Are There Benefits or Harm From Pressure Targeting During Lung-Protective Ventilation?

Neil R MacIntyre MD FAARC and Curtis N Sessler MD

Introduction
Design Features of Mechanical Breaths and the Potential Impact on Ventilator-Induced Lung Injury
The Case for Pressure Targeting
The Variable-Flow Feature of Pressure Targeting Enhances Patient-Ventilator Synchrony
Pressure-Targeted Ventilation Can Be in Accordance With the ARDS Network Strategy
The Case for Flow/Volume Targeting
Controlling Tidal Volume Has Been the Focus of Most Clinical Trials That Reduced VILI
It Is Easier to Limit Tidal Volume if You Set Tidal Volume
Head-to-Head Comparisons to Date Show No Obvious Advantages to Pressure Targeting Over Established Flow/Volume-Targeted Strategies

Summary
Mechanically, breath design is usually either flow/volume-targeted or pressure-targeted. Both approaches can effectively provide lung-protective ventilation, but they prioritize different ventilation parameters, so their responses to changing respiratory-system mechanics and patient effort are different. These different response behaviors have advantages and disadvantages that can be important in specific circumstances. Flow/volume targeting guarantees a set minute ventilation but sometimes may be difficult to synchronize with patient effort, and it will not limit inspiratory pressure. In contrast, pressure targeting, with its variable flow, may be easier to synchronize and will limit inspiratory pressure, but it provides no control over delivered volume. Skilled clinicians can maximize benefits and minimize problems with either flow/volume targeting or pressure targeting. Indeed, as is often the case in managing complex life-support devices, it is operator expertise rather than the device design features that most impacts patient outcomes. Key words: lung-protective mechanical ventilation; ventilator-induced lung injury; patient-ventilator synchrony; pressure-regulated volume control. [Respir Care 2010;55(2):175–180. © 2010 Daedalus Enterprises]
Introduction

The lung can be injured when it is stretched excessively by positive-pressure ventilation. This has been well demonstrated in numerous animal models, where excessive lung stretch during positive-pressure ventilation produced ventilator-induced lung injury (VILI) indistinguishable from acute lung injury (ALI) and the acute respiratory distress syndrome (ARDS). Importantly, VILI is more than just alveolar injury. VILI is associated with cytokine release and bacterial translocation that are implicated in the systemic inflammatory response and multiple-organ dysfunction that results in VILI-associated mortality.

The primary trigger for VILI appears to be physical over-stretch produced by excessive volume, rather than simply from the pressure applied. Illustrating this point is the classic study by Dreyfus et al, in which rat lungs exposed to high pressures and volumes were clearly injured, whereas rat lungs exposed to similar high pressures but with chest bindings that prevented volume expansion suffered no injury. Accordingly, Dreyfus and others emphasize regional hyperinflation from regional high-volume ventilation, or “volutrauma,” as the key cause of VILI.

More recently, several large clinical trials clearly demonstrated that limiting pressure and volume during mechanical ventilation reduces VILI and improves survival. These studies also suggested that VILI may be more than simply a consequence of excessive end-inspiratory stretch. For example, excessive tidal stretch (ie, repetitive cycling of the lung with tidal volume \(V_T > 9\) mL/kg), even in the setting of low end-inspiratory pressure, may also contribute to VILI. Other factors include frequency of stretch, the acceleration/velocity of stretch, and the shear stress phenomenon that occurs when injured alveoli are repetitively opened and collapsed during the ventilatory cycle (ie, cyclical atelectasis). Vascular pressure elevation may also contribute to VILI.

VILI probably develops regionally when low-resistance/high-compliance units receive a disproportionately high regional \(V_T\) in the setting of high alveolar distending pressure. Regional protection of these healthier lung units is the rationale for lung-protective ventilation strategies that focus on lower (and safer) distending pressures and volumes. Today, most clinicians agree that the principles of the ARDS Network low-\(V_T\) strategy should be applied to all patients with ALI/ARDS, and perhaps to all those at risk for ALI/ARDS. This lung-protective strategy is based on limiting the \(V_T\) to 4–8 mL/kg predicted body weight (PBW) and limiting the end-inspiratory stretching pressure (as reflected in the end-inspiratory plateau pressure \(P_{plat}\)) to < 30–35 cm H\(_2\)O. Importantly, these targets should be a higher priority than gas exchange, as long as pH is above 7.15 and \(P_{O_2}\) is above 55 mm Hg.

Design Features of Mechanical Breaths and the Potential Impact on Ventilator-Induced Lung Injury

On most modern mechanical ventilators the gasdelivery algorithm is one of 2 types: flow/volume-targeted, or pressure targeting with time or flow cycling (Fig. 1). With flow/volume targeting the clinician sets the inspiratory flow and the volume cycling criteria. Airway pressure is thus the dependent variable (ie, varies relative to lung mechanics and patient effort). With pressure targeting the clinician sets an inspiratory pressure target and either time or flow cycling criteria. Flow and volume are then the dependent variables (ie, vary relative to lung mechanics and patient effort). With pressure targeting the clinician sets an inspiratory pressure target and either time or flow cycling criteria. Flow and volume are then the dependent variables (ie, vary relative to lung mechanics and patient effort). With flow/volume targeting, changes in compliance, resistance, or patient effort will change airway pressure, but not flow. In contrast, with pressure targeting, changes in compliance, resistance, or effort will change flow and \(V_T\), but not airway pressure.

An important clinical question is whether the pressure-targeted modes have advantages over the more traditional flow/volume-targeted modes. For example, in the presence of an active patient inspiratory effort, pressure targeting, with its variable flow, may enhance comfort and thereby reduce sedation requirements, which could accelerate the ventilator-withdrawal process. One could also speculate that pressure targeting might provide a more reliable end-inspiratory pressure limit than a flow-targeted/volume-cycled breath, and this may have utility in patients with worsening mechanics. However, in a patient with improving mechanics or increasing effort, a fixed pressure target may result in an excessive \(V_T\). Arguments for pressure targeting versus flow/volume targeting are presented in more detail below.
The Case for Pressure Targeting

The Variable-Flow Feature of Pressure Targeting Enhances Patient-Ventilator Synchrony

Patient-ventilator interactions may become increasingly difficult to synchronize when the flow (and volume) delivery from the ventilator is reduced to protect the lung. Under these circumstances, patient flow demand may exceed the clinician-set flow pattern, resulting in dysynchronous interactions and excessive inspiratory muscle loading.18-20 Indeed, clinical studies have shown that reducing ventilator flow delivery during assisted breaths often increases muscle loading and dyspnea.21-27 It would thus seem reasonable that a small-VT strategy with a variable-flow, pressure-targeted mode might be more synchronous than a fixed-flow, flow/volume-targeted mode.28

Clinical studies have shown that variable-flow pressure-targeted breaths often improve patient-ventilator synchrony, compared to fixed-flow volume/volume-targeted breaths.26-29 In a study of the effects of V̇ₚ, Cinnella et al compared flow/volume-targeted ventilation with pressure-targeted ventilation at moderate (8 mL/kg) and high (12 mL/kg) V̇ₚ.26 They found that pressure-targeted ventilation reduced patient work of breathing and improved synchrony during moderate V̇ₚ, but not during high V̇ₚ. Kallet et al found, in patients with ALI and ARDS, that patient work of breathing was reduced approximately 15% with pressure-targeted ventilation, compared to flow/volume-targeted ventilation, at comparable levels of respiratory drive and minute ventilation.27 Yang et al found, in patients with ALI and small-VT ventilation, that pressure-targeted ventilation yielded better dyssynchrony scores and a slower respiratory rate than flow/volume-targeted ventilation.29 Interestingly, this slower rate resulted in less intrinsic positive end-expiratory pressure (PEEP), which is itself a factor for dyspnea and assisted breath triggering delays.

Pressure-Targeted Ventilation Can Be in Accordance With the ARDS Network Strategy

Pressure-targeted ventilation can provide small-VT, pressure-limited ventilation with all of the features of the ARDS Network algorithm.8 Specifically, inspiratory pressure can be set to deliver a V̇ₚ of 4–8 mL/kg PBW and a Pplat < 30–35 cm H₂O. Set breathing frequencies, inspiratory/expiratory ratios, and expiratory pressure settings can also all mimic the ARDS Network protocol. Moreover, the set pressure limit will automatically decrease V̇ₚ in the setting of worsening mechanics, in accordance with the ARDS Network’s algorithm.

However, as noted above, there are 2 theoretical concerns about the use of pressure-targeted breaths to provide the ARDS Network lung-protective strategy: excessive V̇ₚ in the setting of improving mechanics, and excessive V̇ₚ if the patient makes vigorous efforts. The importance of these issues and their management are addressed below.

While pressure targeting will limit end-inspiratory pressure in the setting of worsening lung mechanics (a potential benefit), the converse is also true: it will also allow an increase in V̇ₚ if mechanics improve (a potential harm). An upper-V̇ₚ-limit alarm can mitigate this effect. Alternatively, many modern ventilators can provide a volume feedback mechanism to adjust the inspiratory pressure target within a certain range (various trade names include pressure-regulated volume control, auto-flow, and volume assist). The clinician sets the desired V̇ₚ, and the ventilator adjusts the pressure target to achieve that volume. With these modes, worsening mechanics will increase the pressure target, and improving mechanics will lower the pressure target. Conceptually these algorithms provide the volume guarantee of the volume-cycled breath combined with the variable-flow feature of the pressure-targeted breath. A more complex variant of these feedback modes is adaptive support ventilation, which uses a “minimal work” calculation to adjust pressure-targeted breaths.

Similar to the effects of improving mechanics, there is concern that strong patient efforts during pressure targeting will increase V̇ₚ to an excessive level. While this can certainly be true, there are 3 reasons this may not be an important down side to pressure targeting. First, this phenomenon generally occurs in the recovery phase of lung injury, when patient strength and respiratory drive are recovering. It is important that the clinician recognize that recovery and reduce the inspiratory pressure setting to as low as possible (eg, 5 cm H₂O), and then strongly consider whether ventilatory support is still required. Indeed, in one study that raised this large-V̇ₚ concern,26 the minimal pressure applied to those patients (10 cm H₂O) may have been excessive. Second, if a patient has a strong drive during pressure targeting, he or she is likely also to have it during flow/volume targeting. In the latter situation, V̇ₚ is limited but the “flow hunger” without a ventilator response will often require extra sedation, which may not be desired. Third, the feedback control modes of pressure targeting described above might address this issue by providing variable flow while automatically minimizing the inspiratory pressure.

Any time a mechanically ventilated patient has an increased respiratory drive, it is important to assess the etiology. If it is due to recovery, as described above, the drive should certainly not be blunted with sedation, and the need for the current level of mechanical support should be re-evaluated. On the other hand, if the increased respiratory drive is from pain, agitation, or some inappropriate respiratory system stimulus (eg, dyspnea), treating the source (including sedation/opioids), along with avoiding either
inappropriate manual or automatic reductions in ventilatory support, would be important.

**The Case for Flow/Volume Targeting**

**Controlling Tidal Volume Has Been the Focus of Most Clinical Trials That Reduced VILI**

As discussed earlier, classic studies that explored the relative roles of alveolar hyperinflation versus excessive transpulmonary pressure by modifying extrathoracic or pleural pressure provided important evidence that lung injury occurs with lung hyperinflation, regardless of the inflation pressure (ie, excessive airway pressure not accompanied by alveolar over-distention is not injurious). These findings support a strategy in which control of $V_T$ should take precedence over control of inspiratory pressure. As a consequence, most clinical trials of lung-protective principles, including the pivotal ARDS Network randomized controlled trial, have specifically targeted $V_T$ with flow/volume-targeted continuous mandatory ventilation. In those trials, low $V_T$ was generally accompanied by acceptable $P_{plat}$. For example, Roupie et al found, in patients with ARDS, that when $V_T$ was set at 6.5 mL/kg, only 10% of the patients had $P_{plat}$ that exceeded the upper inflection point (oversretch point) on the pressure-volume curve. Importantly, most of these studies provided for further clinician-set $V_T$ reduction if $P_{plat}$ was judged excessive (> 30–35 cm H$_2$O).

**It Is Easier to Limit Tidal Volume if You Set Tidal Volume**

Restricting $P_{plat}$ to < 30–35 cm H$_2$O with a pressure-targeted strategy does not reliably guarantee low $V_T$. For example, in a secondary analysis of data from the ARDS Network low-$V_T$ trial, Hager et al found that 50% of the patients randomized to 12 mL/kg $V_T$ had $P_{plat}$ ≤ 31 cm H$_2$O on day 1, and they found a benefit from $V_T$ reduction from 12 mL/kg to 6 mL/kg PBW regardless of $P_{plat}$ before the $V_T$ reduction. Their analysis of those data and review of other clinical studies and animal experiments led them to conclude that there is no “safe” $P_{plat}$ below which the benefit of $V_T$ reduction disappears.

In attempting to provide small-$V_T$, lung-protective ventilation, Kallet et al found that with pressure-targeted ventilation $V_T$ “markedly” exceeded the $V_T$ target of 6 mL/kg PBW in 40% of patients with ALI/ARDS—twice the rate observed with flow/volume-targeted ventilation. Interestingly, the volume feedback mode, pressure-regulated volume control, yielded similar results to pressure-targeted ventilation: 40% of the patients had low-$V_T$ violations.

Regardless of the ventilation mode, it is likely that clinician adjustment of ventilator settings to achieve other goals, such as correcting hypoxemia or reducing patient-ventilator dysynchrony, could violate the low-$V_T$ goal. With pressure targeting one would adjust inspiratory pressure and/or inspiratory time, secondarily impacting $V_T$. In contrast a flow/volume-targeted setting adjustment would require an explicit change in $V_T$ to violate this key target—an adjustment that clinicians may be more reluctant to make.

Similar efficacy among approaches may not necessarily translate into equivalent effectiveness when research results are applied at the bedside. There is considerable evidence that clinicians have not reliably applied low-$V_T$ ventilation. Indeed, in a survey of intensive care respiratory therapists and nurses, Rubenfeld et al identified “unwillingness to relinquish ventilator control” as a primary barrier to initiating lung-protective ventilation.

With a written protocol, however, clinician adherence to low-$V_T$ strategies seems to be improved. This particular protocol focused on defining the proper $V_T$, based on PBW, in an explicit manner, which is important, because successful implementation of new treatment algorithms requires simplicity and familiarity. Explicitly setting $V_T$, rather than setting airway pressure and repeatedly measuring $V_T$, is certainly simpler and thus seems intuitively advantageous for achieving widespread adoption. This would be especially true in a clinical setting where a particular mode, such as flow/volume-targeted ventilation, has been used traditionally and clinical expertise with that mode is high.

**Head-to-Head Comparisons to Date Show No Obvious Advantages to Pressure Targeting Over Established Flow/Volume-Targeted Strategies**

Very few studies have directly compared flow/volume-targeted and pressure-limited strategies for lung-protective ventilation in ARDS, and most have had confounding issues. The most extensive study was performed recently by Meade et al, who compared these approaches in a large international multicenter randomized controlled trial. The objective was to compare the flow/volume-targeted lung-protective ventilation of the ARDS Network strategy to the pressure-targeted lung-protective ventilation strategy used by Amato et al, which provided $V_T$ of 6 mL/kg PBW and an aggressive PEEP strategy. These 2 approaches yielded no difference in 28-day mortality (32.3% vs 28.4%, respectively, $P = .20$) or in barotraumas (9.1% vs 11.2%, $P = .33$). Though outcomes were similar, it is important to consider that the primary goal of both approaches was $V_T$ of 6 mL/kg PBW, and that there were important differences beyond pressure targeting versus flow/volume targeting (ie, higher PEEP and higher $P_{plat}$ in the pressure-targeted group), confounding the comparison.
It is often stated that pressure targeting is more synchronous than flow/volume targeting, but not all clinical trial results have supported that notion. Chiumello et al. found, in patients with acute respiratory failure, that when the peak inspiratory flow during flow/volume-targeted ventilation was properly adjusted to support a given VT, there were no differences in work of breathing or airway occlusion pressure 0.1 s after the onset of inspiratory effort, compared to pressure-targeted ventilation. Kallet also found, in a group of patients with ALI receiving small VT, that pressure-targeted ventilation had patient work reduction similar to that obtained with carefully titrated flow/volume-targeted ventilation. Taken together, these studies suggest that if pertinent mechanical parameters (eg, peak flow and VT) are adjusted properly by skilled clinicians, flow/volume targeting can produce patient-ventilator synchrony similar to that with pressure targeting in many patients.

**Summary**

Both pressure-targeted and flow/volume-targeted modes can effectively provide lung-protective ventilation. However, these modes prioritize different parameters, so their behavior under changing respiratory-system mechanics and patient effort is different. Both modes have advantages and disadvantages (Table 1) that can be important in specific circumstances, and skilled clinicians can maximize benefits and minimize problems with either mode. Indeed, as is often the case in managing complex life-support devices, it is the expertise of the operator, rather than the device design features, that most impact patient outcomes.

### Table 1. Pressure-Targeted Versus Flow/Volume-Targeted Ventilator Breaths

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{\text{plat}}$</td>
<td>Limits $P_{\text{plat}}$ in low compliance/high resistance</td>
<td>Reduces $P_{\text{plat}}$ in high compliance/low resistance</td>
<td>Reduces $P_{\text{plat}}$ in high compliance/low resistance</td>
</tr>
<tr>
<td>Good</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bad</td>
<td>Maintains $P_{\text{plat}}$ in high compliance/low resistance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V_T$</td>
<td>Reduces $V_T$ in low compliance/high resistance</td>
<td>Maintains $V_T$ in high compliance/low resistance</td>
<td>Maintains $V_T$ in high compliance/low R</td>
</tr>
<tr>
<td>Good</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bad</td>
<td>Increases $V_T$ in high compliance/low resistance</td>
<td>Maintains $V_T$ in low compliance/low resistance</td>
<td>Maintains $V_T$ in low compliance/low resistance</td>
</tr>
<tr>
<td>Increase $V_T$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-Ventilator Synchrony</td>
<td>Variable flow can help</td>
<td>Fixed flow can harm</td>
<td>Variable flow can help</td>
</tr>
</tbody>
</table>

$P_{\text{plat}} = \text{plateau pressure}$  
$V_T = \text{tidal volume}$

### REFERENCES


Discussion

MacIntyre: One thing you didn’t bring up is that, while we both were addressing the issues of V_T going higher as patient effort got better or as compliance got better, the flip side is that if compliance decreases and the lung gets stiffer, volume-targeted ventilation will drive the plateau pressure higher and higher, whereas a pressure-targeted mode will decrease the V_T.

Hess: I have several questions. You used the terms dysynchrony and discomfort interchangeably; do we have any data that patients who are dysynchronous are necessarily uncomfortable?

MacIntyre: You’re right, that was probably an oversimplification on my part. I think the two are correlated, but I think it is possible to be a bit out of sync with the ventilator but not know it and therefore not be uncomfortable. I think there are other factors that can make patients uncomfortable that really have little to do with dysynchrony, but, having conceded some of your point, I would argue that dysynchrony and discomfort are often found together.
Hess: That brings me to my second question. If your \( V_T \) and my \( V_T \) are 6 mL/kg, why is it that if you intubate me and you put me on the ventilator, and you ventilate me with 6 mL/kg, that I should suddenly be more comfortable with a larger \( V_T \) and less dysynchronous with a larger \( V_T \) if that’s what my \( V_T \) should be to begin with?

MacIntyre: You bring up an interesting point, and it’s a very complicated topic. Setting the frequency-\( V_T \) pattern is not just a mechanical function, there are cortical functions, stretch receptors, blood-gas receptors, pH receptors, and muscle receptors that all come into play. When you injure the lung—make it stiffer or more obstructive—or irritate the airway or impose a high-resistance device, those factors also come into play. So the ideal mechanical \( V_T \), which we think is around 6 mL/kg based on mechanical factors, may be completely overwhelmed by all these other inputs into the respiratory drive that can create a demand for a higher flow or a higher \( V_T \) than we might otherwise want.

Hess: Let me suggest that if I get ARDS and you intubate me, I have a higher dead space. I have a higher \( CO_2 \) production if I’m a little septic, and that makes me acidic. I think that acidosis can be what drives me to want to have a higher \( V_T \). One thing that I have found very effective many times when patients are dysynchronous with the ARDS Network is to just dial up the rate to the point where the patient seems to be getting better. For example, we have a protocol to reduce \( V_T \) to 35 breaths/min.

MacIntyre: Or whatever it took before substantial air-trapping started to develop.

Hess: Just anecdotally, a mistake that I’ve seen (though not as much any more) when clinicians set up ARDS Network ventilation is that they turn down the \( V_T \) and leave the respiratory rate setting where it was, and patients would get very dyssynchronous.

MacIntyre: Fair point.

Gay: While I respect the idea that we can tolerate larger \( V_T \) when the patient seems to be getting better in the pressure-support mode, I would ask you this: how good are we at seeing when somebody’s getting ARDS, much less when somebody’s getting better from ARDS? I’m struck by Ogie Gajic’s data: he keeps a very robust database for us, and he looked at patients 48 hours before they were actually diagnosed with ARDS. The patients who were on non-ARDS higher \( V_T \) had a much higher mortality, even if they were switched to low \( V_T \) when ARDS was eventually diagnosed. So if we have as much trouble figuring out when they’re getting better from ARDS as we do deciding when they get ARDS, how are we going to feel comfortable with your kind of strategy?

MacIntyre: The ARDS Network rule for acidosis was to increase frequency in an effort to protect the \( V_T \), so I would argue that, while you may have to increase \( V_T \), the ARDS Network protocol said that if acidosis was deemed to be an issue, you could increase the \( V_T \), but it also recommended going with frequency first.

MacIntyre: You bring up a very good point. Peter. The Mayo Clinic studies are fascinating because they started off looking at the intubated patients who did not have ARDS and were interested in who would develop ARDS on the ventilator, and the original studies showed that \( V_T \) was far the strongest predictor. The second strongest predictor was transfusions. They instituted a protocol to reduce \( V_T \) in everybody, not just ARDS patients, and the rate of developing ARDS on the ventilator went down.

My way of looking at this is that lung protection is not about trying to protect the sick lung regions, but the healthier lung regions. If we get too hung up and too zealous about trying to open up and recruit sick, atelectatic, flooded alveoli, we tend to forget the healthy alveoli elsewhere in the lung that may be over-distended. If you buy into that concept, it makes sense that you should apply lung-protective ventilation to everybody, because whether they’re obstructed, or had a stroke, or have unilateral or lobar pneumonias, you’re trying to protect the healthier lung regions, so reducing the \( V_T \) and plateau pressure in virtually everybody makes sense.


Siobal: At San Francisco General we use a computerized charting system. As soon as you type in the \( V_T \), it calculates their mL/kg for ideal body weight, so it’s staring you in the face every time you chart it. So in our practice now we very rarely see patients over 8 mL/kg, and if it gets above 10 mL/kg, that’s staring you in the face and you tend to lower it. Our
defaults are between 6 and 8 mL/kg now when we set somebody up on the ventilator. But we don’t calculate it for spontaneous breathing, which we probably should.

**MacIntyre:** Yes. During spontaneous and assisted breaths we tend not to be rigorous about that. People say, “Well, they’re getting 10 mL/kg,” and my response is, at least don’t make it worse: turn the pressure-support down to as low as 5 cm H2O, and if the patient still insists on 10 mL/kg, you have to either sedate them to blunt the respiratory drive, or live with it and perhaps take the tube out. I don’t see any other way around it. I prefer to take the tube out.

**Sessler:** I think the dyssynchrony issues are more complex than we sometimes state, and we tend to lump together the types of dyssynchrony. The most common dyssynchrony is ineffective triggering.

**MacIntyre:** Right.

**Sessler:** Double-triggering is the next most common. But those are opposite extremes. If one has higher VT or more intrinsic PEEP or whatever, we’ve got more ineffective triggering, but we’ve all seen more double-triggering with the lower-VT ventilation, and as we give them a little more VT or make some subtle adjustments we can eliminate that. Pohlman et al looked at a very high rate of double-triggering in some patients receiving low-VT ventilation, and how that often resulted in very high cumulative VT for that paired breath. This may be a marker—something to keep an eye out for—in terms of violation of the low-VT strategy.


**MacIntyre:** We were focusing on what we call flow dyssynchrony. But triggering dyssynchrony and cycling dyssynchrony are as important, and in some patients even more important. One of the beauties of pressure-targeted modes is that you can extend the inspiratory time to try to get more in touch with the patient’s spontaneous inspiratory time and improve cycling synchrony. Similarly, you can adapt the flow-cycling setting for pressure support.

**Fessler:** I think this issue of patient comfort and dyssynchrony is quite important. We’ve gotten comfortable with the tradeoffs between oxygenation and lung protection, but there’s another tradeoff, I think, between sedation and lung protection. We’ve all alluded to the fact that to strictly adhere to a lung-protective strategy often requires more sedation. Most of the flow receptors in a human are in the nose and the larynx, which are bypassed by the endotracheal tube, so it’s not immediately apparent that changing the flow pattern is going to relieve a patient’s dyspnea, particularly if they’re still getting a VT that’s smaller than their stretch receptors want, or if they’re still acidotic. I think this issue needs to be clarified.

**MacIntyre:** I agree the tube bypasses some of the receptors, but there are receptors in the chest wall, muscles, and lung as well, which I think are affected by a host of factors. One approved proportional-assist ventilator is designed to keep up with patient flow and volume demands. One concern is that you lose control of the VT with that approach. Again, there are tradeoffs here.

**Branson:** I have 3 questions. First, people ask me, “Does the VT in the patient actually matter if the plateau pressure stays less than 25 cm H2O?” Second, in pressure-control ventilation, when the patient’s VT goes higher it’s because of patient effort, and doesn’t the patient’s muscle effort improve the distribution of ventilation and potentially reduce VILI for a given VT? Third, Curt mentioned that recent paper about dyssynchrony index and duration of ventilation, but it’s another one of those things where we don’t really know if it’s cause and effect. Is the patient really sick and therefore dyssynchronous and therefore on the ventilator for a long time, or does the dyssynchrony keep them on the ventilator for a long time?


**MacIntyre:** Those are very provocative questions. I’ll give you my take. I agree with Curt; I’m not convinced there is a safe plateau pressure. We argued this at our first respiratory controversies Journal Conference. I think the ARDS Network data, when divided by quartiles, suggest that even with plateau pressure down in the teens there still seemed to be a benefit to having a smaller VT.

Regarding the distribution of VT with patient effort, yes, Dr Habashi at the Cowley Shock Trauma Center at University of Maryland, and his APRV [airway pressure-release ventilation] folks would argue vehemently that spontaneous efforts do distribute gases in the lung better. I think some data support that notion.

You brought up another point, though, Rich, which is, if a patient adds pressure from the muscle side and you’re adding pressure from the ventilator side, those two work together to create the actual end-inspiratory transpulmonary pressure, so if the ventilator is supplying 20 cm H2O and the patient is pulling 15 cm H2O, that is a transpulmonary pressure of 35 cm H2O. I think APRV supporters tend to forget that those set inflation pressures are the end-inspiratory distending pressure of the lung. They ignore the fact that the ap-
plied pressure adds to the negative pressure to create the total transpulmonary pressure. So I have at least a theoretical concern with that.

And regarding whether dyssynchrony results in poor outcomes, one study suggested that bad dyssynchrony does correlate with longer time on the ventilator and maybe even higher mortality, although the difference was not statistically significant. At the very least, I think that dyssynchrony leads to more sedation, and I think you could argue at least circumstantially that that is likely to delay getting the patient off the ventilator.


**Epstein:** One study showed that the more sedated you are, the more ineffective efforts you make, probably because of reduction in drive. The clinical importance is uncertain. Another paper found that patients who had more ineffective triggering had a longer duration of mechanical ventilation and shorter 28-day ventilator-free survival. That was ineffective triggering measured in the first 24 hours of mechanical ventilation. It’s not clear which is the cart and which is the horse.


**Branson:** Scott, I reviewed that paper, and I think the number-one cause of ineffective triggering is intrinsic PEEP. The cart and the horse are still undecided for me. In our surgical population, with very few COPD [chronic obstructive pulmonary disease] patients, we see very few ineffective triggers, unless there’s too much pressure support and the VT is too large and the patient doesn’t have time to exhale.


**Epstein:** That study had no patients with COPD.

**Branson:** Right, that’s my point, I just don’t see many missed triggers in patients who don’t have obstructive lung disease.

**Sessler:** It’s an interesting observation. I can’t think of a plausible mechanism by which ineffective triggering—let’s say 10–20% ineffective triggers—would increase your likelihood of dying. So to me it seems like it is an independent marker if you factor in APACHE [Acute Physiology and Chronic Health Evaluation] scores and everything else, but I think the cause is unclear.

**Epstein:** There is a mechanism whereby it could injure the diaphragm. When a muscle contracts but simultaneously lengthens (that’s called an eccentric contraction), that injures the muscle. That is what might happen during an ineffective triggering, as the muscle is trying to contract but cannot shorten, and may lengthen if this occurs during expiration.

**Siosis:** I think triggering might be a good thing for patients who are going to be on the ventilator for a long time, because it may keep the diaphragm toned, so weaning might be easier.

**Siobal:** I think triggering might be a good thing for patients who are going to be on the ventilator for a long time, because it may keep the diaphragm toned, so weaning might be easier.

**Maclntyre:** I side a little bit with Scott on this one, because I don’t think we appreciate the triggering difficulties as much as we should. It can be subtle, and these little feeble efforts by the diaphragm may not even be appreciated by the clinician; it’s only when you have an EMG [electromyogram] or an esophageal balloon in there that you can see what’s really going on.

**Branson:** I keep looking at new triggers, and there have been at least 3 case reports in which a brain-dead patient was not taken off the ventilator because the heartbeat was triggering the ventilator. Well, how much more sensitive does it need to be? And then we have NAVA [neurally adjusted ventilatory assist], which is not just triggering but also controlling the breath, which is probably more important. We worry about dyssynchrony, but I’m not sure it’s a cause and effect.

**Maclntyre:** I think the reason dyssynchrony is associated with adverse outcomes is not necessarily the dyssynchrony itself, although I accept Scott’s notion that may be there is damage. I think it just drives us to put more and more sedation on these patients to make them look better, and then it’s just that much more difficult to get them off. They get stuck on the ventilator.