Inverse Ratio Ventilation in ARDS
Rationale and Implementation

Theodore W. Marcy, M.D., F.C.C.P.,† and
John J. Martin, M.D., F.C.C.P.‡

Conventional ventilatory support of patients with the adult respiratory distress syndrome (ARDS) consists of volume-cycled ventilation with applied positive end-expiratory pressure (PEEP). Unfortunately, recent evidence suggests that this strategy, as currently implemented, may perpetuate lung damage by overinflating and injuring distensible alveolar tissues. An alternative strategy—termed inverse ratio ventilation (IRV)—extends the inspiratory time, and, in concept, maintains or improves gas exchange at lower levels of PEEP and peak distending pressures. There are two methods to administer IRV: (1) volume-cycled ventilation with an end-inspiratory pause, or with a slow or decelerating inspiratory flow rate; or (2) pressure-controlled ventilation applied with a long inspiratory time. There are several real or theoretical problems common to both forms of IRV: excessive gas-trapping; adverse hemodynamic effects; and the need for sedation in most patients. Although there are many anecdotal reports of IRV, there are no controlled studies that compare outcome in ARDS patients treated with IRV as opposed to conventional ventilation. Nonetheless, clinicians are using IRV with increasing frequency. In the absence of well-designed clinical trials, we present interim guidelines for a ventilatory strategy in patients with ARDS based on the literature and our own clinical experience. (Chest 1991; 100:494-504)

Two methods to administer IRV: (1) volume-cycled ventilation with an end-inspiratory pause, or with a slow or decelerating inspiratory flow rate; or (2) pressure-controlled ventilation applied with a long inspiratory time. These strategies may improve gas exchange while limiting or decreasing the peak airway pressures. We review the physiologic principles relevant to the use of IRV, and suggest an alternative to the current practice of applying IRV with pressure-preset ventilation.

**Physiologic Principles**

Respiratory Mechanics in ARDS

Diffuse lung injury is one of the defining characteristics of ARDS. However, despite the widespread tissue injury and the diffuse infiltrates present on the frontal chest roentgenogram, there does not appear to be a homogeneous distribution of gas exchange abnormalities and mechanical alterations. When performed within the first ten days of illness onset, computed tomographic (CT) scans demonstrate marked heterogeneity in the roentgenographic density of the lung (Fig 1). There are areas that have the density of normally aerated tissue, as well as areas that appear poorly aerated or consolidated. Recent studies suggest that in patients with severe ARDS, only one third to one half of the lung tissue participates in tidal gas exchange. There is often a striking gravitational distribution of the infiltrates. Areas of consolidation appear more extensively in dependent portions of the lung. Positional changes of the patient will quickly and markedly alter this distribution, suggesting that a portion of the nonaerated lung is recruitable.

Analyses of gas exchange using inert gas techniques also suggest that ARDS alters lung function in a nonhomogeneous pattern. As would be expected, the proportion of venous
admixture correlates with the proportion of nonaerated lung. However, a significant fraction of lung units appears to have normal V/Q ratios despite the marked increases in shunt and dead space.

Several recent studies have further defined the respiratory system mechanics of ARDS. Using gas dilution methods, aerated lung volume at FRC was significantly less in patients with ARDS than in other patients requiring mechanical ventilation. However, the total lung volume at FRC was often within normal limits. One explanation for the disparity between aerated and total lung volume is that flooding of alveoli with edema fluid and inflammatory debris forces gas out of the lung.

Investigators have determined the static pressure-volume (P-V) relationships in patients with ARDS from measurements of gas volume, airway pressure, and esophageal pressure during stepwise inflation and deflation of the chest. Early in the disease process, the inflation portion of the P-V curve is typically flat before exhibiting an inflection point at low lung volumes (Fig 2). Significant hysteresis tends to be present in that the volume of aerated lung is greater during deflation than during inflation at the same transpulmonary pressure. Application of PEEP often decreases the hysteresis and abolishes the inflection point (Fig 2).

These observations are consistent with collapse and reopening of airways and alveoli during the different phases of the respiratory cycle. In addition, the surface tension of alveoli may be higher than normal at low lung volumes due to depleted or dysfunctional surfactant. Together, these mechanical alterations require a higher transpulmonary pressure on inflation than that required during deflation. However, the respiratory system compliance of patients with early ARDS, when measured as the slope of the deflation limb of the P-V curve, is comparable to that in other ventilated patients. In early ARDS, specific compliance, which is defined as the ratio of lung compliance to the aerated lung volume at FRC, is comparable to anesthetized normal subjects. Inflection points and hysteresis become less evident with progression of the lung injury and the loss of recruitable lung volume.

Airflow resistance is increased in patients with ARDS. In large part, this may reflect a decrease in the number of functioning airways (corresponding to a smaller aerated lung volume) rather than any alteration in the caliber of individual airways. Alternatively, there may be significant differences in the impedance characteristics (resistance and compliance) among lung units. This may cause a wide variation in the time required for both alveolar volume and pressure in different lung units to approach equilibrium. Although this point is controversial, poorly aerated lung units may have a longer "time constant" than that of aerated regions. These units may not approach full inflation during an inflation period of standard duration.

In summary, CT scans, gas exchange analyses, and measurements of thoracic mechanics suggest that acute lung injury affects lung function in a nonhomogeneous distribution. For any given transpulmonary pressure, there is a decrease in the absolute volume of aerated lung tissue. However, while certain lung units are not aerated due to edema or atelectasis, other lung units are normally aerated and have normal compliance and V/Q ratios. Thus, the functioning lung in ARDS is not so much stiff as it is small. The ventilator must apply...
high pressures to the airway to deliver a tidal volume of "standard size" (10 mL/kg) into these small lungs. These high applied pressures place normally compliant alveoli at risk for overdistension or rupture.

**Pathophysiology of Barotrauma**

Gas extravasated from alveoli during ventilatory support for ARDS is visible roentgenographically as pneumothoraces, pulmonary interstitial emphysema, pneumomediastinum, pneumoperitoneum, and tension air cysts. Certain forms of barotrauma may also cause systemic complications. It is well known that pneumothoraces under tension can cause hemodynamic compromise and collapse. In addition, interstitial gas under pressure can rupture into pulmonary venules to enter the systemic circulation. These systemic gas emboli may cause unexpected (and possibly unrecognized) myocardial and cerebrovascular damage.

Forms of barotrauma that occur from the rupture of alveoli and the extravasation of alveolar gas may not be the only manifestation of tissue injury. In animal models of barotrauma, several investigators have provoked a diffuse lung edema and injury indistinguishable from that in ARDS in normal animals ventilated with moderately high peak airway pressures (30 to 50 cm H2O). Although not yet supported by data from patients, the implication of these studies is that lung edema may be perpetuated or extended by the very technique designed to compensate for it.

The incidence of barotrauma increases with elevations of airway pressure, the requirement for high levels of PEEP, and the presence of underlying lung disease. However, we do not fully understand how these factors interact or their relative contributions to the risk of barotrauma. Early animal investigations by Macklin and Macklin into the pathophysiology of pneumothoraces demonstrated that alveolar disruption appeared to occur in alveoli that bordered the bronchovascular sheath. These studies suggested that alveolar rupture occurs when an excessive pressure gradient exists across this boundary. Subsequent studies demonstrated that alveolar volume was also an important factor leading to the disruption of alveolar tissue. Therefore, clinical situations that lead to alveolar hyperinflation, including the application of high distending pressures or the development of air-trapping, should accentuate the risk of barotrauma (Fig 3).

Peak airway pressures (PAP) over 40 to 50 cm H2O are associated with an increased risk of alveolar rupture during mechanical ventilation. The incidence of barotrauma exceeds 40 percent in patients exposed to a PAP above 70 cm H2O. Under these situations, it is likely—that barotrauma occurs because of the coinciding increases in peak alveolar pressure and volume. Because the normal lung is inflated to total lung capacity with transpulmonary pressures of 35 cm H2O, there is an emerging consensus that peak alveolar pressure (or transpulmonary pressures exceeding 35–40 cm H2O) may increase the risk of tissue rupture. Above this pressure, normal alveoli are almost certainly over-disturbed and fragile alveoli may rupture.

Ventilator-induced alveolar edema may occur at relatively low levels of PAPs. Dreyfuss and colleagues reported that rats had impressive alveolar flooding with proteinaceous edema and microvascular injury when exposed to 20 minutes of PAPs of 45 cm H2O (Fig 4). A similar form of lung injury occurred with negative pressure ventilation when tidal volumes were equivalent to those during positive pressure ventilation. This degree of injury did not occur if the transpulmonary pressure was maintained at a normal level by means of chest strapping, despite high applied peak airway pressure. High transpulmonary pressures and alveolar overdistension are unlikely to be the only causative factors in barotrauma. In neonates, significant barotrauma can occur during high-frequency ventilation even with modest peak and mean alveolar pressures. In animal models of ARDS, large tidal volumes contributed to increased lung edema even if PAPs, end-inspiratory lung volume, and pulmonary capillary wedge pressures were held constant. These and other data suggest that a variety of factors influence the risk of barotrauma: maximal distending pressures, mean airway pressure, the "mechanical stress of hyperventilation,"

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**Figure 3.** Schematic diagram of the distal bronchovascular sheath and surrounding alveoli in the normal state (left panel) and after alveolar hyperinflation. With high transpulmonary pressures and alveolar distention, the pressure gradient between the alveoli and the perivascular interstitium leads to rupture of gas into the bronchovascular sheath. This gas then moves towards the mediastinum, subcutaneous tissues, and the retroperitoneal space. Gas in the mediastinum may cause pleural rupture, creating a pneumothorax (from reference 35, with permission).
Fig. 4. An electron micrograph demonstrates severe injury of the alveolar-capillary membrane of a rat ventilated with a peak airway pressure of 45 cm H2O for 20 minutes. At the right side, the epithelial lining is destroyed, denuding the basement membrane (arrows). There are also hyaline membranes (HM) composed of cell debris and fibrin (f). Two endothelial cells (En) of another capillary are visible inside the interstitium (In). At the lower left side, a monocyte fills the lumen of a third capillary with a normal blood-air barrier (AS = alveolar space) (from reference 7, with permission).

sue fragility, secretion retention, surfactant depletion, shear forces, and the duration of ventilation.

MANAGEMENT PRINCIPLES

The ideal ventilatory strategy would relieve the patient of an excessive breathing workload, assure optimal gas distribution, and recruit collapsed or flooded alveoli without causing barotrauma or adverse hemodynamic effects. To accomplish ventilation, conventional ventilators must create cyclical differences in transpulmonary pressure. To improve oxygenation, the ventilator must apply a sufficiently high maximal transpulmonary pressure to open airways, recruit nonaerated alveoli, and reduce shunt. The ventilator must then maintain a minimum level of transpulmonary pressure to prevent re-collapse of these airways and alveoli during exhalation.

Unfortunately, it is not possible to dissociate entirely the adverse effects of high transpulmonary pressure (barotrauma, hemodynamic compromise) from the pressure-dependent objectives of assuring adequate alveolar ventilation and oxygenation. Instead, the pattern and magnitude of applied pressure must be manipulated to optimize gas exchange with a minimum of alveolar hyperinflation and adverse hemodynamic effects. An understanding of the relationship between applied pressure and the pressures that determine alveolar volume may provide guidance for this manipulation.

Importance of Mean Airway Pressure

During positive pressure ventilation of a passive subject, mean airway pressure (MAP) is the pressure measured at the airway opening, averaged over the entire respiratory cycle, and reflects the average pressure applied by the ventilator. Under these same conditions, mean alveolar pressure (MAvP) is the average pressure acting to distend the alveoli against the combined recoil of lung and chest wall. In the setting of lung edema, MAvP corresponds directly to alveolar recruitment, shunt reduction, and blood oxygenation. During conventional ventilation, MAvP rises with increases in minute ventilation, elevations of end-expiratory pressure (PEEP), or with alterations of the inspiratory flow pattern. Although MAvP cannot be measured directly during the tidal cycle, it can be estimated from a mathematical relationship of MAvP to MAP. Provided inspiratory and expiratory resistances are identical, MAP and MAvP are equivalent. If expiratory resistance exceeds inspiratory resistance, MAvP will exceed MAP by an amount that depends both on the minute ventilation (VE)
and the difference between inspiratory (RI) and expiratory resistance (Rx). MAIvP = MAP - Rx + MAIvP - Rx, therefore, increases in MAP will increase MAIvP by a variable amount depending on the Ve and the relative differences of the resistances during expiration and inspiration. As a result, MAP is a major determinant of oxygenation. 5-8, 21 In addition to its important effect on oxygenation, MAP is a key determinant of hemodynamic compromise during mechanical ventilation. 5-8, 30

In summary, in a patient passively ventilated with positive pressure, MAP is a determinant of oxygenation because it alters MAIvP and, thus, alveolar recruitment. MAP in turn, is a function of the Ve and the pattern of applied airway pressure. One practical approach to ventilator management in ARDS patients may be to use inspiratory flow patterns that augment MAP yet limit peak airway and alveolar pressures.

Several investigators observed that arterial oxygenation is directly related to MAP during neonatal respiratory distress syndrome. 4,8-10, 21, 30 Based on these observations they argued that MAP is the common mediator of improved oxygenation. Clinicians subsequently used a variety of different inspiratory flow patterns to adjust MAP independently of PEEP and the pressure gradient required for tidal volume delivery. These methods include the deliberate use of low inspiratory flow rates, an end-inspiratory pause, or pressure-preset ventilation that combines decelerating flow with protracted inspiratory times.

However, other experimental studies suggest that the inspiratory flow patterns themselves can affect gas exchange independently of MAP. 5, 8-10, 21, 30 There is improved gas exchange and less intrapulmonary shunt with ventilatory patterns that prevent end-expiratory pressure from falling to zero even if MAP and tidal volume are kept constant. 5, 8-10, 21 A certain level of end-expiratory pressure may prevent collapse of unstable airways and alveoli during expiration, and may reduce the depletion or inactivation of surfactant. The latter is an important effect, as increases in alveolar surface tension may favor edema formation. 21

The conventional approach to ventilatory support in ARDS is volume-cycled ventilation with supraphysiologic tidal volumes of 10 to 15 ml/kg, and flow rates that maintain an inspiratory-expiratory (I:E) ratio considerably lower than 1:1. 8 Increments of PEEP are added in an effort to both recruit nonaerated alveoli and to prevent airway closure and alveolar collapse at end-expiration. However, for a constant tidal volume and respiratory compliance, progressive increments in PEEP must elevate peak alveolar pressures (Fig 5), increasing the risk of disrupting or damaging fragile lung units with normal compliance. In addition, at constant tidal volume and MAP, increases in PEEP expand the dead space and raise the Ve required to maintain PaCO₂ constant. 51

Conceptual Basis for Inverse Ratio Ventilation in ARDS

Inverse ratio ventilation manipulates MAP in a manner different from the conventional approach. As the expiratory time fraction falls, the I:E ratio increases, inverting when the inspiratory time exceeds the expiratory time. In concept, prolongation of the inspiratory time can maintain MAP and tidal volume at lower levels of PEEP and peak alveolar pressure, provided that excessive end-expiratory gas trapping does not occur. If excessive gas trapping occurs, end-expiratory alveolar pressure will rise above that corresponding to the initial level of applied PEEP. 21, 26 This will either increase peak alveolar pressure during volume-cycled ventilation or decrease delivered volume during pressure-preset ventilation. 47

Sustained elevations in airway pressure may recruit lung units more effectively than transient increases. 51-53 Non-aerated alveoli may require sustained traction in order to open, 54 and some lung units with prolonged ventilatory "time constants" may require a prolonged inspiratory time to inflate fully. A few reports in the literature, as well as our own clinical experience, suggest that the ultimate benefit of IRV may be time dependent, with maximal benefits observed only after hours of application. 44-47

Sustained alveolar inflation appears to decrease dead space, perhaps by facilitating the mixing of gas in well and poorly enhancing the efficacy of collateral ventilation or by perfused regions. 51-53-55 This dead space reduction reduces Ve requirements, allowing lower tidal volumes and lower peak cycling pressures. As inspiratory time falls, the subsequent development of auto-PEEP acts to prevent end-expiratory collapse of unstable alveoli and airways. In patients with ARDS, who do not have dynamic airway collapse, increments of applied PEEP will increase end-expiratory pressure above that due to auto-PEEP. 45

Sustained inflation times, with or without an inverted ratio, should be of most use when lung units are still recruitable. In ARDS, this is most likely to occur early in the disease process. 45 There is little rationale, theoretical or empirical, for raising MAP if alveolar recruitment does not occur; tissue oxygen delivery will decline if increases in MAP compromise cardiac output.

Methods of Delivering Inverse Ratio Ventilation

There are two general methods to administer IRV: 1) pressure controlled (pressure preset), time-cycled ventilation with a long inspiratory line (Fig 6); or 2) volume cycled ventilation applied with either an end-inspiratory pause, or with a slow or decelerating inspiratory flow rate (Fig 7). During pressure-controlled IRV (PC-IRV), the ventilator applies an approximately square wave of servo-controlled pressure to the airway. As with any pressure-limited mode of ventilation, the volume actually delivered varies with respiratory system compliance and resistance. Furthermore, any level of auto-PEEP will exert a direct (and often undetected) opposing pressure. 47 Therefore, careful monitoring of exhaled volume and Ve is mandatory. It is possible that the decelerating flow pattern of PC-IRV may provide better gas distribution than volume-cycled ventilation with constant flow. 51-53-55 However, compared with the latter technique, PC-IRV may generate greater shear forces—the maximal rate of change in pressure and volume—at the beginning of inspiration (Fig 6). It is not known if this difference in shear forces contributes significantly to the risk of tissue injury.

Although volume-cycled ventilation with IRV has been described for some time, there have been only a few studies in which patients with ARDS were treated with volume-cycled IRV (VC-IRV). 30-56 Recent reports suggest that IRV
Pressure Controlled Inverse Ratio Ventilation

![Diagram of Pressure Controlled Inverse Ratio Ventilation](image)

is almost always implemented with pressure preset ventilation in adult patients. Yet, the application of PC-IRV requires sophisticated electronic circuitry or software, unlike VC-IRV. Despite its infrequent use, VC-IRV is an attractive alternative to PC-IRV and may overcome some of the potential problems of PC-IRV.

A ventilator can be set to deliver VC-IRV by slowing a constant inspiratory flow rate, by adding an additional end-inspiratory pause, or by decelerating flow into a "ramp" pattern (Fig 7). For an equivalent tidal volume, I:E ratio, and respiratory system impedance, an inspiratory pause provides a greater MAP than either the slow flow or decelerating flow techniques. However, the slow flow and the decelerating flow methods reduce the peak airway pressure (though not alveolar) pressure.

The potential advantages of VC-IRV over PC-IRV include: (1) availability of this mode on all adult ventilators; (2) the delivery of a guaranteed tidal volume; (3) precise manipulation of the inspiratory flow pattern; and (4) decreased peak inspiratory flow rates with similar or lower shear force. However, the use of VC-IRV poses its own hazards, especially if peak inflation pressures are not carefully monitored. Peak alveolar pressures can vary with changes in respiratory mechanics, frequency, or flow settings, and may inadvertently exceed the desired level. When this occurs, the clinician must adjust the tidal volume or end-expiratory alveolar pressure. With tidal volume fixed, end-expiratory pressure declines with higher flow rates or with decreases

Volume Controlled Inverse Ratio Ventilation

![Diagram of Volume Controlled Inverse Ratio Ventilation](image)

Figure 7. Schematic diagram of flow, and airway and alveolar pressures during three different forms of volume-controlled inverse ratio ventilation (VC-IRV): slow inspiratory flow, constant flow with an end-inspiratory pause, and decelerating flow. Airway pressures are indicated with the thick line. Alveolar pressure during the respiratory cycle is indicated by the shaded area. For equivalent tidal volume, frequency, and I:E ratio, the constant flow with an end-inspiratory pause has the highest mean airway pressure. As during PC-IRV, there is expiratory flow and positive alveolar pressure (auto-PEEP) at the end of the expiratory phase.
in pause length, frequency, or the PEEP setting. Fortunately, when there is a continuous display of the airway pressure, the clinician can estimate and monitor the peak alveolar pressure from the pressure observed during the end-inspiratory pause. Peak airway pressure is also a useful measurement as it reflects changes in both MAP and end-expiratory alveolar pressure (Fig 8).

Risks Associated with Inverse Ratio Ventilation

There are several real or theoretical problems common to both forms of IRV. As expiratory time falls, there may be air trapping in lung units with high respiratory resistance. Although a certain level of end-expiratory alveolar pressure is expected and desirable, disadvantaged units may become hyperinflated. In one uncontrolled study of PC-IRV for ARDS patients, pneumothoraces occurred during 23 percent of the IRV attempts. Prolonged inflation times or excessive air trapping may have exacerbated the tendency for lung rupture. However, we believe that the incidence of pneumothoraces was high because large tidal volumes (15 to 20 ml/kg) were delivered. The incidence of pneumothoraces was not as high in other studies of IRV that used smaller tidal volumes. Whatever its role in creating tissue damage, increases in MAP may exacerbate or extend barotrauma that has already occurred. Therefore, the ventilator should be adjusted to provide the lowest MAP associated with adequate oxygenation.

It is important to focus on the alveolar pressure when comparing volume-controlled ventilation with PC-IRV. During volume controlled ventilation, the peak airway pressure always exceeds the peak alveolar pressure. In contrast, during PC-IRV, the "peak" or set airway pressure and the peak alveolar pressure will equilibrate. Therefore, a peak airway pressure equivalent to that observed during volume controlled ventilation will result in a higher peak alveolar pressure during PC-IRV.

The second potential problem with IRV is that cardiac output may fall as MAP and auto-PEEP increase. It is possible to select I:E ratios that improve gas exchange without adverse hemodynamic consequences. In ten patients with ARDS placed on IRV, Cole and colleagues observed a decrease in cardiac output and oxygen delivery with I:E ratios of 4:1, but not with I:E ratios of 1:1 or 1.7:1. Similarly, Abraham and Yoshihara did not see hemodynamic changes when they converted nine ARDS patients from conventional ventilation to IRV (I:E ratios of 2:1).

A third problem with IRV is that most patients do not tolerate inverted I:E ratios without sedation. Some critically ill patients require both deep sedation and paralytic medications to accept this mode of ventilation. This is particularly important in VC-IRV. If the patient is allowed to trigger the ventilator during VC-IRV, dysynchrony is almost inevitable, and alveolar pressures will increase dangerously from gas trapping. Sedation and paralysis add certain risks, including apnea during ventilator disconnection, adverse pharmacologic effects, impaired secretion clearance, regionalatelectasis, enhanced muscle catabolism, and the inability to monitor neurologic status. Nevertheless, sedation is mandatory during VC-IRV because of the danger of the patient causing inadvertent increases in frequency and associated gas trapping.

Fourth, the delivered tidal volume is relatively small when peak alveolar pressure is maintained at 35-40 cm H2O and end-expiratory pressure is maintained above 7-10 cm H2O. It may seem logical to raise respiratory frequency to maintain normal levels of PaCO2. However, increasing the frequency during PC-IRV may actually reduce the alveolar ventilation (47), and increasing the frequency during VC-IRV may result in dangerous elevations in MAP and peak airway pressures, as noted above. Therefore, it is often necessary—and perhaps desirable—to maintain a controlled hypercapnia in these patients, achieving an adequate acid-base status (pH = 7.35) with judicious use of bicarbonate or other buffer infusions.

Although there are many anecdotal reports, no controlled studies compare outcome in ARDS patients treated with IRV as opposed to conventional ventilation. Similarly, we do not know if IRV has any physiologic advantages over conventional ventilation if MAP is held constant during the two ventilatory strategies. Reports of the clinical application of IRV are limited to observations of gas exchange and, in some studies, oxygen delivery. Three studies did not control for the effects of sedation and paralysis that were instituted at conversion to IRV. Only one of two studies that controlled for the effects of sedation and paralysis observed a significant increase in oxygen delivery. No study has evaluated whether IRV alters survival of patients with ARDS.

Implementation of Inverse Ratio Ventilation

IRV is a common ventilatory strategy in neonatal care. Clinicians are employing IRV with increasing frequency in adult patients with severe ARDS, despite the lack of convincing supportive data from clinical trials. There is a

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![Graph of predicted peak airway pressure (PAP), mean alveolar pressure (MAvP), and auto-PEEP as a function of I:E ratio](image.png)

**Figure 8.** Graph of the predicted peak airway pressure (PAP), mean alveolar pressure (MAvP), and auto-PEEP as the I:E ratio (or inspiratory time percentage) is increased during volume-controlled ventilation. Predictions were made using a model of constant flow, volume-controlled ventilation in a respiratory system with low compliance (0.04 L/cm H2O) expiratory resistance greater than inspiratory resistance (20 vs 10 cm H2O/L·s-1) and ventilator settings of 1 L tidal volume at a frequency of 20 min-1. At I:E ratios exceeding 2:1, the airway and alveolar pressures rise hyperbolically.

**Percentage Inspiratory Time**

- I:E 1:4
- I:E 1:2
- I:E 1:1
- I:E 2:1
- I:E 4:1

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distinct rationale for the use of IRV in ARDS. However, there are no physiologic guidelines for its safe and effective implementation. In fact, some published studies suggest techniques that may actually increase the risk of barotrauma, in that they recommend the use of conventional or supraconventional tidal volumes.46

On the basis of our review of the relevant literature and our own clinical experience, we use a ventilatory strategy for patients with ARDS that has proved to be safe and effective in our practice. We emphasize that we have not conducted a clinical trial that compares important outcome variables. Nonetheless, as IRV has already become a widely employed therapeutic option, we offer these interim guidelines prior to the findings of well-designed clinical trials.

Routine Management

Once the diagnosis of ARDS is established, we initiate conventional volume-cycled ventilation, usually with the assist-control mode, using tidal volumes of 7 to 10 ml/kg. We add a minimum of 7 cm H2O of PEEP at the supine position alone is associated with a substantial fall in lung volume that PEEP helps to restore. Furthermore, PEEP diminishes end-expiratory lung unit collapse, hysteresis, and the formation of lung edema fluid.14.19.41.44 Additional increments of PEEP are added as needed to reduce Fio2 requirements to safe levels. In a patient with adequate cardiovascular reserves, we accept an Fio2 and PEEP level that provides an arterial oxygen saturation of greater than 85 percent. If the PEEP exceeds 10 cm H2O, cardiac outputs are monitored with a pulmonary artery catheter.

We aggressively control respiratory infections, work to clear secretions, and reposition the patient frequently (if tolerated) to maximize volume recruitment and minimize alveolar collapse.75-76 Tidal volume is adjusted to maintain peak alveolar (plateau) pressures at, or less than, 35 cm H2O. As suggested by animal experiments using high cycling pressures,77 even lower peak alveolar pressures may be necessary to avoid lung injury. To limit cycling pressures, we occasionally use unusually small tidal volumes (6 to 8 ml/kg) at respiratory rates that avoid an unnecessarily high ventilation, maintaining pH at approximately 7.35 with bicarbonate infusions, if necessary, to compensate for CO2 retention.

Sedatives, supplemented with a paralytic agent if necessary, are used if patients have high cycling pressures, are not breathing synchronously with the ventilator, or have refractory hypoxemia despite PEEP. Sedation and paralysis may improve the effectiveness of PEEP by eliminating expiratory muscle activity (increasing FRC) or by decreasing oxygen demand and raising the oxygen saturation of venous blood.78 Paralytic therapy is discontinued as soon as feasible. We prefer to withdraw paralytic therapy temporarily at least one to two times a day to assess neurologic status and to minimize muscle atrophy.

Extended Inspiratory Time Ventilation Including IRV

We consider prolongation of the I:E ratio an option only when conventional ventilation is unable to provide adequate oxygenation without excessive amounts of PEEP, toxic levels of Fio2 or high peak distending pressures. Prolongation of the I:E ratio is likely to be most effective early in the disease process when there are still recruitable lung units. We consider the process of prolonging the I:E ratio to be a continuum aimed at raising MAP to the minimum effective level. Some patients may not require inversion of their I:E ratio. Unfortunately, many patients do not achieve sufficient benefit from IRV to justify its hazards. In such cases, IRV is discontinued after an evaluation period.

It is critically important to monitor patients carefully during transition to this mode of ventilation and for the entire duration of its use. With almost no exceptions, we follow indices of gas exchange, hemodynamics, Ve, and airway pressure frequently whenever we employ strategies designed to increase MAP. Unless there is a clear contraindication, every patient converted to extended inspiration time ventilation should have a pulmonary artery catheter in place to monitor cardiac output and central vascular pressures. Continuous pulse oximetry allows real time monitoring of oxygenation, permitting rapid changes in ventilator settings. We do not use capnometry routinely; instead we rely on following Ve and arterial blood gases to gauge the efficiency of ventilation. Airway pressure can be measured continuously at the pressure tap near the endotracheal tube. The tap is connected to the bedside monitor with pressure transducer tubing and connectors available for hemodynamic monitoring. This transducer and tubing is then dedicated to gas pressure measurement. This arrangement provides a continuous tracing of the airway pressure and the pause pressure, an estimate of peak alveolar pressure. Occlusion of the expiratory port at end-expiration gives an estimate of the total end-expiratory pressure (applied PEEP plus auto-PEEP).

We normally use volume-cycled ventilation to prolong the I:E ratio for the following reasons: (1) all adult ventilators can deliver this mode; (2) the tidal volume and Ve ventilation are guaranteed; (3) the I:E ratio can be varied in finer gradations than that usually available with PC-IRV; and (4) most clinicians are familiar with the use of volume-cycled ventilation. Pressure-controlled ventilation is an alternative method that has its own advantages. First, the maximal airway pressure is tightly controlled by the ventilator—a feature that may make PC-IRV safer than VC-IRV. Second, patients may not require as much sedation to tolerate PC-IRV.75 Even if the patient triggers the ventilator or breathes dys synchronously with the ventilator, alveolar pressures will not rise excessively; instead, tidal volume would fall as auto-PEEP increased at the higher respiratory rates. However, under these circumstances, minute ventilation can drop significantly, causing progressive respiratory acidosis. We prefer to precisely control tidal volume and Ve with VC-IRV, while accepting the need for careful airway pressure monitoring and the necessity for effective sedation. Other practitioners and institutions may decide differently (Table 1).

If not already initiated, the patient is deeply sedated and paralytic agents are added when necessary. This step prevents dysynchronous breathing, enhances comfort, and allows MAP to reflect lung distention; there are no active expiratory efforts that would increase MAP above that related to applied airway pressure. Tidal volume, frequency, inspiratory time, and PEEP are adjusted within the guidelines already discussed.
Either constant flow with an inspiratory pause (CFVC) or decelerating flow (DFVC) can be used to prolong the I:E ratio during volume cycled ventilation (VC-IRV). There may be little physiologic difference between these two methods, provided both deliver the same tidal volume over an identical time period. Both decelerating flow and an inspiratory pause have been shown to improve gas exchange. MAP can be adjusted by altering the delivered tidal volume, flow rate, frequency, PEEP, or pause length. Most ventilators currently in use permit finer adjustments of the peak flow rate than the end-inspiratory pause time. Thus, there tends to be more precise control of MAP by altering flow rate than pause time. In addition, the peak airway pressure will be lower with decelerating flow than with constant flow (Fig 7). For these reasons, we prefer DFVC.

When initiating DFVC, we change the inspiratory flow pattern from constant flow to decelerating flow without altering PEEP or the peak flow rate. This reduces PAP while increasing inspiratory time and MAP. To avoid overdistention, it is critical to begin with a peak flow setting of at least four times the Ve requirement and then to decrease slowly to lower flow rates. The high pressure alarm ("pop-off" threshold) is set at 45 to 50 cm H2O, 10 cm H2O above the intended peak tidal inflation pressure. Blood pressure, heart rate, and arterial oxygen saturation are carefully followed during these adjustments. As the peak flow rate falls to its theoretical limit—Ve itself—the airway and alveolar pressures rise hyperbolically (Fig 8). End-expiratory airway and alveolar pressures are nearly equivalent during DFVC (Fig 7). Nevertheless, the addition of a brief inspiratory pause (0.2 s) enables us to monitor the end-inspiratory alveolar pressure directly.

We adjust tidal volume, frequency, and applied PEEP to maintain end-inspiratory alveolar pressure at 35-40 cm H2O. We maintain the total end-expiratory pressure (determined by end-expiratory port occlusion) between 10-15 cm H2O by altering the level of applied PEEP. Although substantial levels of auto-PEEP can be generated in patients with ARDS with I:E ratios higher than 3:1, auto-PEEP seldom reaches levels of 10-15 cm H2O with ratios of 2:1 or lower.

If DFVC is not available on the ventilator, we will use CFVC. During initiation of CFVC, we vary the MAP by increasing the length of the inspiratory pause rather than by adjusting the peak flow setting. As before, the flow rate is set at four times the minute ventilation. We usually adjust the pause percentage rather than the absolute pause time. Alarm settings and targets for end-inspiratory and end-expiratory pressure are similar to that during DFVC. Pause length is increased until the oxygen saturation is adequate or until the I:E ratio is 2:1.

We select this range of I:E ratios primarily for two reasons. First, we are concerned about the effect of ratios higher than 2:1 on hemodynamics. The second and equally important reason for limiting the I:E ratio to less than 2:1 is that at higher ratios, alveolar pressure becomes strikingly sensitive to changes in the duration of expiration (Fig 8). Once again, we emphasize it may not be necessary to invert the ratio to achieve adequate oxygenation.

Once there are clear signs of improving oxygen exchange, we reduce the inspiratory time by decreasing the length of the inspiratory pause (CFVC) or by increasing the inspiratory flow rate (DFVC). We continue to decrease the inspiratory time as tolerated until conventional ventilation is reestablished.

### Summary

The precise modes and settings needed for optimal ventilation in ARDS are currently unknown and are likely to be different for each individual patient. However, existing evidence supports an approach that prevents peak alveolar pressure from exceeding 35 to 40 cm H2O, and maintains end-expiratory alveolar pressures above 7 to 10 cm H2O. Working within these limits, tidal volume, frequency, and inspiratory duration are adjusted to attain appropriate levels of ventilation and oxygen exchange.

In closing, we emphasize that although the use of IRV is widespread and theoretically defensible for ARDS patients, there are no controlled clinical evaluations of IRV. The same comments apply to our own use of VC-IRV. Until there is more investigational and clinical experience, these methods are unproven and experimental. Therefore, they must be applied cautiously and with full awareness of their potential benefits and hazards.

### References


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Table 1 — Comparison of Volume-Controlled (VC-IRV) and Pressure-Controlled (PC-IRV) Inverse Ratio Ventilation

<table>
<thead>
<tr>
<th>VC-IRV</th>
<th>PC-IRV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>Available on all ventilators</td>
<td>Peak distending pressures precisely controlled</td>
</tr>
<tr>
<td>Guaranteed minute ventilation</td>
<td>Some patients may tolerate without deep sedation</td>
</tr>
<tr>
<td>Precise control of flow pattern</td>
<td>Larger experience published in the literature</td>
</tr>
<tr>
<td>Familiar mode to most clinicians (Peak inspiratory flow lower than PC-IRV)</td>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>Peak alveolar pressures can vary; pressures must be monitored carefully</td>
<td>Tidal volume varies with changing respiratory mechanics; minute ventilation must be monitored carefully</td>
</tr>
<tr>
<td>Deep sedation usually necessary to prevent dysynchronous breathing</td>
<td>Not available on all ventilators</td>
</tr>
<tr>
<td>Not a familiar mode to many clinicians</td>
<td></td>
</tr>
<tr>
<td>? Greater shear forces</td>
<td></td>
</tr>
</tbody>
</table>

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with 1:E ratios higher than 3:1, auto-PEEP seldom reaches levels of 10-15 cm H2O with ratios of 2:1 or lower.
14 Maclntyre N, Follet J, Deitz J. Jet ventilation at 100 breaths per minute in adult respiratory failure. Am Rev Respir Dis 1986; 134:897
36 Pierson D. Alveolar rupture during mechanical ventilation: role of PEEP, peak airway pressure, and distending volume. Respir Care 1989; 34:472-86
38 Macklin M, Macklin C. Malignant interstitial emphysema of the lungs and mediastinum as an important occult complication in many respiratory diseases and other conditions: an interpretation of the clinical literature in the light of laboratory experiment. Medicine 1944; 23:291-352
44 Marini J. Paying the piper—the linkage of alveolar ventilation to alveolar pressure. Intensive Care Med 1990; 16:73-4
Inspiratory-expiratory ratio and airway pressure wave form during mechanical ventilation: the significance of mean airway pressure. J Pediatr 1979; 94:114-17


64 Marini J. Should PEEP be used in airflow obstruction? Am Rev Respir Dis 1989; 140:1-3

65 Al-Saady N, Bennett E. Decelerating inspiratory flow waveform improves lung mechanics and gas exchange in patients on intermittent positive-pressure ventilation. Intensive Care Med 1985; 11:68-75


