Review Articles

Medical Progress

Advances in Mechanical Ventilation

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THE chief reason that patients are admitted to an intensive care unit is to receive ventilatory support. In this article, I update the basic principles of mechanical ventilation, which I reviewed in the *Journal* in 1994,[1] and discuss recent advances.

BASIC PRINCIPLES

The indications for mechanical ventilation, as derived from a study of 1638 patients in eight countries,[2] are acute respiratory failure (66 percent of patients), coma (15 percent), acute exacerbation of chronic obstructive pulmonary disease (13 percent), and neuromuscular disorders (5 percent). The disorders in the first group include the acute respiratory distress syndrome, heart failure, pneumonia, sepsis, complications of surgery, and trauma (with each subgroup accounting for about 8 to 11 percent of the overall group). The objectives of mechanical ventilation are primarily to decrease the work of breathing and reverse life-threatening hypoxemia or acute progressive respiratory acidosis.

Virtually all patients who receive ventilatory support undergo assist-control ventilation, intermittent mandatory ventilation, or pressure-support ventilation; the latter two modes are often used simultaneously.[2] With assist-control ventilation, the most widely used mode, the ventilator delivers a set tidal volume when triggered by the patient's inspiratory effort or independently, if such an effort does not occur within a preselected time.

Intermittent mandatory ventilation was introduced to provide graded levels of assistance. With this mode, the physician sets the number of mandatory breaths of fixed volume to be delivered by the ventilator; between these breaths, the patient can breathe spontaneously.[3] Patients often have difficulty adapting to the intermittent nature of ventilatory assistance, and the decrease in the work of breathing may be much less than desired.[4]

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Pressure-support ventilation also provides graded assistance but differs from the other two modes in that the physician sets the level of pressure (rather than the volume) to augment every spontaneous respiratory effort.[5] The level of pressure delivered by the ventilator is usually adjusted in accordance with changes in the patient's respiratory frequency. However, the frequency that signals a satisfactory level of respiratory-muscle rest has never been well defined, and recommendations range from 16 to 30 breaths per minute.[6]

New modes of mechanical ventilation are often introduced. Each has an acronym, and the jargon is inhibiting to those unfamiliar with it. Yet each new mode involves nothing more than a modification of the manner in which positive pressure is delivered to the airway and of the interplay between mechanical assistance and the patient's respiratory effort. The purpose of a new mode of ventilation may be to enhance respiratory-muscle rest, prevent deconditioning, improve gas exchange, prevent lung damage, enhance the coordination between ventilatory assistance and the patient's respiratory efforts, and foster lung healing; the priority given to each goal varies.

COORDINATING RESPIRATORY EFFORT AND MECHANICAL VENTILATION

Probably the most common reason for instituting mechanical ventilation is to decrease the work of the respiratory muscles. The inspiratory effort expended by patients with acute respiratory failure is about four times the normal value, and it can be increased to six times the normal value in individual patients.[7] Critically ill patients in whom this increased level of effort is sustained indefinitely are at risk of inspiratory-muscle fatigue, which can add structural injury to already overworked muscles.[8] It is sometimes thought that the simple act of connecting a patient to a ventilator will decrease respiratory effort. Yet unless the settings are carefully selected, mechanical ventilation can actually do the opposite.

With careful selection of ventilator settings, inspiratory effort can be reduced to the normal range.[9] But eliminating inspiratory effort is not desirable because it causes deconditioning and atrophy of the respiratory muscles.[10] Surprisingly, researchers have not attempted to determine the desirable target for reducing inspiratory effort in patients with acute respiratory distress. To reduce effort markedly requires that the ventilator cycle in unison with the patient's central respiratory rhythm (Fig. 1). For perfect synchronization, the period of mechanical inflation must match the period of neural inspiratory time (the duration of inspiratory effort), and the period of mechanical

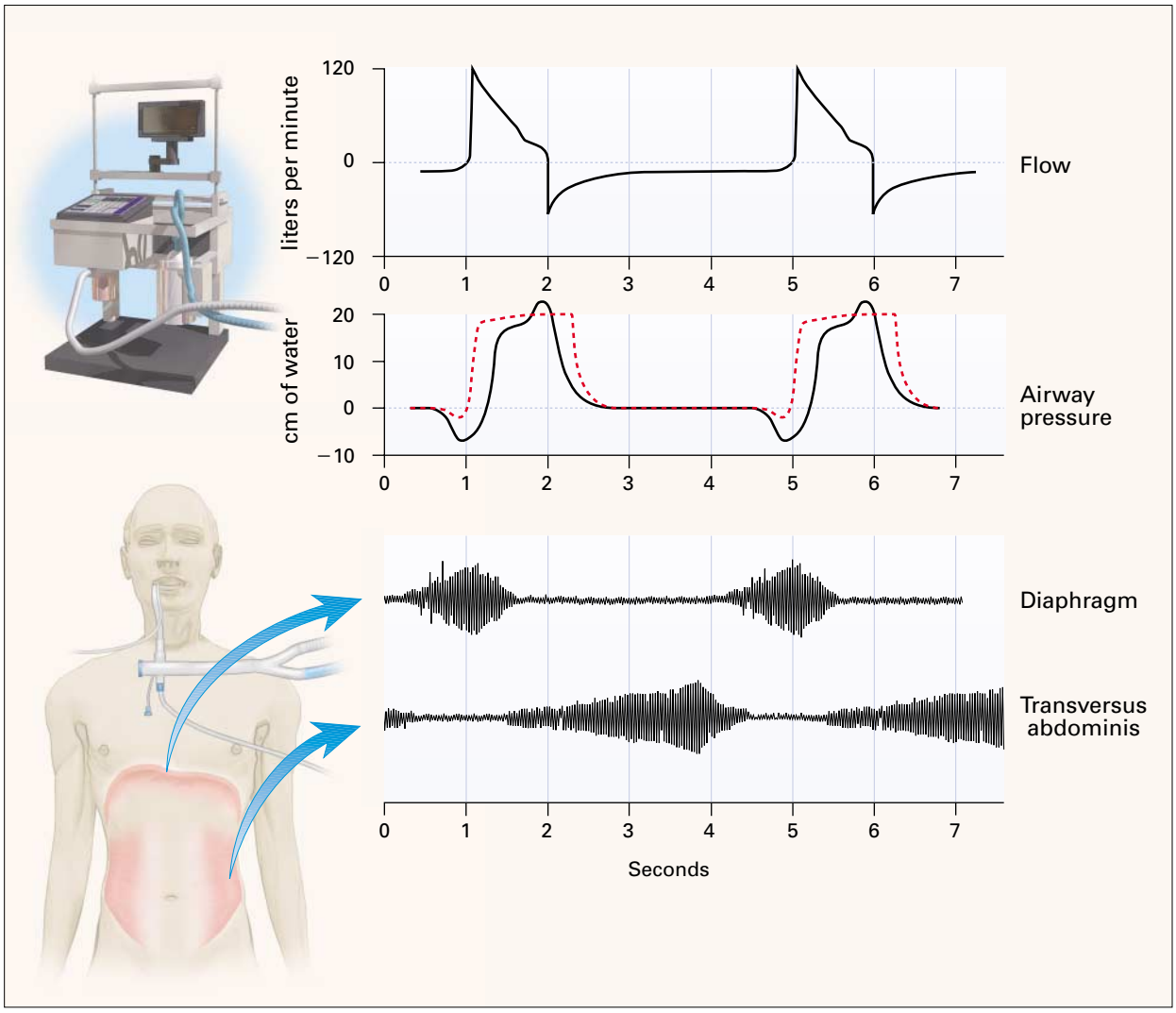

Figure 1. Flow, Airway Pressure, and Inspiratory and Expiratory Muscle Activity in a Patient with Chronic Obstructive Pulmonary Disease Who Received Pressure-Support Ventilation at an Airway Pressure of 20 cm of Water.

The electromyograms in the lower portion of the figure show inspiratory muscle activity in the patient's diaphragm and expiratory muscle activity in the transversus abdominis. The patient's increased inspiratory effort caused the airway pressure to fall below the set sensitivity (−2 cm of water), and inadequate delivery of flow by the ventilator resulted in a scooped contour on the airway-pressure curve during inspiration. While the ventilator was still pumping gas into the patient, his expiratory muscles were recruited, causing a bump in the airway-pressure curve. That the flow never returned to zero throughout expiration reflected the presence of auto–positive end-expiratory pressure. The broken red line shows airway pressure in another patient, who generated just enough effort to trigger the ventilator and in whom there was adequate delivery of gas by the ventilator. Data are from Jubran et al.[6] and Parthasarathy et al.[11]

inactivity must match the neural expiratory time.[12,13] Difficulties in synchronization can arise at the onset of inspiratory effort, at the onset of flow delivered by the ventilator, during the period of ventilator-induced inflation, and at the switch between inspiration and expiration.

Almost all patients who undergo mechanical ventilation receive some form of assisted ventilation, with the patient's inspiratory effort triggering the ventilator. To ensure that the ventilator does not cycle too often, the clinician sets a threshold for airway pressure that will trigger the ventilator. This threshold, referred to as set sensitivity, is usually −1 to −2 cm of water.[14] To reach this threshold, the patient must initiate an inspiratory effort. But when the threshold is reached, inspiratory neurons do not simply switch off. Consequently, the patient may expend considerable inspiratory effort throughout the machine-cycled inflation.[15]

The display of airway pressure and flow tracings

on ventilator screens has increased awareness that inspiratory effort is frequently insufficient to trigger the ventilator. At high levels of mechanical assistance, up to one third of a patient's inspiratory efforts may fail to trigger the machine.[9,16,17] Surprisingly, unsuccessful triggering is not the result of poor inspiratory effort; indeed, the effort is more than a third greater when the threshold for triggering the ventilator is not reached than when it is reached.[9] Breaths that do not reach the threshold for triggering the ventilator have higher tidal volumes and shorter expiratory times than do breaths that do trigger the ventilator. Consequently, elastic-recoil pressure builds up within the thorax in the form of intrinsic positive end-expiratory pressure (PEEP), or auto-PEEP.[9] To trigger the ventilator, the patient's inspiratory effort first has to generate a negative intrathoracic pressure in order to counterbalance the elastic recoil and then must reach the set sensitivity. The consequences of wasted inspiratory efforts are not fully known, but they add an unnecessary burden in patients whose inspiratory muscles are already under stress.

The inspiratory flow rate is initially set at a default value, such as 60 liters per minute. If the delivered flow does not meet the patient's ventilatory needs, inspiratory effort will increase.[15] Sometimes the flow is increased in order to shorten the inspiratory time and increase the expiratory time, especially in patients with inspiratory efforts that are insufficient to trigger the ventilator. But an increase in flow causes immediate and persistent tachypnea, and as a result, the expiratory time may be shortened.[18] In one study, for example, increases in inspiratory flow from 30 liters per minute to 60 and 90 liters per minute caused increases in the respiratory rate of 20 and 41 percent, respectively.[19]

In studies of interactions between the patient's respiratory effort and mechanical ventilation, remarkably little attention has been paid to the switch between inspiration and expiration. With the use of pressure-support ventilation, ventilatory assistance ceases when the patient's inspiratory flow falls by a preset amount (e.g., to 25 percent of the peak flow).[5] Air flow changes more slowly in patients with chronic obstructive pulmonary disease than in other patients, and patients often start to exhale while the ventilator is still pumping gas into their chests.[6,11] In 5 of 12 patients with chronic obstructive pulmonary disease who were receiving pressure support of 20 cm of water, expiratory muscles were recruited during ventilator-induced inflation.[6]

IMPROVING OXYGENATION AND PREVENTING LUNG INJURY

A primary goal of mechanical ventilation is to improve arterial oxygenation. Improvement is achieved partly through the use of endotracheal intubation to ensure the delivery of oxygen to the airway and partly through an increase in airway pressure. Satisfactory oxygenation is easily achieved in most patients with airway obstruction. The main challenge arises in patients with alveolar-filling disorders, especially the acute respiratory distress syndrome — a form of noncardiogenic pulmonary edema resulting from severe acute alveolar injury. It has long been recognized that arterial oxygenation can be achieved at a lower inspired oxygen concentration by increasing airway pressure. The goal of using the lowest possible oxygen concentration to achieve an arterial oxygen saturation of approximately 90 percent has not changed in decades. What has changed is how this goal is viewed in relation to other factors, particularly ventilator pressures. In recent years, there has been a growing tendency to be more concerned about high airway pressures than about oxygen toxicity, although this shift has been based on a consensus of opinion rather than on data from studies in patients and animals.

From the outset, clinicians recognized that mechanical ventilation could rupture alveoli and cause air leaks.[20] In 1974, Webb and Tierney showed that mechanical ventilation could also cause ultrastructural injury, independently of air leaks.[21] Their observations went largely unnoticed until a decade later, when several investigators confirmed and extended them. Alveolar overdistention causes changes in epithelial and endothelial permeability, alveolar hemorrhage, and hyaline-membrane formation in laboratory animals.[22]

Diffuse infiltrates on chest radiographs originally led clinicians to infer that lung involvement was homogeneous. But computed tomography (CT) reveals a patchy pattern: about one third of the lung is unaerated, one third poorly aerated, and one third normally aerated.[23,24] A ventilator-induced breath will follow the path of least impediment, travelling preferentially to the normally aerated areas. As a result, these regions are vulnerable to alveolar overdistention and the type of ventilator-induced lung injury found in laboratory animals[25] (Fig. 2).

A new era of ventilatory management began in 1990, when Hickling et al.[26] reported that lowering the tidal volume caused a 60 percent decrease in the expected mortality rate among patients with the acute respiratory distress syndrome. In a subsequent trial, Amato et al.[27,28] randomly assigned patients to a conventional tidal volume (12 ml per kilogram of body weight) or to a low tidal volume (less than 6 ml per kilogram). Mortality was decreased by 46 percent with the lower tidal volume. In a recent study of 861 patients, the Acute Respiratory Distress Syndrome Network[29] confirmed this benefit: mortality was decreased by 22 percent with a tidal volume of 6 ml per kilogram as compared with a tidal volume of 12 ml per kilogram. Lowering the tidal volume, however, failed to improve the outcome in three controlled trials.[30-32] The discrepant findings can be explained by differences in trial design. Increased survival was de-

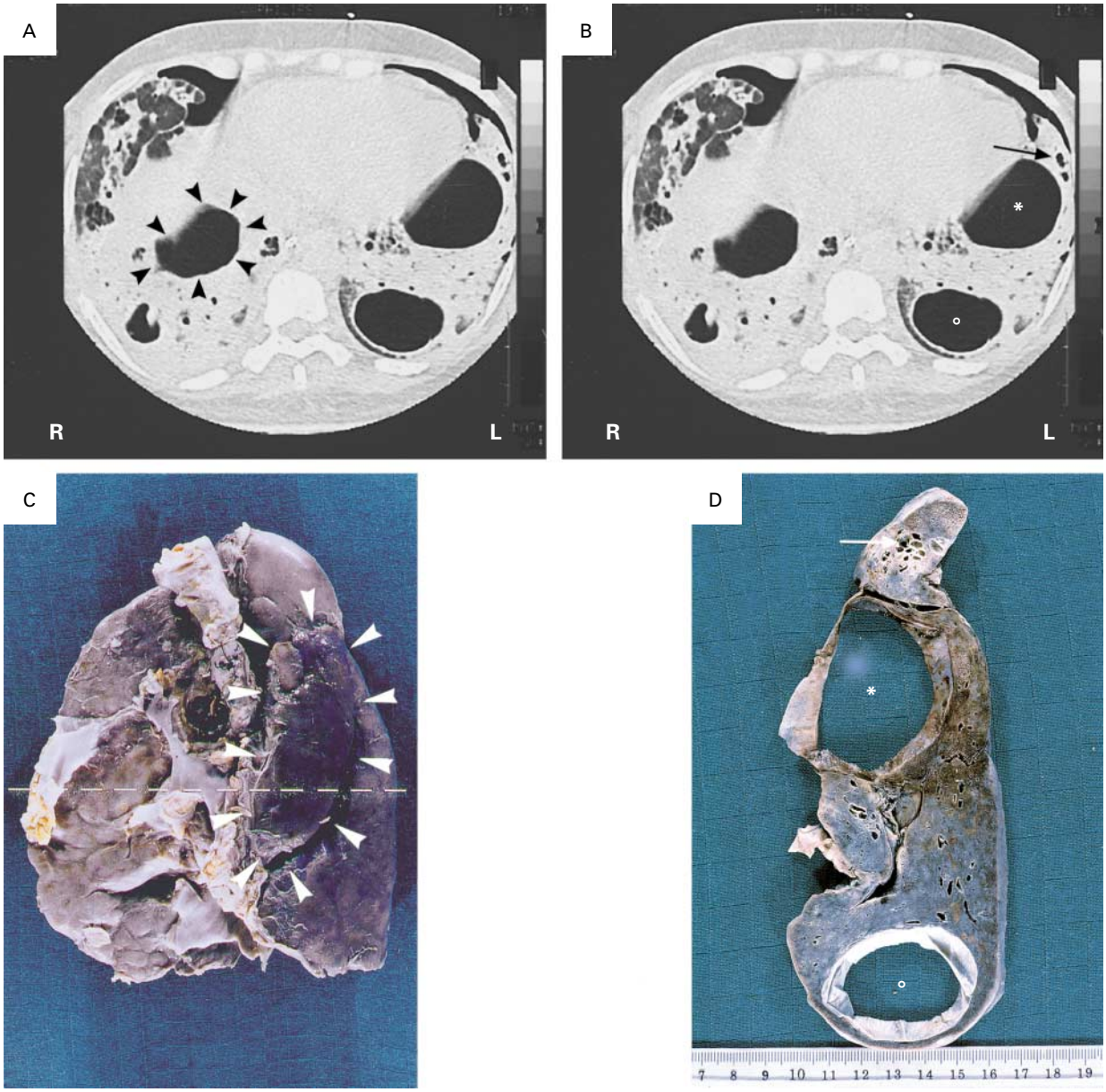

Figure 2. Lung Injury Caused by Mechanical Ventilation in a 31-Year-Old Woman with the Acute Respiratory Distress Syndrome Due to Amniotic-Fluid Embolism.

The patient had undergone mechanical ventilation for eight weeks with tidal volumes of 12 to 15 ml per kilogram of body weight, peak airway pressures of 50 to 70 cm of water, positive end-expiratory pressures of 10 to 15 cm of water, and a fractional inspired oxygen concentration of 0.80 to 1.00 in order to achieve a partial pressure of carbon dioxide that was less than 50 mm Hg and a partial pressure of oxygen that was 80 mm Hg or higher. Computed tomography (CT) performed two days before the patient died revealed a paramediastinal pneumatocele in the right lung (Panel A, arrowheads) and numerous intraparenchymal pseudocysts in the left lung (Panel B, black arrow, open circle, and asterisk).

At autopsy, both lungs were removed and fixed by intrabronchial infusion of formalin, alcohol, and polyethylene glycol at an insufflation pressure of 30 cm of water. Panel C shows the paramediastinal pneumatocele in the right lung (arrowheads); the horizontal broken line is the level of the CT section. Panel D shows a 1-cm-thick section of the left lung, corresponding to the CT section. Small pseudocysts are present (arrow), and two large pseudocysts (asterisk and open circle) have compressed and partially destroyed the parenchyma. The development of these lesions in a patient without a history of chronic lung disease indicates the harm that may result with the use of high tidal volumes and airway pressures. The photographs were kindly provided by Dr. Jean-Jacques Rouby, Hôpital de la Pitié–Salpêtrière, Paris.

monstrable only when the patients undergoing conventional ventilation had a mean pressure during an end-inspiratory pause (the so-called plateau pressure, a surrogate for peak alveolar pressure) that exceeded 32 cm of water.[33]

The pressures pertinent to ventilatory management are the peak inspiratory pressure, plateau pressure, and end-expiratory pressure. Patients with airway obstruction may have a very high peak pressure without any increase in the plateau pressure. Indeed, the gradient between the two is directly related to the resistance of the airway to airflow. An increase in the peak inspiratory pressure without a concomitant increase in the plateau pressure is unlikely to cause alveolar damage. The critical variable is not airway pressure itself but transpulmonary pressure — airway pressure during the end-inspiratory pause minus pleural pressure. The normal lung is maximally distended at a transpulmonary pressure between 30 and 35 cm of water, and higher pressures cause overdistention. Patients with stiff chest walls, such as those with the acute respiratory distress syndrome due to a nonpulmonary disorder (e.g., abdominal sepsis), have an elevated pleural pressure. In such patients, the airway plateau pressure may exceed 35 cm of water without causing alveolar overdistention.

Clinical decisions based on plateau pressure must take into account the relation between lung volume and airway pressure in the individual patient. The pressure–volume curve in patients with the acute respiratory distress syndrome typically has a sigmoid shape with two discrete bends, called inflection points (Fig. 3).[34] Some investigators believe that a plateau pressure above the upper bend causes alveolar overdistention. Reducing the tidal volume lowers the plateau pressure, but at the cost of hypercapnia. In a study in which 25 patients with the acute respiratory distress syndrome underwent mechanical ventilation with a tidal volume of 10 ml per kilogram, 20 had a plateau pressure that was 2 to 14 cm of water above the upper bend of the pressure–volume curve.[35] Lowering the plateau pressure to a value that fell below the upper bend required a 22 percent decrease in the tidal volume, causing the partial pressure of carbon dioxide to increase from 44 to 77 mm Hg.[35] The partial pressure of carbon dioxide, in turn, can be decreased by as much as 28 percent by removing tubing and thus decreasing dead space and increasing the frequency of ventilator-induced breaths. By virtue of their stiff lungs, patients with the acute respiratory distress syndrome who do not have an underlying airway obstruction can tolerate a frequency of 30 breaths per minute without gas trapping.[36] Severe hypercapnia can have adverse effects, including increased intracranial pressure, depressed myocardial contractility, pulmonary hypertension, and depressed renal blood flow.[37,38] The view that these risks are preferable to the higher plateau pressure required to achieve normocapnia represents a substantial shift in ventilatory management.

Lowering the tidal volume is not without hazards. In addition to the potential harm of hypercapnia, the volume of aerated lung may be decreased,[39] with a consequent increase in shunting and worsening oxygenation. One means of minimizing the loss of lung volume is the use of sighs (i.e., single breaths of large tidal volume). In one study, increasing the plateau pressure by at least 10 cm of water during sighs, applied three times a minute over a period of one hour, caused a 26 percent decrease in shunting, with a 50 percent increase in the partial pressure of oxygen.[40] It is unknown whether sighs used at this low frequency cause injury from alveolar overdistention.

The more usual way of improving oxygenation is through the use of PEEP with the intention of recruiting previously nonfunctioning lung tissue. Selecting the right level of PEEP for a given patient with the acute respiratory distress syndrome is difficult, because the severity of injury varies throughout the lungs. PEEP can recruit atelectatic areas but may overdistend normally aerated areas.[41,42] In a study involving six patients with acute lung injury, for example, the use of PEEP at 13 cm of water resulted in the recruitment of nonaerated portions of lung, with a gain of 320 ml in volume, but three patients had overdistention of already aerated portions of lung, with an excess volume of 238 ml.[43]

Overall, about 30 percent of patients with acute lung injury do not benefit from PEEP or have a fall in the partial pressure of oxygen.[23,44,45] With the patient in the supine posture, PEEP generally recruits the regions of the lung closest to the apex and sternum.[23] Conversely, PEEP can increase the amount of nonaerated tissue in the regions close to the spine and the diaphragm.[23] Among patients in the early stages of the acute respiratory distress syndrome, those with pulmonary causes, such as pneumonia, are less likely to benefit from PEEP than are those with nonpulmonary causes, such as intraabdominal sepsis or extrathoracic trauma.[46] This distinction may be related to the type of morphologic involvement: pulmonary causes of the syndrome are characterized by alveolar filling, whereas nonpulmonary causes are characterized by interstitial edema and alveolar collapse. In the later stages of the acute respiratory distress syndrome, remodeling and fibrosis may eliminate this distinction between pulmonary and nonpulmonary causes.

To select the right level of PEEP, some experts recommend bedside calculation of the pressure–volume curve. With the ventilators currently used in the United States, calculating the pressure–volume curve is logistically difficult and technically demanding.[34] Yet many ventilators have a computer screen, and minor software modifications would make it feasible to calculate the curve in as little as two minutes — as with the ventilators available in France.[47] Providing

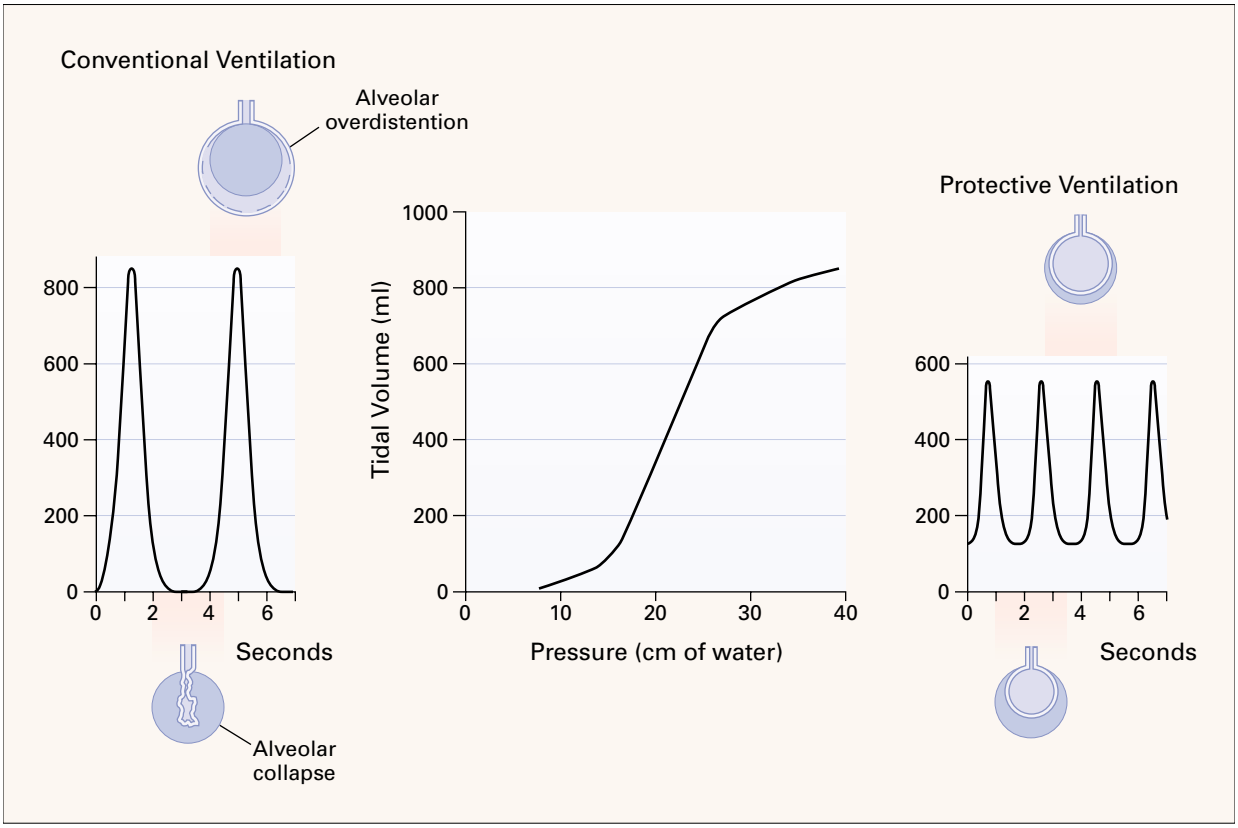

Figure 3. Respiratory Pressure–Volume Curve and the Effects of Traditional as Compared with Protective Ventilation in a 70-kg Patient with the Acute Respiratory Distress Syndrome.

The lower and upper inflection points of the inspiratory pressure–volume curve (center panel) are at 14 and 26 cm of water, respectively. With conventional ventilation at a tidal volume of 12 ml per kilogram of body weight and zero end-expiratory pressure (left-hand panel), alveoli collapse at the end of expiration. The generation of shear forces during the subsequent mechanical inflation may tear the alveolar lining, and attaining an end-inspiratory volume higher than the upper inflection point causes alveolar overdistention. With protective ventilation at a tidal volume of 6 ml per kilogram (right-hand panel), the end-inspiratory volume remains below the upper inflection point; the addition of positive end-expiratory pressure at 2 cm of water above the lower inflection point may prevent alveolar collapse at the end of expiration and provide protection against the development of shear forces during mechanical inflation.

this option on ventilators would increase clinicians' experience with the use of pressure–volume curves in ventilatory management.

Even if the pressure–volume curve is not calculated at the bedside, it is useful to select the PEEP level according to this conceptual framework. A level above the lower bend in the pressure–volume curve is thought to keep alveoli open at the end of expiration and thus prevent the injury that can result from shear forces created by the opening and closing of alveoli.[48-50] This level of PEEP may also prevent an increase in the amount of nonaerated tissue and, thus, atelectasis. However, the notion that the lower bend signals the level of PEEP necessary to prevent end-expiratory collapse and that pressures above the upper bend signal alveolar overdistention is a gross oversimplification. The relation between the shape of the pressure–volume curve and events at the alveolar level is confounded by numerous factors and is the subject of ongoing research and debate.[51-55] An understanding of this relation is also impeded by the difficulty in distinguishing collapsed lung units from fluid-filled units on CT.

Most patients with the acute respiratory distress syndrome have an increase in the partial pressure of oxygen when there is a change from the supine to the prone position. In a study of 16 patients, for example, 12 had an increase of 9 to 73 mm Hg in the partial pressure of oxygen, and 4 had a decrease of 7 to 16 mm Hg.[56] The mechanism responsible for the improvement in the partial pressure of oxygen is not clear. The attribution of this improvement to lung recruitment has not been proved.[56] It is now posited that a prone position causes ventilation to be distrib-

uted more evenly to the various regions of the lungs,[57,58] improving the relation between ventilation and perfusion.[59,60]

DISCONTINUING MECHANICAL VENTILATION

Because mechanical ventilation can have life-threatening complications, it should be discontinued at the earliest possible time. The process of discontinuing mechanical ventilation, termed weaning, is one of the most challenging problems in intensive care, and it accounts for a considerable proportion of the workload of staff in an intensive care unit.[2]

When mechanical ventilation is discontinued, up to 25 percent of patients have respiratory distress severe enough to necessitate the reinstitution of ventilatory support.[61,62] Our understanding of why weaning fails in some patients has advanced considerably in recent years. Among patients who cannot be weaned, disconnection from the ventilator is followed almost immediately by an increase in respiratory frequency and a fall in tidal volume — that is, rapid, shallow breathing[63] (Fig. 4). As a trial of spontaneous breathing is continued over the next 30 to 60 minutes, the respiratory effort increases considerably, reaching more than four times the normal value at the end of this period.[7] The increased effort is mainly due to worsening respiratory mechanics. Respiratory resistance increases progressively over the course of a trial of spontaneous breathing, reaching about seven times the normal value at the end of the trial; lung stiffness also increases, reaching five times the normal value; and gas trapping, measured as auto-PEEP, more than doubles over the course of the trial.[7] Before weaning is started, however, the respiratory mechanics in such patients are similar to those in whom subsequent weaning is successful.[66] Thus, unknown mechanisms associated with the act of spontaneous breathing cause the worsening of respiratory mechanics in patients who cannot be weaned from mechanical ventilation.

In addition to the increase in respiratory effort, an unsuccessful attempt at spontaneous breathing causes considerable cardiovascular stress.[67] Patients can have substantial increases in right and left ventricular afterload, with increases of 39 and 27 percent in pulmonary and systemic arterial pressures, respectively,[64] most likely because the negative swings in intrathoracic pressure are more extreme. At the completion of a trial of weaning, the level of oxygen consumption is equivalent in patients who can be weaned and in those who cannot. But how the cardiovascular system meets the oxygen demand differs in the two groups of patients.[64] In those who are successfully weaned, the oxygen demand is met through an increase in oxygen delivery, mediated by the expected increase in cardiac output on discontinuation of positive-pressure ventilation. In patients who cannot be weaned, the oxygen demand is met through an increase in oxygen extraction, and these patients have a relative decrease in oxygen delivery.[64] The greater oxygen extraction causes a substantial decrease in mixed venous oxygen saturation, contributing to the arterial hypoxemia that occurs in some patients.[64]

Over the course of a trial of spontaneous breathing, about half of patients in whom the trial fails have an increase in carbon dioxide tension of 10 mm Hg or more.[7] The hypercapnia is not usually a consequence of a decrease in minute ventilation.[63] Instead, hypercapnia results from rapid, shallow breathing, which causes an increase in dead-space ventilation. In a small proportion of patients who cannot be weaned, primary depression of respiratory drive may be responsible for the hypercapnia.[7]

The discontinuation of mechanical ventilation needs to be carefully timed. Premature discontinuation places severe stress on the respiratory and cardiovascular systems, which can impede the patient's recovery. Unnecessary delays in discontinuation can lead to a host of complications. Decisions about timing that are based solely on expert clinical judgment are frequently erroneous.[68-70] Several functional measures are used to aid decision making. The level of oxygenation must be satisfactory before one attempts to discontinue mechanical ventilation. Yet in many patients with satisfactory oxygenation, such attempts fail. The use of traditional predictors of the success or failure of attempts — maximal inspiratory pressure, vital capacity, and minute ventilation — frequently has false positive or false negative results.[71] A more reliable predictor is the ratio of respiratory frequency to tidal volume (f/V_T).[72] The ratio must be calculated during spontaneous breathing; calculating it during pressure support markedly impairs its predictive accuracy.[68] The higher the ratio, the more severe the rapid, shallow breathing and the greater the likelihood of unsuccessful weaning. A ratio of 100 best discriminates between successful and unsuccessful attempts at weaning. In a case of clinical equipoise — that is, a pretest probability of 50 percent — an f/V_T of 80, which has a likelihood ratio of 7.5, is associated with almost a 95 percent post-test probability of successful weaning.[73] If the f/V_T is higher than 100, the likelihood ratio is 0.04 and the post-test probability of successful weaning is less than 5 percent.

Several groups of investigators have evaluated the predictive value of f/V_T.[74-78] Its positive predictive value — the proportion of patients who are successfully weaned among those for whom the ratio predicts success — has generally been high (0.8 or higher). The negative predictive value — the proportion of patients who cannot be weaned among those for whom the ratio predicts failure — has sometimes been reported to be low (0.5 or less). Low negative predictive values have often been reported for patients with a high likelihood of successful extubation — for example, patients undergoing routine postop-

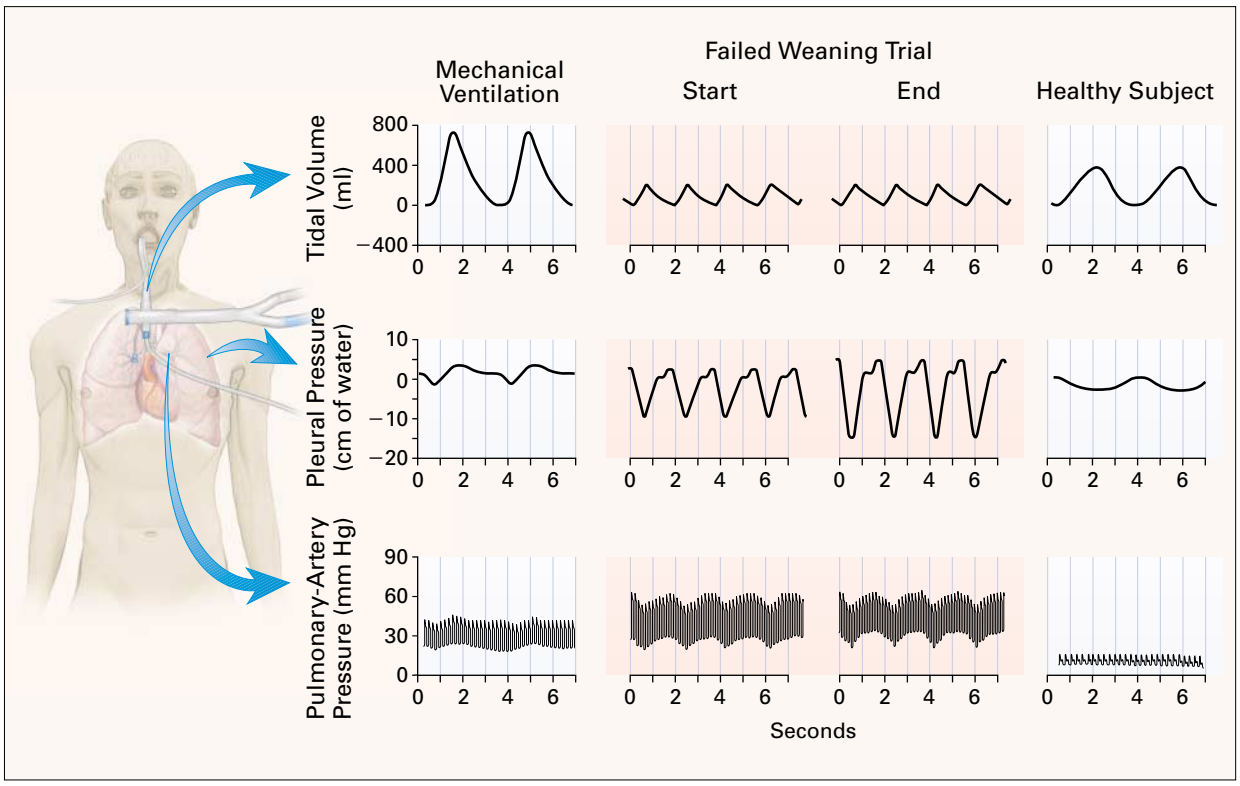

Figure 4. Tidal Volume, Pleural Pressure, and Pulmonary-Artery Pressure in a Patient Undergoing Assist-Control Ventilation and at the Start and End of a Failed Trial of Spontaneous Breathing.

During mechanical ventilation, the patient's inspiratory effort is in the normal range and the pulmonary-artery pressure is 45/22 mm Hg (systolic/diastolic). At the start of the trial of spontaneous breathing, the tidal volume falls to 200 ml, the respiratory frequency increases to 33 breaths per minute, there are swings in pleural pressure of 11 cm of water, and the pulmonary-artery pressure at the end of expiration is 60/28 mm Hg. At the end of the trial, 45 minutes later, the tidal volume and respiratory frequency are unchanged, there are swings in pleural pressure of 19 cm of water, auto–positive end-expiratory pressure is 4 cm of water, and the pulmonary-artery pressure is 60/31 mm Hg. The values in a healthy subject are tidal volume, 380 ml; respiratory frequency, 17 breaths per minute; pleural-pressure swings, 3 cm of water; and pulmonary-artery pressure, 18/8 mm Hg. Data are from Tobin et al.[63,64] and Jubran et al.[7,65]

erative ventilatory assistance and patients who have tolerated initial trials of weaning.[75,76]

There are four methods of weaning.[79] The oldest method is to perform trials of spontaneous breathing several times a day, with the use of a T-tube circuit containing an enriched supply of oxygen. Initially 5 to 10 minutes in duration, the trials are extended and repeated several times a day until the patient can sustain spontaneous ventilation for several hours. This approach has become unpopular because it requires considerable time on the part of intensive care staff.

The two most common approaches, intermittent mandatory ventilation and pressure support, decrease ventilatory assistance gradually by respectively lowering the number of ventilator-assisted breaths or the level of pressure. When a minimal level of ventilatory assistance can be tolerated, the patient is extubated. The minimal level of assistance, however, has never been well defined. For example, pressure support of 6 to 8 cm of water is widely used to compensate for the resistance imposed by the endotracheal tube and ventilator circuit.[80] A patient who can breathe comfortably at this level of pressure support should be able to tolerate extubation. But if the upper airways are swollen because an endotracheal tube has been in place for several days, the work engendered by breathing through the swollen airways is about the same as that caused by breathing through an endotracheal tube.[81] Accordingly, any amount of pressure support overcompensates and may give misleading information about the likelihood that a patient can tolerate extubation.

The fourth method of weaning is to perform a single daily T-tube trial, lasting for up to two hours. If this trial is successful, the patient is extubated; if the trial is unsuccessful, the patient is given at least

24 hours of respiratory-muscle rest with full ventilatory support before another trial is performed.[82]

Until the early 1990s, it was widely believed that all weaning methods were equally effective, and the physician's judgment was regarded as the critical determinant. But the results of randomized, controlled trials clearly indicate that the period of weaning is as much as three times as long with intermittent mandatory ventilation as with trials of spontaneous breathing.[61,62] In a study involving patients with respiratory difficulties on weaning, trials of spontaneous breathing halved the weaning time as compared with pressure support[62]; in another study, the weaning time was similar with the two methods.[61] Performing trials of spontaneous breathing once a day is as effective as performing such trials several times a day[62] but much simpler. In a recent study, half-hour trials of spontaneous breathing were as effective as two-hour trials.[83] However, this study involved all patients being considered for weaning, not just those for whom there were difficulties with weaning.

A two-stage approach to weaning — systematic measurement of predictors, including f/V_T, followed by a single daily trial of spontaneous breathing — was compared with conventional management in a randomized trial.[69] Although the patients assigned to the two-stage approach were sicker than those assigned to conventional weaning, they were weaned twice as rapidly. The rate of complications and the costs of intensive care were also lower with two-stage management than with conventional management.

When patients can sustain spontaneous ventilation without undue discomfort, they are extubated. About 10 to 20 percent of such patients require reintubation.[61,62] Mortality among patients who require reintubation is more than six times as high as mortality among patients who can tolerate extubation.[83,84] The reason for the higher mortality is unknown; it is not clearly related to the development of new problems after extubation or to complications of reinserting the tube. Indeed, the need for reintubation may simply be a marker of a more severe underlying illness.

In a controlled trial involving patients who could not sustain spontaneous ventilation, the patients who were extubated and then received noninvasive ventilation through a face mask had a shorter mean overall period of ventilatory support (10.2 days) than those who remained intubated and were weaned by decreasing pressure support (16.6 days).[85] Although this result is promising, it is not clear how many such patients or which ones could benefit from this approach.

OTHER APPROACHES TO MECHANICAL VENTILATION

Noninvasive ventilation, an approach that is becoming more widespread, was reviewed in the *Journal* in 1997.[86] Two new approaches under investigation are liquid ventilation[87] and proportional-assist ventilation[16]; they have not yet been approved for general clinical use.

CONCLUSIONS

Since my previous overview of mechanical ventilation in the *Journal,* we have gained a better understanding of the pathophysiology associated with unsuccessful weaning and have learned how to wean patients more efficiently. We have also learned how ventilator settings influence survival in patients with the acute respiratory distress syndrome. Less progress has been made in determining how the ventilator can best be used to achieve maximal respiratory-muscle rest, which is the most common reason for providing mechanical ventilation. Although further research may lead to unexpected new insights, an important challenge for researchers is to identify elements of our current knowledge that can be incorporated into a clinical management scheme to improve the outcome for patients who require ventilatory assistance.

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