

Applications of Airway Pressure Release Ventilation

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Abstract The purpose of this review is to cover the definition and mechanism of airway pressure release ventilation, its advantages, and applications in acute lung injury.

Keywords Acute lung injury · Pressure release ventilation · Respiratory distress syndrome · Mechanical ventilation

Introduction

Airway pressure release ventilation (APRV) is a relatively new mode of ventilation, having first been described in 1987 by Stock et al. [1]. It first became commercially available in the mid-1990s. It has been described as continuous positive airway pressure (CPAP) with an intermittent pressure release phase. It has gained popularity recently due to the decreased need for sedation and neuromuscular blockade while using this mode of ventilation. It has also been identified as a safe alternative for ventilating patients with acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) [2]. APRV has also

been shown to facilitate spontaneous breathing, decreased peak airway pressures, and improved oxygenation and ventilation compared to other modes of ventilation.

Terminology

Although there is no consistent vocabulary for describing the settings of APRV, there are some commonly understood and accepted terms. These include pressure high (P High), pressure low (P Low), time high (T High), and time low (T Low). P High is the higher and P Low is the lower of the two airway pressure levels, respectively. P Low can also be thought of as the peak end expiratory pressure (PEEP). T High is the length of time at which the pressure is at P High. T Low is the length of time at which the pressure is at P Low, or the length of time when the airway pressure is released. On this mode of ventilation, the mean airway pressure can thus be calculated: $(P \text{ High} \times T \text{ High}) + (P \text{ Low} \times T \text{ Low}) / (T \text{ High} + T \text{ Low})$.

One aspect of APRV is its similarity to another mode of ventilation, namely, biphasic positive airway pressure (BIPAP). The main difference between APRV and BIPAP is the difference of timing in high and low pressure levels. T High on APRV would be longer than intermittent positive airway pressure (IPAP) on BIPAP [3].

Application of and Indications for APRV

Stock et al. [1] were first to describe APRV and are credited with its introduction. They found that in canines APRV was associated with lower peak inspiratory pressure (PIP) and better oxygenation than was continuous mandatory ventilation. Garner [4] performed the first patient trial with

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14 adults and confirmed the animal study findings. Rasanen [5] (from the Stock et al. research group) studied APRV in canines and found that it resulted in less circulatory interference than did continuous mandatory ventilation. Martin [6] used a neonatal lamb model of oleic acid injury and found that APRV provided similar gas exchange at lower PIP. A multi-institution trial of APRV, which included 50 patients, showed that APRV successfully controlled PaCO₂ in 47 patients [7]. As in previous trials, APRV was associated with significantly lower PIP (55%) than was conventional ventilation. Additional trials with patients in acute respiratory failure [8] after cardiac surgery [9] and in postoperative respiratory failure [10] again confirmed that APRV provided similar gas exchange and lower PIP than conventional ventilation. Putensen et al. [11] conducted an animal study in which they used the multiple inert gas elimination technique (MIGET) and found that APRV provided better ventilation/perfusion (V/Q) matching than pressure support ventilation (PSV). That report confirmed the contention that the role of APRV is to establish lung volume and allow spontaneous breathing. The V/Q differences were all associated with the presence of spontaneous breathing. Sydow et al. [12] compared APRV to volume-controlled inverse-ratio ventilation in 18 patients in acute respiratory failure. Each mode was provided in random sequence for 24 h. APRV provided better gas exchange and lower PIP. Calzia et al. [13] introduced the term “biphasic CPAP” in a study of 19 patients after coronary bypass surgery. They compared biphasic CPAP to PSV and found that PIP and work of breathing (WOB) were both greater during biphasic CPAP. Rathgeber et al. [14] performed the largest trial of any reviewed in the present report; they compared continuous mandatory ventilation, intermittent mandatory ventilation (IMV), and biphasic CPAP in 596 post-cardiac-surgery patients. Patients were randomized into three groups with 123 patients in the continuous mandatory ventilation group, 431 patients in the IMV group, and only 42 patients in the biphasic CPAP group. Patients in the biphasic CPAP group had about a 3–4-h shorter intubation. Patients in the continuous mandatory ventilation group required greater sedation and analgesia than those in the IMV or biphasic CPAP group. Rathgeber et al. concluded that the maintenance of spontaneous breathing during biphasic CPAP improves patient comfort and thus reduces pain and anxiety. Staudinger [15] compared the oxygen cost of breathing during BIPAP and PSV for 20 patients receiving long-term ventilation in a medical intensive care unit. They found no difference in any of the measured variables. They concluded that both BIPAP and PSV are acceptable for partial ventilatory support of those patients. Kazmaier et al. [16] compared BIPAP, IMV, and PSV in 24 patients after cardiac surgery and found no difference in gas exchange or hemodynamic

variables. PIP was lower with BIPAP than with IMV or PSV. In an animal study of oleic acid lung injury, Neumann and Hedenstierna [17] found that APRV provided better oxygenation than did CPAP because of the higher mean airway pressure. In a comparison of APRV and PSV at equal airway pressures, Putensen et al. [18] found that APRV provided better V/Q matching in patients who had ALI. That study evaluated APRV with and without spontaneous breathing and again highlighted the importance of spontaneous breathing for V/Q matching. Kaplan et al. [19] compared APRV to pressure-controlled inverse-ratio ventilation in 12 ALI patients. APRV provided lower airway pressure, better cardiac performance, and was associated with less vasopressor use. These results may have been due to the positive effects of spontaneous breathing or the lower intrinsic PEEP with APRV. Perhaps the most often cited study of APRV versus continuous mandatory ventilation is the study by Putensen et al. [20] of 30 trauma patients suffering from acute respiratory distress syndrome. They randomized patients (15 in each group) to receive APRV or pressure-controlled continuous mandatory ventilation. The APRV group had better gas exchange, hemodynamic performance, and lung compliance and required less sedation and fewer vasopressors. The APRV group had shorter duration of ventilation (15 vs. 21 days) and a shorter intensive care unit stay (23 vs. 30 days).

Based on clinical and experimental data, APRV is indicated as an alternative mode of ventilation for patients with ALI, ARDS, and atelectasis after major surgery. During the introduction of general anesthesia and post-surgery, alveolar derecruitment can take place by placing the patient on APRV mode of ventilation and the clinician can extend the time spent in P High. This will create the potential for alveolar recruitment and improved oxygenation. APRV can hardly be considered a new mode at this point. The evidence is strong that APRV provides lower PIP than does continuous mandatory ventilation.

When converting the patient from a more conventional mode of ventilation to APRV, the prior ventilator settings must be taken into consideration, along with the patient's clinical picture. The P High may be set by using the plateau pressure on the conventional mode as the initial P High. The initial maximum level of P High is normally 35 cmH₂O. P Low initially set at zero produces a minimal amount of expiratory resistance. The rapid drop in pressure facilitates acceleration of expiratory flow rates. The T High is set initially at 4.0 s. The mean airway pressure is lower when the initial setting is less than 4.0 s; this could contribute to airway closure and decrease alveolar surface area for gas exchange. T Low is initially set between 0.5 and 1.0 s, most commonly at 0.8 s initially. These settings (P High/P Low 35/0, T High/T Low 4.0/0.8) result in a mean airway pressure of 29.2 cmH₂O [3]. The advantages of

these settings over conventional modes is that the mean airway pressure is maintained at 29 cmH₂O and also limits the peak or plateau pressure to 35 cmH₂O while still producing a satisfactory tidal ventilation.

When using APRV as the initial mode of ventilation, standard parameters are implemented and adjusted accordingly (Table 1). The plateau pressure must be monitored while adjusting settings as this is currently the

Table 1 Airway pressure release ventilation (APRV)

Terminology:

P High: PEEP high, elevated baseline pressure

P Low: PEEP low, low pressure (not actually reached due to T Low setting)

T High: Time at which P High is maintained (minimum 4 s)

T Low: Time at which P High is terminated; set to achieve expiratory flow from patient ends at about 50–75% of peak expiratory flow

TOP: Threshold opening pressure

Goals:

1. Increase (recruit) and maintain lung volume (P High and T High)
2. Decrease elastic WOB
3. Limit derecruitment; set T Low to ensure expiratory flow from patient ends at about 50–75% of peak expiratory flow
4. Keep in mind that patients do not have to be breathing. APRV promotes spontaneous breathing, but at high P High levels this can be uncomfortable. The goal is to allow spontaneous breathing within 24–48 h of APRV application

Set-up—adults

Newly intubated

P High: set at desired plateau pressure (typically 20–35 cmH₂O)

P Low: 0 cmH₂O

T High: 4–6 s

T Low: 0.2–0.8 adjust for expiratory flow from patient ends at about 50–75% of peak expiratory flow

Transition from conventional ventilation

P High: plateau pressure in volume-cycled mode or peak airway pressure in pressure-cycled mode

P Low: 0 cmH₂O

T High: 4.5 s

T Low: 0.2–0.8 adjust expiratory flow from patient ends at about 50–75% of peak expiratory flow

Ventilation

PCO₂ High

1. Reassess release volume and ensure expiratory flow from patient ends at about 50–75% of peak expiratory flow
2. Increase minute ventilation: shorten T High (increase rate) and increase P High simultaneously (see Precautions in Table 2)
3. Increase alveolar ventilation: increase P High or P High and T High simultaneously
This seems opposite to what is appropriate, but increasing time for gas exchange (alveolar ventilation) may help rather than increase a minute volume that is inefficient at CO₂ clearance
4. If your patient has been spontaneously breathing, assess for oversedation

PCO₂ Low

1. Decrease minute ventilation: lengthen T High (decrease rate)
2. Only decrease P High (2 cmH₂O increments) if your oxygenation is within desired range

Oxygenation

PaO₂ Low

1. Reassess release volume and ensure expiratory flow from patient ends at about 50–75% of peak expiratory flow
2. Increase P High to recruit by reaching TOP
3. Increase P High and T High simultaneously
4. Lengthening T High (decreasing the rate) increases gas mixing and recruits lung units with high resistance time constants. This will also increase your mean airway pressure
5. Assess hemodynamics

PaO₂ High

1. Decrease FiO₂
2. Only decrease P High (2–4 cmH₂O increments) if your pH is within desired range

best available estimate of maximum alveolar pressure. Although primarily demonstrated in animals, a transalveolar pressure greater than 30 cmH₂O is associated with alveolar overdistension and lung injury. Occasionally, a slightly higher P High of 40–45 cmH₂O may be needed to either oxygenate or ventilate patients who have low-compliance respiratory systems (i.e., patients with morbid obesity chest wall edema or abdominal distension).

A T High of 4.0 s is a desirable minimum. This provides an almost continuous airway pressure level that maintains alveolar recruitment and optimizes compliance and oxygenation. The T High can be progressively lengthened by 0.5–2.0-s increments to a goal of 12–15 s, as improvement in the patient's lung mechanics allows. The increased duration of T High allows for a reduction in atelectrauma and a reduction in the development of iatrogenic ALI.

P Low is set at zero because this allows for the least amount of resistance to exhalation. The concern for alveolar collapse is minimized with the use of a short T Low (between 0.5 and 0.8 s), which adequately maintains end expiratory lung volumes [2, 3]. T Low has been extensively studied, and its settings vary to some degree depending on the disease process. Optimizing the release time allows a balance of adequate lung ventilation without excessive lung volume loss. It has been suggested that a T Low of 1.5 s is the relative normal, which allows for complete emptying of the lungs. A long T Low can cause atelectasis, alveolar derecruitment, and airway closure. A short T Low can cause dead-space ventilation from inadequate ventilation. In clinical practice, the clinician does not calculate the T Low for each patient but rather approximates the expiratory flow restriction on the expiratory flow of gas waveform. The lung dynamics must be taken into consideration when setting T Low for each patient. For instance, low compliance states such as ARDS will have shorter expiratory time constants and thus a shorter T Low. Disease states with high resistance, such as asthma, will have longer expiratory time constants and will need longer release times. T Low is set and adjusted when flow from the patient ends at about 50–75% of peak expiratory flow. This can be determined by saving a screen and calculating peak expiratory flow or it can be estimated (Fig. 1). The expiratory flow curves are informative in the initial assessment, but once a patient is on APRV, continuous assessment is made with arterial blood gas analysis. APRV is time cycled, pressure limited, and time/pressure triggered [21].

When transitioning to APRV it may take several hours to appreciate the improvement in oxygenation. It has been observed that the maximum beneficial effect of oxygenation occurs approximately 8 h after implementation of APRV [3].

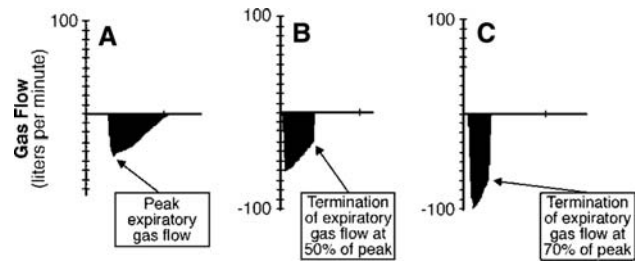


Fig. 1 Time low is set and adjusted when flow from patient ends at 50 to 75% of peak expiratory flow rate

Weaning from APRV

The process of weaning from APRV involves mainly manipulating P High and T High. The primary goal when weaning from APRV is essentially to achieve a state of CPAP, where the water pressure is gradually lowered. At the same time, the patient tidal volume respiratory rate and oxygenation are closely monitored. This is achieved by reducing P High and T High by what is commonly referred to as “dropping and stretching.” In other words, by “dropping” or decreasing P High by 2–3 cmH₂O at a time and “stretching” or extending T High by 0.5–2.0 s at a time, the goal of achieving a state of CPAP is thus achieved. After arriving at this point, the clinician may either directly extubate or lower the CPAP level or continue to wean the patient off CPAP while monitoring oxygenation and ventilation. The drop-and-stretch method ultimately leads to a more gradual reduction in mean airway pressure and thus promotes a more gradual conversion to CPAP mode (Table 2). The advantage of this mode of weaning is prevention of derecruitment post-extubation and therefore avoidance of hypoxia. No trial has been conducted to assess this method of weaning.

APRV and Acute Lung Injury/Adult Respiratory Distress Syndrome

Compared with healthy volunteers, total lung volume, including both aerated and non-aerated portions, is reduced by more than 20% in patients with acute lung injury [1, 22]. Because no effective pharmacologic therapy has been identified, treatment is supportive.

The elevated airway pressure and supraphysiologic end-inspiratory volume encountered during positive pressure ventilation have been implicated as secondary sources of direct lung injury, termed barotrauma and volutrauma. More recently, excess end-tidal alveolar stretch appears to be one of the most important contributing factors causing lung injury. Overdistension lung injury is associated with a variety of pathophysiologic abnormalities, including

Table 2 Wean the P High if PaO₂ is within desired range

“Drop and Stretch”

Simultaneously reduce P High (2–4 cmH₂O increments) and lengthen T High (decrease rate) as the patient’s spontaneous breathing begins to contribute to the total minute ventilation

Precautions

1. If you decrease T High (increase the rate) to increase minute ventilation (for CO₂ clearance) you must keep in mind that the Paw and gas exchanging surface area will be reduced. This may actually cause an increase in CO₂ if you do not simultaneously increase P High
2. P High and T High reduction (increase in rate) may produce less mean alveolar volume (lung volume) and will result in shorter emptying time, so keep in mind you may need to adjust the T Low
3. T Low should not be extended solely to lower CO₂ as this may lead to airway closure (derecruitment)

increased endothelial permeability. In addition to volutrauma caused by regional overdistension, the repeated opening and closing of atelectatic lung units, called atelectrauma, has also been implicated as an important mechanism in ventilator-induced lung injury (VILI). This injury pattern has been ascribed to the excessive shear force applied to lung tissue immediately adjacent to atelectatic regions during tidal ventilation [1].

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 tidal volume by raising the airway pressure above the set PEEP, 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, the risk of overdistension injury may be reduced. In contrast, conventional ventilation raises airway pressure, elevating lung volumes and potentially increasing the risk of overdistension. With APRV, as airway pressure is briefly interrupted, the release volume is driven by gas compression and lung recoil stored during the P High time period or 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 and pressure required to distend the lung and chest wall [2].

Historically, conventional ventilation limits recruitment to brief cycle intervals at end-inspiratory 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 breathes [23]. Reapplication of the same distending pressure with improved recruitment is likely to produce recurrent shear forces and does not attenuate potential lung injury.

The use of APRV to optimize mean airway pressure and lung volume provides a greater surface area for gas exchange. Allowing sustained duration (T High) at 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 exchange within the anatomic dead space results in a greater equilibration of gas concentration in all lung regions, thus resulting in improved oxygenation and reduced dead-space ventilation [2]. Increasing mean airway pressure will increase recruitment and improve compliance. It is not clear if overdistension could happen in normal areas of the lung.

Effects and Benefits of Spontaneous Breathing During Mechanical Ventilation: Lung Recruitment and Ventilation and Perfusion Matching

Several experimental and clinical studies have shown that in ALI spontaneous breathing during APRV improves oxygenation and increases cardiac output when compared with controlled mechanical ventilation [18, 24]. In the absence of spontaneous breathing, APRV is identical to pressure-controlled inverse-ratio ventilation.

Spontaneous breathing is possible in any phase of the mechanical ventilator cycle with APRV, a technique that provides ventilatory support by way of time-cycled switching between two different CPAP levels. In patients with severe ALI, unsupported spontaneous breathing with APRV has been observed to improve arterial oxygenation over that in patients with controlled mechanical ventilation alone, or breath-to-breath inspiratory assistance with pressure support ventilation [24]. Moreover, that clinical investigation and other experimental studies have shown a reduction in intrapulmonary shunting [24, 25]. Putensen et al. [24] recently demonstrated an increase in oxygenation and oxygen delivery as well as a substantial and progressive improvement of end-expiratory lung volume with spontaneous breathing, whereas oxygenation, oxygen delivery, and end-expiratory lung volume remained low in the absence of spontaneous breathing in the porcine model of oleic acid-induced lung injury. Another major finding in

this computed tomography study was that spontaneous breathing was associated with considerably less non-aerated lung tissue and increased aeration. The negative correlation between end-expiratory lung volume and amount of non-aerated lung combined with the correlation with venous admixture suggests that recruitment of non-aerated lung tissue is the major factor in the improvement of end-expiratory lung volume during APRV with spontaneous breathing, and that the redistribution of gas to dependent, well-perfused lung regions mainly explains improved oxygenation and reduction in intrapulmonary shunting during spontaneous breathing [25, 26].

Spontaneous breathing has been shown to increase end-expiratory lung volume and to reopen non-aerated lung tissue by means of diaphragmatic contraction. Diaphragmatic contraction is a more efficient way to acquire tidal volume than positive-pressure ventilation because it increases the recruitment of atelectatic lung in dependent regions. Mechanical breathes shift ventilation to non-dependent lung regions as the passive respiratory system accommodates the displacement of gas into the lungs. However, spontaneous breathing during APRV results in a more dependent gas distribution when the active respiratory system draws gas into the lungs and flow follows a similar time course. 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.

Conceptually, superimposed spontaneous breathes 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 [17].

In addition to the beneficial effects on lung recruitment, spontaneous ventilation has a beneficial effect on spatial distribution of pulmonary blood. The reduction in intrapulmonary shunting and the increase in arterial oxygenation, in conjunction with increased pulmonary compliance, can be attributed to the recruitment of previously non-ventilated (atelectatic) lung areas. This assumption is corroborated by the results of studies on animals that showed a decrease in atelectasis demonstrated by computer tomography when one of the phrenic nerves was stimulated during anesthesia [27]. Furthermore, improved distribution of pulmonary perfusion during spontaneous breathing with APRV/BIPAP could contribute to a decrease in intrapulmonary shunting and an increase in arterial oxygenation. Spontaneous breathing during APRV/BIPAP also decreases non-perfused but well-ventilated dead-space areas and improves the V/Q matching in other areas of the lung [28].

It has been demonstrated in both animal models and human studies that when spontaneous breathing is superimposed on pressure-controlled ventilation, ventilation is

better matched to perfusion. More ventilation and more blood flow were found in the dependent lung areas near the diaphragm during APRV with spontaneous breathing than without, whereas no difference was detected in non-dependent and apical lung areas [18]. This difference in ventilation and blood flow resulted from an increase in ventilated and perfused lung tissue as well as an increase in ventilation and blood flow in the dependent dorsal region during spontaneous breathing [18]. Similar to prone positioning, diaphragmatic tone and spontaneous breathing improve transalveolar pressure gradients in dependent lung regions resulting in a reduction in physiologic dead space, decreased intrapulmonary shunt, and improved gas exchange.

APRV, Sedation, and Neuromuscular Blockade

Recognizing the importance of limiting sedation and neuromuscular blockade in critically ill patients receiving mechanical ventilation, APRV is unique in that it allows a prolonged inspiratory phase without the need for heavy sedation and paralysis. Excessive sedation and use of neuromuscular blocking agents (NMBA) have been associated with increased duration of mechanical ventilation in patients with acute respiratory failure. Reducing the duration of mechanical ventilation decreases patient exposure to artificial airways, sedation, NMBAs, and aspiration of pharyngeal secretions and, therefore the likelihood of ventilator-associated pneumonia [2].

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 breathes [29] (Fig. 2). In addition, because APRV uses an open-breathing system, patients can

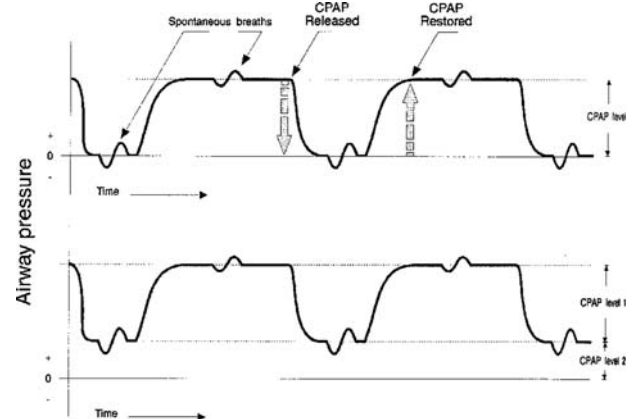


Fig. 2 Spontaneous tidal volumes maintain a sinusoidal flow pattern similar to spontaneous breath

exhale or cough throughout the respiratory cycle. When ventilating with a closed exhalation system, an actively breathing patient can inhale freely but cannot exhale freely until the ventilator switches to the exhalation phase of the breath cycle. If the inspiratory time is longer than the patient's neural inspiratory time and he/she tries to exhale prematurely or cough, the patient will likely experience expiratory resistance and discomfort. The patient may also experience disruption of breath delivery if the breath cycles off early due to a high-pressure alarm violation. Studies show that this has the potential for increasing oxygen consumption and inducing myocardial ischemia [29]. It may be necessary to dampen the patient's respiratory drive through increased sedation in order to prevent this problem from occurring. Ventilators with APRV or BIPAP have the ability to actively control the exhalation valve during the inspiratory phase of a pressure-controlled breath. The valve pressure is managed at or close to the set pressure target. Flow is readily available for inhalation and when a patient exhales or coughs, the ventilator maintains the target pressure by releasing the excess pressure. Since patients are more comfortable and breathing efforts do not disrupt breath delivery with this type of system, it may not be necessary to sedate patients to the point of eliminating respiratory drive when using extended inspiratory times. When a ventilation mode that supports spontaneous breathing, such as APRV, is used, a Ramsay score of 2-3 can be targeted, i.e., an awake, responsive, and cooperative patient [30]. In a retrospective study of over 600 heart surgery patients, a reduction in consumption of analgesics and sedatives was observed when patients were allowed to breathe spontaneously from an early stage with APRV/BIPAP. Preliminary data show that maintaining spontaneous breathing with APRV/BIPAP in patients with multiple trauma over an observation period of more than 10 days leads to significantly lower consumption of analgesics and sedatives than when controlled ventilation is used for 72 h followed by weaning [30]. APRV has been associated with a 70% reduction in NMBA requirements and a 30-40% reduction in sedation requirements when compared with conventional ventilation [5, 10, 12, 18, 19]. In addition, some studies suggest decreased ventilator days and intensive care and hospital length of stay are the results of using APRV [2, 20].

Effects of APRV on the Cardiovascular System, Renal Function, and Splanchnic Perfusion

Experimental and clinical studies show that in intermittent mandatory ventilation (IMV) and APRV/BIPAP, spontaneous breathing of 10-40% of the total expired minute ventilation at unchanged volume exhaled or airway

pressure limits results in an increase in cardiac output. A simultaneous rise in right ventricular end-diastolic volume during spontaneous breathing in APRV/BIPAP is an indication of improved venous return to the heart [28]. Conversely, ventilatory support of each individual inspiration with pressure support ventilation and identical airway pressures produces no increase or very little increase in cardiac output [28, 31]. Kaplan et al. [19] investigated whether APRV can safely enhance hemodynamics in patients with ALI/ARDS compared with pressure control ventilation (PCV). During APRV, the cardiac index rose from $3.2 \pm 0.4/\text{min}/\text{m}^2$ for PCV to $4.6 \pm 0.3/\text{min}/\text{m}^2$, whereas oxygen delivery increased from 997 ± 108 to $1409 \pm 146 \text{ ml}/\text{min}/\text{m}^2$ and central venous pressure decreased from $18 \pm 4 \text{ cmH}_2\text{O}$ for PCV to $12 \pm 4 \text{ cmH}_2\text{O}$ for APRV. Urine output increased by 0–83 for PCV to 0–96 for APRV [19].

The decrease in intrathoracic pressure associated with spontaneous breathing also has significant effects on the cardiovascular functions of patients on APRV. The descent of the diaphragm into the abdomen during a spontaneous breathing effort simultaneously decreases pleural pressures and increases abdominal pressure. This effectively lowers right atrial (RA) pressure while compressing abdominal viscera, propelling blood into the inferior vena cava. 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. These changes in venous return and cardiac output, coupled with an increase in recruitment of atelectatic lung, likely contribute to the improvement in arterial oxygenation using APRV with spontaneous breathing.

The advantages of spontaneous breathing are not limited to the thorax. Hering et al. [32] hypothesized that partial ventilatory support using APRV with spontaneous breathing provides better cardiopulmonary and renal function than full ventilatory support using APRV without spontaneous breathing. Effective renal blood flow and glomerular filtration rate were higher during APRV with spontaneous breathing ($858 \pm 388 \text{ ml}/\text{min}/\text{m}^2$ and $94 \pm 47/\text{min}/\text{m}^2$) than during APRV without spontaneous breathing and the same minute ventilation ($714 \pm 236/\text{min}/\text{m}^2$ and $82 \pm 35/\text{min}/\text{m}^2$, $P < 0.05$). Maintaining spontaneous breathing during ventilatory support may, therefore, have the advantage of preventing deterioration of renal function in patients with ARDS [32].

Effective renal blood flow was significantly increased and glomerular filtration rate was higher with the addition of spontaneous breathing with APRV in patients with acute lung injury in the absence of preexisting renal dysfunction [1]. Improved splanchnic perfusion has also been identified in porcine lung injury models reporting an increased

Table 3 Advantages of APRV

1. APRV uses lower peak and mean airway pressures
2. Increases cardiac index
3. Decreases central venous pressure
4. APRV increases oxygen delivery
5. Reduces the need for sedation and paralysis
6. APRV also improves renal perfusion and urine output when spontaneous breathing is maintained. The benefits of APRV may be related to the preservation of spontaneous breathing
7. Maintaining the normal cyclic decrease in pleural pressure, augmenting venous return, and improving cardiac output
8. The need for sedation is decreased
9. During PPV atelectasis formation can occur near the diaphragm, when activity of this muscle is absent (paralysis). However, if spontaneous breathing is preserved, the formation of atelectasis is offset by the activity of the diaphragm

mucosal-submucosal blood flow to the stomach and small and large bowels. These benefits are attributed to improvement in systemic blood flow and arterial blood oxygenation (Table 3).

Because APRV is a pressure-controlled ventilator mode, tidal volume is variable. As a result there is a potential risk of delivering excess tidal volumes to patients using pressure-controlled modes. Because mechanically delivered volumes are dependent on lung compliance, preset levels of P High and P Low and the release time, if lung or chest wall compliance improves, tidal volume will increase in proportion. With pressure-supported spontaneous breathes, potentially dangerously high tidal volumes may be generated at the P High setting due to aggregate tidal volumes. On APRV, a reduction in respiratory system compliance would reduce mechanically delivered tidal volume; however, this would likely be compensated by spontaneous ventilation.

In addition, Neumann et al. [17] demonstrated that oxygenation is better with CPAP than with partial MV support using APRV secondary to possible rapid lung collapse during the phases of airway pressure release below the CPAP level. Theoretically, in patients with ALI, vigorous respiratory efforts from P High with or without pressure support could result in excessive transpulmonary pressures causing regional overdistension and contributing to lung injury. In addition, shearing of terminal lung units and vascular endothelium may occur during rapid deflation below some lower inflection point of the pressure-volume curve. This has the potential to occur during the release phase of APRV.

Due to the effort of spontaneous breathing, APRV carries the potential for increased energy expenditures secondary to the increased work of breathing. However, attempts to prove this theory have not translated into higher VO_2 or VCO_2 [15]. The patient's work for breathing can also be minimized by the addition of pressure support to the patient's spontaneous breathes.

Patients with obstructive lung disease may require closer monitoring while receiving APRV. Practitioner determination of the release time ideally provides adequate time for CO_2 clearance, yet not too long to allow derecruitment. Patients with obstructive lung disease have increased resistance, making it even more challenging to achieve both of these goals.

In addition, a retrospective review by Dart et al. reported that APRV had to be terminated in a patient with a closed head injury secondary to an increase in intracranial pressure [33, 34]. It is not clear whether the rise in intracranial pressure was secondary to a rise in pCO_2 or a decrease in venous return because of elevated intrathoracic pressure. APRV is also contraindicated in patients with large bronchopleural fistulas.

As with any new technology, staff stress and subsequent increased risk to the patient may be noted with the implementation of APRV. Adequate and appropriate on-site training coupled with off-site support will help reduce the risks associated with the introduction of APRV. Transferring patients to subacute areas may result in the lack of access to ventilators capable of delivering APRV, which results in converting the patient to a more conventional mode of ventilation. Similarly, traveling to other departments may require temporary discontinuation of APRV thus increasing the potential risks of transport (Table 4).

Conclusion

APRV is a unique mode of ventilation that allows patients to breathe spontaneously during the entire cycle of ventilation. The ability to spontaneously breathe during APRV is associated with improved alveolar recruitment, ventilation-perfusion matching, and global system perfusion while reducing the demand for sedation and NMBA [1]. An adequately designed and powered study to demonstrate a

Table 4 Disadvantages of APRV

1. APRV is a pressure targeted mode of ventilation, volume delivery depends on lung compliance, airway resistance and patient's spontaneous effort
2. APRV does not completely support CO₂ elimination, but relies on spontaneous breathing
3. With increase Raw (e.g. COPD), the ability to eliminate CO₂ may be more difficult than the limited emptying of the lung and short release periods
4. If spontaneous efforts are not matched during the transition from P High to P Low and P Low to P High, it may lead to increased work load and discomfort for the patient
5. Limited staff experience with this mode may make implementation of its use difficult
6. Large bronchopleural fistula
7. Increase intracranial pressure

reduction in mortality and days on APRV in comparison to a lung-protective strategy on conventional mode ventilation has not been performed.

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