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

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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.

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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).[1-3] Importantly, VILI is more than just alveolar injury. VILI is associated with cytokine release[4,5] and bacterial translocation[6] 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.[7] Accordingly, Dreyfuss and others emphasize regional hyperinflation from regional high-volume ventilation, or "volutrauma," as the key cause of VILI.[3,7]

More recently, several large clinical trials clearly demonstrated that limiting pressure and volume during mechanical ventilation reduces VILI and improves survival.[8-11] 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.[11] Other factors include frequency of stretch,[12] the acceleration/velocity of stretch,[13] and the shear stress phenomenon that occurs when injured alveoli are repetitively opened and collapsed during the ventilatory cycle (ie, cyclical atelectasis).[14,15] Vascular pressure elevation may also contribute to VILI.[16]

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.[17] 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[8] 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_2O. 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.

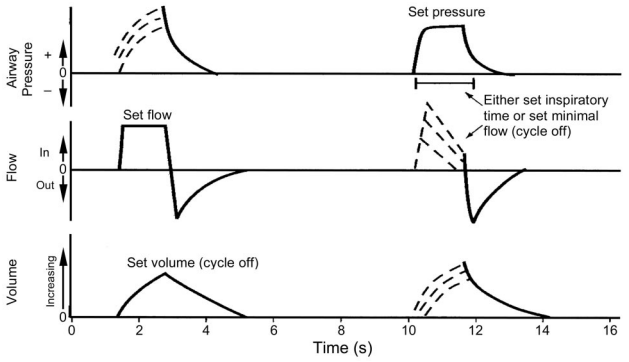

Fig. 1. Breath design. The left-hand curves depict a flow/volume-targeted breath. The right-hand curves depict a pressure-targeted breath. The solid lines indicate clinician-set ventilation parameters. The dashed lines indicate ventilation parameters affected by respiratory-system mechanics and patient effort.

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

On most modern mechanical ventilators the gas-delivery algorithm is one of 2 types: flow/volume targeting, 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 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 dyssynchronous 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-V_T 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 flow/volume-targeted breaths.[26-29] In a study of the effects of V_T, Cinnella et al compared flow/volume-targeted ventilation with pressure-targeted ventilation at moderate (8 mL/kg) and high (12 mL/kg) V_T.[26] They found that pressure-targeted ventilation reduced patient work of breathing and improved synchrony during moderate V_T, but not during high V_T. 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-V_T 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-V_T, pressure-limited ventilation with all of the features of the ARDS Network algorithm.[8] Specifically, inspiratory pressure can be set to deliver a V_T of 4–8 mL/kg PBW and a $P_{plat} < 30–35$ cm H_2O. 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 V_T 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 V_T in the setting of improving mechanics, and excessive V_T 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 V_T if mechanics improve (a potential harm). An upper-V_T-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 V_T, 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 V_T 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 H_2O), and then strongly consider whether ventilatory support is still required. Indeed, in one study that raised this large-V_T concern,[30] the minimal pressure applied to those patients (10 cm H_2O) 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, V_T 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 reevaluated. 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).[7] 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,[8] 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 (overstretch point) on the pressure-volume curve.[31] Importantly, most of these studies provided for further clinician-set V_T reduction if P_{plat} was judged excessive ($> 30–35$ cm H_2O).

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

Restricting P_{plat} to $< 30–35$ cm H_2O 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 $P_{plat} \leq 31$ cm H_2O on day 1,[32] 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.[30] 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 dyssynchrony, 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.[33,34] 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.[35]

With a written protocol, however, clinician adherence to low-V_T strategies seems to be improved.[36] 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,[37] 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[8] to the pressure-targeted lung-protective ventilation strategy used by Amato et al,[10] 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.

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

	Pressure-Targeted	Flow/Volume-Targeted	Pressure-Regulated Volume-Control/Volume Support
P_{plat}			
Good	Limits P_{plat} in low compliance/high resistance	Reduces P_{plat} in high compliance/ low resistance	Reduces P_{plat} in high compliance/ low resistance
Bad	Maintains P_{plat} in high compliance/ low resistance	Increases P_{plat} in low compliance/ high resistance "Sucked down" with effort	Increases P_{plat} in low compliance/ high resistance
V_T			
Good	Reduces V_T in low compliance/high resistance	Maintains V_T in high compliance/ low resistance	Maintains V_T in high compliance/ low R
Bad	Increases V_T in high compliance/low resistance Increases V_T with great patient effort	Maintains V_T in low compliance/ high resistance	Maintains V_T in low compliance/ high resistance
Patient-Ventilator Synchrony			
Good	Variable flow can help		Variable flow can help
Bad		Fixed flow can harm	

P_{plat} = plateau pressure
V_T = tidal volume

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[23] 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 V_T, 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 V_T, that pressure-targeted ventilation had patient work reduction similar to that obtained with carefully titrated flow/volume-targeted ventilation.[30] Taken together, these studies suggest that if pertinent mechanical parameters (eg, peak flow and V_T) 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.

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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. That, of course, is what the ARDS Network protocol says to do: if the pressure is too high you're supposed to reduce the V_T.

Hess: I have several questions. You used the terms dyssynchrony and discomfort interchangeably; do we have any data that patients who are dyssynchronous 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 synch 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 dyssynchrony, but, having conceded some of your point, I would argue that dyssynchrony 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 dyssynchronous 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 acidotic. 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 dyssynchronous with the ARDS Network is to just dial up the rate to the point where the patient is not as acidotic, and they get more synchronous with the ventilator.

MacIntyre: So you're trading synchrony for lung protection.

Hess: I'm saying that, many times, if you dial up the V_T and get rid of the acidosis, the dyssynchrony can go away.

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.

Hess: All the way up 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;[1] 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?

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MacIntyre: You bring up a very good point, Peter. The Mayo Clinic studies[1,2] 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 by 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.

1. Gajic O, Dara SI, Mendez JL, Adesanya AO, Festic E, Caples SM, et al. Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. Crit Care Med 2004;32(9):1817-1824.
2. Yilmaz M, Keegan MT, Iscimen R, Afessa B, Buck CF, Hubmayr RD, Gajic O. Toward the prevention of acute lung injury: protocol-guided limitation of large V_T ventilation and inappropriate transfusion. Crit Care Med 2007;35(7):1660-1667.

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/H_2O, 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 V_T or more intrinsic PEEP or whatever, we've got more ineffective triggering, but we've all seen more double-triggering with the lower-V_T ventilation, and as we give them a little more V_T 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-V_T ventilation, and how that often resulted in very high cumulative V_T for that paired breath.[1] This may be a marker—something to keep an eye out for—in terms of violation of the low-V_T strategy.

1. Pohlman MC, McCallister KE, Schweickert WD, Pohlman AS, Nigos CP, Krishnan JA, et al. Excessive V_T from breath stacking during lung-protective ventilation for acute lung injury. Crit Care Med 2008; 36(11):3019-3023.

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 V_T 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 V_T with that approach. Again, there are tradeoffs here.

Branson: I have 3 questions. First, people ask me, "Does the V_T in the patient actually matter if the plateau pressure stays less than 25 cm H_2O?" Second, in pressure-control ventilation, when the patient's V_T 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 V_T? Third, Curt mentioned that recent paper[1] 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?

1. Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive Care Med 2006; 32(10):1515-1522.

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.[1,2] 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 V_T.

Regarding the distribution of V_T 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 H_2O and the patient is pulling 15 cm H_2O, that is a transpulmonary pressure of 35 cm H_2O. 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[3] 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.

1. Respiratory controversies in the critical care setting: part I. Respir Care 2007;52(4): 406-493.
2. Respiratory controversies in the critical care setting: part II. Respir Care 2007; 52(5):494-645.
3. Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. Intensive Care Med 2006; 32(10):1515-1522.

Epstein: One study showed that the more sedated you are, the more ineffective efforts you make, probably because of reduction in drive.[1] 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.[2] 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.

1. de Wit M, Pedram S, Best AM, Epstein SK. Observational study of patient-ventilator asynchrony and relationship to sedation. J Crit Care 2009;24(1):74-80.
2. de Wit M, Miller KB, Green DA, Ostman HE, Gennings C, Epstein SK. Ineffective triggering predicts increased duration of mechanical ventilation. Crit Care Med 2009;37(10):2740-2745.

Branson: Scott, I reviewed that paper,[1] 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 V_T is too large and the patient doesn't have time to exhale.

1. de Wit M, Miller KB, Green DA, Ostman HE, Gennings C, Epstein SK. Ineffective triggering predicts increased duration of mechanical ventilation. Crit Care Med 2009;37(10):2740-2745.

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.

Gentile: Ineffective triggering we don't see much any more because everybody is on flow triggering and the ventilators have gotten much better. Even in COPD patients we don't see a lot of ineffective triggering any more.

I don't think many people would disagree that lung protection is good, but we're trying to balance it now. Some people mention the sedation thing. When the ARDS Network trial was done, everybody was put on a set rate, but sedation practices have changed; people are triggering much earlier in their ventilator course if they're on a rate at all. Some people go on a PEEP of 10 cm H_2O and a pressure of 12 cm H_2O for their entire ventilator course, so that is the most difficult thing—trying to control for V_T when the patient is "driving the car."

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.

MacIntyre: 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.

MacIntyre: 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.