Analytic Reviews

High-Frequency Oscillatory Ventilation (HFOV) and Airway Pressure Release Ventilation (APRV): A Practical Guide

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Despite advances in ventilator management, 31% to 38% of patients with adult respiratory distress syndrome (ARDS) will die, some from progressive respiratory failure. Inability to adequately oxygenate patients with severe ARDS has prompted extensive efforts to identify what are now known as alternative modes of ventilation including high-frequency oscillatory ventilation and airway pressure release ventilation. Both modalities are based on the principles of the open-lung concept and aim to improve oxygenation by keeping the lung uniformly inflated for an extended period of time.

Although a mortality benefit has not been proven, some patients may benefit from these alternative modes of ventilation as rescue measures while the underlying process resolves. The purpose of this article is to review the evidence and mechanisms underlying each modality and to describe the fundamental steps in initiating, adjusting, and terminating these modes of ventilation.

Keywords: alternative mechanical ventilation; open lung; APRV; HFOV

Introduction

Inability to adequately oxygenate patients with acute lung injury (ALI) or adult respiratory distress syndrome (ARDS) has prompted extensive efforts to identify what are now known as alternative modes of ventilation. Animal studies demonstrate that mechanical ventilation with large tidal volumes and high airway pressures leads to severe alterations in permeability, pulmonary edema, and diffuse alveolar damage similar to the pathologic findings characteristic of ARDS.[1,2] Mechanisms thought to be involved in ventilator-induced lung injury (VILI) include

excessive stretch of the alveoli (volutrauma), shear injury due to repetitive alveolar collapse and reopening (atelectrauma), and excessive pressure within the alveoli (barotrauma).

Application of low tidal volume/low plateau pressure strategies during conventional ventilation in adults with ALI or ARDS results in decreased duration of mechanical ventilation and mortality relative to high tidal volume/high plateau pressure ventilation.[3,4] However, 31% to 38% of patients proceed to die, some from progressive respiratory failure, indicating that conventional ventilation with lung protective strategies may not be adequate.[3,4] Although a mortality benefit has not been proven, such patients may benefit from alternative modes of ventilation as rescue measures to maintain oxygenation while the underlying process resolves.

High-frequency oscillatory ventilation (HFOV) and airway pressure release ventilation (APRV) are 2 commonly used alternative modes of mechanical ventilation in this patient population. Both modalities are based on the principles of the open-lung concept (OLC) and aim to improve oxygenation by

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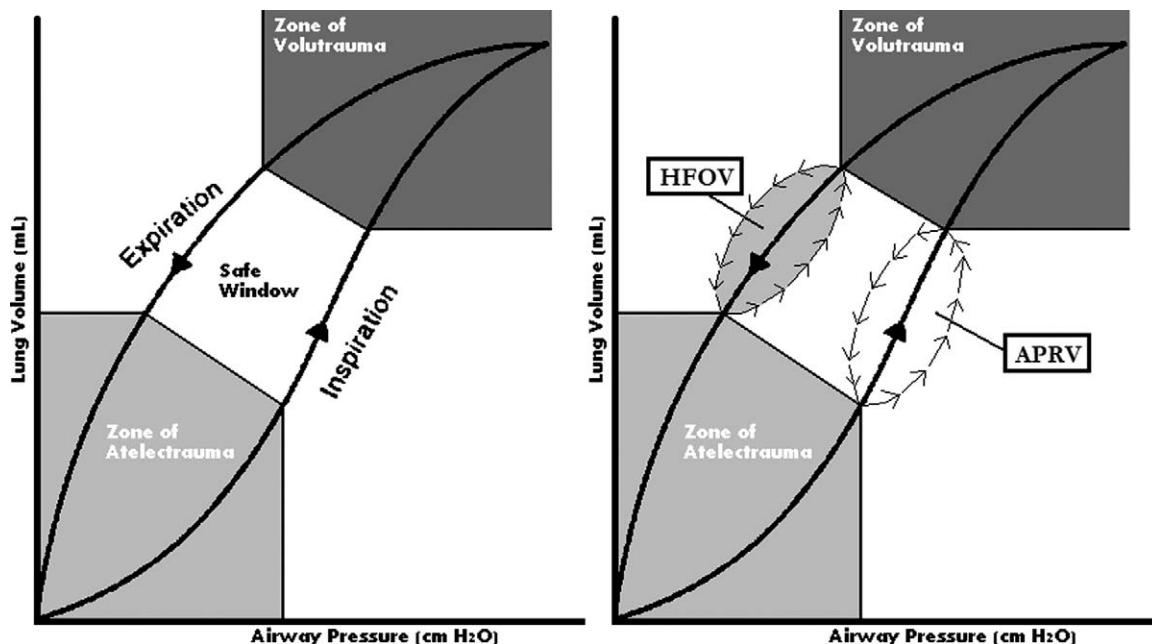
Figure 1.   Pressure-volume curve comparing regions of ventilation using high-frequency oscillatory ventilation (HFOV) and airway pressure release ventilation (APRV). Note that ventilation with HFOV occurs on the expiratory limb, whereas ventilation with APRV occurs on the inspiratory limb of the curves.

keeping the lung uniformly inflated for an extended period of time. The OLC was originally coined by Lachmann in 1992 and highlights the importance of maintaining open alveoli while minimizing over-distension and atelectrauma.[5] In general, either mode could be considered when the fraction of inspired oxygen (FiO_2) is greater than 60%, positive end-expiratory pressure (PEEP) is greater than 15 cm H_2O, plateau pressure is greater than 30 cm H_2O, and the arterial oxygen saturation is less than 90%.[6]

The purpose of this article is to review the evidence and mechanisms underlying each modality and to describe the fundamental steps in initiating, adjusting, and terminating these modes of ventilation. Discussion is limited to adult patients. It is assumed that the reader has a sound understanding of the pathophysiology of ARDS and VILI.

High-Frequency Oscillatory Ventilation

High-frequency oscillatory ventilation has been identified as an alternative method of applying low tidal volume, controlled pressure ventilation in the setting of ARDS.[7] Traditionally used with great success in neonatology, HFOV has recently been

recognized as potentially useful in adult patients with ARDS.[7] Its use in adults is based on the hope that it will improve oxygenation without further injuring the lung. The only HFOV approved for use in adults is the Sensormedics 3100B (Viasys Health-care, Yorba Linda, CA).

Rationale Behind HFOV

Patients who develop ARDS or ALI have reduced lung compliance and impaired oxygenation.[8] High-frequency oscillatory ventilation attempts to deal with potential risks of mechanical ventilation, baro-trauma, volutrauma, atelectrauma, and oxygen toxicity and can be considered when conventional ventilation fails to safely and adequately provide respiratory support. High frequency ventilation is generally considered beneficial for patients with severe pulmonary failure because (*a*) it uses much smaller tidal volumes than conventional ventilation, (*b*) it maintains the lungs/alveoli open on the deflation limb of the pressure-volume curve (Figure 1) at a relatively constant airway pressure and thus may prevent atelectrauma and barotrauma,[9] and (*c*) it improves ventilation/perfusion (V/Q) matching by ensuring uniform aeration of the lung.[9] It is possible

Table 1. Suggested Initial Settings for APRV and HFOV

HFOV[10]		APRV	
Frequency		T_{high}	4-6 seconds
pH < 7.1	4 Hz	T_{low}	0.6-0.8 seconds based on T-PEFR[a]
pH 7.1-7.19	5 Hz	P_{high}	Same as plateau pressure on CV or
			P_{aw} + 2-4 cm H_2O if transition from HFOV
pH 7.2-7.35	6 Hz	P_{low}	0
pH > 7.35	7 Hz	Fio_2	100%
Amplitude (power)	70-90 cm H_2O		
P_{aw}	5 cm H_2O > plateau pressure on		
	CV to max of 35 cm H_2O		
Bias flow	40 L/min		
Inspiratory time	33%		
Fio_2	100%		

NOTES: APRV = airway pressure release ventilation; CV = conventional ventilation; HFOV = high-frequency oscillatory ventilation; P_{aw}, mean airway pressure.
[a] T_{low} may have to be greater than 1 second in patients with severe obstructive lung disease.

that adults with severe ARDS may benefit from HFOV due to the long and variable time constant required for filling of noncompliant alveoli. Such alveoli may experience atelectrauma even with low tidal volume, moderate PEEP conventional ventilation. Similarly, less fibrotic segments of the lung may experience cyclic volutrauma due to preferential air flow into these segments with conventional ventilation. Various studies have used different criteria for determining when HFOV should be instituted in adults, but a consensus article that sought to adhere to lung protective strategies of mechanical ventilation while maintaining adequate gas exchange, suggested its use when conventional ventilator settings require an Fio_2 greater than 70% and PEEP greater than 14 cm H_2O or when the arterial pH is less than 7.25 with a tidal volume that is greater than 6 cm^3/kg and a plateau pressure that is greater than 30 cm H_2O.[10]

Several studies in adults have shown that oxygenation improves after implementation of HFOV, but mortality benefit has not been demonstrated in randomized trials.[11,9,12-14] However, these studies were not powered sufficiently to detect small changes in mortality. In a study by Fort et al,[9] HFOV was evaluated in terms of safety and effectiveness in patients with ARDS.[9] This prospective study included patients with mean peak inspiratory pressure of 54.3 ± 12.7 cm H_2O, Pao_2/Fio_2 ratio of 68.6 ± 21.6, and PEEP of 18.2 ± 6.9 cm H_2O. High-frequency oscillatory ventilation was instituted after varying periods of conventional ventilation (5.12 ± 4.3 days). A lung volume recruitment strategy was used concurrently. During the study, 76% of

patients demonstrated improved gas exchange and an overall improvement in Pao_2/Fio_2 ratio. Cardiac output was not compromised in any of the patients despite increases in mean airway pressure, lending credence to the fact that HFOV is both a safe and an effective means to augment oxygenation in adult patients with severe ARDS failing conventional ventilation. Thus, patients who need maximal alveolar recruitment to keep the Fio_2 below toxic levels may benefit from HFOV.

Mechanics of High-Frequency Oscillatory Ventilation

The variables that are controlled directly on the 3100B ventilator are respiratory frequency, amplitude of ventilation (also called the power or ΔP), mean airway pressure (P_{aw}), bias gas flow rate, percentage of inspiratory time, and Fio_2. Suggested initial ventilator settings are noted in Table 1. The core of the HFOV system consists of a piston assembly that incorporates an electronic control circuit, or square-wave driver, which powers a linear drive motor (Figure 2). This motor consists of an electrical coil within a magnet, similar to a permanent magnet speaker. When a positive polarity is applied to the square-wave driver, the coil is driven forward. The coil is attached to a rubber bellows, or diaphragm, to create a piston. When the coil moves forward, the piston moves forward, resulting in the creation of the inspiratory phase. When the polarity becomes negative, the electrical coil and the attached piston are
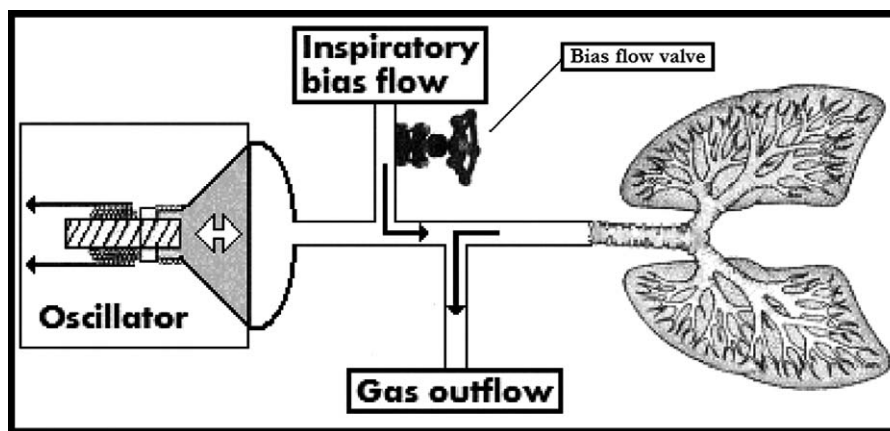
Figure 2. Basic design of the high frequency oscillating ventilator. A bias gas flow is moved rapidly by a piston-driven assembly.
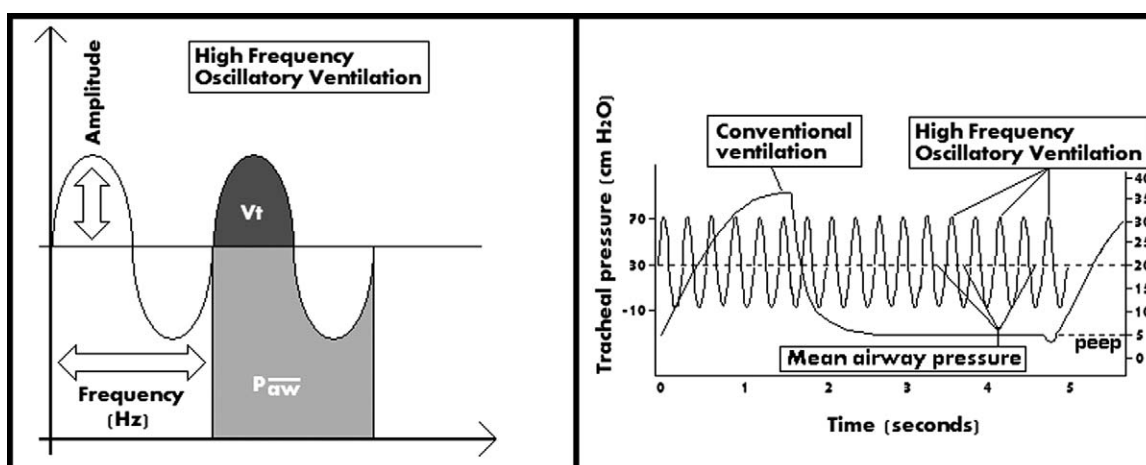

Figure 3. Waveforms depicting the key variables that are controlled during high frequency oscillation as compared to conventional ventilation. The y-axis on the left depicts changes in airway pressure seen with high frequency oscillatory ventilation and the y-axis on the right depicts changes in peak airway pressure with conventional ventilation. Note that tracheal pressure becomes negative at peak expiration, thereby making expiration an active process. Also note that as amplitude increases, delivered minute ventilation increases. A background tracing of pressure versus time using a respiratory rate of 12 and inspiratory to expiratory ratio of 1:3 with conventional ventilation is presented for comparison.

driven away from the patient, creating the expiratory phase. By moving rapidly, the diaphragm oscillates a constant stream of gas, called the bias gas flow, through the airways. It is recommended that the lung be aggressively recruited prior to the start of HFOV to ensure that all the potentially recruitable alveoli are open.

The speed of oscillation is set by manipulating the frequency (Figure 3). One Hertz is equal to 1 breath per second, that is, 60 breaths per minute. A frequency of 5 Hz gives a frequency of 5 breaths per second or 300 breaths per minute. An important point to remember is that given a fixed inspiratory to expiratory time ratio, as frequency is increased, the excursion of the piston is limited by the time allocated for each breath cycle. Therefore, changes in frequency are *inversely* proportional to the amplitude and thus delivered tidal volume (see below). Alveoli with short-time constants for air flow (high lung compliance and low airway resistance) can be ventilated more effectively at higher frequencies than those which have longer time constants (low lung compliance or high airway resistance). Frequency selection also directly affects the pressure cycles

Table 2.   Ventilator Adjustments Based on Blood Gas Results

HFOV	APRV
Hypoxemia	
• Increase Fio_2	• Increase Fio_2
• Increase P_{aw} by 2 cm H_2O to max 40 cm H_2O	• Recruitment maneuver
• Recruitment maneuver in cases of recurrent hypoxemia	• Increase T_{high}
• Increase bias flow	• Increase P_{high} to max 40 cm H_2O
	• Adjust T_{low} to keep T-PEFR > 50%
Hypercapnea/acidemia	
• Decrease frequency to nadir of 3 Hz	• Ensure patient is spontaneously breathing
• Increase power to max 90 cm H_2O	• Increase T_{low}
• Introduce endotracheal cuff leak	• Increase P_{high} and T_{high} to increase minute ventilation

NOTES: APRV = airway pressure release ventilation; HFOV = high-frequency oscillatory ventilation; Fio_2 = Fraction of inspired oxygen; P_{aw} = Mean Airway Pressure; T-PEFR = Terminal peak expiratory flow rate.

applied to the lung. A smaller percentage of the circuit change in pressure is transmitted at higher frequencies. Whereas the normal lung can be ventilated over a wide pressure range without inducing injury, the lung with poor compliance has a very limited zone of safety.[15] As frequency increases, the zone of safe pressure widens, making it easier to maintain more of the lung homogenously aerated.[15] Unfortunately, there is no simple formula for estimating the ideal frequency for an individual patient, and clinical judgment combined with arterial blood gas measurements is needed (Tables 2 and 3). Use of frequency lower than 3 Hz is not recommended because the depth of oscillation increases markedly, which may result in increased risk of barotrauma. In addition, the frequency should not be raised higher than 7 Hz in adults. Frequency is adjusted in 1 Hz increments based on the Pco_2 (see below).

The amount of polarity voltage (also called power, amplitude, or ΔP) applied to the electrical coil determines the distance that the piston is driven toward/away from the patient's airway. Therefore, increasing the polarity voltage increases the piston movement or amplitude. The easiest way to conceptualize this is to view it as the means by which tidal volumes are delivered and removed about the mean airway pressure (Figure 3). The greater the piston displacement, the more volume delivered to the patient. The extent to which the amplitude increases depends on the resistance the piston encounters to forward movement. For example, when the oscillator is used in a patient with low compliance or high airway resistance, the piston meets greater pressure during the inspiratory phase, resulting in lesser change in the effective tidal volume. In addition, as

Table 3.   Summary of Important Respiratory Therapy and Nursing Considerations With Regard to HFOV Use and Routine Maintenance

Perform thorough suction before connecting to the oscillator

Perform recruitment maneuver before connecting to the oscillator

Use closed system suction catheter

Avoid disconnection from the ventilator

Check for changes in pitch/rhythm of delivered breaths

Check chest/thigh wiggle and changes in chest/thigh wiggle

Always humidify gases

If oscillator stops during suctioning; silence alarm, pull back catheter and restart oscillator

Obtain blood gases and chest x-ray 2 hours after HFOV commencement and at least daily thereafter

Ensure appropriate education regarding the oscillator for relatives of the patient

NOTE: HFOV = high-frequency oscillatory ventilation.

depicted in Figure 3, expiration is an active process in HFOV. This is because negative displacement of the diaphragm results in subatmospheric pressure. Generally, the starting power setting should be 70 to 90 cm H_2O. Most commonly, this variable is adjusted to obtain a slight wiggle to the level of the patient's thigh, though it has been recommended that the starting setting be $Pco_2 + 20$ cm H_2O. As described below, subsequent adjustments are made based on the Pco_2.

The mean pressure adjust control mechanism allows for adjustments in P_{aw}. This control varies the resistance placed on a mushroom-shaped control valve on the patient circuit at the terminus of the expiratory limb. Following manual recruitment efforts, increasing the P_{aw} keeps alveoli open at a constant pressure, thus minimizing or avoiding

atelectrauma from shearing forces. As with all forms of mechanical ventilation, increases in mean airway pressure result in enhanced oxygenation. Although increasing P_{aw} increases the transpulmonary pressure, it does not affect cardiac output in euvolemic patients.[9] As discussed below, the mean pressure-adjust control is bias flow dependent. Most authors recommend a starting P_{aw} 5 cm H_2O above the last plateau pressure noted during conventional ventilation with a maximal starting P_{aw} of 35 cm H_2O. Based on outcome studies on conventional ventilation, the goal is to keep the P_{aw} less than 30 cm H_2O. Mean airway pressure should be adjusted in increments of 2 cm H_2O based on the oxygen saturation. Patients who have recurrent hypoxemic events that resolve with recruitment should have their P_{aw} increased.

Bias flow is the rate at which gas flows through the ventilator circuit. The generally accepted starting bias flow rate is 40 L/min, and the maximal flow possible on the 3100B is 60 L/min. An increase in bias gas flow will increase P_{aw}, thereby improving oxygenation. The maximal flow may be needed to maintain P_{aw} in patients with a large air-leak, such as bronchopleural fistulae. However, the maximal flow rate is not sufficient to support significant spontaneous respiratory efforts and is one reason that patients must be deeply sedated or pharmacologically relaxed while on HFOV.

In conjunction with amplitude, mean airway adjust, bias flow, and frequency control, the percentage of inspiratory time can also be adjusted. Because the endotracheal (ET) tube contributes at least 50% of the total airway resistance during expiration, the inspiratory time setting should always be less than 50% to minimize the risk of air trapping and volu- and barotraumas.[16] Inspiratory time of 33% is optimal because it results in a drop in the mean intrapulmonary pressure as a result of higher flow-dependent ET tube resistance during inspiration. This is due to higher flow rates during the shortened inspiratory phase.[16] Increasing the inspiratory time will improve both oxygen (by increasing P_{aw}) and CO_2 exchange (by increasing delivered tidal volume), though it can also increase the risk of lung injury. Because of this, it is the variable least commonly altered to address blood gas values.

Gas Exchange

Tidal volumes delivered using the 3100B are not measured and are estimated to be 1 to 2 cm^3/kg—

approximately the volume of anatomic dead space. There are several mechanisms postulated to explain gas transport under these nonphysiologic conditions (Figure 4), and the reader is referred to more definitive sources for greater detail of information.[17,18] Briefly, the gas transport in the most proximal airway occurs by convection, and gradually transitions into a mixture of convection and diffusion and finally purely diffusion as one progresses along the airway tree.[17] Bulk flow can still provide conventional gas delivery to proximal alveoli with low regional dead space volumes.[18] There is also the presence of coaxial flow, wherein the gas in the center of large airways and the ET tube flows inward while gas on the periphery flows outward. This can develop because of the asymmetric low profile of high velocity gases.[18] Dispersion phenomena can produce mixing of fresh and residual gas along the flow front of gas through a tube. Pendelluft flow refers to flow of gas between adjacent alveoli with different impedance, as seen in ARDS.[17,18] Collateral ventilation and cardiogenic mixing also play a role.[17] Finally, augmented molecular diffusion can occur at the alveolar level secondary to the added kinetic energy from the oscillations.[16-18] The importance of each of these mechanisms is debated, and it has been suggested that a combination of all the above factors may be in play simultaneously during HFOV.[16,17,19]

As with any form of mechanical ventilation, oxygenation on HFOV can be improved by either increasing the Fio_2 or increasing the mean airway pressure. As noted above, the mean airway pressure can be increased directly or it can be adjusted by increasing the inspiratory time. Increases in P_{aw} result in greater alveolar recruitment and subsequent improvement in V/Q matching. However, increasing P_{aw} to a point where perialveolar vessels collapse from alveolar overdistention can result in both seemingly paradoxical hypoxemia and/or barotrauma to the lung. Because P_{aw} is affected by many variables, such as inspiratory time or ET cuff leak (discussed below), one must be cognizant of the fact that a change in one variable may affect the other variables and vice versa.

Ventilation on HFOV is facilitated by the extremely efficient mixing of gas in the airways. Carbon dioxide removal is approximately proportional to the product of oscillation frequency and the amplitude squared.[20] Thus, changes in tidal volume have a greater impact on CO_2 clearance than changes in respiratory rate. This explains why decreasing the
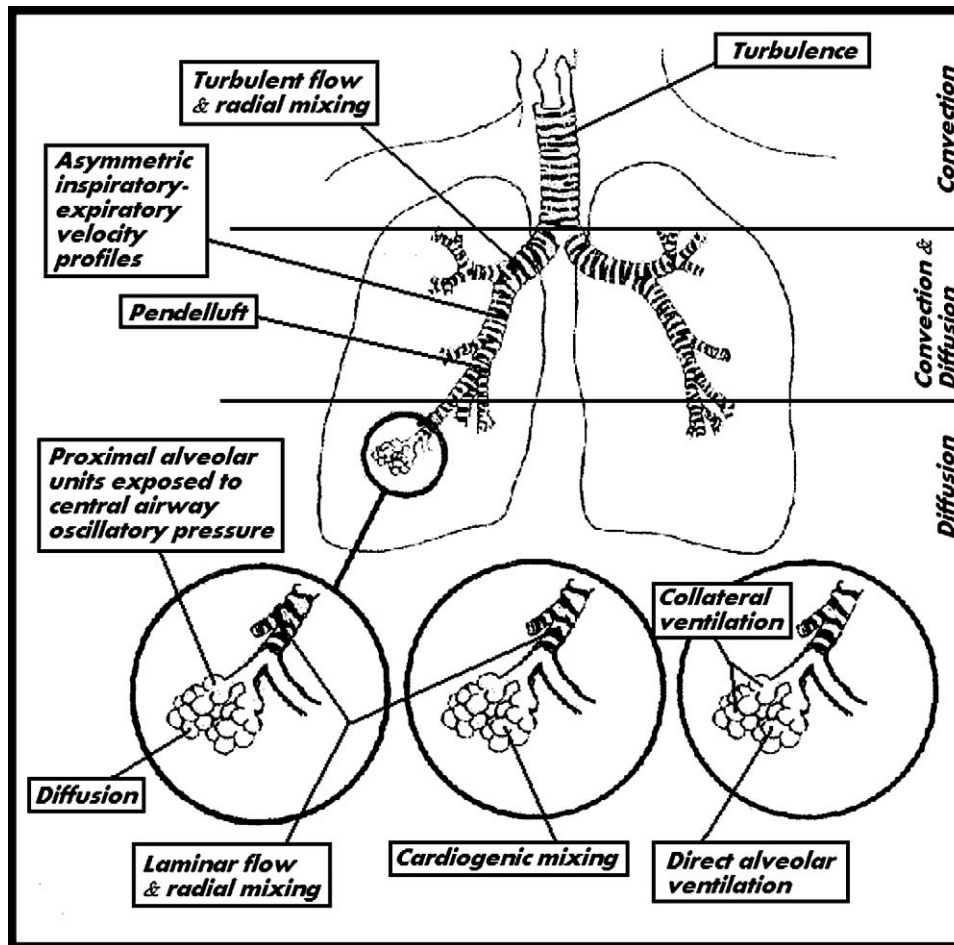
Figure 4. Possible mechanisms to account for gas exchange at various levels of the bronchoalveolar tree during high frequency oscillation.

frequency results in an increase in CO_2 clearance— that is, decreasing the frequency results in an increase in delivered tidal volume. Furthermore, even the smallest adjustments in amplitude or changes in lung compliance and delivered tidal volume have a great effect on ventilation. Consequently, CO_2 elimination is controlled primarily by adjusting amplitude first and then by adjusting frequency.[20] Lastly, ventilation can also be augmented by decreasing the anatomic dead space. This can be done by deflating the cuff of the ET tube sufficiently to decrease the P_{aw} 5 to 8 cm H_2O (and compensating for this decrease by manually increasing the P_{aw} again). However, this may result in an increased risk of aspiration or derecruitment of the lung, though adverse outcomes have not been reported in studies on adult patients.

Because there is no bulk flow of gas, significant respiratory acidosis is common at the start of HFOV. Patients who have significant preexisting acidemia may need to be temporized with intravenous buffering solutions while CO_2 exchange stabilizes. Table 4 lists the factors associated with decreased tidal volume delivery and thus impaired ventilation with HFOV.

To summarize, oxygenation is improved by increasing mean airway pressure, Fio_2, or percentage of inspiratory time. Ventilation (CO_2 exchange) is improved by decreasing frequency, increasing power, increasing inspiratory time, or creation of a cuff leak. The risks and benefits of changes in each variable have to be considered. Table 2 list suggested ventilator adjustments based on arterial blood gas results.

Interaction With Spontaneous Breathing

Spontaneous breaths contribute useful lung reexpanding forces.[21,22] Much like in APRV, spontaneous

Table 4. Factors Contributing to Decreased Tidal Volume Delivery With HFOV

Decreased endotracheal tube diameter
Mucous plug or alveolar edema fluid accumulation
Decreased ventilator power or amplitude
Decreased percentage of inspired time
Decreased respiratory system compliance
Increased endotracheal tube length
Increased ventilator frequency

NOTE: HFOV = high frequency oscillatory ventilation.

breaths on HFOV help maintain end-expiratory alveolar expansion in dependent lung regions and improve V/Q distributions.[23,24] A significant reduction in days on ventilator was observed when spontaneous breathing efforts were allowed in patients with ALI/ARDS.[22] However, vigorous spontaneous respiratory efforts, especially in large size patients, may contribute to sudden pressure variations that activate equipment alarms, interrupt oscillations, and produce significant oxygen desaturation. It is for this reason that the early HFOV trials in adults recommended administration of muscular blockade. Current sedation protocols attempt to maintain the patient's ability to breathe spontaneously with small tidal volumes while suppressing deep breaths or coughing, thus minimizing potential complications related to myopathy/neuropathy of prolonged neuromuscular blockade.[25,26]

Weaning From HFOV

There is no consensus on how to wean patients from HFOV to conventional ventilation. However, a protocol used in 2 randomized trials called for the P_{aw} to decrease in increments of 2 cm H_2O to a goal of 30 cm H_2O after the FiO_2 had been weaned to less than 60%.[13,14] The FiO_2 was then weaned to 40% if the oxygen saturation (SaO_2) remained greater than 88%. Finally, the P_{aw} was weaned again to a final goal of 20 to 25 cm H_2O. The patient was then transitioned to a lung protective volume-controlled mode of ventilation if the SaO_2 remained greater than 88% for 24 hours. Initial conventional ventilation settings were designed to ensure that the mean airway pressure remained 20 to 25 cm H_2O. The patient was considered to fail this transition and was converted back to HFOV if the SaO_2 decreased to less than 88% in the first 48 hours following transition. This protocol is supported by other studies that suggest that weaning the P_{aw} to less than 20 cm H_2O prior to transitioning to conventional ventilation can cause derecruitment of alveoli and hypoxemia.[25] In instances where the initial P_{aw} is greater than 35 cm H_2O and the FiO_2 is greater than 60%, some authors suggest weaning the P_{aw} and FiO_2 concurrently to try to minimize excess stretch and barotrauma on the alveoli as quickly as possible. In these instances, the P_{aw} should be weaned to 35 cm H_2O initially, then the FiO_2 should be weaned to less than 60%, and then the protocol outlined above can be followed.

Complications and Drawbacks of HFOV

Despite research showing benefits of HFOV, use of oscillatory ventilation is rare in adult patients, and comfort level is generally low among medical personnel using this equipment,[27] consequently resulting in difficulty with troubleshooting and adjusting the ventilator. Possible complications include overdistention/underdistention of the lung, pneumothorax, ET occlusion from secretions, and hemodynamic compromise. Other limitations include inability to transport the patient and deliver nebulized medications.

The possibility of lung overdistention on HFOV due to trapping of gas has been investigated.[28] Because this cannot be measured directly, the exact extent to which this is a problem is controversial, but there is no difference in the reported rate of pneumothorax between HFOV and conventional ventilation.[13]. Lung underdistention can also be a problem under HFOV. Although controversial, small tidal volumes delivered at a constant mean airway pressure may actually exacerbate or result in progressive atelectasis, one of the problems HFOV is thought to overcome. This underscores the importance of recruiting the lung at the start of HFOV.

Continuous positive intrathoracic pressure impedes venous return to the heart and therefore cardiac output. This can result in hypotension when patients are transitioned from conventional ventilation to HFOV. Patients must be euvolemic prior to initiation of HFOV to minimize this risk, and the bedside practitioner should be ready to volume resuscitate the patient as needed. As previously described, systemic hypotension may also be worsened by transient acidemia.

Metered dose inhalers are largely ineffective during HFOV, with only about 25% of a nebulized medication being detectable at the end of the ET tube.[29]

Better methods to deliver aerosolized medications with HFOV are being developed.

Patient transport during HFOV may be a significant logistical problem because there is no portable version of the equipment. However, an effective protocol for transport of patients on HFOV has been described.[7] This mechanism involves clamping the ET tube while on HFOV, transition to a self-inflating bag with 20 cm H_2O PEEP valve, unclamping of the ET tube with vigorous manual ventilation during transport, and reversal of these procedures once an oscillatory ventilator has been set up at the trip destination.[7] Recruitment maneuvers can be used as needed to reestablish oxygenation. This protocol notwithstanding transport of such patients is potentially dangerous and should be minimized.

Unique Aspects Regarding HFOV

There are a number of specific respiratory therapy and nursing aspects that should be highlighted with regards to patients on HFOV (Table 3). The sight of someone being "oscillated" can be disturbing for the family and friends of the patient. Hence, it is important to ensure adequate education regarding expectations provided to the patient's family and friends.

It is difficult to appropriately auscultate the chest while a patient is on HFOV. Physicians and nurses must rely on chest x-ray and objective measures (eg, vital signs, ventilator readings, and blood gas analysis) to detect new lung pathology. Daily chest x-ray is needed to ensure adequate lung expansion.

A closed system suction unit should be used on HFOV because disconnecting the patient to suction can potentially lead to derecruitment. Unless otherwise indicated, suctioning for the first 24 hours is not necessary. When using a closed system suction system, it is important to draw back the suction catheter all the way from the ET tube upon completion. Ideally, the patient should be thoroughly suctioned before HFOV is commenced. Once the patient is oscillated, every attempt must be made to try not to disconnect the patient from the oscillator to prevent derecruitment.

All clinical staff need to be trained in recognition of HFOV-related complications. This is especially important with HFOV because the ventilator is poorly alarmed to alert the bedside staff to possible complications. Clinical assessment and experience are needed to recognize ET tube obstruction (increase in amplitude with an increase in P_{aw}, decrease in SpO_2, and increase in PcO_2), tension pneumothorax (decrease in SpO_2, disparity in the height of the left and right chest walls, and a fall in blood pressure), or pulmonary overdistension (fall in blood pressure, increased central venous pressure, and decreased SpO_2). Observation of the patient for equal and continuous chest wiggle should be performed upon initiation of HFOV and followed closely thereafter. Chest wiggle diminishes if the ET tube has moved or is obstructed. Chest wiggle on one side only may indicate that the patient has developed a pneumothorax or has a main-stem intubation. Chest wiggle assessments should be performed following any patient repositioning.

Airway Pressure Release Ventilation

Airway pressure release ventilation represents another open-lung mechanical ventilation strategy. Airway pressure release ventilation was designed to provide the oxygenation benefits of a near-permanent recruitment maneuver, while augmenting ventilation for patients with low-compliance lung disease.[30] Stock et al[31] were first to describe APRV in 1987 and are credited with its introduction.

Airway pressure release ventilation has been described as continuous positive airway pressure (CPAP) with regular, brief, intermittent releases in airway pressure.[30] It can therefore be thought of as a time-cycled, pressure-limited mode of mechanical ventilation, which operates by cycling between 2 pressure levels within a high-flow (demand-valve) CPAP circuit that allows spontaneous breathing at any phase of the ventilatory cycle. This mechanism may reduce the need for heavy sedation[31-33] and requires patient involvement, thus precluding the use of paralysis.

The degree of ventilatory support with APRV is determined by the duration of the 2 CPAP levels and the distending pressure used to recruit alveoli with each mechanical cycle.[31,34] The tidal volume generated depends mainly on respiratory compliance and the difference between the CPAP levels; because, P_{low} is usually set at zero, tidal volume is dependent on P_{high}. Of interest, when spontaneous breathing is absent, APRV is indistinguishable from inverse ratio pressure-controlled, time-cycled ventilation.[31,34]

Rationale Behind APRV

Lungs of patients with ALI/ARDS are often characterized by heterogeneity of threshold opening pressures across different lung areas.[35] The cyclic change in pressure and tidal volume that is characteristic of conventional ventilation may preferentially fill and overdistend alveoli with a short-time constant for filling (ie, nonfibrotic alveoli) while inducing atelectrauma in fibrotic alveoli with a longer time constant for filling. Airway pressure release ventilation aims to minimize this risk by keeping the lung inflated for an extended period of time while minimizing the exhalation (or release) phase.

Compared to conventional ventilation, APRV is associated with significantly lower peak/plateau airway pressures for a given tidal volume.[30] In a multicenter, prospective crossover trial of patients with ALI, Rasanen et al[36] demonstrated a 55% reduction in peak airway pressures compared with conventional ventilation while maintaining similar oxygenation and ventilation. By keeping the lung expanded for an extended period of time and allowing minimal time for exhalation, APRV may produce nearly complete recruitment while minimizing lower volume-induced lung injury associated with cyclic recruitment and atelectrauma.[30] However, as opposed to HFOV, APRV allows for a brief exhalation period. It is known that ARDS is a heterogeneous process whereby less fibrotic regions of the lung receive inspiratory flow preferentially while less compliant alveoli collapse earlier during exhalation. Therefore, APRV could theoretically cause VILI by inducing volutrauma during the inhalation phase and atelectrauma during the release phase in patients with ARDS. As discussed below, ventilator adjustments based on the flow-versus-time and pressure-versus-time curves are needed to minimize this risk.

There is evidence that points to important differences between ventilation distribution during spontaneous breathing and controlled mechanical ventilation.[37] During spontaneous breathing, the posterior muscular sections of the diaphragmatic muscle move more than the anterior tendon plate. Thus, in a supine patient, the dependent portions of the lungs are better ventilated during spontaneous breathing. Because in conventional methods of ventilation the diaphragm remains more passive, and because of the complex interactions between abdominal and thoracic forces, mechanical ventilation tends to be distributed more towards the anterior, nondependent, and relatively less perfused areas of the lung.[38] Paralysis and heavy sedation further inhibit diaphragmatic contraction leading to cephalad migration and further compression of dorsal inferior lung parenchyma. Therefore, more atelectasis is observed in the dorsal lung areas, which are closer to the diaphragm. By recruiting alveoli and reestablishing functional residual capacity at a more favorable point on the pressure-volume curve, APRV can "unload" inspiratory muscles and decrease the work of breathing associated with acute restrictive lung disease.[39] Spontaneous breathing, therefore, might require less effort. The ability to have variable gas flow and accommodate spontaneous ventilation is a key difference between HFOV and APRV. Spontaneous breathing with APRV in experimental lung injury models was associated with less atelectasis by computed tomographic evidence.[40] Furthermore, Neumann et al[41] demonstrated that allowing spontaneous breathing with APRV decreased intrapulmonary shunt by increasing ventilation of aerated-dependent lung tissue and opening atelectatic lung parenchyma.[41]

Although relatively weak, there is evidence that use of APRV may be associated with decreases in multiorgan failure and perhaps mortality (when compared to mortality in the ARDSNet trial),[4,35] as well as significant decrease in the need for sedatives as compared to volume-controlled ventilation in postcardiac surgery patients.[42] Furthermore, when compared to pressure-controlled ventilation, APRV has been associated with higher cardiac index and lower systemic and pulmonary vascular resistance.[33,43] In early clinical studies, APRV was demonstrated to be a feasible alternative to conventional mechanical ventilation in patients with ALI of mild-to-moderate severity.[36]

Mechanics of APRV

The 5 major parameters that need to be adjusted when using APRV are FiO_2, P_{high} (high pressure), T_{high} (time spent at the high pressure), P_{low} (low pressure), and T_{low} (time spent at the low pressure). The P_{high} and T_{high} are the main determinants of mean airway pressure and thus are directly correlated with oxygenation.[35] Because mean airway pressure also directly correlates with mean alveolar
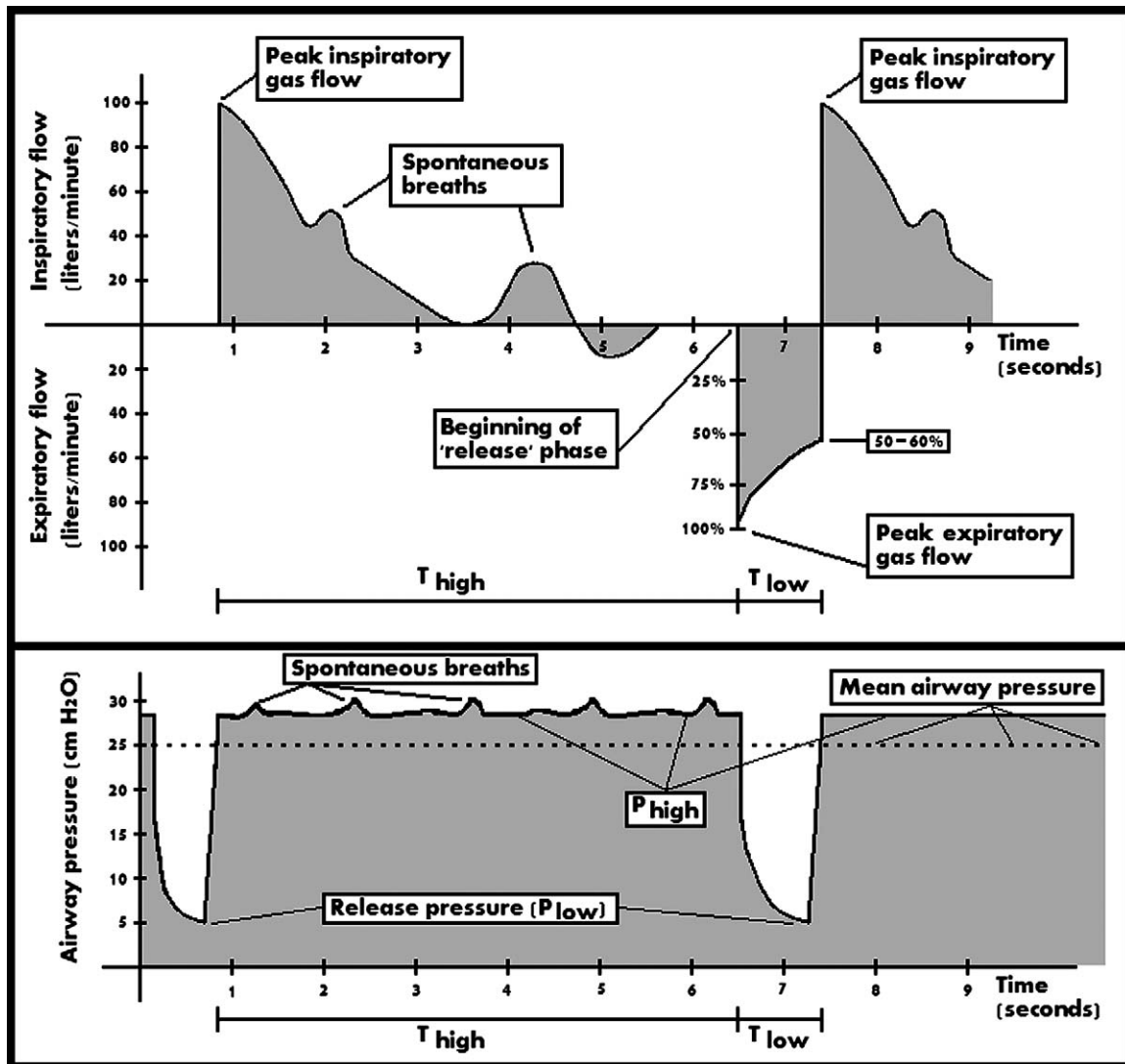
Figure 5. Pressure versus time and flow versus time graphs seen with airway pressure release ventilation. Note that spontaneous breaths are present during the respiratory cycle. Furthermore, note that T_{low} is set such that end-expiratory flow is 50% to 60% of peak expiratory flow.

volume (thus alveolar-capillary diffusion surface area), P_{high} and T_{high} are directly related to gas exchange. The pressure gradient between P_{high} and P_{low}, T_{low}, and the patient's spontaneous minute ventilation are the main determinants of alveolar ventilation, thus, CO_2 clearance. Suggested initial ventilator settings are noted in Table 1.

The P_{low} and T_{low} regulate end-expiratory lung volume and should be optimized to prevent alveolar closure and associated derecruitment while maximizing alveolar ventilation. Generally, the majority (80%-95%) of the total cycle time ($T_{high} + T_{low}$) should be spent at P_{high} to optimize mean alveolar

volume and thus maximize potential gas exchange. To minimize derecruitment, the T_{low} should be set such that expiration ends when expiratory flow equals 50% to 75% of peak expiratory flow rate (PEFR; Figure 5). Because the flow curve shown on the ventilator is a summation of all alveoli, it is possible that severely fibrotic alveoli with a short-time constant for exhalation will collapse and sustain atelectrauma if exhalation time is extended. Moreover, VILI may be possible even with this recommended exhalation time.

Newly intubated adult patients who are started on APRV should have their P_{high} set at the desired plateau

pressure. If a patient is transitioning from conventional ventilation, their P_{high} should be set at their most recent plateau pressure (usually 20-35 cm H_2O). When transitioning from HFOV to APRV, the patient should be placed on P_{high} equal to mean P_{aw} plus 2 to 4 cm H_2O.[35] Regardless of when the patient was intubated or prior mode of ventilation, P_{low} is set at 0 cm H_2O, T_{high} between 4 and 6 seconds, and T_{low} between 0.6 and 0.8 seconds based on the expiratory flow measurements.[35] Pressure$_{low}$ is set to zero to optimize the pressure gradient during the release phase, thus maximizing exhalatory flow and alveolar ventilation. Despite the set P_{low}, the release phase (T_{low}) is very brief, preventing an airway pressure of zero. Time$_{low}$ is kept brief to prevent actual alveolar collapse or derecruitment. Of note, patients with obstructive lung disease should have their initial T_{low} set between 0.8 and 1.5 seconds and adjusted based on the expiratory flow measurements.[35] In both scenarios, the pressure-time curve can be used to confirm that the airway pressure never reaches zero.

Special Measured Parameters

The PEFR is the maximal expiratory flow rate achieved during the release phase of APRV. It is a function of the pressure gradient between P_{high} and P_{low}, lung volume, compliance of the lung and thorax, and the airway resistance. Peak expiratory flow rate termination (T-PEFR) is a measured parameter that represents the expiratory flow rate at the end of the release phase of the APRV cycle. Peak expiratory flow rate termination is useful in guiding APRV adjustments, when used as a ratio of PEFR.[35] To keep things practical, a ratio of T-PEFR to PEFR of 60% is ideal. However, because of individual variability, a ratio between 50% and 66% may be used successfully (Figure 5).

Gas Exchange

As with HFOV, a large part of gas exchange occurs through convection and diffusion during the inspiratory phase of APRV. Alveolar recruitment results in improved V/Q matching, intrapulmonary shunting, and arterial oxygenation relative to conventional ventilation.[23] The increase in arterial oxygenation supports the notion of ongoing recruitment of previously nonventilated lung areas, especially when coupled with improved pulmonary compliance. The improvement in oxygenation occurs gradually over a period of 24 hours and results from gradual pulmonary recruitment.[44]

As with all modes of ventilation, oxygenation is increased by increasing the Fio_2 or the mean airway pressure. The mean airway pressure in APRV is increased by increasing the P_{high} or the T_{high}. Increasing the P_{high} beyond 30 cm H_2O risks inducing barotrauma, however, may be indicated in patients with poor thoracic or abdominal compliance.[35]

Airway pressure release ventilation is capable of either augmenting alveolar ventilation in the spontaneously breathing patient or facilitating ventilation in the apneic patient.[45] In fact, APRV was initially described as an improved method of ventilatory support in the presence of ALI and hypercarbia.[31] Airway pressure release ventilation augments CO_2 removal by improving V/Q matching and decreasing intrapulmonary shunting. A limiting factor for carbon dioxide clearance is the gradient between alveolar and arterial CO_2. This gradient is refreshed during the "release" phase of APRV when fresh gas is exchanged in the alveolar tree. The optimal release frequency is variable and depends upon a number of factors including CO_2 production, V/Q mismatch, shunt, and cardiac output. As noted above, CO_2 exchange may decrease as the T_{high} increases because the respiratory frequency decreases.[35] This phenomenon is similar to that observed with decreased CO_2 clearance with increasing I:E ratios.

Although the bulk of CO_2 exchange occurs during the release phase, other mechanisms such as cardiogenic mixing and spontaneous breathing also affect on alveolar ventilation. Cardiogenic mixing results in CO_2 movement toward central airways during the T_{high} (or breath-hold) period, improving the ventilatory effectiveness of the release.[46] The addition of spontaneous breaths during the T_{high} period further enhances recruitment and ventilation efficiency.[35] Manipulation of T_{high} must be tailored to each patient because of the number of factors involved with CO_2 removal. Table 2 lists recommended ventilator adjustments based on blood gas results.

Weaning From APRV

Patients with adequate or improving oxygenation while on APRV can be progressively weaned by

lowering the P_{high} and extending the T_{high}. As a result, the number of timed releases is decreased and the machine minute ventilation is reduced. This forces the patient to increase spontaneous minute ventilation to maintain constant total minute ventilation. This can be equated to a progressive spontaneous breathing trial and a relatively "smooth" transition toward CPAP. Some authors believe that the ultimate weaning target of APRV is CPAP, and that pressure-assisted breathing (pressure support) may actually be counter-productive.[35] Patients can be transitioned back to conventional ventilation when the P_{high} is less than 20 cm H_2O, the T_{high} is greater than 6 seconds, and the Fio_2 is less than 40%. Although it has not been studied, transitioning to conventional ventilation may expedite weaning in an environment where care providers are not as familiar with APRV.

Complications and Drawbacks of APRV

In general, APRV is not indicated in patients who are not breathing spontaneously. Although APRV can oxygenate adequately in the absence of spontaneous breathing, the patient's spontaneous breaths contribute a significant amount of the total minute ventilation. Because many of the proposed advantages of APRV (improved gas exchange, reduced dead space, possible decreased requirement for sedation and analgesia, and improved hemodynamics) are thought to be due to the preservation of spontaneous breathing, the absence of spontaneous breathing renders benefits of APRV relatively ineffective.[47]

As with HFOV, intravascular volume often needs to be augmented in patients on APRV to offset the decrease in venous return to the heart, which results from prolonged positive intrathoracic pressure. However, as opposed to HFOV, these cardiovascular side effects may be minimized on APRV by reducing mechanical ventilation to a level that provides adequate support for existing spontaneous breathing while avoiding overly high levels of positive airway pressure.[48] Periodic reduction of intrathoracic pressure achieved by maintaining spontaneous breathing during mechanical ventilation promotes venous return to the heart and increased cardiac output and oxygen delivery.[49] Moreover, the periodic release of positive intrathoracic pressure also augments venous return to the heart.

Other relative contraindications to APRV include patients with severe obstructive pulmonary conditions who are unable to empty their lungs in less than 2 seconds.[18] This group includes patients with severe asthma and chronic obstructive pulmonary disease (COPD).

Conclusion

Both HFOV and APRV have been shown to improve oxygenation in patients with ARDS. The important difference between APRV and HFOV is that APRV allows spontaneous ventilation via an elaborate pressure-release valve mechanism, while HFOV is often incompatible with spontaneous breathing. Consequently, APRV may be associated with reduction in the need for or degree of sedation and therefore may be associated with decreased number of ventilator days. Conversely, HFOV aims to keep the lung open at all times, has less of a theoretical chance of causing VILI by inducing volu- or atelectrauma, and mandates sedation. Lastly, APRV ventilators are battery powered and therefore can be used during patient transport. This can be a distinct advantage for patients who need ongoing intervention or testing. To date, there has not been either equivalency or superiority studies comparing these 2 modalities.

A series of randomized, prospective studies are needed to compare outcomes from use of either modality both as initial therapy for evolving ARDS and as rescue modalities for patients who fail accepted conventional ventilation strategies. It is possible that either APRV or HFOV may be equivalent to (if not superior to) low tidal volume and moderate PEEP ventilation due to the concerns regarding ongoing volu- and atelectrauma described above.

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