Acute Respiratory Distress Syndrome

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ABSTRACT

Acute respiratory distress syndrome (ARDS) is a syndrome of injured lung due to any systemic inflammatory responses. The decline in ARDS mortality mostly attributed to improvements in standard supportive care. There are still no data from any large multicenter randomized clinical trial ever demonstrated to reduce mortality other than the recommended by the National Institutes of Health (NIH) ARDS Network published in 2000.

Key words: ARDS, acute respiratory failure, acute lung injury.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) involved only up to 3% of ICU patients but its mortality rate reached 40 to 60%. This mortality rate is more than 20% higher than the other form of acute respiratory failure (ARF).

ARDS was first described by Ashbaugh in 1967 and was termed as adult respiratory distress syndrome. The term differentiates the disease from similar syndrome in neonates. However, in the recognition that ARDS may occur in children, the term of adult was changed to acute for the typical of acute onset that defines the syndrome.

ARDS may complicate a vast spectrum of critical illnesses. It is primarily an inflammatory phenomenon. Regardless of the site of origin of the insult, a systemic inflammatory response injures the lungs, as well as other organs. It is possible that the inflammatory response of the lung is worse than the other site of the body due to combinations of factors including the positive pressure of mechanical ventilation.

Acute lung injury (ALI) is a term for milder form of ARDS. In ALI, the oxygen partial pressure may be reached in arterial blood (PaO₂) by a same oxygen fraction or concentration in the inspired air of the patient (FiO₂), is higher than ARDS. Numerically ALI is defined by PaO₂/FiO₂ = 201 - 300 while PaO/FiO₂ ≤ 200 is categorized as ARDS.

DIAGNOSIS OF ARDS

The diagnostic criteria that is now widely accepted for ARDS is the criteria published by the American European Consensus Conference in 1994. This criteria require acute onset of bilateral radiographic infiltrates which is consistent with pulmonary edema but without any clinical evidence of left sided heart failure (pulmonary artery wedge pressure or PAWP ≥18 mmHg if measured). Along with the criteria mentioned, ALI/ARDS is then defined when PaO₂/FiO₂ is ≤ 300.

COMPLICATIONS OF ARDS

Complications in ALI/ARDS may be directly due to the disease or as an effect of the treatment. The mortality in ALI/ARDS is significantly affected by the occurrence of other complication. Yet the majority of deaths are due to complication occurred (especially sepsis and multiorgan dysfunction) rather than the primary respiratory failure. Survival in ALI/RDS is ultimately depends on the successful prevention and support to the complications.

ALI/ARDS is a pulmonary manifestation of systemic disorders with several similarities to sepsis. Such in SIRS/sepsis, multiorgan dysfunction or failure may complicate ALI/ARDS. This multiorgan dysfunction may be due to the underlying processes, such as multiple trauma, infection and sepsis, or directly due to the hypoxemic state of ALI/ARDS. Maintaining organ perfusion is critical in managing ALI/ARDS to prevent multiorgan dysfunction.

Pulmonary infection or pneumonia may induce ALI/ARDS while ventilator associated pneumonia (VAP) is a common complication in ALI/ARDS patients manage by mechanical ventilator. ALI/ARDS patients are often die due to uncontrolled infection. Fever, purulent secretions, new pulmonary infiltrates and elevated white blood count should raise the suspicion of VAP,
although ARDS may also present with this symptoms.\textsuperscript{14} Appropriate early empirical antibiotic therapy is crucial to determine the outcome of this complication. Local resistance pattern is required in this situation and microbacterial culture and antibiotics resistance test should directly be done.

Pulmonary embolism and deep vein thrombosis (DVT) due to prolonged lying down are also common complication of ARDS patients. Thrombo-embolism prophylaxis should be administered in immobile patients of more than three days. Method of prophylaxis is beyond the scope of this article to discuss.

Barotrauma due to the use of mechanical ventilator may lead to pneumothorax, pneumatocele, pneumomediastinum, subcutaneous emphysema or air embolus. Pneumothorax or air embolus should always be considered in sudden, unexplained worsening respiratory distress and hypoxemia or hemodynamic instability in a mechanically ventilated patient. Chest tube should be placed directly especially if it is under tension. Subcutaneous emphysema and pneumomediastinum can be treated with analgesia.

Other complication of prolonged mechanical ventilation used in ALI/ARDS patients is critical illness polynueapathy which may be related to neuropathy or myopathy or both. The use of corticosteroids or neuromuscular blocker agents may induce this complication.\textsuperscript{15}

TREATMENT OF ARDS

The management of ARDS consists of two important measures; there are supportive therapy and mechanical ventilation. While low tidal volume strategy in mechanical ventilation proved to reduce the ARDS mortality by 10\%, the over time decline in mortality mostly reflects improvements in standard supportive care.\textsuperscript{3,4} The principles of the supportive therapy in ALI/ARDS are:

1. Fluid and hemodynamic management
2. Nutritional management
3. Inciting factor treatment
4. Management of complication

FLUID AND HEMODYNAMIC MANAGEMENT

Appropriate targets for hemodynamic and fluid status in ALI/ARDS are hard to define. The principle idea is to reduce left atrial pressure to reduce the formation of pulmonary edema, yet to keep an adequate intravascular volume to maintain cardiac output and tissue perfusion.\textsuperscript{16,17} This principle result to a conservative fluid strategy rather than a liberal fluid constitution.

NUTRITIONAL SUPPORT

Overfeeding or high carbohydrate diet should be avoided due to the risk of high respiratory quotient and a resultant rise in CO\textsubscript{2} production. In acute respiratory failure high lipid and low carbohydrate diet have been shown to lessen the duration of mechanical ventilation (but the report did not mention the outcome on mortality rate).\textsuperscript{18}

Enteral feeding should be preferred to parenteral route when there is no contraindication for enteral usage. Lack of enteral feeding may promote bacterial translocation from the intestine.\textsuperscript{19,20} Theoretically parenteral feeding may also increase the risk of nosocomial infection.

A trial showed that diet rich in fish oil, gamma-linoleic acid, and antioxidant lessen the duration of mechanical ventilation and lower organ failure in ALI/ARDS cases but it failed to show any decrease in mortality.\textsuperscript{21}

No data has been available to judge the optimal time of feeding initiation.

INCITING FACTOR TREATMENT

Treatment for any underlying factor of ALI/ARDS is critical to enhance the chance of survival. Around 40\% of septic patients developed ARDS.\textsuperscript{1} Appropriate antibiotic, guided by a resistance test, should be given when an infection such as pneumonia or sepsis is the precipitating factor. Invasive diagnostic procedure including bronchoscopy may be warranted especially in immunocompromised patients.

The presence of multiple predisposing disorders should always be considered for it substantially increases risk,\textsuperscript{11} as does the presence of secondary factors including chronic alcohol abuse, chronic pulmonary disease, and serum ascidosis.\textsuperscript{12}

In patients with unknown source, intra-abdominal process should be considered. Surgical management in the right time for intra abdominal source control is associated with better outcomes.

MECHANICAL VENTILATION

A variety of modes of mechanical ventilation have been used anecdotally. There are still no data from any large multicenter randomized clinical trial ever demonstrated to reduce mortality other than the recommended by the National Institutes of Health (NIH) ARDS Network published in 2000.\textsuperscript{22} The recommendation is to use low tidal volume ventilator strategy. This strategy showed a 22\% reduction in mortality rate compare to higher tidal volume. Other strategy such as
high level of PEEP, prone positioning, lung recruitment maneuver and inhaled nitric oxide proved to improved oxygenation but have no benefit in mortality rate.

The low tidal volume strategy also called lung protective ventilation strategy because high tidal volume and high plateau pressure may harm an injured lung. The protocol for the protective lung strategy of the ARDS Network consist of the use of maximally 6 ml/kg body weight and/or plateau pressure less than 30 cm H$_2$O. The body weight used in this strategy is the ideal (predicted) body weight of patient’s height.

To use this strategy our initial setting is usually volume assist/control with PEEP 18 mmHg and FiO$_2$ 100%. Tidal volume is started from 4 ml/kg BW. Every one hour we observed SpO2 and the plateau pressure (it is recommended also to monitor PaO$_2$ using a PaO$_2$ continuous monitor) and then adjusted in steps of 1 ml/kg BW every 1 hour until 6 ml/kg BW. While adjusting the tidal volume, plateau pressure should be monitored. When the tidal volume has reached 6 ml/kg BW, while the plateau pressure is still below 30 cm H$_2$O, then the ventilator setting is kept to this position. If the plateau pressure has reached 30 cm H$_2$O before the tidal volume reach 6 ml/kg BW, then the tidal volume is kept in 4-5 ml/kg BW. To meet to the minimal minute ventilation needed to keep a normal CO$_2$ and pH level, the respiratory rate should be adjusted but not more than 35/minute.

This strategy is targeted to maintain arterial oxygenation at PaO$_2$ 55 – 80 mmHg or SpO$_2$ ≥ 88% - 95%. If the initial settings result in SpO2 > 95 % or PaO$_2$ using continuous PaO$_2$ monitor > 80 mmHg, PEEP and FiO$_2$ can be reduced in combination as listed in table 1. By reducing PEEP, the plateau pressure may also be decreasing below 30 cm H$_2$O so if the tidal volume is still < 6 ml/kg BW, then we may rise the tidal volume to 6 ml/kg BW.

The summary of the protective lung strategy is listed in table 1.

| Table 1. Summary of The Protective Lung Strategy by The NIH ARDS Network 2000 |
| Mode of Ventilator | Volume control/assist initially, Pressure support when weaning |
| Predicted Body Weight | Male : 50 + 0.91 [(height in cm) – 152.4], Female : 45.5 + 0.91 (height in cm) – 152.4 |
| Tidal Volume | Adjust q1-2h by 1 ml/kg until 6 ml/kg. Observe inspiratory plateau pressure (Pplat, 0.5 sec inspiratory pause) every 4 hours and after each change in PEEP or Vt. If Pplat > 30 cm H$_2$O decrease Vt to 5 or 4 ml/kg. If Pplat < 25 cmH$_2$O while Vt still 6 ml/kg, increase Vt by 1 ml/kg. |
| Respiratory Rate | Adjust RR (as long as ≥ 35/min) in accordance to Vt to Maintain minute ventilation, pH 7.30 -7.45 and PCO$_2$ ≥ 25 mmHg. |
| I : E ratio | 1 : 1 to 3, no inverse ratio |
| PaO$_2$ or SpO$_2$ | Maintain PaO$_2$ 55 – 80 mm Hg or SpO$_2$ 88 – 95 % |
| PEEP/FiO$_2$ combination | Set combination of PEEP and FiO$_2$ to maintain thr above PaO$_2$ or SpO$_2$ with the following: PEEP/FiO$_2$ (mmHg%): 5/30-40, 8/40-50, 10/50-70, 12/70, 14/70-80, 16/90, 18/90-100, 19-25/100 |
| Acid-base Management | pH < 7.3, increase RR until pH ≥ 7.3 or RR ≥ 35 /min. pH < 7.3 while RR ≥ 35 /min, consider bicarbonate IV pH < 7.15, increase Vt (Pplat may exceed 30cm H$_2$O) pH > 7.45, decrease RR (especially when patient is not breathing spontaneously) but not below 6/ minute. |
| Weaning criteria | PaO$_2$/FiO$_2$ > 200 with FiO$_2$ < 40% and PEEP < 8 cm H$_2$O No neuromuscular blocking agents Apparent inspiratory effort while ventilator rate is decreased to 50% of baseline level for not more than 5 minutes. Systolic blood pressure > 90 mm Hg, without vassopressor support. |
Table 2. PEEP and FiO2 Combination to Maintain PaO2 55–80 mmHg or SpO2 88–95%

<table>
<thead>
<tr>
<th>PEEP</th>
<th>5</th>
<th>8</th>
<th>10</th>
<th>10</th>
<th>10</th>
<th>12</th>
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<td>FiO2</td>
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<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
<td>0.7</td>
<td>0.8</td>
</tr>
<tr>
<td>PEEP</td>
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<td>18-25</td>
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<tr>
<td>FiO2</td>
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OTHER THERAPY

Such as in SIRS/sepsis, ALI/ARDS is a severe inflammatory process, including its procoagulant state. Anti inflammatory and anti coagulant treatment strategy is widely studied to facilitate the resolution of ALI/ARDS. However, there is still no established pharmacologic therapy to this proposes.

Glucocorticoid therapy was found useless in the early phase of ALI/ARDS. Glucocorticoid therapy is still suggested in the late phase of ALI/ARDS to hasten the resolution of fibroproliferative process. However, the possible complication of using high doses corticosteroids (including polyneuropathy) should always be weighted in critically patients.

Most ALI/ARDS patients have mild to moderate pulmonary arterial hypertension. Fatal outcome may be seen in patients with progressive rise in pulmonary vascular resistance. Vasodilators including nitric oxide, sodium nitroprusside, hyalurazine, alprostadel (prostaglandin E1), and epoprosterol (prostacyclin) have been studied for ARDS, but until now on, there is still no vasodilator agent proven to be effective in reducing mortality. The use of vasodilator may be limited to patients who have really developed sign of pulmonary hypertension such as right ventricular overload.

Other therapy such as N-acetylcystein, surfactant, and ketoconazole appeared to fail in large randomized trials. Concentrations of activated protein C are low in ARDS. Intravenous drotecogin alfa activated, a recombinant activated protein C is considered to be studied for ALI/ARDS to modulate fibrinolysis, but there is still no established result to endorse its routine use.

REFERENCES