Management of post traumatic respiratory failure

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For patients who have been critically injured, acute respiratory distress syndrome (ARDS) represents the first step on the final common pathway to death. The lung, when compromised from a variety of direct and secondary stressors, exhibits a pathophysiology that is uniform and classic. Pulmonary physiology is exquisitely sensitive to a systemic inflammatory state, and the respiratory system is generally the first system to demonstrate evidence that the patient is failing to meet the physiologic challenges of their injury.

Acute respiratory distress syndrome was described first by Ashbaugh [1] in the mid-1960s. Coincidently, trauma surgeons involved with the Vietnam conflict identified morbidity in their patients that they called “DaNang Lung.” The recognition of these syndromes was caused in part to improvements in non-pulmonary critical care, because the patients were able to survive hemorrhage, infection, and renal insufficiency to reach the point where ARDS could manifest fully.

The characteristics of ARDS include acute onset of severe hypoxemia accompanied by characteristic radiographic changes in the absence of cardiogenic pulmonary edema (Box 1). Several criteria have been used to standardize the definition of ARDS, but the most widely used is from the American–European Consensus Conference on ARDS of 1994 [2]. Although variations exist between the different classification systems, in general, there is agreement on which patients in fact have ARDS [3]. The advantage of the American–European consensus criteria is that these variables are based upon patients and their disease state as opposed to interventions of the intensive care specialist. Some classifications are contingent upon ventilator settings, and because these are affected by practitioner style, these classifications are less objective and consequently less helpful.

Because ARDS frequently is the first step in a more generalized cascade of decompensation, it is important to understand the pathophysiology and epidemi-
ology of ARDS. Perhaps the most important single aspect of managing a patient with ARDS is to identify the inciting event and treat that problem aggressively. Unless the underlying stressor can be managed effectively, whether it is a direct lung insult such as aspiration or contusion or some distant process such as missed injury, the patient will deteriorate progressively and die. This article’s aim is to provide an approach to the management of ARDS such that patients in this situation will survive the pulmonary compromise while the underlying issues are addressed.

**Etiology**

Acute respiratory distress syndrome is caused by either direct insult to the lung or a pulmonary response to a distant stressor. The primary local causes of ARDS

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**Box 1. Criteria for diagnosis of acute respiratory distress syndrome**
(from the American–European Consensus Conference)

- Acute onset
- Bilateral infiltrates on chest radiograph
- Pulmonary artery wedge pressure < 18 mm Hg
- PaO2:FiO2 ratio < 200 is ARDS
- PaO2:FiO2 ratio < 300 is Acute lung injury


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Fig. 1. Clinical onset of ARDS after initiating events. (*Reprinted from* Hudson LD, Milberg JA, Anardi D, Maunder RJ. Clinical risks for development of the acute respiratory distress syndrome. Am J Respir Crit Care Med 1995;151:293–301; with permission.)
injured patients are aspiration, inhalation, and pulmonary contusion. Indirect stressors such as sepsis, massive transfusion, ischemia/reperfusion, fat emboli, and missed injury also may generate the stress necessary to develop ARDS. In general, the classic radiographic findings and physiology of ARDS follow the inciting event in a fairly rapid fashion (Fig. 1). The recognition of progressive hypoxemia and the development of a diffuse infiltrate pattern on the chest radiograph should alert the clinician to the probability of some significant event within the preceding 24 to 48 hours. Historically, ARDS has carried a mortality of between 50% and 80%. Evolution in general critical care and pulmonary/respiratory critical care has reduced that rate gradually to the 25% to 35% range. Nevertheless, ARDS still represents one of the most lethal conditions encountered, with 50% of the survivors still on the ventilator in the ICU 3 weeks after onset and 50% still hospitalized for 6 weeks or more [4].

Pathophysiology

Acute respiratory distress syndrome is essentially a local inflammatory response of the capillary–alveolar membrane to systemic inflammatory up-regulation. It affects the endothelial layer of the circulatory system and the epithelial layers of the bronchoalveolar system. This is accompanied by failure of the hemostatic and immunologic barrier functions of the capillary–alveolar membrane and the gas exchange functions. The acute period is marked with an exudative phase, wherein the lung becomes populated with inflammatory cells and protein-rich fluids. The loss of integrity at the capillary alveolar membrane results in the flooding of the alveoli. This pathologic accumulation of protein rich, inflammatory fluid in the lung alveolar spaces and interstitial fluid leads to the characteristic heavy lung of ARDS. The decreased compliance, poor diffusion capabilities, and characteristic radiographic and pathologic appearance of the injured lung that is characteristic of other pulmonary edema states with the exception of ARDS are caused by a local insult and development of edema without an elevated intravascular volume or pressure. There is no cardiogenic component to ARDS, and, by definition, the diagnosis requires normal pulmonary arterial filling pressures in the presence of noncardiogenic pulmonary edema. This physiology will continue as long as the inflammatory state is up-regulated, and the underlying inflammatory source is present. If, however, the patient is treated in such a fashion that the underlying stressor is removed, and general principles of critical care are maintained, the lung will recover. Following this phase, there is a variable degree of fibroproliferative scarring of the lung as the patient recovers and the lung is repopulated with its normal cellular constitution.

The normal alveolar epithelium experiences changes in permeability and surfactant function related to type 2 alveolar cell loss. This leads to compromise of its barrier and gas exchange function. The capillary endothelium responds to cellular injury with platelet aggregation, the sequestration of polymorphonuclear (PMN) leukocytes, and compromise of the bacterial barrier. The neutrophils
themselves are sequestered in a reasonably unique fashion. They have periodic stops in transit through the pulmonary circulation that are not related to selectin mediation but do result in longer transit times than for the red cells. The PMNs become increasingly less deformable, and this stiffening facilitates the adhesion and migration across the capillary membrane.

With systemic inflammation, the neutrophils decrease in the systemic circulation [5], and their concentration is increased greatly in the pulmonary circulation (Fig. 2). These inflammatory cells release proteases, reactive oxygen metabolites, and amplify cytokines that generate the cascade that exacerbates the acute lung injury. In addition, neutrophil apoptosis is decreased significantly, thereby allowing the inflammatory state to continue to up-regulate in the injured and failing lung [6].

The cytokines that amplify and maintain the system of acute lung injury are produced by the PMN leukocytes, the monocytes, the interstitial structural cells, and the actual endothelium of the pulmonary circulation. Through the typical intermediaries of tumor necrosis factor-α (TNF-α), interleukin (IL)-1, IL-6, and IL-1β, activated neutrophils and alveolar macrophages are stimulated to release leukotrienes, toxic oxidants, platelet activating factor, and various proteases. These inflammatory compounds create an environment that injures the alveolus at the cellular level, leading to epithelial sloughing, necrosis of type 1 alveolar cells, and the denudation of the basement membrane. This results in the development of a state characterized by a hyaline membrane deposition and the

Fig. 2. Disappearance of PMNs from circulation in MOF/ARDS. (Reprinted from Botha AJ, Moore FA, Moore EE, Sauaia A, Banerjee A, Peterson VM. Early neutrophil sequestration after injury: a pathogenic mechanism for multiple organ failure. J Trauma 1995;39:411–7; with permission.)
accumulation of protein-rich edema fluid. In addition, extravascular third space lung water is increased greatly, and the lung, as a consequence, becomes wet, heavy, and relatively noncompliant.

For patients who survive the acute phase of respiratory distress and begin to heal from their underlying injuries and complications, the resolution of acute lung injury and ARDS has several predictable components. The alveolar epithelium is repopulated by differentiation of type 2 alveolar cells. The edema fluid in the recovering alveolus is transported along sodium channels in the apical and posterior/lateral aspects of the type 2 cells. Proteinaceous material in the hyaline membranes is cleared by alveolar cell endocytosis and diffusion between the alveolar epithelial cells. The actual remodeling of the alveolus is conducted by fibroplastic processes of interstitial granulation and fibrosis. Eventually, the proteinaceous exudate is cleared; the type 2 cellular matrix is re-established; the scarring and interstitial granulation are matured, remodeled, and somewhat resolved, and the bronchial epithelium is repopulated. Functional recovery continues for a number of months following resolution of the acute phase to near premorbid levels [7].

When a patient has suffered an acute lung injury or ARDS, they invariably require support in the form of mechanical ventilation. A thorough understanding of respiratory mechanics and the interaction between a compromised patient and the ventilator is essential for caring for patients with ARDS.

**Ventilator-induced lung injury**

The lungs of one man may bear, without injury, as great of force as those of another man can exert; which by the bellows cannot always be determined [8].

Mechanical ventilation provides positive pressure ventilation as opposed to the normal negative aspiratory force generated with spontaneous breathing. The lung is like any other variably compliant material. There is a sigmoidal compliance curve that has a central area of uniform elasticity sandwiched between areas of relatively poor compliance (Fig. 3). The point on the pressure:volume curve where the lung relaxes into a zone of easy and uniform inflation is called the lower inflection point and is related to the lung volume where most distensible alveoli have been recruited. After a zone of comfortable ventilation, the lung becomes more resistant to further distention. The point on the pressure:volume curve where this occurs is called the higher inflection point. It is the goal of the intensive care specialist to maintain the tidal volume between these two areas of transition on the pulmonary pressure:volume curve. If the tidal volume falls below the lower inflection point, atelectasis and loss of functional residual capacity occur. If the tidal volumes are such that the higher inflection point is surpassed, a spike of pressure at the end of each ventilation will occur, leading to lung injury through excessive volume and pressure. Because the lung is regionally heterogeneous, not all alveoli are in a similar state of distention. This creates the opportunity for overdistention of previously functional alveolar units if posi-
tive pressure is used in an attempt to recruit further functional residual capacity from the transition zones between aerated and atelectatic lung.

Barotrauma to the lung is apparent grossly, microscopically, and biochemically in patients who have been overventilated. The development of subcutaneous emphysema, spontaneous pneumothoraces, interstitial emphysema, and pneumomediastinum have been described following large tidal volume–high pressure ventilation. The concept that it was volume and not pressure that was responsible for ventilator-induced lung injury first was proposed by Dreyfuss [9] in 1988. He demonstrated that by limiting the volume of pulmonary distention, injury as measured by lung edema was reduced, regardless of imposed pressure. The specific cellular level physiology with the ventilator-induced volutrauma or barotrauma includes diffuse alveolar damage, increased microvascular permeability, increased fluid filtration, and consequently pulmonary edema. Both circumferential and longitudinal tension in the alveolar wall have been identified as responsible. By activating stress-related cation channels, there are increases in intracellular calcium that lead to a 3.7 times increased capillary filtration coefficient when compared with similarly treated lungs that have had these calcium channels chemically blocked. The phenomenon of atelectasis/recruitment in a repeated cycle also has been demonstrated to be related to increased lung injury. This repeated opening and closing of the microairways of the lungs is prevented best by setting the positive end expiratory pressure (PEEP) at a level above the lower inflection point of the pressure volume curve.

Muscedere [10] demonstrated that tidal volumes producing airway pressures below the lower inflection point lead to increased lung injury and loss of pulmonary compliance. Tremblay [11] demonstrated a biologic mechanism for ventilator-induced lung injury (Fig. 4). Tremblay’s group showed increased levels of
cytokines, including TNFα, IL-1β, IL-6, MIP-2, INFγ, and IL-10, in low PEEP ventilatory strategies when compared with low tidal volume moderate PEEP or moderate tidal volume high PEEP ventilatory modes. Ranieri [12] demonstrated that protective ventilation was associated with decreased concentrations of numerous cytokines in the bronchoalveolar lavages of damaged lungs.

The combination of biochemical injury and biophysical injury from mechanical ventilation creates a cycle of injury that amplifies the inflammatory state. The effects of inflammatory cells and mediators that have been activated in the lung—impaired oxygen delivery and increased bacteremia secondary to loss of barrier function—serve to amplify the inflammatory state that is associated with multiple system organ failure.

Treatment strategies for acute respiratory distress syndrome

Effective care of the patient with ARDS requires a multi-faceted approach. Although the pulmonary insufficiency demonstrated by these patients is compelling, successful outcome is unlikely without attention to numerous other factors. The primary components of treatment include: treatment of the inciting clinical disorder, fluid and hemodynamic management, management of infection, nutrition, and mechanical ventilation and supportive oxygen delivery.
Only by providing an integrative and aggressive posture in all of these areas can the intensive care specialist support the patient such that they can survive the days and weeks necessary to recover from ARDS.

Acute respiratory distress syndrome may be secondary to direct lung insult or to a systemic inflammatory response generated by a distant catastrophe. In the absence of known aspiration, inhalation, or pulmonary contusion, it is likely that a secondary source of stress is driving the inflammatory state that is manifesting as ARDS. It is important to seek and treat extrapulmonary sources of infection and consider acute pancreatitis, focal ischemia, and other intra-abdominal catastrophes. All nonviable tissue in wounds or areas of low flow needs to be debrided, and aggressive pulmonary toilet must be maintained to prevent secondary insult that will exacerbate the problem.

The basic controversy surrounding fluid management in pulmonary failure is related to the issue of oxygen delivery and cardiac preload that results from a relatively replete intravascular physiologic state versus a relatively dry state that is intended to reduce the amount of extravascular lung water. Because true ARDS is a noncardiogenic pulmonary edema that is related to injury of the capillary integrity and loss of fluid from the vascular space in the lung, excessive diuresis cannot preferentially pull water from the lung. Patients should be maintained in a euvoletic state, and diuresis should be reserved for excessive total body water situations. Part of the dilemma arises when intensive care specialists use excessive distending and end-expiratory pressures to increase oxygenation. This creates an impediment to venous return and the equivalent of tamponade physiology. This condition necessitates the use of high filling pressures and results in a critically ill patient who requires many liters in excess of an optimal and physiologic state of hydration to compensate for inappropriately high ventilator-induced intrathoracic pressures.

Humphrey demonstrated that treatments designed to reduce the pulmonary arterial pressure and overall total body water were associated with a reduced mortality in ARDS [13]. Others, however, have shown that, although one can decrease the number of days on the ventilator and in the ICU [14], there was no survival benefit. The basic goal of cardiopulmonary critical care is to provide adequate oxygen delivery to all distant tissue beds in the body. This is caused in part by the oxygenation of the blood and cardiac output and hemoglobin concentration. The basic principles of this approach are to resuscitate a patient to normal hemodynamics; limit the intrathoracic pressure, facilitating venous return and cardiac output; limit oxygen consumption with sedation, analgesia, and thermoregulation, and use fluids as necessary for volume and packed red blood cells for increased oxygen carrying capacity.

Both pulmonary and extrapulmonary infections are common in patients with ARDS. This may be the initiating event that is driving the inflammatory state or may be caused by the decreased resistance of the critically ill ventilated patient to infection in general and pneumonia in particular. Nosocomial pneumonia, while infrequently a cause of ARDS, often is associated with the syndrome. Aggressive immune surveillance using bronchoalveolar lavage and endoscopically directed
protected specimen brushing has demonstrated an overall 15% incidence of pneumonia in ARDS patients [15], and in those with clinical characteristics of pneumonia there is a 55% incidence. Fagon has shown that the overall mortality in ARDS may be reduced by the aggressive use of bronchoscopic-directed protected brushing for immune surveillance in treatment of suspected ventilator-associated pneumonia [16].

It is essential to provide adequate nutrition to the critically ill patient. A patient with ARDS generally will require full protein and calorie nutrition, and it is the standard of care to provide this early in the hospital stay, preferably by the enteric route [17]. The immunomodulating effect of TPN and the risk of catheter-associated sepsis and the reduction of bacterial translocation from the gut seem to favor an enteric route [18,19]. Finally, many patients with ARDS have multiple organ failure, including acute renal insufficiency. Full protein/calorie nutrition should be provided to patients in this condition without regard to the nitrogenous loads that are obligatory with such management. Although patients who require dialysis are by nature more critically ill than those who do not, it is better that patients have full nutrition and, if necessary, dialysis than to have nutrition withheld.

**Ventilator management**

There are many approaches to the ventilation of the critically ill patient. The literature is replete with descriptions, comparisons, and prospective studies that fail to demonstrate improvement of survival. Survival as an outcome measure for a patient with ARDS is frequently the result of a complex interplay of many variables and serves as a poor measure of the effectiveness of any particular modality. Because the situations are diverse and complex, much information can be gleaned from reviewing simple physiologic studies related to oxygenation and local pathophysiology in the lung. Nevertheless, the most important patient-centered outcome remains survival to hospital discharge. The only strategies of ventilation that have been shown to reduce mortality are related to volume-limited or open lung approaches [20,21].

The principle of protective ventilation is to ventilate the patient on the steep and homogenous portion of the pressure volume curve. This requires that the level of PEEP be set above the lower inflection point and that a tidal volume and pressure limitation be used such that a full distention the lung never reaches the higher inflection point. In general, this is between 6 and 8 cc of tidal volume per kilogram of body weight [22]. The effect of this approach is to limit the amount of atelectatic collapse and recruitment and prevent shunt through unaerated portions of the lung. The open lung ventilation strategy of Amato was based on the same principles of recruitment and prevention of over distension. The goal was to use a tidal volume of smaller than 6 cc/kg with a driving pressure of less than 20 cm of water and a plateau pressure of less than 40 cm of water. The PEEP was preset at 2 cm above the lower inflection point or at 16 cm of water, and
recruitment maneuvers were used with 40 seconds of 35 to 40 cm of pressure. All patients received similar standards of aggressive critical care to include pulmonary arterial catheterization, protocolized sedation, and the use of gastrointestinal (GI) prophylaxis. The study was terminated after enrollment of the 53rd patient with a demonstration of a survival benefit of 62% in the treatment group versus 29% in the control group.

The Acute Respiratory Distress Syndrome Network conducted a randomized prospective multi-institutional trial that demonstrated similar conclusions. Holding all other variables equal, to include the linking of various levels of inspired oxygen with PEEP, the two groups varied only in the amount of tidal volume and plateau pressures used for ventilation. The traditional tidal volume group received a 12 mL/kg breath with plateau pressures of less than 50 mL of water, while the treatment group received 6 cc/kg tidal volume and plateau pressures of less than 30 mL of water. The treatment group had significantly decreased mortality (31% versus 39.8%), earlier liberation from the ventilator at 28 days (65.7% versus 55%), and a significantly decreased number of nonpulmonary organ failures. All other aspects of mechanical ventilation of the patient with ARDS remain controversial.

Although it is apparent that limiting both pressure and tidal volume are important, it is less clear how best to address issues of recruitment, prevention of atelectasis, pulmonary toilet, and reduction of shunt. In general, as the shunt fraction increases, clinicians tend to use more inspired oxygen and higher levels of PEEP [23]. With current understanding of ventilator-induced lung injury, it is readily apparent that the optimal settings on the ventilator are those that provide adequate oxygen delivery with the lowest levels of inspired oxygen, tidal volume, plateau pressure, and PEEP. To accomplish this, it is intuitive to use means other than direct positive pressure for alveolar recruitment. These means including pulmonary toilet and positioning to allow for full distention and recruitment of the lung.

Fig. 5 demonstrates one approach to determining the optimal level of PEEP [24]. The goal of this approach is to optimize oxygen delivery by integrating and optimizing the effect of PEEP on oxygen saturation and cardiac output. As the PEEP is increased, the arterial saturation of the blood will continue to increase in a fairly linear fashion. At some point, however, the amount of intrathoracic pressure will begin to compromise venous return and cardiac output, and consequently oxygen delivery, will decrease. There is, in any particular individual at any particular time, a point at which increasing the PEEP can be demonstrated to have diminishing returns measured by saturation of the mixed venous blood of the pulmonary artery. Because SvO2% represents oxygen saturation of blood returning from the periphery, the clinician can determine the effect of interventions with regard to oxygen delivery and consumption rapidly. The clinical goal of a SvO2 between 70% and 80% correlates well with the physiologic characteristics of hemoglobin dissociation. With all other things being equal, if a best PEEP curve is conducted over a reasonably short period of time, the optimal PEEP can be determined in a protocolized and reproducible fashion. The specifics of the
process are: the approximate lower inflection point of the pressure volume curve is estimated, and the PEEP incrementally is increased above this level with titration for optimization of the SvO2 with the SvO2 preservation or enhancement of the static compliance. The best PEEP is defined at the level of PEEP that provides the highest SvO2 without compromising compliance.

Recruitment maneuvers use extrinsically applied and sustained pressures to open the lung, prevent atelectasis, optimize functional residual capacity, and reduce shunt. There are various methods described, all with utility. Pelosi recommends three consecutive sighs at 45 cm of water [25]. Grasso is a proponent of 40 cm of water held for 40 seconds [26], and Patroniti has advocated a continuous positive airway pressure (CPAP) 20% higher than the peak pressure for 3 to 5 seconds each minute [27]. Although all of these measures have been shown to increase oxygenation and improve compliance, none have been shown to affect overall mortality in patients with ARDS.

These approaches are unlikely to have much effect in a patient who has been kept supine and immobilized with lungs damaged by an acute or subacute inflammatory process. This is because there is no possible way that extrinsically applied pressure can open the densely atelectatic and dependent portions of the
lung. The West zones of the lung adapt to a patient in the supine position. Zone 2 of the lung is the area where there is good V/Q matching. It is the goal of the intensive care specialist to increase the percentage of the lung that is in zone 2, decreasing shunt fraction and hypoxemia. A logical and clinically applicable way to do this is with the use of intermittent prone positioning. By placing the patient in a prone position, the aerated and heavy atelectatic portions of the lung are reversed, and gravity is used to open up areas of previous shunt [28]. The use of prone positioning is somewhat controversial, in part because of technical difficulties with the maneuver and in part because of misinterpretation of the literature. Gattinoni and the Prone Supine Study Group [29] failed to demonstrate an overall survival benefit of prone positioning in a multi-institutional prospective trial. The study did not evaluate ARDS in trauma patients primarily, however, nor did it use a particularly aggressive protocol for intermittent prone positioning. It is interesting, however, that in a posthoc analysis, those patients with the most severe morbidity and physiology did show survival benefit with intermittent prone positioning. The conclusion that prone positioning is of limited utility is premature, particularly with young acutely injured patients or those who have ARDS from sepsis. The application of an early, aggressive, and protocol-driven method for positional therapy in selected patients does yield significant improvements in oxygen index and survival.

A protocolized approach to the treatment of acute respiratory distress syndrome

The Trauma Unit of Legacy Emanuel Hospital has developed and instituted a protocol for managing patients with ARDS [30]. If standard measures fail to improve the PF ratio (paO2/FiO2) to greater than 200, the Pulmonary Failure Protocol is instituted. This protocol is an algorithm designed to optimize oxygen delivery relative to consumption (DO2:VO2) while limiting inspired oxygen (FiO2). This is accomplished by treating the three determinants of delivery: oxygenation, cardiac output, and oxygen-carrying capacity, while minimizing excessive oxygen consumption and limiting ventilator-induced lung injury. At all times, FiO2 is titrated to provide an O2 saturation of greater than 93%.

The first step in the protocol is the placement of an oximetric PA catheter (Opticath, Abbott Laboratories, North Chicago, Illinois) to guide fluid and cardiac therapy. The management goal is to provide for a DO2:VO2 ratio of roughly 4:1 as indicated by an SvO2 of 70% to 75%. This endpoint is used to direct overall management, because it responds rapidly to interventions and is related to a physiological state of oxygen delivery that is sufficient to meet oxygen demand.

The second protocol step is to optimize the level of PEEP provided by the ventilator. The optimal PEEP is defined as the level of PEEP that is associated with the highest SvO2 while maintaining or enhancing the static compliance and the abdominal compartment or intracranial pressures as clinically indicated. In collaboration with the physicians, the respiratory therapists at the bedside ac-
complish this by following a best PEEP protocol designed to select a level of PEEP that optimizes oxygen delivery. The pressure:volume characteristics of the patient and circuit are evaluated with a graphics attachment to the ventilator (Servo 390, Siemens, Elma, Sweden), and the approximate lower inflection point of the pressure:volume (PV) curve is estimated \([9,24]\). The PEEP is increased incrementally above this level, with titration for optimization of the \(\text{SvO}_2\) and preservation or enhancement of the static compliance \((\text{Cs}, \text{measured with two second-end aspiratory and expiratory pauses: } \text{Cs} = \frac{\text{P}_\text{plateau} - \text{PEEP}}{\text{TV}_{\text{uncorrected}}} )\).

The author considers the best PEEP as the level of PEEP that provides the highest \(\text{SvO}_2\) without compromising compliance. A flowchart of this procedure is created for each best PEEP trial, and the level of PEEP to be used is determined from the data. The patient is “best PEEPed” during each nursing shift, following each positional change, and with major clinical changes in the patient’s condition. The \(\text{SvO}_2\), used as an indirect measurement of oxygen delivery, provides almost instantaneous feedback concerning therapeutic changes. These trended data allow physicians to avoid the use of PEEP levels that improve the \(\text{SaO}_2, \text{PaO}_2, \text{and P:F ratio but impair venous return, cardiac output, and, ultimately, oxygen delivery.}

The third step is to optimize cardiac performance with a goal cardiac index of greater than 2.5 l/min/m\(^2\). The PA catheter is used to monitor volume status. Infusions and diuresis or renal replacement therapies are employed to maintain the pulmonary capillary wedge pressure between 13 and 18 mm Hg. As the volume status is being managed, selected inotropes are employed to increase contractility and reduce systemic and pulmonary vascular resistance to normal or low normal levels. The wedge pressure is reassessed continuously as cardiac function, systemic resistance and capacitance, body position, and PEEP affect this measure. The actual wedge pressure is determined by briefly removing the patient from the ventilator and allowing the airway pressures to dissipate before measurement.

Patients are sedated to prevent resistance to mechanical ventilation and to decrease oxygen consumption \((\text{VO}_2)\) when necessary. In general, opiate and benzodiazepine infusions are sufficient, although neuromuscular blockade is required occasionally. Paralytic agents are used in continuous infusion and are titrated to maintain two twitches in a chain of four impulses delivered by a neuromuscular stimulator placed over the facial or median nerve.

After each major therapeutic maneuver, the patient is re-evaluated, and attempts are made to wean the \(\text{FiO}_2\) to attain an \(\text{FiO}_2\) of less than or equal to 50% while maintaining an \(\text{SvO}_2\) of greater than 70% with a \(\text{SaO}_2\) of greater than 90%. The patient’s oxygen carrying capacity is maintained at a hematocrit of 35% with the judicious use of packed red blood cell transfusions. Liberal weaning criteria are permitted, and relative hypercapnia \((\text{pCO}_2 44 – 60)\) is tolerated. Patients who cannot be weaned to an \(\text{FiO}_2\) of 50% and in whom the PF ratio remains below 200, have intermittent prone positioning (IPP) instituted.

The procedures for IPP are standardized by protocol. Eligible patients are proned for 6 hours and returned to supine for 6 hours. The schedule is designed to balance nursing workload, patient safety, and the observation that dependent atelectasis occurs in the prone position also. The protocol at the author’s institution
is designed to gradually decrease the marginal zones of atelectasis and recruit the marginal areas for ventilation. This schedule is maintained until the P:F ratio is greater than 250 in the supine position; the patient is on a FiO₂ of less than 50%, and the PEEP is stable. Occasionally, patients oxygenate much better in the prone position and are managed with a regimen of prone for 8 hours and supine for 4 hours.

If a patient cannot be managed with these methods, then heparin-bonded extracorporeal membrane oxygenation (ECMO) is considered. Patients on ECMO are turned every 8 hours secondary to the added risks of accidental dislodgement and kinking of the cannulas. After ECMO is discontinued, the patient is treated with the standard 6-hour schedule of IPP. For any trip from the ICU (ie, to the operating room, CT scanner, invasive radiology), the patient is maintained on the Servo ventilator with previously determined settings.

Details of the author’s methodology for IPP have been reported previously [34]. Using the techniques described, the author been able to use IPP safely and effectively for patients with open abdomens, recent sternotomy or thoracotomies, intracranial monitors, removed cranial bone flaps, high flow cannulas, including ECMO and continuous venous hemofiltration (CVVH) lines, external fixators, unstable fractures, incomplete spine clearance, known thoracic, lumbar and cervical spine fractures, and patients on balloon pumps. With a prompt and consistent application of this protocol the author has been able to manage virtually all patients with ventilator settings considered to be within the safe range. Thus far, the only patients not treatable with IPP have been those with bilateral fronto–temporal craniectomy flaps removed. Within 24 hours, the author has been able to reduce all patients to a tidal volume of less than 8 mL/kg, peak airway pressures of less than 35 cm of water, inspired oxygen of less than 50%, and PEEP less than 16. For patients suffering from ARDS following trauma, the author has experienced an 86% survival rate, and although some patients have died with ARDS, none have died from hypoxemia.

The author also aggressively uses extracorporeal membrane oxygenation when necessary. This therapy has been applied to all patients who fail to oxygenate despite implementation of the protocol. With this aggressive approach, the author has been able to further prevent ventilator-induced lung injury and support the most critically compromised patients while they stabilize and recover. The logic of ECMO for severe pulmonary failure is that borderline patients may be salvaged if their lungs are allowed to rest and heal rather than endure the extreme levels of ventilator support necessary to oxygenate and ventilate them. In the population of injured patients, ECMO has been used primarily for acute cardiac support, rewarming, and oxygenation during resuscitation [23–25], and for the management of acute and severe respiratory failure.

Poor pre-ECMO DO₂/VO₂ (low SvO₂) and hemodynamic instability requiring veno-arterial perfusion were associated with mortality, as was acute renal failure. These correlations indicate once again that shock and poor tissue perfusion lead to multiple organ failure and death. Respiratory failure without shock, or when shock has been prevented by resuscitation, is more often reversible. Even
when perfusion and oxygen delivery are maintained by prolonged veno-arterial bypass, organs that have been damaged irreversibly by ischemia may not recover. These observations explain the importance of prompt and complete resuscitation criteria, and the early use of ECMO if it is to be used as a resuscitative measure. This is also true when ECMO is used for respiratory failure, and the author has shown the independent association of early ECMO use with survival [31]. Overall, the author has experienced greater than 50% survival with patients treated with ECMO who are completely refractory to all other maneuvers [31].

Outcome after acute respiratory distress syndrome

Increasingly, interest has been directed toward assessing the long-term consequences of critical illness, and particularly ARDS. Several studies have looked specifically at components of recovery with a goal of describing the outcome after ARDS. Ultimate survival is contingent on three primary factors: underlying etiology, comorbidities, and modes of therapy. It appears that sepsis is a more lethal etiology than others and that extrapulmonary organ dysfunction, in particular chronic liver disease, is associated with poor outcome. In addition, failure to respond to treatment as measured both physiologically and with the persistence of PMNs in the bronchoalveolar lavage load is associated with increased mortality.

Pulmonary function returns to near normal by 6 months, with the exception that carbon monoxide diffusion capacity remains low for as long as 12 months following hospitalization [32]. Integrated studies have been done by several investigators. Davidson et al demonstrated that the quality of life as measured by the SF-36 (Medical Outcomes Study Short Form 36) was compromised significantly in the physical function, general health, and mental health domains for patients with ARDS compared with matched controls [33]. Herridge et al have presented an excellent study with 3, 6, and 12-month follow-up of 100 ARDS survivors [34]. The study included physical examination, pulmonary function testing, a walk test, and a quality-of-life evaluation. They demonstrated that although lung function essentially had returned to baseline, patients were plagued with muscle weakness and fatigue, and for many, these limitations continued for the 1-year study period. Approximately 50% of the patients had returned to work, and those who had not returned to work reported limitations primarily related to physical function, fatigue, and weakness. The distance patients were able to walk was shorter than predicted and inversely related to the severity of the ARDS by the lung injury score and by use of steroids during the ICU stay. At 12 months following hospitalization, all domains of the SF-36 (except role emotional) were below those of an age- and gender-matched control population. The role physical and physical functioning domains improved dramatically during the year; however the effect of hospitalization continued to manifest in mental, general, and physical health domains. Overall, although only 6% of the patients had persistent pulmonary morbidity, the survivors as a group were limited functionally primarily
because of muscle strength and wasting. Additionally, they had not returned to baseline physically, emotionally, or occupationally.

References


