AnaesthesiaUK

Print this page!

ARDS – Introduction to Management

Resource: Respiratory

ARDS – Introduction to Management

Dr John Griffiths DICM MRCP FRCA MA
CriticalCareUK Editor

Focus on the management of ARDS

The initial management of acute respiratory distress syndrome (ARDS) consists of emergency intubation with support of ventilation, oxygenation, haemodynamics and general ICU supportive care. The goal of fluid management is to maintain the intravascular volume at the lowest level that is consistent with adequate organ perfusion. It is important to address and treat the precipitating cause wherever possible in an attempt to limit the evolving inflammatory cascade. An enormous amount of research has gone into specific treatment strategies for ARDS above and beyond the normal management strategies and organ support that characterise a modern ICU. However, no treatment has been shown conclusively to be of benefit in ARDS.

Focus on low tidal volumes

"Lung-protective" ventilation strategies use smaller tidal volumes in an attempt to protect the lung from both overdistension (VALI – 'Ventilator Associated Lung Injury') and dampen or prevent the release of inflammatory mediators that may drive the inflammatory response. If a respiratory acidosis develops through the use of low tidal volumes, this is often tolerated ("permissive hypercapnia"). The true level of hypercapnic acidosis that is safely tolerated, and its true effect on patient outcome, remains open to debate. In the last 10 years, five randomized, controlled trials have focused on lung-protective strategies (Table 1). The most important trial was conducted by the Acute Respiratory Distress Network ("ARDSnet").

The ARDSnet Trial
The ARDSnet conducted a multicentre, prospective, randomised, controlled trial from 1996 to 1999 to determine whether the use of low tidal volumes would improve clinical outcomes in ARDS. The trial compared "traditional ventilation" (tidal volume of 12 ml/kg of predicted body weight and a plateau airway pressure of <50 cm H_2O) with "low tidal volume" ventilation (tidal volume of 6 ml/kg of predicted body weight and a plateau pressure of <30 cm H_2O). The lower tidal volume group displayed a 22% lower 28-day mortality rate, significantly more ventilator-free days and a lower incidence of non-pulmonary organ failure. The groups did not differ in the incidence of barotraumas or in the use of neuromuscular blocking agents.

However, a subsequent meta-analysis of the five low versus high tidal volume prospective, randomised, controlled studies highlighted that the two beneficial trials compared low tidal volume ventilation with control arms with airway pressures high enough (34-37 cm H_2O) to potentially increase control mortality rates. In this meta-analysis, Eichacker concluded that, given this situation, low tidal volumes might mistakenly appear beneficial. The applicability of the ARDSnet trial to UK practice has also been questioned, as the ventilator mode and settings used in the study are not commonly used on the ICU in the UK. However, at the current time, the findings of this trial have been widely endorsed throughout the critical care fraternity, and are an integral part of the Surviving Sepsis guidelines.

Table 1 Randomised, prospective studies of protective ventilatory strategies in patients with ARDS.

Reference	*n*	'Protective group'	Control group	Mortality
Stewart (1998)	120	Vt <8 ml/kg PIP <30 cm H_2O PEEP levels similar in both groups	Vt 10–15 ml/kg PIP <50 cm H_2O	No difference
Brochard (1998)	116	Vt <10 ml/kg Pplat <25 cm H_2O PEEP levels similar in both groups	Vt 10 ml/kg Normocapnia	No difference
Amato (1998)	53	Vt <6 ml/kg PIP <40 cm H_2O PEEP 2 cm above LIP of static PV curve	Vt 12 ml/kg Normocapnia	Lower in "protective" group (45 vs 71%)
Brower (1999)	52	Vt 5–8 ml/kg Pplat <30 cm H_2O PEEP levels similar in both groups	Vt 10–12 ml/kg Pplat <45–55 cm H_2O	No difference
ARDSNet (2000)	861	Vt 6 ml/kg Pplat <30 cm H_2O PEEP slightly higher in first few days	Vt 12 ml/kg Pplat <50 cm H_2O	Lower in "protective" group (31 vs 40%)

Vt = tidal volume; PIP = peak inspiratory pressure; Pplat = end-inspiratory plateau pressure; PEEP = positive end-expiratory pressure; LIP = lower inflection point of PV curve

Adapted from Moloney E and Griffiths M (2004)

Focus on PEEP

PEEP has been applied in ARDS and acute lung injury in an attempt to improve oxygenation and prevent lung shear-stress injury associated with the cyclical opening and closing of collapsed alveoli ("atelectrauma"). In the face of ARDS, most clinicians would apply a PEEP of 5-10 cm H_2O. However, it is important to balance the beneficial effect of PEEP on arterial oxygenation and its adverse effects such as cardiovascular compromise and increased airway pressures and over-distension. The ARDSnet group performed a randomised, controlled trial to determine whether higher levels of PEEP would improve clinical outcomes in patients with ARDS. All patients received mechanical ventilation with a tidal-volume goal of 6 ml/kg of predicted body weight and an end-inspiratory plateau-pressure limit of 30 cm H_2O. Mean PEEP was 8.3 cm H_2O in the lower group and 13.2 cm H_2O in the higher group. There were no significant differences between the groups in the mortality rate or number of ventilator-free days, ICU-free days, or organ-failure free days.

Focus on prone positioning

Two large randomised trials have compared the effects of prone positioning on mortality from ARDS. In both trials there was a significant improvement in oxygenation when patients were turned prone. However, this did not translate into improved clinical outcome. The rates of displacement of endotracheal tubes, vascular catheters and thoractomy tubes were similar in the two groups in one trial but increased in the prone group in the other trial (see Prone positioning and ARDS article in this resource).

Focus on artificial surfactant

Patients with ARDS have decreased production and biochemical alterations of endogenous surfactant. Lack of surfactant contributes to atelectasis, shunts, poor gas exchange and increased rates of ventilator associated pneumonia. However, although artificial surfactant is of benefit in neonates with idiopathic respiratory distress syndrome, the results in adults with ARDS have been disappointing, and its use is not justified at the current time. It is interesting to note that the post hoc analysis of the use of recombinant protein C-based surfactant in ARDS patients suggested a trend towards a survival benefit on the "direct" lung injury group. This effect may be related to an improvement in gas exchange. However, further studies are needed to evaluate the significance of these findings.

Focus on nitric oxide and prostacyclin therapy

Inhaled nitric oxide can selectively vasodilate the pulmonary vascular and reduce pulmonary hypertension, decrease shunting and improve gas exchange in ARDS.

There are no systemic effects because nitric oxide is scavenged rapidly by haemoglobin. However, numerous large clinical trials have failed to demonstrate that the improvements in oxygenation seen in patients treated with nitric oxide translate into improved outcome. Inhaled prostacyclin vasodilates the pulmonary bed as effectively as nitric oxide but does not result in the same improvements in oxygenation.

Focus on corticosteroids

Corticosteroids have no role in the acute management of ARDS. However, a small trial in 1998 suggested a survival benefit if high-dose corticosteroids are given as a treatment for the later "fibroproliferative" phase. A recent trial set out to repeat the findings of this earlier controversial study. In this trial, 180 patients with ARDS of at least 7 days' duration were randomised to receive either methylprednisolone or placebo in a double-blind fashion. Although, overall, 60-day mortality was similar between the two groups, methylprednisolone was associated with significantly increased 60- and 180-day mortality rates among patients enrolled at least 14 days after the onset of ARDS. Methylprednisolone therapy increased the number of ventilator-free and shock-free days during the first 28 days, in association with an improvement in oxygenation, with fewer days of vasopressor therapy. As compared with placebo, methylprednisolone did not increase the rate of infectious complications but was associated with a higher rate of neuromuscular weakness. Despite the improvement in cardiopulmonary physiology, the results of this study do not support the routine use of methylprednisolone for persistent ARDS. In addition, starting methylprednisolone therapy more than 2 weeks after the onset of ARDS may increase the risk of death.

Focus on high-frequency oscillation

High frequency oscillatory ventilation (HFOV) is, in theory, a "lung-protective" mode of ventilation. HFOV provides efficient gas exchange by using very low tidal volumes and high respiratory rates. The application of a constant mean airway pressure in HFOV allows the maintenance of alveolar recruitment while avoiding low end-expiratory pressure and high peak pressures. The mean airway pressure generated by HFOV is usually higher than that generated by conventional ventilation (tidal volumes of 10 ml/kg). The first randomized, controlled trial comparing HFOV with a conventional ventilation strategy in 148 adults with ARDS has recently been completed. Although this study expands on previous studies confirming that HFOV is effective and safe, and not associated with significant haemodynamic effects, there was no significant difference in mortality between the groups. One of the limitations of this (and almost all of the other older studies of ventilation strategy) was that HFOV was not compared with the current gold standard low-tidal volume approach used by the ARDSnet trial.

Focus on partial liquid ventilation

In partial liquid ventilation, perfluorocarbon-filled lungs are ventilated with conventional gas mechanical ventilation. Perfluorocarbons characteristically settle in the dependent lung regions, commonly affected in

ARDS. Partial liquid ventilation has the ability to increase gas exchange by recruiting atelectatic lung regions, redistributing pulmonary blood flow and reducing total lung water. It is also postulated that perfluorocarbons possess anti-inflammatory properties. Although partial liquid ventilation has been shown to be practical and safe in ARDS, a recent randomised, prospective study against conventional ventilation showed no difference in outcome. However, again, no attempt was made to control the tidal volume in the conventional ventilation group.

Focus on Extracorporeal Membrane Oxygenation (ECMO)

This treatment is very expensive, and at present has not been associated with improved survival benefits in the adult ARDS population. A large UK single centre trial ("CAESAR") is looking at the role of ECMO in adults with severe ARDS.

Key learning points

- Mechanical ventilation with smaller tidal volumes (6 ml/kg predicted body weight) is associated with improved survival
- Prone positioning and low-dose inhaled nitric oxide both improve oxygenation but are not associated with improved survival
- The optimal level of PEEP is yet to be determined
- Exogenous surfactant may improve oxygenation but has no significant effect on survival
- No other drug therapy has been shown to improve survival
- The true roles of high-frequency oscillatory ventilation, partial liquid ventilation and ECMO are yet to be determined

Key references

Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, Takagaki TY, Carvalho CR. Effect of a protective ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998; 338: 347–354.

Brochard L, Roudot-Thoraval F, Roupie E, Delclaux C, Chastre J, Fernandez-Mondejar E, Clementi E, Mancebo J, Factor P, Matamis D, Ranieri M, Blanch L, Rodi G, Mentec H, Dreyfuss D, Ferrer M, Brun-Buisson C, Tobin M, Lemaire F. Tidal volume reduction for prevention of ventilator-induced lung injury in acute respiratory distress syndrome. Am J Respir Crit Care Med 1998; 158: 1831–1838.

Brower RG, Shanholtz CB, Fessler HE, Shade DM, White P Jr, Wiener CM, Teeter JG, Dodd-o JM, Almog Y, Piantadosi S. Prospective, randomized, controlled clinical trial comparing traditional versus reduced tidal volume ventilation in acute respiratory distress syndrome patients. Crit Care Med 1999; 27: 1492–1498.

The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000; 342: 1301-1308.

Stewart TE, Meade MO, Cook DJ, Granton JT, Hodder RV, Lapinsky SE, Mazer CD, McLean RF, Rogovein TS, Schouten BD, Todd TR, Slutsky AS. Evaluation of a ventilation strategy to prevent barotraumas in patients at high risk for acute respiratory distress syndrome. N Engl J Med 1998; 338: 355–361.

Eichacker PQ, Gerstenberger EP, Banks SM, Cui X, Natanson C. Meta-analysis of acute lung injury and acute respiratory distress syndrome trials testing low tidal volumes. Am J Respir Crit Care Med 2002; 166: 1510-1514.

Moloney ED, Griffiths MJD. Protective ventilation of patients with acute respiratory distress syndrome. Br J

Anaesth 2004; 92: 261–270.

The National Heart, Lung and Blood Institute ARDS Clinical Trials Network. Higher versus lower positive end-expiratory pressure in patients with the acute respiratory distress syndrome. N Engl J Med 2004; 351:327-336.

Gattinoni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, Malacrida R, Di Giulio P, Fumagalli R, Pelosi P, Brazzi L, Latini R; Prone-Supine Study Group. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 2001; 345: 568-573.

Guerin C, Gaillard S,Lemasson S, Ayzac L, Girard R, Beuret P, Palmier B, Le QV, Sirodot M, Rosselli S, Cadiergue V, Sainty JM, Barbe P, Combourieu E, Debatty D, Rouffineau J, Ezingeard E, Millet O, Guelon D, Rodriguez L, Martin O, Renault A, Sibille JP, Kaidomar M. Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. JAMA 2004; 292: 2379-2387.

Spragg RG, Lewis JF, Walmrath HD, Johannigman J, Bellingan G, Laterre PF, Witte MC, Richards GA, Rippin G, Rathgeb F, Hafner D, Taut FJ, Seeger W. Effect of recombinant surfactant protein C-based surfactant on the acute respiratory distress syndrome. N Engl J Med 2004; 351: 884-892.

Sokol J, Jacobs SE, Bohn D. Inhaled nitric oxide for acute hypoxemic respiratory failure in children and adults. Cochrane Database Syst Rev 2000; (4): CD002787.

Dellinger RP, Zimmerman JL, Taylor RW, Straube RC, Hauser DL, Criner GJ, Davis K Jr, Hyers TM, Papadakos P. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: results of a randomized phase II trial. Inhaled Nitric Oxide in ARDS Study Group. Crit Care Med 1998; 26: 15-23.

Meduri GU, Headley AS, Golden E, Carson SJ, Umberger RA, Kelso T, Tolley EA. Effect of prolonged methylprednisolone therapy in unresolving acute respiratory distress syndrome: a randomized controlled trial. JAMA 1998; 280: 159-165.

Steinberg KP, Hudson LD, Goodman RB, Hough CL, Lanken PN, Hyzy R, Thompson BT, Ancukiewicz M; National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. N Engl J Med 2006; 354: 1671-1684.

Hurst JM, Branson RD, Davis K Jr, Barrette RR, Adams KS. . Comparison of conventional mechanical ventilation and high-frequency ventilation: a prospective randomized trial in patients with respiratory failure. Ann Surg 1990; 211: 486–491.

Derdak S, Mehta S, Stewart TE, et al. High-frequency oscillatory ventilation for acute respiratory distress syndrome in adults. Am J Respir Crit Care Med 2002; 166: 801–808.

Mehta S, Lapinsky SE, Hallet DC, Merker D, Groll RJ, Cooper AB, MacDonald RJ, Stewart TE. A prospective trial of high-frequency oscillation in adults with acute respiratory distress syndrome. Crit Care Med 2001; 29: 1360–1369.

Wunsch H, Mapstone J, Takala J. High-frequency ventilation versus conventional ventilation for the treatment of acute lung injury and acute respiratory distress syndrome: a systematic review and Cochrane analysis. Anesth Analg 2005; 100: 1765-1772.

Hirschl RB, Conrad S, Kaiser R, Zwischenberger JB, Bartlett RH, Booth F, Cardenas V. Partial liquid ventilation in adult patients with ARDS: a multicentre phase I–II trial. Ann Surg 1998; 228: 692–700.

Hirschl RB, Croce M, Gore D, Wiedemann H, Davis K, Zwischenberger J, Bartlett RH. Prospective, randomized, controlled pilot study of partial liquid ventilation in adult acute respiratory distress syndrome. Am J Respir Crit Care Med 2002; 165: 781–787.