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.

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
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 maneuver (e.g., P_{high} 40–50 cm H_{2}O and T_{high} 30–60 secs).

Conventional volume ventilation limits 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.

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 breathing 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_{2}O and T_{high} 30–60 secs).

Conventional volume ventilation limits 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 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).
Phigh, T high, P low, and T low. Time parameters in APRV are independent rather than following precise adjustment.

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

<table>
<thead>
<tr>
<th>Author (yr Published)</th>
<th>Study</th>
<th>Measurements</th>
<th>Findings</th>
<th>Study design</th>
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<td>Stock (1987)</td>
<td>APRV vs. IPPV; dogs with ALI (n = 10)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>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</td>
<td>Animal study, small n, and short-term observations</td>
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<tr>
<td>Garner (1988)</td>
<td>APRV vs. conventional ventilation, patients after cardiac surgery (n = 14)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>APRV had similar effects on blood gases but with significantly fewer adverse hemodynamic effects</td>
<td>Observational, crossover trial</td>
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<tr>
<td>Rasanen (1988)</td>
<td>APRV vs. conventional ventilation vs. CPAP; anesthetized dogs (n = 10)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>APRV increased V E more than CPAP; APRV provided similar gas exchange to conventional ventilation, but with fewer adverse hemodynamic effects</td>
<td>Animal studies, small n, and short-term observations</td>
</tr>
<tr>
<td>Martin (1991)</td>
<td>APRV vs. CPAP vs. conventional ventilation vs. spontaneous breathing; neonatal sheep with oleic-acid lung injury (n = 7)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>APRV provided similar gas exchange with lower PIP, but no hemodynamic advantage was identified</td>
<td>Animal studies, small n, and short-term observations</td>
</tr>
<tr>
<td>Davis (1993)</td>
<td>APRV vs. SIMV; surgery patients with ALI (n = 15)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>APRV provided 30% lower PIP, less venous admixture (14 vs. 21%), and better oxygenation; no difference in hemodynamics</td>
<td>Prospective, crossover trial</td>
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<tr>
<td>Putensen (1994)</td>
<td>APRV (with and without spontaneous breathing) vs. PSV; anesthetized dogs (n = 10)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>APRV provided similar gas exchange to conventional ventilation, but with fewer adverse hemodynamic effects</td>
<td>Animal studies, small n, and short-term observations</td>
</tr>
<tr>
<td>Sydow (1994)</td>
<td>APRV vs. volume-controlled inverse-ratio ventilation; patients with ALI; 24-hr observation periods (n = 18)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>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</td>
<td>Prospective, randomized, crossover trial</td>
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<tr>
<td>Calzia (1994)</td>
<td>BiPAP vs. CPAP; patients after bypass surgery (n = 19)</td>
<td>WOB and PTP</td>
<td>No difference</td>
<td>Prospective, crossover trial</td>
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<tr>
<td>Rathgeber (1997)</td>
<td>BiPAP vs. conventional ventilation vs. SIMV; patients after cardiac surgery (n = 596)</td>
<td>Duration of intubation, sedation requirement, analgesia requirement</td>
<td>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</td>
<td>Prospective, randomized, controlled, open trial over 18 months, uneven randomization</td>
</tr>
<tr>
<td>Kozmaier (2000)</td>
<td>BiPAP vs. SIMV vs. PSV; patients after coronary artery bypass (n = 24)</td>
<td>Blood gases, hemodynamics, lung volume, airway pressure, f, V T, V E</td>
<td>No differences in blood gases or hemodynamics</td>
<td>Prospective, crossover trial with short-term observations</td>
</tr>
<tr>
<td>Putensen (2001)</td>
<td>APRV vs. pressure controlled conventional ventilation; patients with ALI after trauma (n = 30)</td>
<td>Gas exchange, hemodynamics, sedation requirement, hemodynamic support, duration of ventilation, ICU stay</td>
<td>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</td>
<td>Randomized controlled, prospective trial, small n; the conventional ventilation group received paralysis for the first 3 days, potentially confounding results</td>
</tr>
<tr>
<td>Varpula (2003)</td>
<td>Combined effects of proning and SIMV PC/PS vs. APRV; patients with ALI (n = 45)</td>
<td>Blood gases, oxygenation (PaO2/FiO2 ratio), hemodynamic, sedation requirement</td>
<td>Oxygenation was significantly better in APRV group before and after proning; sedation use and hemodynamics were similar</td>
<td>Prospective, randomized intervention study</td>
</tr>
</tbody>
</table>

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.


In addition to F iO2 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
decrease in PaCO₂ as machine frequency decreases. This has been previously described and is similar to improved CO₂ clearance with increasing IE ratios (47–51). Despite the intermittent nature of ventilation, CO₂ delivery to the lung is continuous as cardiac output transfers CO₂ into the alveolar space, provided airways remain open (52). During the brief Tlow, released gas is exchanged with fresh gas to regenerate the gradient for CO₂ diffusion. In addition, cardiogenic mixing results in CO₂ movement toward central airways during the Thigh or breathhold period (46, 53–55), improving the efficacy of the release for ventilation. The addition of spontaneous breaths during the Thigh period at Phigh (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 Thigh may sacrifice alveolar ventilation and oxygenation. Reducing Thigh 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 (P̄high − P̄low), inspiratory lung volume (P̄high), the potential energy (recoil or compliance of the thorax and the amount of energy stored during Thigh), and downstream resistance (artificial airway). P̄low and Tlow 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 T̄high (80–95% of the total cycle time) occurs at the P̄high or CPAP level. To minimize derecruitment, the time (T̄low) at P̄low 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 T̄high, T̄low 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 P̄high phase. Active exhalation during the P̄high 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 (T̄low) 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 airflow 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 P̄low 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 Tlow 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-

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**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, CO₂-enriched gas is released to accommodate CO₂ into the alveolar space, provided airway-continuous as cardiac output transfers air to the lung is maintained, improving the efficacy of gas exchange. 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 H₂O, peak expiratory flow rate (PEFR) is delayed, whereas a P_low of 0 cm H₂O 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, setup, 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
- 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$_2$O 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$_2$O)
- Note: $P_{high}$ >35 cm H$_2$O may be necessary in patients with decreased thoracic/abdominal compliance or morbid obesity (73, 74). With a $P_{high}$ >25 cm H$_2$O, use of noncompliant ventilator circuit is recommended to minimize circuit volume compression (75, 76).
  - $P_{low}$—0 cm H$_2$O
  - $T_{high}$—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$_2$O
  - $T_{high}$—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$_2$O
  - $P_{low}$—0 cm H$_2$O
  - $T_{high}$—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$_2$O)
- Note: $P_{high}$ >30 cm H$_2$O may be necessary in patients with decreased thoracic/abdominal compliance or morbid obesity (73, 74). With a $P_{high}$ >25 cm H$_2$O, use of noncompliant ventilator circuit is recommended to minimize circuit volume compression (75, 76).
  - $P_{low}$—0 cm H$_2$O
  - $T_{high}$—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$_2$O
  - $T_{high}$—3–5 secs
  - $T_{low}$—0.2–0.8

Transition from HFOV$^b$

- $P_{high}$—$mPaw$ on HFOV plus 2–4 cm H$_2$O
  - $P_{low}$—0 cm H$_2$O
  - $T_{high}$—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$_2$O)
- Note: $P_{high}$ >25 cm H$_2$O may be necessary in patients with decreased thoracic/abdominal compliance (73, 74). With a $P_{high}$ >25 cm H$_2$O, use of noncompliant ventilator circuit is recommended to minimize circuit volume compression (75, 76).
  - $P_{low}$—0 cm H$_2$O
  - $T_{high}$—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$_2$O
  - $T_{high}$—2–3 secs
  - $T_{low}$—0.2–0.4

Transition from HFOV$^b$

- $P_{high}$—$mPaw$ on HFOV plus 0–2 cm H$_2$O
  - $P_{low}$—0 cm H$_2$O
  - $T_{high}$—2–3 secs
  - $T_{low}$—0.2–0.4

Continues
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).

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\textsubscript{high}, or P\textsubscript{high} and T\textsubscript{high} simultaneously

Adjustment of P\textsubscript{high} to recruit by achieving TOP

Adjustment of T\textsubscript{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\textsubscript{low} by 0.05–0.1 increments to achieve 50% T-PEFR

If T-PEFR ≤50%, decrease T\textsubscript{low} to achieve minimum T-PEFR of 50%

Increase alveolar ventilation (preferred method)—increase P\textsubscript{high} or P\textsubscript{high} and T\textsubscript{high} simultaneously

Increase minute ventilation—decrease T\textsubscript{high} and increase P\textsubscript{high} simultaneously (see precautions below)

Weaning

Simultaneously reduce P\textsubscript{high} and increase T\textsubscript{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\textsubscript{high} ≤16 and T\textsubscript{high} ≥12–15 sec (APRV = 90% CPAP)

Wean CPAP (with automatic tube compensation) and consider extubation when CPAP 5–10 cm H\textsubscript{2}O

Precautions

Adjustment of T\textsubscript{low} differs with lung disease, lung volume and artificial airway size. T\textsubscript{low} values provided are typical but not absolute; see goals for OLD and RLD

If minute ventilation is increased by decreasing T\textsubscript{high} in an attempt to improve CO\textsubscript{2} clearance, mPaw and gas exchanging surface area will be reduced; more so if P\textsubscript{high} is not simultaneously increased as CO\textsubscript{2} may paradoxically increase (see text for details). May need to decrease T\textsubscript{low} as T\textsubscript{high} reduction may produce less mean alveolar volume (lung volume) and will result in shorter emptying time.

T\textsubscript{low} should not be extended solely to lower CO\textsubscript{2} as this may lead to airway closure (derecruitment) (38, 56, 71). Additionally, T\textsubscript{low} should not be viewed as an expiratory time as the patient may exhale throughout the respiratory cycle if permitted (58).

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 visceral 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 descent 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\textsubscript{high}. The addition of

Table 2. Continued

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<th>Ventilation</th>
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<td>Increase minute ventilation—decrease T\textsubscript{high} and increase P\textsubscript{high} simultaneously (see precautions below)</td>
<td>Increase alveolar ventilation (preferred method)—increase P\textsubscript{high} or P\textsubscript{high} and T\textsubscript{high} simultaneously</td>
<td>Progress to CPAP with automatic tube compensation when P\textsubscript{high} ≤16 and T\textsubscript{high} ≥12–15 sec (APRV = 90% CPAP)</td>
<td>Wean CPAP (with automatic tube compensation) and consider extubation when CPAP 5–10 cm H\textsubscript{2}O</td>
<td>Adjust T\textsubscript{low} differently with lung disease, lung volume, and artificial airway size. T\textsubscript{low} values provided are typical but not absolute; see goals for OLD and RLD</td>
</tr>
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**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); mPaw during HFOV is equal to CPAP; mPaw during APRV is typically 2–4 cm H\textsubscript{2}O 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.
PSV to APRV contradicts limiting airway pressure and lung distension during ventilation by not restricting lung inflation to the P$_{\text{high}}$ level. PSV above P$_{\text{high}}$ may lead to significant elevation in transpulmonary pressure (Fig. 6). When PSV is triggered during the P$_{\text{high}}$ phase, the higher baseline lung volume distends further as the sum of P$_{\text{high}}$, PSV, and pleural pressure raises transpulmonary pressure. The additional lung distension above P$_{\text{high}}$ 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$_{\text{mus}}$) (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 dysynchrony, 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 NMBAs 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 H2O) 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 NMBAs use essentially eliminated from routine practice at STC.

Weaning from Airway Pressure Release Ventilation

Patients with improved oxygenation on APRV (e.g., FIO2 <40% with Spo2 ≥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 PacO2. 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, the weaning the 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 NMBAs 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 autot-cycling 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
compared with a protective conventional ventilation strategy.

CONCLUSION

Clinical and experimental studies with APRV demonstrate improvements in physiological endpoints 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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REFERENCES


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 $P_{\text{high}}$ and increasing $T_{\text{high}}$ 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 $P_{\text{high}}$ 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 compensation remains active). Reprinted from ICON educational supplement 2004 with permission.


22. Hutchison AA, Leaderstorf MR, Habashi NM: Airway pressure release ventilation in a preterm infant with severe bronchopulmonary dysplasia. 10th Annual REAson meet-

ing; June 27–28, 2004; University of War-


55. Rose G, Cassidy S, Johnson R: Diffusing capacity at different lung volumes during


spontaneously. N Engl J Med 1996; 335:
1864–1869
cations of extubation delay in brain-injured
patients meeting standard weaning criteria.
Am J Respir Crit Care Med 2000; 161:
1530–1536
102. Ibrahim EH, Tracy L, Hill C, et al: The
occurrence of ventilator-associated pneu-
monia in a community hospital: risk factors
and clinical outcomes. Chest 2001; 120:
555–561
103. Cook DJ, Walter SD, Cook RJ, et al: Inci-
dence of and risk factors for ventilator asso-
ciated pneumonia in critically ill patients.
of a nursing-implemented sedation protocol
on the duration of mechanical ventilation.
Crit Care Med 1999; 27:2609–2615
105. Ely EW, Meade MO, Haponik EF, et al: Me-
chanical ventilator weaning protocols
driven by nonphysician health-care profes-
sionals: evidence-based clinical practice
guidelines. Chest 2001; 120:454S–463S
pneumonia. State of the art. Am J Respir
Crit Care Med 2002; 165:867–903
107. Craven DE, Steger KA: Epidemiology of
nosocomial pneumonia: new perspectives
on an old disease. Chest 1995; 108(suppl):
1S–16S
oral care and cough reflex sensitivity
in elderly nursing home patients. Chest
2004; 126:1666–1670
peak flows and extubation outcomes.
Chest 2003; 124:286–286
110. Hotman C, Baum M, Putensen C, et al: Biph-
asic positive airway pressure (BiPAP)—a new
mode of ventilatory support. Eur J Anaesthesiol
1994; 11:37–42
111. The Acute Respiratory Distress Syndrome
Network: Ventilation with lower tidal vol-
umes as compared with traditional tidal vol-
umes for acute lung injury and the acute
2000; 342:1301–1308
112. Kallet R, Corral W, Silverman H, et al: Im-
plementation of a low tidal volume ventila-
tion protocol for patients with acute lung
injury and the acute respiratory distress
syndrome. Respir Care 2001; 46:1024–1037
113. Kallet RH, Luce JM: Detection of patient-
ventilator asynchrony during low tidal vol-
ume ventilation, using ventilator waveform
graphics. Respir Care 2002; 47:183–185
114. Kallet RH, Alonso JA, Martin L, et al, for the
NIH NHLBI ARDS Network: Incidence of
respiratory distress or patients ventilator
dysynchrony during low tidal volume ven-
tilation in patients with acute lung injury.
Respir Care 2001; 46:1122
115. Kallet RH, Alonso JA, Martin L, et al, for the
NIH NHLBI ARDS Network: Sedation and neu-
romuscular blocking agent requirements
during initiation of low tidal volume ven-
tilation in patients with acute lung injury
(ALI). Respir Care 2001; 46:1122
116. Kallet RH, Alonso JA, Martin L, et al, for the
NIH NHLBI ARDS Network: Characteristics of
acute lung injury patients exhibiting re-
spiratory distress or dysynchrony during
low tidal volume ventilation. Respir Care
2001; 46:1122
117. Kallet RH, Corral W, Hayden D, et al, for the
NIH NHLBI ARDS Network: Does high level
minute ventilation demand limit imple-
mentation of the Acute Respiratory Distress
Syndrome (ARDS) Network low tidal vol-
ume ventilation protocol? Respir Care
2001; 46:1122
118. Eichacker PQ, Gerstenberger EP, Banks
and acute respiratory distress syndrome tri-
als testing low tidal volumes. Am J Respir
Crit Care Med 2002; 166:1510–1514
Interhospital transport of the extremely ill
patient: The mobile intensive care unit. Crit
Care Med 2000; 28:79–85
120. Navarrete-Navarra P, Rodriguez A, Reynolds
H, et al: Acute respiratory distress syn-
drome among trauma patients: trends in
ICU mortality, risk factors, complications
and resource utilization. Intensive Care
Med 2001; 27:1133–1140
tubation after spontaneous breathing auto-
matic tube compensation, t-tube, or pres-
sure support ventilation. Acta Anaesthesiol
Scand 2002; 46:973–979
122. Gajic O, Dara S, Mendez J, et al: Ventilator-
associated lung injury in patients without
acute lung injury at the onset of mechanical
ventilation. Crit Care Med 2004; 32:
1817–1824
123. Derdak S: High-frequency oscillatory venti-
lation for acute respiratory distress syn-
drome in adult patients. Crit Care Med
2001; 29(suppl):S317–S323
pressure release ventilation by mask. Crit
Care Med 1988; 16:1250–12