Does Airway Pressure Release Ventilation Offer Important New Advantages in Mechanical Ventilator Support?

Timothy R Myers RRT-NPS and Neil R MacIntyre MD FAARC

Airway pressure-release ventilation (APRV) is a mechanical ventilation strategy that is usually time-triggered but can be patient-triggered, pressure-limited, and time-cycled. APRV provides 2 levels of airway pressure (P_{high} and P_{low}) during 2 time periods (T_{high} and T_{low}), both set by the clinician. APRV usually involves a long T_{high} and a short T_{low}. APRV uses an active exhalation valve that allows spontaneous breathing during both T_{high} and T_{low}. APRV typically generates a higher mean airway pressure with a lower tidal volume (V_T) and lower positive end-expiratory pressure than comparable levels of other ventilation strategies, so APRV may provide better alveolar recruitment at a lower end-inflation pressure and therefore (1) decrease the risk of barotrauma and alveolar damage in patients with acute lung injury or acute respiratory distress syndrome (ALI/ARDS), and (2) provide better ventilation-perfusion matching, cardiac filling, and patient comfort than modes that do not allow spontaneous breaths. However, if the patient makes a spontaneous breath during T_{high}, the V_T generated could be much larger than the clinician-set target V_T, which could cause the end-inflation transpulmonary pressure and alveolar stretch to be much larger than intended or produced in other ventilation strategies. It is unknown whether a patient's inspiratory effort (and consequent larger V_T) can damage alveoli in the way that mechanically delivered, positive-pressure breaths can damage alveoli in ALI/ARDS. Other ventilation modes also promote spontaneous breaths, but at overall lower end-inflation transpulmonary pressure. There is a dearth of data on what would be the optimal APRV inspiratory-expiratory ratio, positive end-expiratory pressure, or weaning strategy. The few clinical trials to date indicate that APRV provides adequate gas exchange, but none of the data indicate that APRV confers better clinical outcomes than other ventilation strategies. *Key words: airway pressure release ventilation, mechanical ventilation.* [Respir Care 2007;52(4):452–458.

Introduction

Mechanical ventilation is utilized to provide respiratory support for patients who are incapable of maintaining adequate gas exchange unassisted. The basic goals and objectives of mechanical ventilation are well established, and the clinical challenge is to provide adequate support while avoiding lung injury and other adverse effects.[1] Over the last 85 years, approaches to providing mechanical ventilatory support have evolved from simple mimicking of the normal respiratory pattern to applications of sophisticated flow waveforms, inflation/deflation timing, interactive capabilities, lung-recruitment techniques, and the concept of maintaining alveolar patency during exhalation with positive end-expiratory pressure (PEEP). While many of these innovations produce physiologic benefit, interestingly, only the concept of reducing tidal volume (V_T) and end-inflation distending pressure has been shown to improve mortality.[2]

Airway pressure-release ventilation (APRV) is a relatively recent innovation, first described by Stock et al[3] in 1987, and available in the United States since the mid-1990s. APRV can be classified as a time-triggered (and potentially patient-triggered), pressure-limited, time-cycled ventilation mode (Fig. 1). In essence, APRV provides 2 levels of airway pressure (P_{high} and P_{low}) during 2 set time periods (T_{high} and T_{low}). Although most ventilators provide a wide range of potential T_{high} and T_{low} settings, APRV strategies usually involve a long T_{high} and a short T_{low}. Because of this, many think of APRV as a ventilation mode that basically sets a level of continuous positive airway pressure that intermittently time-cycles to a lower airway pressure. A feature of APRV that distinguishes it from older forms of pressure-limited long-inflation-time ventilation strategies (eg, pressure-controlled inverse-ratio ventilation) is the use of a release valve that allows spontaneous breathing during both T_{high} and T_{low}. Although these spontaneous breaths can be unsupported, pressure-supported, or supported by automatic tube compensation, most clinical experience has been with unsupported spontaneous breathing.

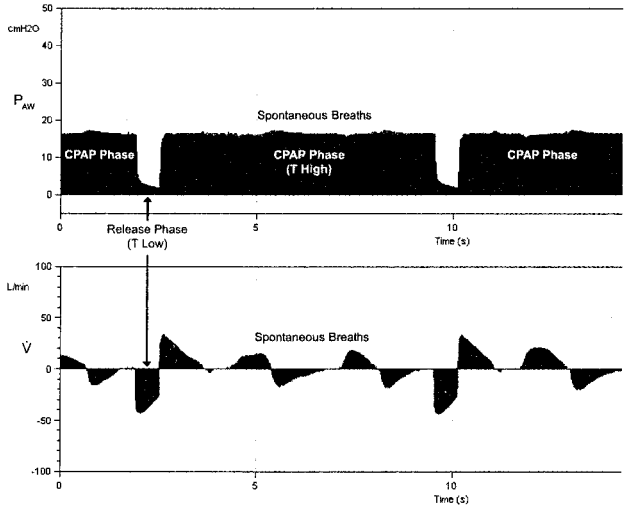

Fig. 1. Airway pressure (P_{aw}) and flow ($\dot{V}$) during airway pressure-release ventilation with a long-inflation period (T_{high}) and short-deflation period (T_{low}) mechanical breath pattern. In this example, the inflation period is labeled "CPAP phase" (continuous positive airway pressure) and the deflation period is labeled "Release phase." Note that spontaneous breathing is occurring during the inflation period. (From Reference 4, with permission.)

Pro: APRV Is an Important New Innovation

Conceptual Advantages

Much of the rationale for APRV is based on the "open lung" concept, which is a mechanical ventilation approach designed to maximize and maintain alveolar recruitment throughout the ventilatory cycle (Table 1).[4–6] With APRV this is accomplished by setting P_{high} well above the closing pressure of recruitable alveoli.[4–6] Thus, the majority of the ventilatory cycle is spent at a pressure and volume well above the lower inflection point of the pressure-volume curve. The set T_{high} generally maintains this pressure (and thus alveolar recruitment) for several seconds, while the set T_{low} is of a duration adequate to assist in CO_2 removal but not be so long as to permit substantial de-recruitment. Put another way, during the long inflation phase, recruitment is maintained, whereas during the brief release, inherent lung recoil properties facilitate ventilation and the slower-emptying alveolar compartments remain expanded through intrinsic PEEP.[7] This "reverse" concept form of ventilation thus provides an alternative way to assist ventilation and maximize and maintain alveolar recruitment (and thereby maximize oxygenation) with substantial mean airway pressure.[4,6]

Timothy R Myers RRT-NPS is affiliated with the Asthma Center, Division of Pediatric Pulmonology, Rainbow Babies and Children's Hospital, Case Western Reserve University, Cleveland, Ohio. Neil R MacIntyre MD FAARC is affiliated with Respiratory Care Services, Duke University Medical Center, Durham, North Carolina.

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Correspondence: Timothy R Myers RRT-NPS, Asthma Center, Division of Pediatric Pulmonology, Rainbow Babies and Children's Hospital, Case Western Reserve University, 11100 Euclid Avenue, Mailstop 6043, Cleveland OH 44106. E-mail: timothy.myers@uhhospitals.org.

Table 1. Theoretical Advantages of Airway Pressure-Release Ventilation

Lung-protective: minimizes ventilator-induced lung injury
Alveolar recruitment or low lung injury
Decreases overinflation or high-volume lung injury
Lower pressure also improves lymphatic drainage, reducing edema
Enhanced gas diffusion
Improves hemodynamic profile
Reduced need for pharmacologic pressor support
Enhanced venous return
Increased cardiac output
Reduced myocardial workload
Provides benefits from spontaneous breathing
Improves ventilation/perfusion matching
Preferentially aerates the dependent lung
Decreases work of breathing
Augments collateral ventilation
Decreases dead-space ventilation by reducing minute ventilation requirement
Decreases need for sedation/neuromuscular blocker

Adapted in part from References 4–6.

Another conceptual advantage to APRV over volume-controlled or pressure-controlled modes is the preservation of spontaneous breathing, the benefits of which are a redistribution of aeration to the dependent lung regions, less need for neuromuscular blockade and sedation, improved cardiac filling, and a better matching of pulmonary ventilation and perfusion.[4,6,8] Also, because spontaneous breathing provides some of the required minute ventilation ($\dot{V}_E$), the ventilator pressure requirement may be less than with other forms of mechanical support.

The unique ventilatory pattern of APRV may have important effects on ventilator-induced lung injury (VILI). VILI is produced by several mechanisms.[9–11] Among the most important is excessive end-inflation lung volume, which over-stretches and physically injures alveoli. Another important VILI mechanism is repetitive opening and closing of injured alveoli. Conceptually, APRV may address both of these mechanisms. First, because spontaneous breaths are allowed, there are fewer mechanical breaths and the mechanical tidal pressure swings may be smaller than in other forms of ventilatory support. Second, because alveolar recruitment is maintained through the long inflation and short deflation periods, lower applied inflation and deflation pressures may be used. Finally, because of better ventilation distribution and ventilation-perfusion matching with spontaneous breathing, the need for ventilator-delivered pressure might be further reduced. It must be emphasized, however, that the relationship between APRV and VILI has not been well studied, so these benefits are purely conceptual. Indeed, as will be discussed later, the concepts underlying these potential benefits can be challenged.

Clinical Evidence Supporting the Use of APRV

A number of simple clinical crossover studies[12–17] have looked at physiologic end points with APRV (Table 2). In general, these studies found that APRV required less applied inflation pressure and less sedation, and APRV often produced better oxygenation than other forms of mechanical ventilation. Spontaneous breathing contributed a substantial amount to the total ventilation in those study patients, so mechanical support was generally less with APRV than with the control strategy. The improved oxygenation probably reflected the substantial mean pressure generated by the prolonged inflation period and the improved distribution with spontaneous breathing.

One crossover study[8] compared various APRV settings and pressure-support settings in 12 patients. APRV with spontaneous breaths, compared to APRV without spontaneous breaths, at a comparable $\dot{V}_E$ required lower inflation pressure and had better cardiac output, P_{aO_2}, and oxygen delivery. When APRV with spontaneous breaths was compared to pressure-support ventilation at comparable inflation pressure or comparable $\dot{V}_E$, APRV provided significantly better oxygenation, cardiac output, and oxygen delivery.

Another crossover study also found better cardiac filling during APRV with spontaneous breaths than during APRV without spontaneous breaths.[18] These cardiovascular benefits are not surprising, given the lower inflation pressure required and the negative inspiratory pressure generated by spontaneous breathing.

Studies have investigated the effects of different T_{low} values on gas exchange during APRV.[4,6] In general, as T_{low} shortens, less time is available for expiration, and intrinsic PEEP develops, which increases mean pressure and reduces V_T. These changes can have important effects on gas exchange and hemodynamics. A well-designed clinical trial addressed this issue in depth,[19] with 35 patients on APRV. T_{high} and T_{low} were initially set at 2.5 s, along with a set pressure-release rate of 12/min that remained unchanged for the remainder of the study period. After obtaining baseline measurements, T_{low} was decreased in 0.5-s increments and T_{high} was simultaneously increased in 0.5-s increments. As expected, shortening T_{low} and prolonging T_{high} significantly increased mean airway pressure and P_{low} in all patient groups. V_T decreased when T_{low} was < 1.5 s; however, $\dot{V}_E$ was unaffected because of parallel increases in the spontaneous respiratory rate.

There have been 2 randomized controlled trials of APRV. One enrolled 30 mechanically ventilated trauma patients at risk for acute respiratory distress syndrome (ARDS).[20] APRV with spontaneous breathing was compared to pres-

Table 2. Clinical Trials of APRV That Have Examined Physiologic End Points

First Author	*n*	Study Design	Key Findings With APRV
Sydow[17]	18	Crossover with APRV vs volume-controlled inverse-ratio ventilation	Lower end-inflation airway pressure, better P_{aO_2}/F_{IO_2}, less neuromuscular blockade
Rasanen[14]	50	Crossover with APRV vs conventional ventilation	Lower end-inflation airway pressure, better P_{aO_2}/F_{IO_2}
Cane[12]	18	Crossover with APRV vs conventional ventilation	Lower end-inflation airway pressure, same P_{aO_2}/F_{IO_2}
Schultz[15]	15	Crossover with APRV vs SIMV	Lower end-inflation airway pressure, same P_{aO_2}/F_{IO_2}
Dart[16]	46	Crossover with APRV vs SIMV or pressure support	Lower end-inflation airway pressure, better P_{aO_2}/F_{IO_2}
Kaplan[13]	12	Crossover with APRV vs pressure-controlled inverse-ratio ventilation	Lower end-inflation airway pressure, less neuromuscular blockade, better oxygen delivery

APRV = airway pressure-release ventilation
P_{aO_2}/F_{IO_2} = ratio of P_{aO_2} to fraction of inspired oxygen
SIMV = synchronized intermittent mandatory ventilation

sure-controlled time-cycled ventilation with sedation and paralysis for 72 hours. After 72 hours the pressure-controlled time-cycled ventilation group was crossed over to APRV. APRV was associated with significant increases ($p < 0.05$) in respiratory-system compliance, P_{aO_2}, cardiac index, and oxygen delivery, as well as significant ($p < 0.05$) decreases in venous admixture shunt and oxygen extraction. In addition, patients initially ventilated with pressure-controlled time-cycled ventilation required significantly ($p < 0.05$) higher doses of sedation and vasopressors for hemodynamic instability. Initial APRV use significantly decreased the duration of mechanical ventilation (APRV 15 ± 2 d, pressure-controlled time-cycled ventilation 21 ± 2 d, $p < 0.05$) and intensive care unit (ICU) stay (APRV 23 ± 2 d, pressure-controlled time-cycled ventilation 30 ± 2 d, $p < 0.05$). Mortality, however, was not affected.

In a more recent randomized controlled trial, Varpula et al[21] assessed the effects of the combination of spontaneous breathing in APRV versus pressure-controlled synchronized intermittent mandatory ventilation with pressure support (SIMV-PS) and prone positioning on gas exchange in 33 patients with ARDS or acute lung injury. APRV significantly improved the ratio of P_{aO_2} to fraction of inspired oxygen (F_{IO_2}) prior to both proning episodes, compared to the SIMV-PS-group ($p = 0.02$). These differences, however, were not maintained during the proning episodes. Importantly, there was no difference in mortality or ICU stay.

Con: APRV Has Not Yet Proven to Be an Important Innovation

Does APRV Really Improve Gas Exchange and Lung Mechanics?

As noted above, numerous studies have purported to show better gas exchange at lower pressure with APRV than with "conventional" ventilation (see Table 2).[12–17] One must be cautious in accepting these claims, however. Specifically, the control strategy in a comparison study must be carefully assessed. In many of these studies, the control strategy involved ventilator settings that included longer inspiratory time, unacceptably higher V_T, or modes that required heavy sedation or paralysis. To be fair, APRV should be compared in a randomized fashion to modes and strategies that are generally accepted as providing safe and effective support, such as the ARDS Network approach.[2] This has not been generally the case.

Does APRV Prevent—or Could It Promote—Ventilator-Induced Lung Injury?

With conventional ventilation, the standard approach to managing hypoxemia is to recruit additional lung units by raising the mean airway pressure with increases in either V_T or PEEP (or both). Unfortunately, these approaches also increase the end-inflation stretch and thus increase the risk of VILI, as noted above.[1,9,10] APRV uses a longer inflation duration rather than a larger V_T or PEEP to recruit atelectatic lung units and thereby better match ventilation and perfusion. APRV can thus increase mean airway pressure without adding to the end-inflation stretch. Because spontaneous breaths are allowed, a lower inflation pressure may be used with APRV than with a comparable level of conventional support.

These effects of APRV have led to the notion that APRV might reduce end-inflation stretch and thus reduce VILI.[4,6] It is important to remember, however, that the intrathoracic inflation pressure generated by the patient's respiratory muscles during the spontaneous breaths will *add* to the end-inflation volume and stretching pressure during APRV. For example, if the set APRV inflation pressure is 28 cm H_2O and the patient generates an additional 12 cm H_2O for the spontaneous breath, then the end-inflation pressure across the alveolar structures (transpulmo-

nary stretching pressure) is 40 cm H_2O, which is a potentially injurious level.[1] The claim that APRV set pressure can be lower than conventional set pressure thus has little meaning when we think about the total end-inflation stretch in a spontaneously breathing patient.

APRV might have additional VILI effects. For example, the alveolar stresses associated with a long inflation time and/or the rapid flow reversals associated with the deflation-reinflation APRV pattern could also have a VILI effect. These have not been well studied, and until further data are available, it would seem premature to state that APRV reduces the risk of VILI—it might actually increase it. Admittedly, these concepts are hypothetical, but nevertheless they should raise at least some concern about the apparent simplicity and safety of APRV.

Does APRV Enhance Spontaneous Breaths, Compared to Other Mechanical Ventilation Approaches?

There is no question that allowing spontaneous patient efforts in a mechanical ventilation strategy will better distribute gas in the lung (especially to basilar lung units), improve cardiac filling, reduce the risk of ventilator-induced diaphragmatic dysfunction (atrophy), and improve comfort.[7] The observation that adding spontaneous breaths to a ventilatory strategy such as APRV improves comfort, cardiac function, and gas exchange thus is not surprising.

However, the claim that sedation needs are less with APRV deserves further scrutiny. This claim is derived from studies that compared APRV with controlled (and often inverse-ratio) ventilation modes that usually require heavy sedation or neuromuscular blockade.[4,6–12] However, in modern ICUs, rarely is controlled ventilation, let alone inverse-ratio ventilation, utilized. Instead, assisted ventilation modes such as volume-assist or pressure-assist control or pressure support with SIMV are used in the vast majority of patients around the world.[22] Indeed, in the one study where sedation needs were carefully examined during APRV versus a patient-triggered spontaneous/assisted mode (SIMV plus pressure support), the sedation needs were identical.[21]

There is also the concern that if patient efforts occur at the onset of an APRV machine inflation and/or deflation period, substantial discomfort and asynchrony can occur. While this is not a common occurrence, clinical studies have shown that it happens in a substantial number of patients.[23]

Can APRV Be Standardized to Allow Consistent Application Across Multiple Caregivers for a Given Patient?

The "optimal" APRV settings are not known. The Δ pressure setting (V_T) and respiratory rate setting are probably straightforward when focused on modest V_T (6–8 mL/kg) and pH (7.20–7.35) targets. Problems come, however, in determining the best deflation time and PEEP settings. In essence, there are 2 schools of thought. First, a short deflation time that produces a long inspiratory-expiratory ratio will give a higher mean pressure, because more intrinsic PEEP is applied. This may reduce the need for applied PEEP (which may facilitate lung emptying) and has been shown to produce less spontaneous breath variability. The V_T, however, will be reduced as intrinsic PEEP increases for a constant maximum applied inflation pressure. The other school of thought is to use a longer deflation time that will shorten the inspiratory-expiratory ratio and minimize the development of intrinsic PEEP. This approach requires more applied PEEP for a given mean pressure, and it appears this may produce more spontaneous breath variability. Unfortunately, there are few data to help us decide which of these approaches is optimal (or if in fact they may be equivalent).

Another unresolved question about setting up APRV is how to address hypoxemia. Specifically, should clinicians add more inflation pressure, apply more PEEP, or create more intrinsic PEEP? If the patient is hypercapnic, should the adjustment be to add more breaths (with shorter inflation times), more inflation pressure, or lengthen deflation time to reduce intrinsic PEEP? Finally, when weaning a patient, should the clinician reduce the V_T, the inspiratory-expiratory ratio, or both? Perhaps one should simply just go to spontaneous breathing trials on a modest level of continuous positive airway pressure. The answers to these questions are unknown, and few data exist with which to make rational decisions.

Because of these uncertainties, clinically applying APRV is problematic. It would thus seem reasonable for institutions that want to utilize APRV to apply it in some sort of uniform way. To do this, a protocol and data-collection sheet should be developed. This will allow the ventilator "philosophy" to be carried over from caregiver to caregiver and shift to shift. Moreover, a data-collection sheet will allow clinical departments to assess protocol performance and adjust accordingly.

Do Clinical Trials Indicate Better Outcomes With APRV?

The ultimate challenge for proponents of any new technique such as APRV is to show better outcomes. Though physiologic improvements appeal to clinicians, it must always be remembered that sometimes the ultimate outcome of a physiologic improvement may be unacceptable. A classic example is from the low-V_T study by the ARDS Network, which found that the high-V_T strategy produced better oxygenation and mechanical functioning over the

first 2 days, but it ultimately produced more VILI and higher mortality.[2]

With APRV there have been 2 randomized controlled trials on outcomes in patients with acute respiratory failure. The first was by Putensen et al.[20] Importantly, and for unclear reasons, the control group strategy in that study required paralysis for the first 3 days. Not surprisingly then, the inflation pressure setting on the ventilator was reduced with APRV, since spontaneous breaths were allowed. However, as noted above, the actual end-inflation transpulmonary pressure and volume during the spontaneous breaths had to be higher but were unmeasured. Interestingly, P_{O_2} improved slightly (but significantly) with the APRV strategy but decreased dramatically from baseline with the control strategy, for unclear reasons. Because of this need for paralysis and worsening of oxygenation, the appropriateness of the control group strategy in that study is called into serious question. The APRV group had a significantly shorter duration of ventilation, intubation, and ICU stay. However, these results must be viewed with great caution, given the problem with the control group.

The other randomized controlled trial was by Varpula et al.[21] They randomized 58 ARDS patients to either APRV or a more rational control group than did the Putensen et al study,[20] in that Varpula et al employed SIMV plus 10 cm H_2O of pressure support. Again, a lower inflation pressure was required with APRV, but recall that the spontaneous breaths during the inflation period probably raised end-inflation volume and transpulmonary pressure to an equivalent or even higher level than the control group. Importantly, this carefully done study showed similar gas exchange, sedation needs, ventilator-free days, and mortality between APRV and a clinically relevant control strategy.

The inevitable conclusion from these 2 clinical trials is that APRV does seem to supply reasonable gas exchange, but an APRV advantage in patient outcomes has yet to be demonstrated. Of note is that a recent evidence-based review gave similar low marks to the evidence in support of APRV for gas exchange or outcomes benefit.[24]

Summary

APRV does provide a higher mean pressure with a lower V_T and PEEP than do comparable levels of other forms of ventilation. Good lung recruitment thus may occur at lower levels of applied end-inflation pressure. However, because spontaneous breaths are encouraged during the inflation period, end-inflation transpulmonary pressure (stretch) will be higher than the applied inflation airway pressure and could be higher than conventional assist-control modes. The spontaneous breaths permitted during APRV improve ventilation-perfusion matching, cardiac filling, and comfort, compared to controlled ventilation. However, this can also be seen on other forms of mechanical ventilation that permit spontaneous efforts and spontaneous or assisted breaths. Though there is conceptual simplicity to APRV settings, there is no consensus or data to help resolve some of the most important questions involving inspiratory-expiratory ratio, PEEP, and weaning strategy. Finally, though the few clinical trials to date show that APRV does supply reasonable gas exchange, none have shown any meaningful clinical outcome benefit over conventional strategies.

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Discussion

Branson: The first patients we put on APRV were in 1985, and we didn't even use a ventilator; we used a CPAP setup, a valve that went back and forth between 30 cm H_2O or 10 cm H_2O of CPAP. It's clear to me that if you want to increase mean airway pressure, whether via APRV or high-frequency oscillation, compared to your PEEP-F_{IO_2} paper from the ARDS Network, you can improve oxygenation. I don't understand why people think that's so amazing, when you go from a PEEP of 12 cm H_2O to—whether its APRV with a P_{high} of 30 cm H_2O or high-frequency oscillation with a mean airway pressure of 30 cm H_2O—those are substantially higher. APRV will work.

I don't think you should ever use it at all in a patient with obstructive lung disease; it should just be contraindicated in that case. But if the patient has low lung volume and is breathing on his own—and a trauma patient will have hypocarbia and hypoxemia—and you begin APRV, you correct that problem. I don't know whether that has any advantage over continuous or intermittent mandatory ventilation or just pressure support.

MacIntyre: You brought up an important concept, Rich: there are a number of ways to improve P_{O_2}. But I think a critical point here is, does improving P_{O_2} translate into a better outcome? The ARDS Network studies had 2 important lessons. Number one was that a larger V_T provided a better P_{O_2} and better compliance (almost certainly because it recruits alveoli and thus improves ventilation-perfusion matching and mechanical ventilation), but the larger V_T also overdistended and injured the alveoli and thus increased the mortality of the higher-V_T patients. So improving gas exchange and mechanical functioning of the lung does not necessarily translate into a better outcome.

The corollary to that was the higher-PEEP vs lower-PEEP ARDS Network trial, in which the higher-PEEP strategy clearly improved gas exchange, allowed dramatic decrease in the F_{IO_2}, and dramatically improved compliance over 7 days in the study, but at the end of the day it didn't make a difference in outcomes. Reducing V_T did the trick, whereas additional PEEP, to make the numbers look better, did not change the ultimate patient outcomes.

Pierson:* In view of your statement, with which I agree completely, how do you limit V_T in a pressure-limited ventilation mode, except with a paralyzed patient?

* David J Pierson MD FAARC, Division of Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle, Washington.

MacIntyre: We do that all the time. Pressure-assist control is our standard ventilation mode. It's very easy to set the inspiratory pressure to a target V_T. If you have a *very* unstable patient, with unstable respiratory drive or unstable mechanics, you could consider using something like a pressure-regulated volume-controlled mode, but, in our experience, we can keep people in the target V_T range using pressure assist-control without a whole lot of difficulty.

Pierson: But in the context of this discussion of APRV, as you pointed out, you don't limit the V_T. You made the point that the transalveolar distending pressure is bigger than you think it is, but also that V_T is bigger than you think it is, right? Aren't you also failing to be able to control the V_T in the context that distending volume is just as important as pressure?

MacIntyre: Distending volume *is* the key driver here, and, sure enough, with pressure-assist control, if you deliver a 6-mL/kg V_T on top of a PEEP, the end-inspiratory volume is the functional residual capacity plus that V_T. But it's the same thing with volume-controlled ventilation, in which the end-inspiratory volume is the functional residual capacity plus the applied V_T. The point is that you can set the inspiratory assistance to whatever level is appropriate for your V_T target.

Pierson: But my point was that the V_T you were giving the patient is constant in a volume-targeted mode, whereas it is *not* controlled or constant with a pressure mode.

MacIntyre: Yes, volume is the dependent variable in pressure-assist control ventilation. What I'm saying, though, is that mechanics don't change that rapidly, and patient efforts don't change that dramatically in most ARDS patients. And if you're concerned, then go to a volume-controlled mode. I have no problem with that. Pressure-regulated volume control will also address that very same issue, to maintain V_T in the target range.

Pierson: One last quibble. In this era of mandated sedation vacations and movement away from sedation drips to bolus use, I think the patient's level of consciousness and air hunger vary quite a bit, and more than they did in the past. So I think V_T in a pressure-limited situation is, by my observation, varying more than what you imply.

MacIntyre: We can obviously argue about this until the cows come home, because neither of us has data on it. But in my institution we like the pressure-target modes, because they tend to require less sedation and, at least in our experience as an ARDS Network center for 10 years, we have gotten very comfortable with reasonably stable V_T in the target range using pressure-targeted ventilation modes.

Kallet: A few points I want to make regarding pressure control ventilation and V_T variation. We recently published a study[1] on V_T stability and work of breathing with volume-regulated and pressure-regulated modes, basically using the ARDS Network protocol. In about 40% of the patients with pressure control or pressure-regulated volume control, there was very poorly controlled V_T, with very large changes in esophageal pressure, but 60% of the patients—who were basically sedated to a Ramsey score of about 4 during the study—were fine. When we looked at the daily reference ventilator checks from our ARDS Network clinical quality-assurance data,[2] about 20–30% of the patients were on an alternative mode. Actually the V_T were pretty tight. So I think if you are at the bedside and really looking at breath-to-breath data, you sometimes can see large variations, but in patients who are kept fairly well sedated, the pressure-regulated modes appeared to work very well most of the time.

On the use of APRV for lung-protective ventilation, I agree with Neil's position. They were originally setting this mode up with a peak pressure of 35 cm H_2O over a PEEP of about 5 cm H_2O. If you assume a representative compliance of 30 mL/cm H_2O, with a pressure differential of 30 cm H_2O, you are talking about a 900 mL volume differential with full equilibration. Even subsequently allowing for a brief release of 1–2 time constants (63–88% equilibration), you are still talking about approximately a 600–800 mL volume change!

And with these APRV studies, they almost never report the release volumes. Sure, I can put someone with ARDS on intermittent mandatory ventilation, like I did 20 or 30 years ago, give them 700–900 mL V_T, and let them breathe spontaneously in between. Their work of breathing is going to be better, and they are going to appear more comfortable than on assist-control with a low V_T. But there are other problems with some of these studies.

Putensen et al,[3] for example, paralyzed people on pressure control ventilation for 3 days while the APRV cohort could breathe spontaneously from the start. And the difference in the duration of mechanical ventilation between the 2 groups was 3 days. This is just disingenuous to claim APRV is superior to assist-control modes, and clinicians need to be careful when they read such claims.

Habashi[4] even claimed that his patients on APRV had a better outcome than the ARDS Network, but he works primarily with a trauma population, whereas in the ARDS Network study most of our patients had pneumonia or sepsis, which carries a higher mortality risk, and trauma patients were a minority. But if you look at the substudies of ARDS Network patients who had trauma, their mortality was about 11%, I think.[5] Neil, you can correct me on that.

1. Kallet RH, Campbell AR, Dicker RA, Katz JA, Mackersie RC. Work of breathing during lung-protective ventilation in patients with acute lung injury and acute respiratory distress syndrome: a comparison between volume and pressure-regulated breathing modes. Respir Care 2005;50(12):1623–1631.
2. Kallet RH, Jasmer RM, Pittet J-F, Tang JF, Campbell AR, Dicker RA, et al. Clinical implementation of the ARDS Network protocol is associated with reduced hospital mortality compared to historical controls. Crit Care Med 2005;33(5):925–929.
3. Putensen C, Zech A, Wrigge H, Zinserling J, Stuber F, Von Spiegel T, Mutz N. Long-term effects of spontaneous breathing during ventilatory support in patients with acute lung injury. Am J Respir Crit Care Med 2001;164(1):43–49.
4. Habashi NM. Other approaches to open-lung ventilation: airway pressure release ventilation. Crit Care Med 2005;33(3 Suppl):S228–S240.
5. Eisner MD, Thompson T, Hudson LD, Luce JM, Hayden D, Schoenfeld D, Matthay MA; Acute Respiratory Distress Syndrome Network. Efficacy of low tidal volume ventilation in patients with different clinical risk factors for acute lung injury and the acute respiratory distress syndrome. Am J Respir Crit Care Med 2001;164(2):231–236.

MacIntyre: They were lower.

Kallet: Yeah, so you have to be very careful. There are people who are pushing a mode, and I think you have to look very carefully and very skeptically both at study designs and interpretation.

Steinberg: One of the compelling data sets for low-V_T ventilation in

acute lung injury is from Ranieri et al,[1] who found lower pulmonary and systemic inflammatory cytokines. Has any similar work been done on APRV compared to volume control or pressure control ventilation? Because, in theory, if APRV is supposed to be more lung-protective, you would expect less inflammatory cytokines.

1. Ranieri VM, Suter PM, Tortorella C, De Tullio R, Dayer JM, Brienza A, et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA 1999;282(1):54–61.

MacIntyre: I don't know of any studies that have looked at cytokines in humans.

Fessler: There are 2 aspects of APRV that make me a little dysphoric. One is the patient-ventilator dyssynchrony that occurs if the patient makes an inspiratory effort as the release phase begins. That's equivalent to sucking on the airway as they attempt to inhale, and it seems like that would decrease patient comfort. The other is the claim that the brevity of the P_{low} phase prevents lung derecruitment during that phase. But if 500 mL come out, then some lung regions will derecruit, and if those 500 mL come out in 0.4 seconds, they are primarily going to come out of the short-time-constant areas, so I would think that APRV would have the same or even greater tendency to derecruit and then reopen certain lung regions than any other mode.

MacIntyre: I agree. Some of the prettier pictures I've seen are from Nieman's group in Syracuse.[1] They studied inflation and deflation with in vivo microscopy, and it's impressive how fast these alveoli can collapse when pressure is suddenly removed.

1. Halter JM, Steinberg JM, Schiller HJ, DaSilva M, Gatto LA, Landas S, Nieman GF. Positive end-expiratory pressure after a recruitment maneuver prevents both alveolar collapse and recruitment/derecruitment. Am J Respir Crit Care Med 2003; 167(12):1620–1626.

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