Management of acute respiratory distress syndrome

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Background: Managing patients with acute respiratory distress syndrome (ARDS) still remains a challenge to the intensivists despite huge accumulation of basic and clinical data and better understanding in its management. The evolution of the concept of ventilator associated lung injury (VALI) in mechanically ventilated patients with ARDS has changed the approach to ventilatory management. Survival of the patients with ARDS may be improved by modifying the mechanical ventilation such that VALI is kept to a minimum. Protective strategy in mechanical ventilation with limited volume and pressure is the only accepted treatment or supportive measure shown to affect the outcome in ARDS patients. Low tidal volume ventilation has been recommended for every patient with ARDS to be used routinely. Protective ventilatory strategy has been accepted as a new gold standard and is being used to evaluate and compare other techniques and modalities. Use of approaches such as prone position ventilation, inhaled nitric oxide and surfactant has failed to improve survival in clinical studies. But these approaches may confer benefits if used in conjunction with the protective strategy.

Key words: Acute respiratory distress syndrome (ARDS); Protective ventilatory strategy; Ventilator associated lung injury (VALI)

Introduction
The reported prevalence of acute respiratory distress syndrome (ARDS) is high in the order of 5-10% of all ICU admissions. 1 It is associated with mortality as high as up to 74%. 2 Managing patients with ARDS still remains as an extreme challenge to the intensivists despite huge accumulation of basic and clinical data and better understanding in its management. Mechanical ventilation is indispensable in support of the patients with ARDS in respiratory failure. The approach to selecting tidal volume, positive end expiratory pressure (PEEP) and ventilatory modes are changing with reported improved pulmonary functions and survivals. There are further additions to the pharmacological therapies to offer improvement in the management of ARDS. Recently, the interest of the researchers has been focused on the study of damage to the lungs due to application of pressure, positive or negative, known as ventilator associated lung injury (VALI) or ventilator induced lung injury (VILI). By modifying mechanical ventilation such that VALI is kept to a minimum may improve survival of patients with ARDS.

In this article, attempt has been made to include definition of ARDS, brief pathophysiology of ARDS, VALI, ventilatory and clinical strategies, alternative and adjunctive modalities and therapies and the general approach to the management of ARDS patients.

Definition
The American-European Consensus Conference defined acute respiratory distress syndrome (ARDS) as “a condition or conditions resulting in impaired gas exchange with ratio of arterial partial pressure to fraction of inspired oxygen (PaO₂/FIO₂) less than 200, regardless of the level of the PEEP; bilateral lung infiltrates on the chest radiograph; and a pulmonary capillary wedge pressure PCWP less than 18mmHg or if not directly measured, the clinical absence of
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Elevated left atrial pressure”. This definition is comprehensive and covers ARDS patients in wide variety of setting. The criteria of diagnosing ARDS include: i) insult to the lung from epithelial (e.g. aspiration) or endothelial (e.g. sepsis) side, ii) bedside finding of tachypnoea, dyspnoea, crackles, iii) diminished lung compliance (<40ml/cmH\(_2\)O), iv) impaired gas exchange (PaO\(_2\)/FIO\(_2\) <200), v) diffuse (three or four quadrants) airspace filling on the chest radiograph and vi) exclusion of high-pressure pulmonary oedema (e.g. PCWP <18mmHg, echocardiographic examination).

Acute respiratory distress syndrome (ARDS) is a syndrome, not a disease and can have several causes fulfilling the above criteria. The syndrome may be the manifestation of several pathophysiologic pathways. The cause for ARDS due to acid aspiration could be direct chemical injury whereas ARDS associated with sepsis and pancreatitis is probably due to systemic inflammation. The details of the pathways remain poorly understood.

Diagnosing the existence of ARDS does not mean diagnosing patient’s underlying problem. While the patient is being given the supportive management, diagnostic and therapeutic interventions must go side by side. Appropriate supportive therapy may transiently make the patient stable but if for example, the underlying source of sepsis in the abdomen is not recognized with appropriate tests (e.g. CT scan), the patient will definitely succumb.

Lung Injury Score (LIS), developed by Murray and colleagues in 1988, based on chest x-ray, hypoxaemia (PaO\(_2\)/FIO\(_2\)) score, lung compliance and PEEP, is the most widely accepted scoring system although several systems have been developed to compare the severity of ARDS in various studies and settings.

An exhaustive list can be prepared to enumerate the causes of ARDS, but by far the most common causes encountered in ICU are pneumonia and gastric acid aspiration through direct injury and sepsis and trauma through indirect injury. The mortality in ARDS is more related to the causes of ARDS than to the lung injury itself. ARDS associated with sepsis has higher mortality as compared to that associated with air embolism.

Pathophysiology

Prevailing knowledge supports that acute lung injury (ALI) and ARDS are the spectrums of the same pathophysiologic processes and will be used as synonyms in this article. It is well known that ARDS results from a pulmonary capillary leak that causes flooding of the lung interstitium and alveolar space with protein rich fluid despite normal pulmonary intravascular pressure, regardless of cause. Obviously this flooding diminishes the lung compliance, which can be evidenced by increased pressure in the monitor. This results in substantial fraction of mixed venous blood passing through the non-ventilated airspaces resulting into right to left intrapulmonary shunt that is relatively refractory to oxygen therapy.

The early phase of ARDS is characterized by the capillary leak or also called non-cardiogenic pulmonary oedema. Pathologically there is diffuse alveolar damage (DAD), that leads to progressive lung inflammation and cellular injury. The early phase of DAD is also called exudative due to the predominance of pulmonary oedema and its consequences. This condition may resolve or progress to diffuse lung fibrosis.

The tracheal fluid at the onset of ARDS has high protein content (70-90% of serum level) in contrast to cardiogenic pulmonary oedema and can have diagnostic value early in the course of oedemagenesis but not later.

The chest x-ray finding in ARDS is described as diffuse lung infiltrates. Marked inhomogeneity of alveolar flooding is evidenced in CT scan. This suggests that the application of large tidal volumes and PEEP may result in over distension of relatively spared lung regions before recruitment of flooded alveoli thus demanding the newer protective strategy to be discussed later.

Hyaline membrane formation in the alveolar space becomes prominent over the days following acute lung injury due to precipitation of serum proteins. Increase in the number of inflammatory cells in the interstitium and necrosis of the type I pneumocytes may occur. Abnormal collagen deposits may follow this by 7-10 days. This phase is also known as proliferative phase of ARDS. The ventilated patients show evidence of large dead space and requirement of large minute ventilation and pulmonary hypertension. There is overall restriction of the lung mechanics. The time course of recovery from proliferative phase may be relatively variable with some patients making a nearly complete recovery in a relatively brief period of time and other showing protracted lung derangements taking many months.

Ventilator Strategies

Ventilator Associated Lung Injury (VALI) and Evolution of Protective Strategy

In 1985, Dreyfuss and co-workers could reproduce the experiments, reported earlier by Webb and Tierney, demonstrating that mechanical ventilation using large tidal volumes and high inflation pressures could cause a fatal lung injury in rats with otherwise normal lungs. They hypothesized that mechanical ventilation with large tidal
volume or high inflation pressure might exacerbate or perpetuate the lung injury in patients suffering from ARDS. This raised two important questions: Did the high inflation pressure or large tidal volume excursions cause the lung injury? Did PEEP attenuate or worsen the injury? Further investigations by Dreyfuss and colleagues\(^\text{16}\) in animals (rats) showed that large tidal volumes were associated with lung injury, but the high inflation pressure in the absence of large tidal volume was not. They were surprised to observe that PEEP had the effect of limiting the injury that occurred in animals ventilated with large tidal volumes and high pressures. The results have been verified in larger animals also. Corbridge and co-workers\(^\text{17}\) in a canine model of oleic acid injury showed that mechanical ventilation with large tidal volume and low PEEP was associated with a worsening of intrapulmonary shunt compared with ventilation with high PEEP and small tidal volumes. This was the first observation that the pattern of ventilation used had an effect on the evolution of acute lung injury.

Other studies\(^\text{18}\) have also supported the idea that PEEP level that maintains lung inflation above a lower inflection point (LIP) on the static pressure-volume curve of the lung results in less lung injury than a PEEP and tidal volume setting that causes the lung to be deflated and inflated repeatedly across the LIP. This is attributed to the larger shear force due to opening and closing during the respiratory cycle. Maintaining tidal inflation above the LIP with PEEP set above the LIP has been termed the "open lung" approach and has been evaluated extensively. However, production of static pressure-volume curve for patients with ARDS is technically difficult, does not always provide clear inflection points, and is of unproven benefits.\(^\text{19}\)

Many clinical studies\(^\text{20, 21, 22, 23}\) have been conducted comparing the outcome of ventilation with small tidal volumes (5-7ml/kg), lower target pressure (peak and plateau-35cmH\(_2\)O) also called protective strategy with that of ventilation with conventional strategy with higher tidal volume and target pressure (peak and plateau). Whether the conventional groups were ventilated in accordance with best practice in the trials is debatable since prescribed limits were exceeded. One of the studies (ARDS Network Study) with 861 patients showed benefit from the protective strategy.\(^\text{23}\) This study perhaps more convincingly shows the negative effect of high tidal volumes and pressures on outcome. This study established the need to limit tidal volume and inflation pressure in ARDS patients. The death rates of patients ventilated with high and conventional (low) PEEP did not differ significantly and optimum PEEP in patients with ARDS could not be defined. We still cannot define the best pressure or the physiological criteria by which PEEP should be adjusted.\(^\text{24}\)

Results of clinical studies\(^\text{25, 26, 27}\) have suggested that mechanical stress is important in determining the outcome of the patients with ARDS. Mechanical ventilation continues to damage the injured lungs despite adopting strategy to maintain low tidal volume. The ventilator associated lung injury (VALI) can have many components\(^\text{28}\) viz. a) volutrauma- damage caused by over distension, b) atelectotrauma- injury associated with repeated recruitment and collapse, theoretically prevented by using PEEP above LIP, c) biotrauma- pulmonary and systemic inflammation caused by the release of mediators from lungs subjected to injurious mechanical ventilation, d) oxygen toxic effects-damage caused by high concentration of inspired oxygen and e) barotraumas-high pressure induced lung damage.

When protective strategy termed ‘open lung approach’ is followed, PEEP is set 2cmH\(_2\)O above the LIP. If LIP cannot be determined then a PEEP of 16cmH\(_2\)O is used. The driving pressure, defined as plateau pressure minus PEEP is kept below 20cmH\(_2\)O, peak pressure restricted to 40cmH\(_2\)O and the respiratory rate kept below 30 breaths per minute. When the patient is disconnected from the ventilator, a recruitment manoeuvre (RM) with use of continuous positive airway pressure (CPAP) of 35cmH\(_2\)O is applied for 40 seconds before re-instituting the previous PEEP.\(^\text{29}\) Recruitment manoeuvres are the processes of periodically briefly raising the transpulmonary pressure to higher level than are achieved during tidal ventilation. Clinical investigators have reported that the possible derecuitment due to reduction in tidal volume while using protective strategy can also be prevented and oxygenation improved by using recruitment manoeuvres.\(^\text{29, 30}\) A recent clinical study\(^\text{31}\) to evaluate the effects of RMs in patients with acute lung injury ventilated with high PEEP has shown that the duration of RM induced recruitment is brief. Greater and more sustained effects are likely with higher RM pressure and with improved RM techniques and effects of RM may be greater in patients in whom there is greater potential for recruitment. Role of RM has been described in children also.\(^\text{32}\)

**Permissive Hypercapnia**

In a retrospective review, Hickling and colleagues\(^\text{33}\) in 1990, reported their experience using low tidal volume pressure limited ventilation (peak inflation pressure not greater than 45cmH\(_2\)O, ideally less than 30cmH\(_2\)O) and permissive hypercapnia (tolerance of PaCO\(_\text{2}\) elevation of 20-30 mmHg or even more and the associated acidosis, as long as the goal of the airway pressure is achieved). It was followed by a prospective descriptive study using the same ventilatory strategy and published the report in 1994.\(^\text{34}\) They excluded the patients with contraindications to hypercapnia and observed that the use of permissive hypercapnia was
associated with far better survival than predicted by APACHE-II score. Similar reports have been published others but the most compelling of all is by Amato and colleagues who using the ‘open lung’ approach (VT <6ml/kg, PC-IRV mode, PEEP <2cmH₂O, PEEP 2cmH₂O above the LIP) and permissive hypercapnia demonstrated more rapid recovery of pulmonary compliance, decreased requirements of high FIO₂, high rate of liberation from ventilator and decreased death associated with respiratory failure. But there are a number of controversial points to be considered in the study. Small sample size, sepsis not as causes of ARDS in both treatment and control arms (mostly leptospirosis and pneumonia), multiple differences between the two groups (PEEP strategy, CO₂ levels, ventilatory modes, minute ventilation) are the issues of concern. In spite of these questions, this study must be considered an important investigation in the ventilatory management of patients with ARDS.

Permissive hypercapnia can be incorporated in the alternative approach to use of open lung PEEP also known as ‘least PEEP strategy’ for the management of patients with ARDS. In this approach, the least PEEP required to maintain haemoglobin saturation of 90% on non-toxic FIO₂ (60-70%). There is less likelihood of alveolar overdistension at any given tidal volume. Since the PEEP is much below LIP, there is chance of lung damage by shear forces of recruitment and collapses.

There may be deleterious effects of permissive hypercapnia, although PaCO₂ as high as 250mmHg (pH as low as 6.72) has been reported to be well tolerated in volunteers. Bronchial asthma patients also frequently have PaCO₂ higher than 100mmHg without showing significant systemic effects. But what happens in the patients with underlying metabolic acidosis by superimposing with respiratory acidosis is not known but can be anticipated to be significantly deleterious.

To avoid unwanted high level of PaCO₂ two simple methods have been advocated. The first one is to reduce circuit dead space, and one may prefer for this reason using a heated humidifier instead of a heat and moisture exchanger, which can add almost 100ml of dead space to ventilator circuit. The other simple feature consists in increasing respiratory frequency above the conventional settings of 12-20/min. This may be achieved by a high respiratory peak flow and no end-inspiratory pause to optimize the inspiratory to expiratory time ratio as used in ARDS Network trial.

Permissive hypercapnia should not be attempted in patients with definite contraindications to its use i.e. elevated intracranial pressure (e.g. cerebral oedema or severe head injury), seizures, pulmonary hypertension and cardiovascular deterioration associated with permissive hypercapnia.

**Alternative and Adjunctive Protective Strategies**

**Prone Position Ventilation**

Prone position oxygenation in ARDS patients is not a new but accepted modality. It has been shown to have improved oxygenation but without survival benefit. However, it remains as underutilized modality mainly due to difficulty of providing nursing and other care. Different hypotheses have been proposed to explain the improvement in oxygenation including increased FRC (functional residual capacity), change in the regional diaphragm motion, better clearance of secretion, and redistribution of perfusion. Another possible reason for the improvement in oxygenation could be improved lymphatic drainage in prone position. Specially designed ICU beds may be used for ventilating the patient in prone position. Being effective and safe, prone position ventilation should be attempted in patients with severe ARDS more commonly.

**Airway Pressure Release Ventilation (APRV)**

APRV has been shown to provide higher mean airway pressure still allowing spontaneous breathing thereby providing better gas exchange and haemodynamics with less need of sedation.

**Inverse Ratio Ventilation (IRV)**

When inspiration to expiration ratio (I: E) is made more than one in either volume cycled or pressure cycled ventilation, it is called inverse-ratio ventilation (IRV). IRV has been found to improve oxygenation in a small subset of patients refractory to conventional ventilation. But there is no way to prospectively identify the patients likely to respond to IRV. The mechanism believed to improve oxygenation in IRV is that it causes alveolar recruitment at lower airway pressure and more optimal distribution of ventilation but the role of volume-controlled IRV remains poorly defined and used only as the last resort in hypoxia refractory to conventional modes of ventilation.

**High Frequency Ventilation (HFV)**

It can be considered logical that ventilation with very small tidal volume at higher frequencies should be associated with less VALI and better outcome if excessive lung excursion is associated with damage of the injured lung in ARDS patients. The tidal volumes and ventilatory rates can be variable in high frequency ventilation. Gas exchange is
poorly understood in high frequency ventilation but it is believed that it occurs through augmented axial diffusion and through bulk flow.\(^{59,60}\) Unfortunately, multiple trials of HFV have failed to demonstrate benefit over mechanical ventilation.\(^{51, 52, 53, 54}\)

**Extra corporeal Membrane Oxygenation (ECMO)/ Intra venous Oxygenation (IVOX)**

Theoretically, oxygenation by ECMO and allowing the lung to rest can be attractive strategy for patients with lung injury. This, however, is not supported by recent outcome study.\(^{35}\) Use of intravenous oxygenation (IVOX) has been reported in ARDS patients.\(^{66}\) In this technique, small membrane lung is actually inserted into the vena cava. This, however, is capable of only limited gas exchange and hence of limited usefulness. ECMO/ IVOX remain only as last resorts in hypoxia refractory to conventional ventilation.

**Liquid Ventilation**

Breathing through liquid medium can be expected to be advantageous when the surface tension at the air-liquid interface of lungs is increased, as it occurs in acute lung injury. When special liquid medium (capable of dissolving large amount of respiratory gases) is used for ventilating the lungs it can offset the collapsing force, decrease the alveolar surface tension with exogenous surfactant and eliminate air-liquid interface by filling the lung with a fluid. The only group of liquids that has the capacity to dissolve respiratory gases and is devoid of significant toxic effects is per fluorocarbons (PFC). PFC passively dissolves oxygen and other respiratory gases. Oxygen solubility is inversely proportional to the number of fluorine atoms present.\(^{57}\) The first use of liquid ventilation with PFC in human was in babies and was described by Greenspan and colleagues\(^{58}\) in 1989. Hirschl and co-workers\(^{59}\) first reported partial liquid ventilation (PLV) in a mixed group of adult, paediatric and neonatal patients in uncontrolled single centre study and concluded that it can be safely used in patients with severe respiratory failure and may improve lung function. Potential benefits of PLV described are improvement in oxygenation, producing liquid PEEP, improvement in lung mechanics and reduction in inflammation. The described problems encountered include pneumothorax, ET tube blocking and uncertain long-term effect.\(^{60}\)

Although liquid ventilation has been shown to be safe in patients with acute lung injury, there has been no improvement in survival or decrease in ventilator requirement. No evidence was found from randomized controlled trials to support partial liquid ventilation in children in a recent review.\(^{61}\) We do not know, if some subset of patients with ARDS responds to partial liquid ventilation. Researches are on the way to evaluate other possible uses of liquid ventilation such as pulmonary drug delivery.

**Pharmacotherapy**

Better understanding of the pathophysiology of ARDS has contributed to development and use of various pharmacotherapeutic adjuncts in ARDS patients. Pharmacotherapeutic adjuncts are used not only for improving oxygenation but also to limit the acute lung injury.

**Inhaled Nitric Oxide (NO)**

Nitric oxide has been extensively studied, as a therapy for ARDS after Roissant and co-workers\(^{62}\) published their initial work using inhaled NO. NO is the final common mediator of vascular smooth muscle relaxation previously known as endothelial derived relaxing factor (EDRF). The activity of NO seems to be terminated in vivo by binding to haemoglobin resulting into the formation of methaemoglobin, which is regarded as the most important risk, associated with its use.

The beneficial effects in the lungs of ARDS patients is produced by selective vasodilatation of pulmonary capillaries and arterioles adjacent to the ventilated alveoli and thus diverting blood to those alveoli which are away from areas of shunt. Initially the pulmonary vascular resistance decreases which is accompanied by decrease in the pulmonary artery pressure at a concentration of approximately 0.1ppm in patients with ARDS whereas improvement in oxygenation occurs at a concentration of 1 to 10ppm.\(^{63}\) Systemic haemodynamic effects do not occur due to rapid inactivation of inhaled nitric oxide by binding to haemoglobin in the blood. This requires it to be given by continuous gas delivery through ventilator circuits.

Some patients with ARDS do not respond to inhaled NO and investigators have speculated increased pulmonary phosphodiesterase type-5 to be partially responsible for its decreased responsiveness and sildenafil is likely to improve the responsiveness.\(^{64}\) Inhaled NO completely reverses the effects of permissive hypercapnia.\(^{65}\) It has been demonstrated that NO decreases H\(_2\)O\(_2\) production and release of IL-6 and IL-8 in neutrophils after 4 days of therapy in ARDS patients.\(^{66}\) NO may also inhibit platelet function at concentrations commonly administered.

Although abundance of literature describing the beneficial physiologic effects of inhaled NO exists, no mortality benefits were shown in a study with 385 ALI/ARDS patients.\(^{67}\) Nonetheless, it is a safe therapy with appropriate monitoring in patients with severe hypoxaemia despite usual measures. Interruption of continuous delivery of NO can
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precipitate life threatening hypoxaemia and right heart failure.68

Prostaglandins
It was thought that prostaglandins might be of some benefit in ARDS patients, since prostaglandin E1 (PGE1) is known to dilate pulmonary artery. But PGE1 is reported to decrease in pulmonary artery pressure and increase in shunt69 and outcome studies failed to demonstrate improvements.70 But some researchers believe that PGE1 may improve oxygen delivery.71 Prostaglandin is associated with hypotension, diarrhoea and fever. Newer mode of delivery by aerosolizing the PGE1 has raised renewed interests of its use again.72 It is associated with enhanced efficacy and diminished side effects.

Surfactants
Clinical investigators of adult ARDS have been interested by the result of surfactant therapy in infants with the respiratory distress syndrome (RDS) of prematurity. In RDS of prematurity, surfactant therapy is associated with improved gas exchange, improved lung mechanics, decreased requirements for continuous positive airway pressure (CPAP), and less barotraumas.73 But prospective study of surfactants in adult ARDS patients showed no benefits with surfactant therapy.74 Exogenous surfactant can still be considered experimental in ARDS patients.

Corticosteroids
Corticosteroids by virtue of their ability to attenuate cell mediated immunity and decrease cytokine release and activation, appear to be ideal agents to interrupt the detrimental cascade of immunologic events that accompany sepsis and ARDS. Corticosteroids have been shown to significantly improve outcome in animals treated with endotoxin75 but, unfortunately, failed to demonstrate benefits in human studies.76 This discrepancy may be due to the fact that animals that obtained a beneficial response was a consequence of earlier treatment with steroids in course of disease than it is possible with human patients. Steroid therapy has not only failed to demonstrate a benefit in outcome but also in gas exchange or lung mechanics. The only condition, which fulfills the criteria of ARDS and responds to steroid therapy, is acute eosinophilic pneumonia.77 Any patient showing high eosinophils count in broncho-alveolar lavage (BAL) should be treated with high doses of steroids. Although it has been anecdotally claimed that high dose steroid therapy may be of some benefit in the proliferative phase of ARDS, it is difficult to discern their role during proliferative phase of ARDS in the absence of well-controlled, randomized trials in debilitated, infection-prone ARDS patients. Recently, use of low dose steroids in acutely ill patients with sepsis has shown a reduction in mortality.78

Activated Protein C
Recently, clinical evaluations have shown those drugs specifically targeting the inflammatory markers are effective. Recombinant human activated protein C, an anticoagulant, is the first anti-inflammatory agent that has been found to be in sepsis79 and hence can be expected to be useful in ARDS associated with sepsis.

Activated protein C inactivates factor Va and VIIIa, thereby preventing the generation of thrombin which in turn decreases inflammation by inhibiting platelet activation, neutrophil recruitment and mast cell degranulation. The direct anti-inflammatory properties include blocking the production of cytokines by monocytes and blocking cell adhesion. Before starting therapy with activated protein C there must be a) proven or suspected infection, b) evidence of systemic response to infection, and c) evidence (criteria) for acute organ dysfunction in clinical practice. Activated protein C is associated with the risk of increased incidence of serious bleeding (intracranial bleeding or requirement of 3 or more than 3 units of blood) as compared to placebo. Activated protein C must be used with caution in patients with international normalized ratio (INR) of more than 3 or a platelet count less than 30,000/cmm. Currently, use of activated protein C is restricted to the more seriously patients who are at eminent risk of death. Activated protein C should be used as an adjunct to supportive therapy when standard care has failed to show improvement and that there are no contraindications.

General Approach of Management85,86

After identifying a patient suffering from ARDS, 100% oxygen should be administered through a high flow mask until trachea can be intubated and mechanical ventilation started. Oxygen supplementation acts as both diagnostic and therapeutic manoeuvre. Hypoventilated patients show dramatic improvement in oxygenation, patients with substantial V/Q mismatching show moderate response, and patients with significant shunt (ARDS patients) show only minimal response.

Non-invasive ventilation is rarely appropriate as the course of ARDS is usually longer than the time that intensivists want to use non-invasive ventilation. The ventilatory mode may depend on the availability of the ventilator and the experience of the intensivists.

Every effort should be made to minimize oxygen consumption by controlling fever and use of sedation and muscle relaxants. To keep the mixed venous oxygen saturation higher, the haemoglobin should be kept at a
minimum of 12gm/dl. Attempts must be made to maintain optimal cardiac output but keeping in mind that excess volume loading can worsen the respiratory condition.

Endotracheal suctioning should be performed without disconnecting the endotracheal tube from the circuit through a sample valve of the connector. Systemic detection of airway colonization of bacteria should be done at least once weekly using broncho-alveolar lavage, since there is high incidence of nosocomial pneumonia and difficulty in diagnosing ventilator-associated pneumonia (VAP) in these patients.\(^3\) Weaning of high pressures, FIO\(_2\) and sedation might be started early on and should be tested repeatedly on daily basis.\(^8\)

### Conclusion

Basic science investigations and clinical studies have brought significant change in the understanding and practice of managing the patients of ARDS in the recent years. The evolution of the concept of VALI in mechanically ventilated patients with ALI or ARDS has changed the approach to ventilatory management. Protective strategy in mechanical ventilation is the only accepted treatment or supportive measure that has been shown to affect the outcome in the patients with ARDS. It is recommended to use low tidal volume ventilation routinely for patients with injured lungs with few exceptions to conditions exacerbated by hypercapnia (e.g. raised ICP). Protective ventilatory strategy (volume and pressure limited) has been accepted as a new gold standard against which newer supportive modalities including partial liquid ventilation, high frequency ventilation, ECMO etc should be tested. Other approaches intended to improve gas exchange in the injured lung that have failed to improve survival in clinical studies, including prone positioning, inhaled NO, surfactants etc could confer benefit if used in conjunction with this protective ventilatory strategy. Based on the present knowledge, it can be concluded that limiting the tidal volume and airway pressure can give the best chances of survival to the ARDS patients.

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