the lungs and chest wall, and during sleep (14–18). In addition to the effect of delivered flow on frequency, investigators have shown that frequency is influenced by delivered tidal volume—an effect seen under isocapnic and hypocapnic conditions, and during wakefulness and sleep (18, 19).

When studying the effects of a change in a ventilator's flow or tidal volume, the results may be influenced unwittingly by simultaneous changes in ventilator inspiratory time. When inspiratory flow is increased and tidal volume kept constant, ventilator inspiratory time must decrease. When tidal volume is increased and inspiratory flow kept constant, ventilator inspiratory time must increase. A series of experiments has been undertaken in healthy volunteers to delineate the separate influences

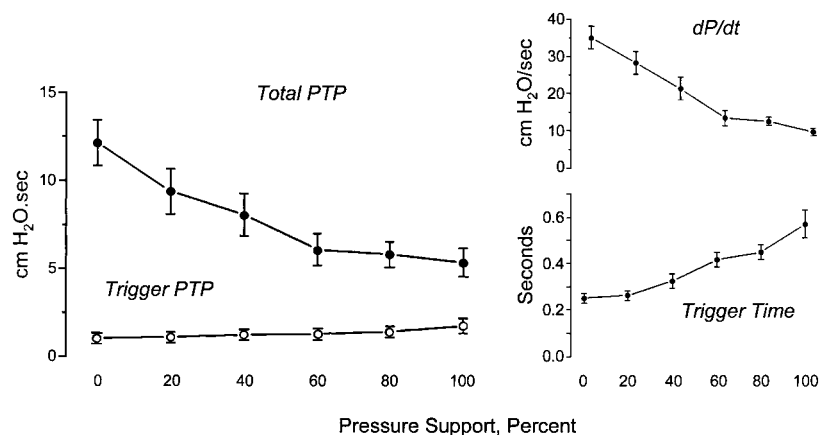


Figure 1. Graded increases in pressure support produced a decrease in total PTP per breath (closed symbols), although PTP during the trigger phase (open symbols) did not change (left panel). The constancy of PTP during triggering probably resulted from different factors becoming operational at different levels of assistance (right panel). At low levels of pressure support, respiratory drive (dP/dt) and intrinsic positive end-expiratory pressure (PEEP_i) were high but triggering time was short, resulting in a large change in pleural pressure over a brief interval. At high levels of pressure support, dP/dt and PEEP_i were low but triggering time was long, resulting in a smaller change in pleural pressure over a longer time. [Based on data from Leung and coworkers (3).]

of these three settings—flow, tidal volume, ventilator inspiratory time—in mediating flow-associated tachypnea (20).

For inspiratory flow of 30, 60, and 90 L/min, the respective frequencies were 12.9, 15.5, and 18.2 breaths/min. Because tidal volume was kept constant, an increase in flow was accompanied by a proportional decrease in ventilator inspiratory time. The increase in frequency was proportional to the decrease in ventilator inspiratory time ($r = -0.69$). When flow and tidal volume were held constant and ventilator inspiratory pauses of as much as 2 s were imposed, frequency again changed as a function of ventilator inspiratory time ($r = -0.86$). When flow was increased from 30 to 60 L/min, and tidal volume adjusted to maintain a constant ventilator inspiratory time, frequency decreased from 17.9 to 16.0 breaths/min. This series of observations shows that imposed inspiratory time can determine frequency independently of delivered inspiratory flow and tidal volume (20). The findings have clinical implications. Clinicians often increase tidal volume to lower carbon dioxide tension. An increase in tidal volume without change in inspiratory flow, however, must be accompanied by a longer inspiratory time, which is likely to decrease frequency. The consequent change in minute ventilation and carbon dioxide will fall short of that intended. (The opposite scenario holds when a lower tidal volume is selected.)

The effects of delivered flow, tidal volume, and inspiratory time on frequency can be interpreted according to current understanding of the Hering-Breuer reflex. First, for a fixed inspiratory time, an increase in inspiratory flow will necessarily increase end-inspiratory lung volume. An increase in delivered volume causes a progressive increase in the activity of the slowly adapting receptors (stretch receptors). This activity is transmitted by the vagus to the brainstem where it inhibits inspiration (negative feedback). Any decrease in neural inspiratory time is also likely to be accompanied by a decrease in neural expiratory time, because the two phases are closely linked (21). Accordingly, decreases in neural inspiratory time and expiratory time secondary to lung inflation are likely to be major factors in explaining flow-associated tachypnea. Second, a decrease in neural inspiratory time fosters the extension of mechanical inflation into neural expiratory time, which, in turn, causes prolongation of neural expiratory time (22, 23). A mechanical expiratory time that exceeds neural inspiration—as can occur with imposed inspiratory pauses, higher tidal volume, or slower flow rates—is thus an important modulator of frequency. In summary, the response of frequency to a change in ventilator settings is complex, because it depends on the relative dominance of physiologic mechanisms acting in different directions. High flows are often used with the intent of lowering PEEP_i by achieving a shorter inspiratory time and, thus, allowing more time for exhalation. The associated tachypnea could cause expiratory time to shorten, and thus increase PEEP_i, or to lengthen, secondary to continuation of mechani-

cal inflation into neural expiration; which of these opposing scenarios prevails has yet to be determined.

MODE-SPECIFIC EFFECTS OF INSPIRATORY UNLOADING

Intermittent mandatory ventilation (IMV) was the first mode designed to provide graded levels of assistance. This mode was introduced as a means of resting the respiratory muscles during machine-supported breaths, while avoiding atrophy and fostering reconditioning by allowing the patient to take some spontaneous breaths (24). More than 15 yr elapsed after the introduction of IMV before it was recognized that patients have difficulty in adapting to the intermittent nature of the assistance (25).

Leung and coworkers (3) undertook a head-to-head comparison of the relative effectiveness of graded levels of IMV and pressure support in unloading the inspiratory muscles. Over the entire span of assistance, the rate of change in effort per minute did not differ between the modes (analyzed in terms of slopes). The efficacy of unloading, however, did differ according to the stages of assistance. From zero assistance up to a medium level of assistance (60% of maximum), the decrease in patient effort per minute was greater with pressure support than with IMV; the converse was observed as ventilator assistance was increased further to a maximal level (Figure 2). The changes in effort per breath and frequency help with understanding the different responses (3). Effort per breath decreased linearly as the rate of IMV was increased. Effort per breath also decreased linearly as pressure support was increased to a medium level, but little thereafter, presumably because pressure support provides assistance only if patients makes some effort. Frequency decreased linearly as pressure support was increased; with IMV, frequency changed little until a high level of assistance was provided. As IMV is increased from a medium to a high level, all of a patient's ventilatory requirements will be met and frequency decreases dramatically; thus, a greater rate of respiratory unloading occurred between medium and high levels of assistance with IMV than with pressure support. Because these two modes are used primarily to provide partial, as opposed to complete, assistance, the greater decrease in patient effort per minute with pressure support at 20 to 60% of assistance makes it a clinically more useful mode than IMV.

Pressure support and IMV are commonly combined in a given patient. In an international survey of mechanical ventilation (26), this combination tied with assist-control ventilation as the most commonly used mode of ventilation in North America (34% for each). The rationale for combining the modes is unclear, but presumably clinicians use pressure support to overcome the work imposed by the endotracheal tube and demand valve during the nonmandatory breaths. Examin-

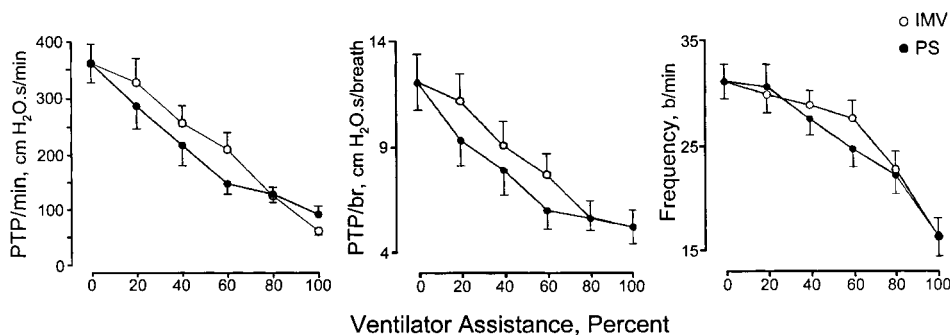


Figure 2. Changes PTP per minute (left panel), PTP per breath (middle panel), and frequency (right panel) as IMV and pressure support (PS) were progressively increased. PS of 100% represents the level necessary to achieve a V_T equivalent to that during assist-control ventilation (10 ml/kg); IMV of 100% is the same ventilator rate as during assist-control ventilation. [Based on data from Leung and coworkers (3).]

ing the response of the respiratory centers to this combination of modes provides useful insight into patient-ventilator interaction. A decrease in the number of mandatory breaths produces a decrease in the average tidal volume (3), with inevitable increase in the dead space-to-tidal volume ratio. To avoid a decrease in alveolar ventilation, the patients increased respiratory drive, inspiratory effort, and frequency. Adding pressure support of 10 cm H₂O caused a decrease in effort at any given IMV rate. Interestingly, the decrease in effort during the mandatory ventilator breaths was related to the decrease in respiratory drive during the intervening breaths ($r = 0.67$) (3). In other words, the reduction in drive during the intervening breaths achieved by adding pressure support was carried over to the mandatory breaths, facilitating greater unloading. Combining IMV and pressure support provides a sometimes useful means of achieving a high level of assistance; the combination has a clinical advantage when it is difficult to achieve a high inspiratory flow in the assist-control mode, as with the Siemens 900C ventilator (Siemens Corporation, New York, NY).

INSPIRATION-EXPIRATION SWITCHING

Patients are commonly ventilated with a volume-cycled mode, such as assist-control or IMV. "Cycling-off" of mechanical inflation, however, may be based only indirectly on volume. Instead, inspiratory flow is commonly preset and the ventilator adjusts inspiratory time to achieve a given tidal volume. This system is more precisely termed time-cycled ventilation. Inflation time is constant with a time-cycled machine, but patients invariably display considerable breath-to-breath variability in inspiratory time (27). Accordingly, a patient's neural inspiratory time may be shorter or longer than the inflation time of the machine. If the machine delivers the set tidal volume before the end of a patient's neural inspiratory time, ventilator assistance will cease while the patient continues to make an inspiratory effort—with double triggering (two ventilator breaths for a single effort) a likely consequence (28).

The algorithm for "cycling-off" of mechanical inflation during pressure support varies among brands, but most manufacturers employ some fall in inspiratory flow (29). With the Siemens 900C ventilator, inflation ceases when inspiratory flow decreases to 25% of the peak value; with the Puritan-Bennett 7200 ventilator (Mallinckrodt, Inc., St. Louis, MO), a decrease in flow to 5 L/min terminates inflation. Such algorithms are problematic in patients with chronic obstructive pulmonary disease, because increases in resistance and compliance produce a slow time-constant of the respiratory system. The longer time needed for flow to fall to the threshold value can cause mechanical inflation to persist into neural expiration. In 12 patients with chronic obstructive pulmonary disease receiving pressure support of 20 cm H₂O, five recruited their expiratory muscles while the machine was still inflating the thorax (30). Interestingly, the patients who recruited their expiratory muscles during mechanical inflation had an average time constant of 0.54 s, compared with an average of 0.38 s in the patients who did not exhibit expiratory muscle activity. The persistence of mechanical inflation into neural expiration is very uncomfortable, as is well recognized with use of inverse-ratio ventilation.

FURTHER IMPLICATIONS

The respiratory work performed by patients receiving partial ventilator assistance can be considerable. For example, when patients receive an IMV of 10 breaths/min or pressure support of 7 cm H₂O—common settings in clinical practice—inspiratory PTP can exceed 200 cm H₂O · s/min (3). Such inspiratory

effort may be sufficient to induce respiratory muscle fatigue or prevent its recovery. Unfortunately, physical examination and most monitoring modalities do not reliably detect such elevated respiratory work. With carefully selected settings, mechanical ventilation decreases respiratory work from intolerable levels to the normal range. Lowering patient effort into the normal range must be balanced against the greater likelihood of nontriggering and complications at high levels of assistance. Patients who are successfully weaned from mechanical ventilation have an elevated inspiratory PTP, averaging about 200 cm H₂O · s/min (2). Thus, the right target for patient effort during assisted ventilation is not known. It is also not known if decreasing patient effort to the normal range, or lower, predisposes to respiratory muscle deconditioning. Circumstantial evidence suggests that assisted ventilation—as opposed to controlled ventilation—is unlikely to produce respiratory muscle atrophy. Surprisingly little spontaneous activity is sufficient to prevent atrophy of a limb muscle (31). Moreover, a strategy requiring assist-control ventilation for at least 22 h a day has been shown to achieve more rapid weaning from mechanical ventilation than strategies employing graded levels of ventilator assistance (32, 33).

Future studies of patient-ventilator interaction need to address the mechanisms that determine synchronization of machine cycling with a patient's intrinsic respiratory rhythm (34). For example, the extent of synchronization may differ considerably during sleep versus wakefulness (35). Also, we need studies that define the level of unloading that avoids muscle fatigue while not fostering respiratory muscle atrophy. Lastly, better and simpler tools for monitoring patient effort are required.

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