Other approaches to open-lung ventilation: Airway pressure release ventilation

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Objective: **To review the use of airway pressure release ventilation (APRV) in the treatment of acute lung injury/acute respiratory distress syndrome.**

Data Source: **Published animal studies, human studies, and review articles of APRV.**

Data Summary: **APRV has been successfully used in neonatal, pediatric, and adult forms of respiratory failure. Experimental and clinical use of APRV has been shown to facilitate spontaneous breathing and is associated with decreased peak airway pressures and improved oxygenation/ventilation when compared with conventional ventilation. Additionally, improvements in hemodynamic parameters, splanchnic perfusion, and reduced sedation/neuromuscular blocker requirements have been reported.**

Conclusion: **APRV may offer potential clinical advantages for ventilator management of acute lung injury/acute respiratory distress syndrome and may be considered as an alternative "open lung approach" to mechanical ventilation. Whether APRV reduces mortality or increases ventilator-free days compared with a conventional volume-cycled "lung protective" strategy will require future randomized, controlled trials. (Crit Care Med 2005; 33[Suppl.]:S228–S240)**

KEY WORDS: airway pressure release ventilation; airway pressure release ventilation; spontaneous breathing; lung protective strategies; acute lung injury; acute respiratory distress syndrome

Airway pressure release ventilation (APRV) was initially described by Stock and Downs (1, 2) as continuous positive airway pressure (CPAP) with an intermittent pressure release phase. Conceptually, APRV applies a continuous airway pressure (P_{high}) identical to CPAP to maintain adequate lung volume and promote alveolar recruitment. However, APRV adds a time-cycled release phase to a lower set pressure (P_{low}). In addition, spontaneous breathing can be integrated and is independent of the ventilator cycle (Fig. 1). CPAP breathing mimics the gas distribution of spontaneous breaths as opposed to mechanically controlled, assisted, or supported breaths, which produce less physiological distribution (3–6). Mechanical breaths shift ventilation to nondependent lung regions as the passive respiratory system accommodates the displacement of gas in to the lungs. However, spontaneous breathing during APRV results in a more dependent gas distribution when the active respiratory system draws gas into the lung as pressure changes and flow follow a similar time course (7–9). As a result, by allowing patients to spontaneously breathe during APRV, dependent lung regions may be preferentially recruited without the need to raise applied airway pressure.

APRV has been used in neonatal, pediatric, and adult forms of respiratory failure (1–4, 6, 10–22). Clinical studies using APRV are summarized in Table 1 (1–4, 12, 18, 23–28).

In patients with decreased functional residual capacity (FRC), elastic work of breathing (WOB) is effectively reduced with the application of CPAP. As FRC is restored, inspiration begins from a more favorable pressure/volume relationship, facilitating spontaneous ventilation and improving oxygenation (29).

However, in acute lung injury/acute respiratory distress syndrome (ALI/ARDS), the surface area available for gas exchange is significantly reduced. Despite optimal lung volume, CPAP mandates that unaided spontaneous breathing manage the entire metabolic load or Co_2 production. However, CPAP alone may be inadequate to accomplish necessary Co_2 removal without producing excessive WOB. In contrast to CPAP, APRV interrupts airway pressure briefly to supplement spontaneous minute ventilation. During APRV, ventilation is augmented by releasing airway pressure to a lower CPAP level termed P_{low}. The intermittent release in airway pressure during APRV provides Co_2 removal and partially unloads the metabolic burden of pure CPAP breathing.

By using a release phase for ventilation, APRV uncouples the traditional requirement of elevating airway pressure, lung volume, and distension during tidal ventilation. Rather than generating a tidal volume by raising airway pressure above the set positive end-expiratory pressure (PEEP) (like in conventional ventilation), release volumes in APRV are generated by briefly releasing airway pressure from P_{high} to P_{low}. Because ventilation with APRV results as airway pressure and lung volume decrease (release volume), the risk of overdistension may be reduced. In contrast, conventional ventilation raises airway pressure, elevating lung volumes, potentially increasing the threat of overdistension (Fig. 2).

Ventilation generated by the release phase of APRV may have additional advantages in ALI/ARDS. Increased elastic recoil is common to restrictive lung diseases such as ALI/ARDS. With APRV, as airway pressure is briefly interrupted, the release volume is driven by gas compression and lung recoil (potential energy) stored during the P_{high} time period or

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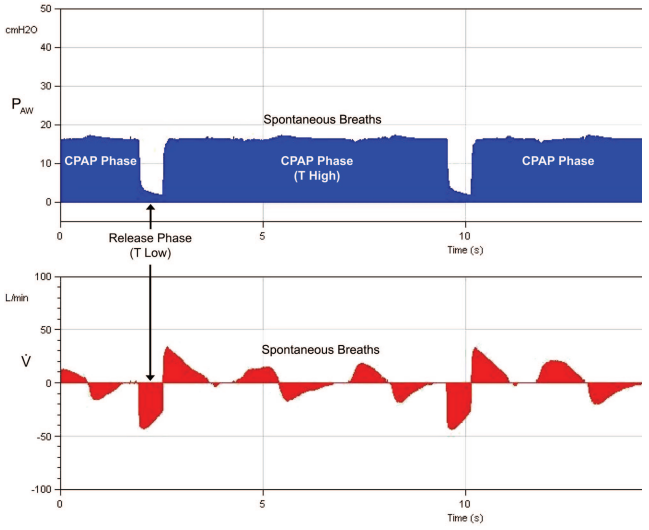

Figure 1. Airway pressure release ventilation is a form of continuous positive airway pressure (*CPAP*). The P_{high} is equivalent to a CPAP level; T_{high} is the duration of P_{high}. The CPAP phase (P_{high}) is intermittently released to a P_{low} for a brief duration (T_{low}) reestablishing the CPAP level on the subsequent breath. Spontaneous breathing may be superimposed at both pressure levels and is independent of time-cycling. Reprinted from ICON educational supplement 2004 with permission.

T_{high}. During conventional ventilation, inspiratory tidal volumes must overcome airway impedance and elastic forces of the restricted lung from a lower baseline resting volume, increasing the energy or pressure required to distend the lung and chest wall. Furthermore, as thoracic compliance decreases, the inspiratory limb of the volume/pressure curve shifts to the right, i.e., more pressure is required to deliver a set tidal volume. However, the expiratory limb remains unaffected by the prevailing volume/pressure relationship and extends throughout all phases of injury (30). APRV uses the more favorable volume/pressure relationship of the expiratory limb for ventilation by applying a near-sustained inflation or recruitment state (31).

Alveolar recruitment is a pan-inspiratory phenomenon. Successful recruiting pressure depends on the yield or threshold opening pressure (TOP) of lung units. ALI/ARDS may have a multitude of TOP distributed throughout the lung (32–35). In addition to TOP, the time-dependent nature of recruitment should also be considered. Although the exact mechanisms are not known, the lung is interdependent and recruitment of air spaces results in radial traction of neighboring alveoli, producing a time-dependent ripple effect of recruitment (36–38).

As lung units recruit, the additional time (T_{high}) at P_{high} provides stability as an "avalanche" of lung units pop open (37, 38). Conceptually, superimposed spontaneous breaths at a high lung volume rather than brief and frequent tidal ventilation between PEEP and end-inspiratory pressure may be more successful in achieving progressive and sustained alveolar recruitment.

Airway opening is dynamic as the lung creeps to the recruited lung volume. Compliance and resistance (time constants) of recently recruited lung units decrease the inflating or sustaining pressure requirements. Therefore, progressive extensions of T_{high} may be critical for sustaining recruitment as time constants evolve (38). Furthermore, the sustained T_{high} period may encourage spontaneous breathing at an upper and open lung volume, improving efficiency of ventilation.

Although recruitment maneuvers may be effective in improving gas exchange and compliance, these effects appear to be nonsustained, requiring repeated maneuvers (39, 40). Alternatively, APRV may be viewed as a nearly continuous recruitment maneuver with the P_{high} providing 80% to 95% of the cycle time creating a stabilized "open lung" while facilitating spontaneous breathing. Fundamentally, assisted mechanical breaths cannot provide the same gas distribution as spontaneous breaths. Therefore, during a recruitment maneuver in a passive respiratory system, the nondependent lung regions distend first until applied airway pressure reaches and exceeds the high TOP of the dependent lung units, increasing the threat of overdistention. Conversely, spontaneous breathing favors dependent lung recruitment through the application of pleural pressure. Spontaneous breaths at the CPAP level (P_{high}) improve dependent ventilation through pleural pressure changes rather than the application of additional applied airway pressure (5, 6, 26). The recruited lung requires less pressure than the recruiting lung. Therefore, maintaining lung volume and allowing spontaneous breathing from the time of intubation by using APRV (CPAP with release) may reduce the need for recurrent high CPAP recruitment maneuvers (41). If a recruitment maneuver is desired during APRV, the P_{high} and T_{high} can be adjusted to simulate a conventional CPAP-type recruitment maneuver (e.g., P_{high} 40–50 cm H_2O and T_{high} 30–60 secs).

Conventional volume ventilation limits its recruitment to brief cyclic intervals at end-inspiration or plateau pressure. Lung regions that are recruited only during brief end-inspiratory pressure cycles produce inadequate mean alveolar volume. Because alveolar volume is not maintained, compliance does not improve, requiring the same inflation pressure on subsequent breaths. Reapplication of the same distending pressure without adequate lung recruitment is likely to produce recurrent shear forces and does not attenuate potential lung injury (42). Conversely, sustained recruitment is associated with increased compliance allowing successful, sequential airway pressure reduction and improving gas exchange by increasing alveolar surface area (4, 42–44). Increased alveolar surface area may improve stress distribution in the lung.

Gallagher and coworkers (45) demonstrated a direct correlation among mean airway pressure, lung volume, and oxygenation. The use of APRV to optimize mean airway pressure/lung volume provides a greater surface area for gas exchange. Allowing sustained duration (T_{high}) of P_{high} and limiting duration and frequency of the release phase (T_{low}) of P_{low} permits only partial emptying, limiting lung volume loss during ventilation. As lung recruitment is sustained, gas redistribution and diffusion along concentration gradients have time to occur. The mixture of alveolar and inspired gas within the anatomic dead space results in a greater equilibration of gas concentrations in all lung regions, improved oxygenation, and reduced dead-space ventilation (26, 46) (Fig. 3).

Table 1. Clinical studies using airway pressure-release ventilation (APRV)

Author (yr Published)	Study	Measurements	Findings	Study design
Stock (1987)	APRV vs. IPPV; dogs with ALI (n = 10)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E	Hemodynamics were not different at equivalent V_E; with APRV, PIP and physiological dead space were lower, mean airway pressure was higher, and oxygenation was better	Animal study, small *n*, and short-term observations
Garner (1988)	APRV vs. conventional ventilation, patients after cardiac surgery (*n* = 14)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E	Similar oxygenation and ventilation at lower peak airway pressure	Observational, crossover trial
Rasanen (1988)	APRV vs. conventional ventilation vs. CPAP; anesthetized dogs (*n* = 10)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E	APRV had similar effects on blood gases but with significantly fewer adverse hemodynamic effects	Animal studies, small *n*, and short-term observations
Martin (1991)	APRV vs. CPAP vs. conventional ventilation vs. spontaneous breathing; neonatal sheep with oleic-acid lung injury (*n* = 7)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E	APRV increased V_E more than CPAP; APRV provided similar gas exchange to conventional ventilation, but with fewer adverse hemodynamic effects	Animal studies, small *n*, and short-term observations
Davis (1993)	APRV vs. SIMV; surgery patients with ALI (*n* = 15)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E	APRV provided similar gas exchange with lower PIP, but no hemodynamic advantage was identified	Prospective, crossover trial with short-term observations
Putensen (1994)	APRV (with and without spontaneous breathing) vs. PSV; anesthetized dogs (*n* = 10)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E, ventilation/perfusion determined by multiple inert-gas-elimination technique	PSV had highest V_E; APRV had higher cardiac output, PaO_2, and oxygen delivery; APRV had better V/Q and less dead space	Animal studies, small *n*, and short-term observations
Sydow (1994)	APRV vs. volume-controlled inverse-ratio ventilation; patients with ALI; 24-hr observation periods (*n* = 18)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E	APRV provided 30% lower PIP, less venous admixture (14 vs. 21%), and better oxygenation; no difference in hemodynamics	Prospective, randomized, crossover trial
Calzia (1994)	BiPAP vs. CPAP; patients after bypass surgery (*n* = 19)	WOB and PTP	No difference	Prospective, crossover trial
Rathgeber (1997)	BiPAP vs. conventional ventilation vs. SIMV; patients after cardiac surgery (*n* = 596)	Duration of intubation, sedation requirement, analgesia requirement	APRV had shorter duration of intubation (10 hrs) than SIMV (15 hrs) or conventional ventilation (13 hrs); conventional ventilation was associated with greater doses of midazolam; APRV was associated with less need for analgesia	Prospective, randomized, controlled, open trial over 18 months, uneven randomization
Kazmaier (2000)	BiPAP vs. SIMV vs. PSV; pPatients after coronary artery bypass (*n* = 24)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, V_E	No differences in blood gases or hemodynamics	Prospective, crossover trial with short-term observations
Putensen (2001)	APRV vs. pressure controlled conventional ventilation; patients with ALI after trauma (*n* = 30)	Gas exchange, hemodynamics, sedation requirement, hemodynamic support, duration of ventilation, ICU stay	APRV was associated with fewer ICU days, fewer ventilator days, better gas exchange, better hemodynamic performance, better lung compliance, and less need for sedation and vasopressors	Randomized controlled, prospective trial, small *n*; the conventional ventilation group received paralysis for the first 3 days, potentially confounding results
Varpula (2003)	Combined effects of proning and SIMV PC/PS vs. APRV; patients with ALI (*n* = 45)	Blood gases, oxygenation (Pa_{O_2}/F_{IO_2} ratio), hemodynamic, sedation requirement	Oxygenation was significantly better in APRV group before and after proning; sedation use and hemodynamics were similar	Prospective, randomized intervention study

IPPV, intermittent positive-pressure ventilation; ALI, acute lung injury; f, respiratory frequency; V_E, minute volume; V_T, tidal volume; PIP, peak inspiratory pressure; CPAP, continuous positive airway pressure; PSV, pressure support ventilation; V/Q, ventilation/perfusion ratio; BiPAP, bilevel positive airway pressure; SIMV, synchronized intermittent mandatory ventilation; WOB, work of breathing; PTP, pressure-time product; ICU, intensive care unit.

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In addition to F_{IO_2} and slope, clinician-controlled APRV parameters are: P_{high}, T_{high}, P_{low}, and T_{low}. Time parameters in APRV are independent rather than an inspiratory:expiratory (I:E) ratio allowing precise adjustment.

The P_{high} and T_{high} regulate end-inspiratory lung volume and provide a significant contribution to the mean airway pressure. Mean airway pressure correlates to mean alveolar volume and is critical for maintaining an increased surface area of open air spaces for diffusive gas movement. As a result, these parameters control oxygenation and alveolar ventilation. Counterintuitive to conventional concepts of ventilation, the extension of T_{high} can be associated with a

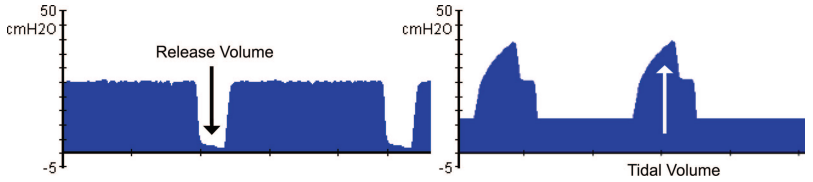

Figure 2. Ventilation during airway pressure release ventilation is augmented by release volumes and is associated with decreasing airway pressure and lung distension. Conversely, tidal volumes during conventional ventilation are generated by increasing airway pressure and lung distension. Reprinted from ICON educational supplement 2004 with permission.

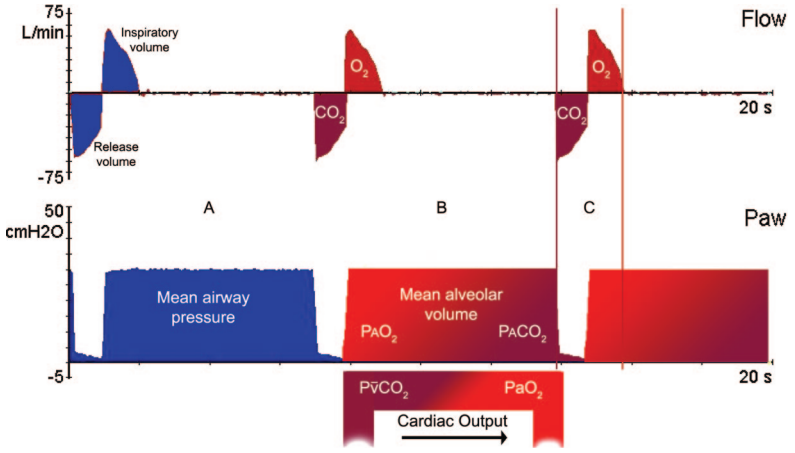

Figure 3. Gas exchange during airway pressure release ventilation. *A*, mean airway pressure (lung volume) provides sustained mean alveolar volume for gas diffusion. *B*, alveolar gas volume combined with cardiac output provides continuous diffusive gas exchange between alveolar and blood compartments despite the cyclic nature of ventilation. *C*, Co_2-enriched gas is released to accommodate oxygen-enriched gas delivered with the subsequent inspiratory cycle. New inspiratory volume is introduced, regenerating diffusion gradients. Reprinted from ICON educational supplement 2004 with permission.

decrease in $Paco_2$ as machine frequency decreases. This has been previously described and is similar to improved Co_2 clearance with increasing I:E ratios (47–51). Despite the intermittent nature of ventilation, Co_2 delivery to the lung is continuous as cardiac output transfers Co_2 into the alveolar space, provided airways remain open (52). During the brief T_{low}, released gas is exchanged with fresh gas to regenerate the gradient for Co_2 diffusion. In addition, cardiogenic mixing results in Co_2 movement toward central airways during the T_{high} or breathhold period (46, 53–55), improving the efficacy of the release for ventilation. The addition of spontaneous breaths during the T_{high} period at P_{high} (higher lung volume) further enhances recruitment and ventilation efficiency (Fig. 3).

The risk of using APRV as a cyclic mode and attempting to increase the machine frequency and minute ventilation by reducing T_{high} may sacrifice alveolar ventilation and oxygenation. Reducing T_{high} will lead to a reduction in mean airway pressure, potentially resulting in airway closure, decreasing alveolar surface area for gas exchange.

In addition to spontaneous breathing, ventilation is augmented during APRV as a result of the release phase. The release phase is determined by the driving pressure differential (P_{high} - P_{low}), inspiratory lung volume (P_{high}), the potential energy (recoil or compliance of the thorax and the amount of energy stored during T_{high}), and downstream resistance (artificial airway). P_{low} and T_{low} regulate end-expiratory lung volume and should be optimized to reduce airway closure/derecruitment and not as a primary ventilation adjustment. Generally, to maintain maximal recruitment, the majority of the time or T_{high} (80–95% of the total cycle time) occurs at the P_{high} or CPAP level. To minimize derecruitment, the time (T_{low}) at P_{low} is brief (usually between 0.2 and 0.8 secs in adults).

Because patients can maintain their native respiratory drive during APRV, spontaneous inspiratory and expiratory time intervals are independent of the T_{high}, T_{low} cycle (56). Thus, the release phase does not reflect the only expiratory time during APRV when patients are breathing spontaneously. Therefore, spontaneous expirations will occur at the upper pressure or P_{high} phase. Active exhalation during the P_{high} phase may result in additional recruitment and volume redistribution analogous to grunting respiration in neonates, thereby improving ventilation/perfusion (V/Q) matching (22, 57–61).

The release time (T_{low}) may be titrated to maintain end-expiratory lung volume (EELV)/(end-release lung volume [ERLV]). The end-release lung volume can be adjusted and continually assessed by using the expiratory flow pattern (Fig. 4). The expiratory gas flow is a result of the inspiratory lung volume, the recoil or drive pressure of the lung, and downstream resistance (artificial airway, circuit, and PEEP valve) (Fig. 5). Experimental data in a porcine ALI model using dynamic computed tomography scanning shows that airway closure occurs rapidly (within 0.6 secs) (38, 62). However, the rapid airway closure in pig models of ALI may be related to poor collateral ventilation as opposed to human lungs. Collateral ventilation may play a significant role in recruitment/derecruitment in ALI (63).

Using a P_{low} of zero allows end-expiratory/release lung volume to be controlled by one parameter (time). The inherent resistance of the artificial airway behaves as a flow resistor/limiter and, if coupled with a brief release time, can effectively trap gas volume to maintain end-release or expiratory pressure (PEEP) (64, 65). During passive expiration or release in patients with ARDS, expiratory time constants are significantly modified (increased threefold) by the flow-dependent resistance of the artificial airway (66, 67).

Because the artificial airway produces a nonlinear, flow-dependent resistive load and the release results from a high lung volume, flow resistance will be highest at the initial portion of the release phase (67–69). The T_{low} or release phase is terminated T-PEFR rapidly before the flow-dependent expiratory load is dissipated, resulting in end-expiratory volume and pressure.

The residual pressure and volume in the lung during the brief release phase typically yields end-release or end-

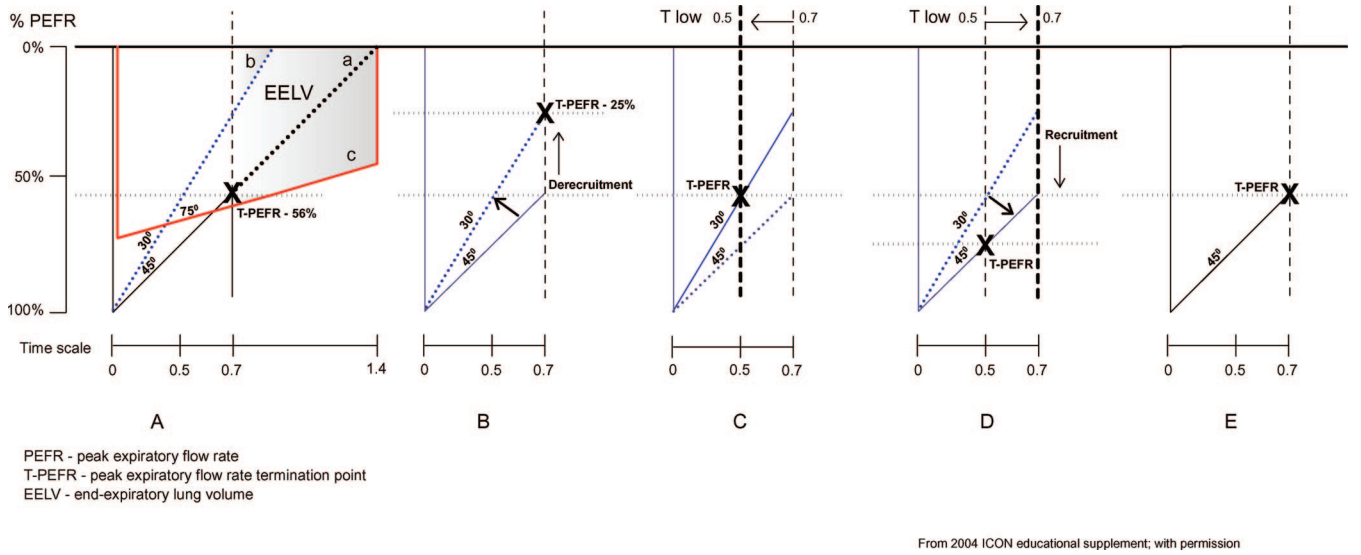

Figure 4. End-expiratory lung volume. Expiratory flow pattern during the release phase of airway pressure release ventilation. Initial portion of expiratory flow limb is the peak expiratory flow rate (PEFR) as a result of P_{high} to P_{low} pressure reduction. Deceleration of gas flow occurs as driving pressure dissipates producing the decelerating limb. PEFR and rate of deceleration are affected by inspiratory lung volume, thoracic recoil, and downstream resistance (artificial airway resistance with P_{low} of zero). *A*, expiratory flow pattern demonstrating normal deceleration at 45° as airways empty sequentially (67). Release time is adjusted to regulate T-PEFR to 60% of PEFR. The flow/time beyond the T-PEFR correlates with the end-release lung volume (ERLV) (end-expiratory lung volume [EELV]). The angle of deceleration (A_{DEC}) can suggest alterations in lung mechanics resulting in altered expiratory gas flow ([a] Normal (45°), [b] restrictive, e.g., decrease thoracic compliance (<45°) [c] obstructive, e.g., OLD, small or obstructed artificial airway (>45°)]. *B*, expiratory flow pattern with lung changes indicating derecruitment. As lung compliance worsens (less end-inspiratory lung volume and increasing thoracic recoil, e.g., increased lung water or decreased thoracic/abdominal compliance), the expiratory flow pattern will become more restricted (the decelerating limb will become steeper, i.e., A_{DEC} <45°) and the set release time will result in a lower T-PEFR and less end-expiratory lung volume (or ERLV); lower ERLV with resulting airway closure/derecruitment. *C*, the release time can be adjusted to limit airway closure and prevent derecruitment. *D*, conversely, as respiratory mechanics improve (lung, thoracic, abdominal compliance), recruitment is reflected as the decelerating limb returns to a 45° angle and the set release time increases the T-PEFR regulating ERLV (EELV). *E*, the release time can be readjusted to maintain T-PEFR at 50% to 75%. Reprinted from ICON educational supplement 2004 with permission.

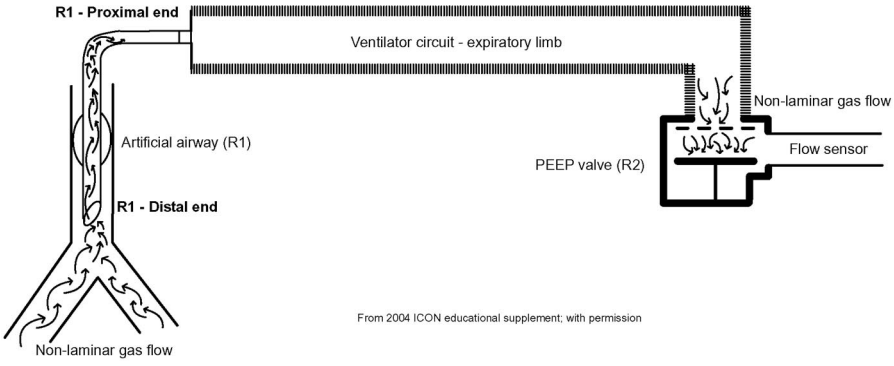

Figure 5. Patient interface to mechanical ventilator circuit and inherent resistance to expiratory flow from artificial airway (R1) and positive end-expiratory pressure (*PEEP*) valve (R2). Because the release occurs from a high lung volume during airway pressure release ventilation, flow resistance develops at the distal end of R1 and R2. The proximal end of R1 decompresses more rapidly than the distal end. Despite zero end-expiratory pressure (ZEEP), flow resistance at R2 (typically measured approximately 8 ft away) contributes to tracheal pressure elevation above end-expiratory pressure. Flow resistance is highest at the onset of the release (>0.2 L/sec) and decreases as expiratory flow rate declines. Release time is terminated after a brief duration before flow resistance dissipates to maintain end-expiratory lung volume (67–69). Reprinted from ICON educational supplement 2004 with permission.

expiratory pressure greater than the P_{low} arbitrarily set at the machine's peep valve (approximately 8 ft away). In fact, commercially available ventilators with tube compensation algorithms for resistance of artificial airways provide inadequate expiratory compensation when PEEP is reduced to atmospheric pressure. The addition of a negative pressure source to briefly lower the end-expiratory pressure to subatmospheric is required to fully compensate the expiratory resistance imposed by the artificial airway (70).

By using a P_{low} >0 cm H_2O, peak expiratory flow rate (PEFR) is delayed, whereas a P_{low} of 0 cm H_2O accelerates PEFR concluding the release phase earlier and enabling the P_{high} phase to be resumed earlier in the cycle. A greater percent of the cycle time at T_{high} increases the potential for recruitment, maintains lung volume, limits derecruitment, and induces spontaneous breathing. See Table 2 for goals, set up, oxygenation, ventilation, weaning, and precautions during utilization of APRV.

Spontaneous Breathing During Airway Pressure Release Ventilation

During APRV, patients can control the frequency and duration of spontaneous inspiration and expiration. Patients are not confined to a preset I:E ratio, and spontaneous tidal volumes maintain a sinusoidal flow pattern similar to normal spontaneous breaths. The ability of critically ill patients to effectively augment

Table 2. Airway pressure release ventilation (APRV) clinical guide

Goals
- Acute (recruitable) restrictive lung disease (RLD)
  - Increase (recruit) and maintain lung volume (P_{high} and T_{high})
  - Decrease elastic WOB with CPAP (P_{high} and T_{high})
  - ATC set at 100% to maximally compensate for artificial airway resistance and decrease resistive WOB imposed by the artificial airway[a]
  - Minimize number of releases to supplement ventilation from spontaneous breathing (71)
  - Limit derecruitment; T_{low} set to ensure T-PEFR is >50 and ≤75%
  - Allow spontaneous breathing within 24 hrs of APRV application
- Acute obstructive lung disease (OLD)
  - Decrease lung volume
  - Maintain P_{high} at or 1–2 cm H_2O above PEEPi
  - Minimize number of releases to supplement ventilation from spontaneous breathing (71)
  - Stint airways; T_{low} set for 25–50% T-PEFR
- Allow spontaneous breathing within 24 hrs of APRV application. May require a brief course of NMBA (<24 hrs) to control high spontaneous breathing frequency and artificial airway contribution to dynamic hyperinflation.

Set-up—adults
- Newly intubated
  - P_{high}—set at desired plateau pressure (typically 20–35 cm H_2O)
  - **Note:** P_{high} >35 cm H_2O may be necessary in patients with decreased thoracic/abdominal compliance or morbid obesity (73, 74). With a P_{high} >25 cm H_2O, use of noncompliant ventilator circuit is recommended to minimize circuit volume compression (75, 76).
  - P_{low}—0 cm H_2O
  - T_{high}—4–6 secs
  - T_{low}—0.2–0.8 secs (RLD)
  - 0.8–1.5 secs (OLD)
- Transition from conventional ventilation
  - P_{high}—plateau pressure in volume-cycled mode or peak airway pressure in pressure-cycled mode
  - P_{low}—0 cm H_2O
  - T_{high}—4–6 secs
  - T_{low}—0.2–0.8 secs (RLD)
  - 0.8–1.5 secs (OLD)
- Transition from HFOV[b]—use noncompliant ventilator circuit
  - P_{high}—mPaw on HFOV ***plus*** 2–4 cm H_2O
  - P_{low}—0 cm H_2O
  - T_{high}—4–6 secs
  - T_{low}—0.2–0.8 secs (RLD)
  - 0.8–1.5 secs (OLD)

Set-up—Pediatrics
- Newly intubated
  - P_{high}—set at desired plateau pressure (typically 20–30 cm H_2O)
  - **Note:** P_{high} >30 cm H_2O may be necessary in patients with decreased thoracic/abdominal compliance or morbid obesity (73, 74). With a P_{high} >25 cm H_2O, use of noncompliant ventilator circuit is recommended to minimize circuit volume compression (75, 76).
  - P_{low}—0 cm H_2O
  - T_{high}—3–5 secs
  - T_{low}—0.2–0.8
- Transition from conventional ventilation
  - P_{high}—plateau pressure in volume-cycled mode or peak airway pressure in pressure-cycled mode
  - P_{low}—0 cm H_2O
  - T_{high}—3–5 secs
  - T_{low}—0.2–0.8
- Transition from HFOV[b]
  - P_{high}—mPaw on HFOV **plus** 2–4 cm H_2O
  - P_{low}—0 cm H_2O
  - T_{high}—3–5 secs
  - T_{low}—0.2–0.8

Set-up—Neonates
- Newly intubated
  - P_{high}—set at desired plateau pressure (typically 10–25 cm H_2O)
  - **Note:** P_{high} >25 cm H_2O may be necessary in patients with decreased thoracic/abdominal compliance (73, 74). With a P_{high}>25 cm H_2O, use of noncompliant ventilator circuit is recommended to minimize circuit volume compression (75, 76).
  - P_{low}—0 cm H_2O
  - T_{high}—2–3 secs
  - T_{low}—0.2–0.4
- Transition from conventional ventilation
  - P_{high}—plateau pressure in volume-cycled mode or peak airway pressure in pressure-cycled mode
  - P_{low}—0 cm H_2O
  - T_{high}—2–3 secs
  - T_{low}—0.2–0.4
- Transition from HFOV[b]
  - P_{high}—mPaw on HFOV **plus** 0–2 cm H_2O
  - P_{low}—0 cm H_2O
  - T_{high}—2–3 secs
  - T_{low}—0.2–0.4

Continues

Table 2. Continued

Oxygenation
Optimize end-expiratory or release lung volume
Reassess release volume to ensure T-PEFR is >50 and ≤75%
If oxygenation poor and T-PEFR ≤50%, decrease release time until T-PEFR 75%
Optimize gas exchange surface area by adjusting mPaw
Increase P_{high} or P_{high} and T_{high} simultaneously
Adjustment of P_{high} to recruit by achieving TOP
Adjustment of T_{high} increases gas mixing and recruits lung units with high resistance time constants
Assess hemodynamics
Ventilation
Assess for oversedation; consider using sedation scale (77)
Optimize end-expiratory or release lung volume; reassess release volume to ensure at 50–75% T-PEFR
If T-PEFR ≥75% and oxygenation is acceptable, consider increasing T_{low} by 0.05–0.1 increments to achieve 50% T-PEFR
If T-PEFR ≤50%, decrease T_{low} to achieve minimum T-PEFR of 50%
Increase alveolar ventilation (*preferred method*)—increase P_{high} or P_{high} and T_{high} simultaneously
Increase minute ventilation—decrease T_{high} and increase P_{high} simultaneously (see precautions below)
Weaning
Simultaneously reduce P_{high} and increase T_{high} for a gradual reduction of mPaw and to increase the contribution of spontaneous to total minute ventilation.
Progress to CPAP with automatic tube compensation when P_{high} ≤16 and T_{high} ≥12–15 sec (APRV = 90% CPAP)
Wean CPAP (with automatic tube compensation) and consider extubation when CPAP 5–10 cm H_2O
Precautions
Adjustment of T_{low} differs with lung disease, lung volume and artificial airway size. T_{low} values provided are typical but not absolute; see goals for OLD and RLD
If minute ventilation is increased by decreasing T_{high} in an attempt to improve Co_2 clearance, mPaw and gas exchanging surface area will be reduced; more so if P_{high} is not simultaneously increased as Co_2 may paradoxically increase (see text for details). May need to decrease T_{low} as T_{high} reduction may produce less mean alveolar volume (lung volume) and will result in shorter emptying time.
T_{low} should not be extended solely to lower Co_2 as this may lead to airway closure (derecruitment) (38, 56, 71). Additionally, T_{low} should not be viewed as an expiratory time as the patient may exhale throughout the respiratory cycle if permitted (58).

ATC, automatic tube compensation; $PEEP_i$, intrinsic PEEP; mPaw, mean airway pressure; PEFR, peak expiratory flow rate; T-PEFR, peak expiratory flow rate termination; HFOV, high-frequency oscillatory ventilation; WOB, work of breathing; APRV, airway pressure release ventilation; TOP, threshold opening pressure.

[a] *In vitro* resistance may be greater than *in vivo* resistance calculations and measurements (commercial tube compensation algorithms) due to deformation, kinks and secretion in the artificial airway (64, 65, 72); [b] mPaw during HFOV is equal to CPAP; mPaw during APRV is typically 2–4 cm H_2O less than CPAP as a result of the release phase (airway pressure interruption) and proximal vs. distal mPaw measurement. Reprinted from ICON Educational Supplement—2004 with permission.

spontaneous ventilation in response to changing metabolic needs may promote synchrony during mechanical ventilation and improve V/Q matching (3–6, 10, 11). In contrast, patients transitioned from spontaneous breathing to mechanical ventilation through the induction of anesthesia exhibit worsening gas exchange and dependent atelectasis on computed tomography scan within minutes (7–9, 76–83). These studies suggest rapid alteration of ventilation distribution when the respiratory system becomes passive.

Most mechanical ventilators monitor airway pressures; however, transpulmonary pressures ultimately determine lung volume change. Although difficult to monitor clinically, the effects of pleural pressure on transpulmonary pressures should not be excluded from management principles. For example, patients with reduced thoracic and abdominal compliance demonstrate higher airway pressure yet may have lower transpulmonary pressure (73, 74).

Spontaneous breathing, diaphragmatic tone, and prone positioning modify pleural pressure, improving transalveolar pressure gradients in dependent lung regions (7, 84–87). Increased dependent lung ventilation during spontaneous breathing recruits alveoli improving V/Q matching without raising applied airway pressure (3–6, 10, 11).

APRV and prone positioning may have an additive effect on recruitment and gas exchange. Varpula demonstrated greater improvement in gas exchange when prone positioning was combined with APRV rather than synchronized intermittent mandatory ventilation (10).

Hemodynamic Effects of Airway Pressure Release Ventilation

The descent of the diaphragm into the abdomen during a spontaneous breathing effort simultaneously decreases pleural pressures and increases abdominal pressure. This effectively lowers the right atrial (RA) pressure while compressing abdominal viscera propelling blood (preload) into the inferior vena cava (IVC). Increasing the mean systemic pressure (MSP)/RA gradient couples the thoracic and cardiac pumps, increasing venous return, improving cardiac output, and decreasing dead space ventilation (88, 89). Conversely, when spontaneous breathing is limited or the diaphragm is paralyzed, the passive decent of the diaphragm is no longer linked with lower pleural/right atrial pressure, minimizing the IVC–right atrial pressure gradient (MSP-RA) and limiting venous return/cardiac output.

Restoration of cardiopulmonary interaction with spontaneous breathing during APRV produces improvements in systemic perfusion. Animal and human studies document improved splanchnic and renal perfusion during APRV with spontaneous breathing (13, 90)

Use of Pressure Support Ventilation with Airway Pressure Release Ventilation

Currently, some ventilator manufacturers incorporate pressure support ventilation (PSV) above P_{high}. The addition of

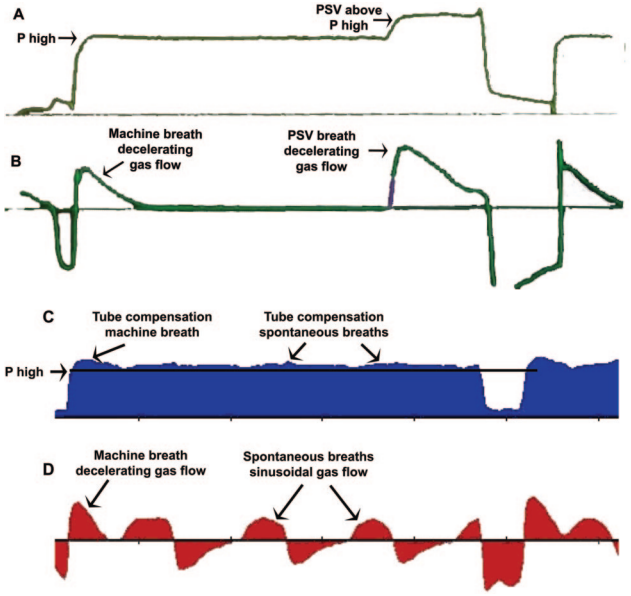

Figure 6. *A*, pressure tracing represents a pressure support ventilation (*PSV*) breath at the P_{high} level. During passive efforts, once the PSV trigger threshold is reached, airway pressure elevates above the P_{high} level. Alternatively, if the patient generates vigorous inspiratory efforts, the transpulmonary pressure differential (sum of PSV, P_{high}, Pmus) can be significant and may result in overdistension. *B*, flow tracing demonstrates a triggered PSV breath with resultant decelerating gas flow as opposed to sinusoidal gas flow typical of spontaneous breathing (see D). *C*, pressure tracing represents airway pressure release ventilation (APRV) with automatic tube compensation; note minimal airway pressure elevation above P_{high}. *D*, spontaneous breaths during APRV with automatic tube compensation, preserving a sinusoidal flow pattern. Reprinted from ICON educational supplement 2004 with permission.

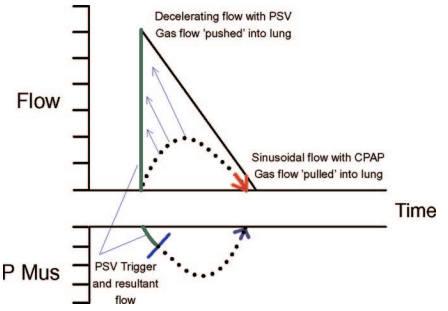

Figure 7. Gas flow pattern comparing pressure support ventilation (*PSV*) and spontaneous breathing. PSV produces a decelerating gas flow pattern because the gas flow and patient effort (*P Mus*) do not follow a similar time course. Typically, patient effort is outpaced by applied flow and pressure development. Gas distribution during PSV is similar to an assisted breath rather than a spontaneous breath. Spontaneous or unassisted continuous positive airway pressure (*CPAP*) breath producing a sinusoidal gas flow pattern as gas flow and patient effort (P Mus) are coupled and follow a similar time course. Spontaneous ventilation (unassisted) is associated with improved ventilation/perfusion distribution, unlike PSV (4, 6, 26, 92–94). Reprinted from ICON educational supplement 2004 with permission.

PSV to APRV contradicts limiting airway pressure and lung distension during ventilation by not restricting lung inflation to the P_{high} level.

PSV above P_{high} may lead to significant elevation in transpulmonary pressure (Fig. 6). When PSV is triggered during the P_{high} phase, the higher baseline lung volume distends further as the sum of P_{high}, PSV, and pleural pressure raises transpulmonary pressure. The additional lung distension above P_{high} and the transpulmonary pressure elevation will not be completely reflected in the airway pressure because the pleural pressure remains unknown (91). Furthermore, the imposition of PSV to APRV reduces the benefits of spontaneous breathing by altering sinusoidal spontaneous breaths to decelerating assisted mechanical breaths as flow and pressure development are uncoupled from patient effort (Fig. 7). Ultimately, PSV during APRV defeats improvements in distribution of ventilation and V/Q matching associated with unassisted spontaneous breathing (4, 6, 26, 92–94). During weaning, even low levels of PSV used to overcome tube resistance may overcompensate and convert patient-triggered efforts to assisted rather than spontaneous breaths, especially if adequate PEEP levels are used (95, 96). If patient efforts are more vigorous, the PSV will undercompensate artificial airway resistance.

Artificial Airway Compensation Algorithms and Airway Pressure Release Ventilation

Computerized ventilator algorithms, which attempt to match inspiratory flow to calculated resistance of the artificial airway during APRV may reduce spontaneous WOB (14). Unlike PSV, tube compensation algorithms apply inspiratory flow in proportion to the pressure drop across the artificial airway resulting from patient effort or flow demands (95, 96). As a result, the dynamic pressure applied to the artificial airway is determined within the breath cycle, limiting over- or undercompensation of artificial airway resistance. Furthermore, as tube compensation is coupled to patient effort, flow and resulting applied airway pressure do not exceed inspiratory pressure generated by the respiratory muscles (P_{mus}) (patient's effort), preserving the sinusoidal flow pattern of spontaneous breathing (97) (Fig. 6). Conversely, applying a fixed airway pressure like PSV may result in both over- and undercompensation of artificial airway resistance as patient effort (flow) varies.

Commercially available ventilators offer forms of tube compensation but vary in the efficiency of the algorithms applied. Although many ventilators may compensate inspiratory resistance effectively, expiratory compensation by lowering PEEP levels to atmosphere or ZEEP (at the initial phase of expiration) may not unload expiratory resistance imposed by the artificial airway. The application of negative airway pressure during the initial expiration phase may be necessary to negate the pressure drop across the artificial airway (70).

Airway Pressure Release Ventilation and Use of Sedation and Neuromuscular-Blocking Agents

Sedation is essential when caring for critically ill and injured patients requiring mechanical ventilation. In severe cases of patient–ventilator dyssynchrony, neuromuscular-blocking agents (NMBAs) are frequently used. Excessive sedation has been associated with increased duration of mechanical ventilation in patients with acute respiratory failure (98–103). Reducing the

duration of mechanical ventilation decreases patient exposure to artificial airways, sedation, and NMBAs and the likelihood of ventilator-associated pneumonia (VAP) (101, 104–106).

The negative impact of sedation and NMBAs on the duration of mechanical ventilation and the risk of VAP is likely to be in part related to depression of the cough reflex, increasing the risk of aspiration of pharyngeal secretions (107). Watando suggested that improved cough reflex may limit aspiration pneumonia in high-risk groups (108). Furthermore, an effective cough may be a predictor of hospital mortality and of successful extubation (109).

Because APRV uses an open breathing system and requires less sedation, patients can exhale or cough throughout the respiratory cycle. As a result, cough and secretion clearance can be facilitated without significant intrathoracic pressure elevation or airway pressure-limiting as would occur with a closed expiratory valve system.

APRV has been associated with a 70% reduction in NMBA requirements and a 30% to 40% reduction in sedation requirements when compared with conventional ventilation (3, 4, 11, 12, 23, 25, 110). In addition, some studies suggest a decrease in ventilator days and intensive care unit and hospital length of stay as a result of using APRV (4).

The ARDS Network (ARDSNet) reported a significant reduction of mortality from 39.8% to 31.0% with a low tidal volume strategy (6 mL/kg of ideal body weight) and a limited inspiratory plateau pressure (30 cm H_2O) using a volume-cycled mode (111). However, patients ventilated using low tidal volumes may experience more dyssynchrony and require additional sedation (Kallet RH, personal communication) (112–118).

Airway Pressure Release Ventilation for Trauma-Associated Acute Respiratory Distress Syndrome: Clinical Experience

APRV has been used at R Adams Cowley Shock Trauma Center (STC) in Baltimore, MD, since 1994 and has become a standard of care. In the early 1990s, STC established a regional advanced respiratory failure service, including the development of ventilation protocols aimed to reduce airway pressure with APRV, prone positioning, and an extracorporeal lung assist technique (119). The STC has logged over 50,000 patient-hours annually on APRV since 1994, developing significant clinical experience with APRV. At STC, the 2-yr period post-APRV implementation for the management of advanced respiratory failure was studied and documented a reduction in ARDS mortality and multisystem organ failure. The mortality rates after the implementation of APRV in patients meeting criteria for ARDS were lower than reported in the ARDSNet trial, 21.4% vs. 31% (120). In addition, sedation requirements were reduced and NMBA use essentially eliminated from routine practice at STC.

Weaning from Airway Pressure Release Ventilation

Patients with improved oxygenation on APRV (e.g., F_{IO_2} $\leq$40% with Sp_{O_2} $\geq$95%) can be progressively weaned by lowering the P_{high} and extending the T_{high}. By decreasing the number of releases, the minute ventilation output of the ventilator is reduced while simultaneously (if permitted) the patient's spontaneous minute ventilation increases, enabling a progressive spontaneous breathing trial (99) (Fig. 8). The total and spontaneous minute ventilation should be carefully monitored during weaning to anticipate changes in Pa_{CO_2}. Eventually, the ventilator's minute ventilation output is significantly reduced or eliminated and the patient has gradually transitioned to pure CPAP. CPAP, when combined with tube compensation, can be used to effectively overcome artificial airway resistance during the final phase of weaning. When used in the final weaning phase, tube compensation may be a useful predictor of successful extubation, particularly in the difficult-to-wean patient who fails PSV and T-piece weaning methods (96). This author believes that progressive extension of T_{high} during APRV weaning increases spontaneous breathing through a gradual transition to pure CPAP (with tube compensation). Therefore, transitioning the weaning APRV patient to PSV (a form of assisted breathing) may be counterproductive and unnecessary (121).

Airway Pressure Release Ventilation and High-Frequency Oscillatory Ventilation

Fundamentally APRV and high-frequency oscillatory ventilation (HFOV) have similar goals. Both techniques focus on maintaining lung volume while limiting the peak ventilating pressure. Maintaining lung volume optimizes V/Q matching, improves gas exchange, and improves stress distribution, minimizing shear forces. During HFOV, the continuous, high-flow gas pattern facilitates a constant airway pressure profile minimizing derecruitment. In contrast to HFOV, APRV actively promotes spontaneous breathing.

In addition, APRV does not require a single-purpose ventilator, effectively uses conventional humidification systems, and is associated with reduced sedation and NMBA use. Furthermore, because ALI can develop in 24% of patients receiving mechanical ventilation who did not have ALI at the onset (122), APRV as a lung protective strategy, may be used earlier rather than at advanced stages of respiratory failure. APRV can be applied as the initial ventilator mode for respiratory failure or typically before HFOV criteria are reached. For patients showing improvement on HFOV, APRV may represent an ideal transition/weaning modality because P_{high} on APRV can be matched to the mean airway pressure (mPaw) during HFOV, permitting continued gradual reduction of lung volume (123).

Noninvasive Ventilation with Airway Pressure Release Ventilation

APRV may also be applied noninvasively pre- or postintubation (124). Noninvasive APRV has the advantage of an adjustable degree of mandatory ventilation without the need for a trigger (only forms of APRV that do not use pressure support), decreasing the likelihood of autocycling from leaks common to noninvasive ventilation.

Future clinical research with APRV should test different algorithms for oxygenation, ventilation, and weaning. In addition, hemodynamic and systemic perfusion during APRV should be assessed. Animal studies should be performed with APRV (coupled with spontaneous breathing) to compare histologic and biomarker evidence of VILI/VALI compared with other mechanical ventilation approaches. The delivery of aerosol medications to the lung is poorly understood during APRV and should be studied. Ultimately, clinical studies should be conducted using a validated, protocolized approach to APRV

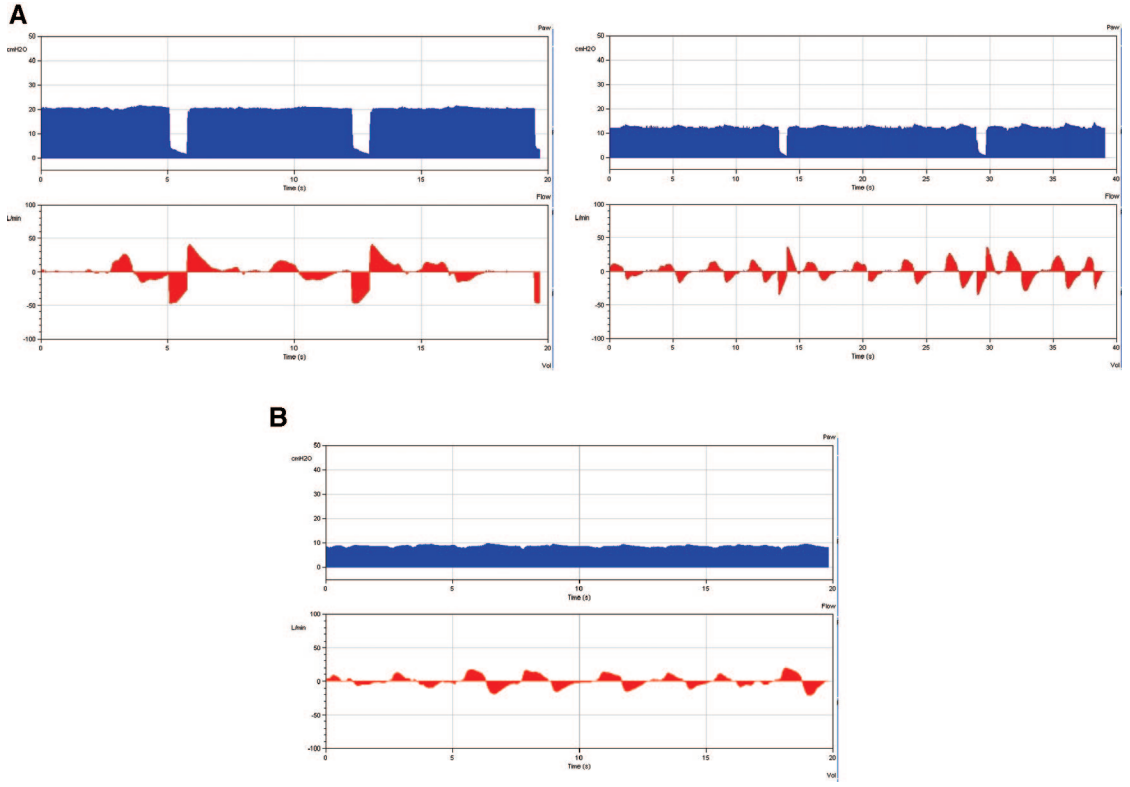

Figure 8. Airway pressure release ventilation weaning and gradual transition to pure continuous positive airway pressure (CPAP). Tube compensation may be used with the onset of spontaneous breathing and is not limited to the final weaning phase. *A*, sequentially decreasing P_{high} and increasing T_{high} simultaneously results in a gradual reduction of mean airway pressure. Mean airway pressure is reshaped to produce a lower and extended pressure profile. *B*, patient's increased spontaneous minute ventilation increases as fewer releases in P_{high} contribute less to the total minute ventilation. Eventually, the release phase provides minimal contribution to the total minute ventilation, and the patient has transitioned to CPAP (tube compensate remains active). Reprinted from ICON educational supplement 2004 with permission.

compared with a protective conventional ventilation strategy.

CONCLUSION

Clinical and experimental studies with APRV demonstrate improvements in physiological end points such as gas exchange, cardiac output, and systemic blood flow (3, 4, 6, 11, 13, 26, 90). APRV facilitates spontaneous breathing and improves patient tolerance to mechanical ventilation by decreasing patient–ventilator dyssynchrony. Additional studies document reduction in sedation and NMBAs with APRV, and some, but not all (10), studies suggest less ventilator days and shorter length of intensive care unit stay (3, 4, 11, 12, 23, 25, 111). An adequately designed and powered study to demonstrate a reduction in mortality or ventilator days with APRV compared with optimal lung protective conventional ventilation has not yet been performed. APRV (combined with tube compensation software) remains unique among potential "open lung" approaches to lung protective mechanical ventilation with the ability to facilitate spontaneous breathing.

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