

The role of prone positioning in the management of Acute Respiratory Distress Syndrome – A Literature Review

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INTRODUCTION AND BACKGROUND

Acute respiratory distress syndrome (ARDS) was first described in 1967 by Ashbaugh during the Vietnam War.^{1,2} It is an important public health problem and is a leading cause of mortality in critically ill patients.³ ARDS is colloquially known as “leaky lung syndrome”.⁴ It is an acute lung injury as a result of a diffuse inflammatory process. It has a varied aetiology and can be triggered by a range of both pulmonary and extra-pulmonary pathological processes. This causes a non-specific reaction affecting the lungs,⁵⁻⁷ namely inflammation damages alveoli, increasing vascular permeability, leading to inflammatory non-cardiac pulmonary oedema and acute respiratory failure, which can subsequently cause life-threatening hypoxaemia.^{2,4,8-11}

The Berlin criteria for ARDS have superseded previous distinction between acute lung injury and ARDS. According to the Berlin Criteria to be diagnosed with ARDS the patient must have all of the following:^{4,5}

- New or worsening respiratory symptoms within 1 week of a defined insult
- New bilateral diffuse opacifications on their chest x-ray
- Pulmonary oedema must not be related to fluid overload or be cardiac related
- Impaired oxygenation.

ARDS affects approximately 7 people per 100,000 of the population per year in Europe¹ and accounts for 7-10% of intensive care admissions.¹ It is likely that ARDS is initiated by an environmental trigger in a genetically predisposed individual.¹² The most commonly identified triggers include pneumonia, burns, trauma and sepsis.^{5,7}

A decade ago ARDS was associated with a 60% mortality rate and, despite this falling, currently 46.1% of patients with severe ARDS do not survive.^{7,8} Death is usually secondary to multi-organ failure, but 20% of patients die as a direct result of the hypoxaemia and respiratory failure.^{4,7} Aetiology is associated with mortality. The mortality rate is 86% if secondary to pneumonia, but only 38% if secondary to trauma.¹³ ARDS is known to be a complex condition with few effective management options.¹⁴ It often requires prolonged intensive care admission and slow weaning of respiratory support.^{2,5}

The severity of ARDS correlates with patient oxygenation ($\text{PaO}_2/\text{FiO}_2$) which is calculated as a ratio of arterial partial pressure of oxygen (PaO_2) and fraction of inspired oxygen (FiO_2).¹⁵ Mild ARDS is defined as $\text{PaO}_2/\text{FiO}_2$ of 200-300mmHg, moderate as a $\text{PaO}_2/\text{FiO}_2$ of 100-200mmHg and severe as a $\text{PaO}_2/\text{FiO}_2$ of less than 100mmHg.⁴

Classically, the first sign of ARDS is tachypnoea followed by development of hypoxaemia, central cyanosis, diffuse fine inspiratory crackles, and finally the

development of the classical ARDS chest x-ray changes.^{7,13} The chest x-ray findings of diffuse patchy or homogenous infiltrates are non-specific and therefore subject to significant inter-observer variability.^{7,12} Central or upper-lobe predominant ground-glass appearance and presence of central airspace consolidation are the most specific radiological findings for ARDS on chest x-ray.¹⁶

Lungs require dry alveoli to facilitate efficient gas exchange. The alveolar-capillary membrane is a selectively permeable membrane which allows control of the quantity of fluid within the alveoli to optimise this.¹⁷ In ARDS this normal physiological process is interrupted, and the lungs become dysfunctional. The pathophysiology can be split into acute and subacute phases.

The acute phase lasts up to 7 days and is when hypoxaemia and chest x-ray changes develop. Pro-inflammatory cytokines activate neutrophils and produce toxic mediators.¹⁷ They damage the alveolar membrane, reducing its integrity and this allows protein rich fluid to diffuse into the alveoli resulting in loss of the oncotic gradient.¹⁷ Fluid consequently uncontrollably enters the alveoli and inactivates the alveoli surfactant.¹⁷ If alveoli become fluid filled and contain non-functional surfactant, once collapsed the alveoli require high pressures to reopen.¹⁷ This can lead to atelectasis, ventilation-perfusion mismatch, reduced lung compliance and inefficient gas exchange.^{1,7,12,17} It has been suggested that there may be some involvement of the renin-angiotensin-aldosterone system which may contribute to the increased permeability of the alveolar membranes.¹⁶ This may be one mechanism to explain the observed element of genetic predisposition to ARDS.

The subacute phase begins around day 5 with persistent hypoxaemia, increasing atelectasis, development of interstitial fibrosis, proliferation of type 2 alveolar cells and further pulmonary complications, such as microvascular thrombosis.¹⁷ During this phase patients either begin to recover or start to develop chronic fibrotic changes.¹²

This literature review is going to summarise the evidence base for the management of ARDS patients focusing upon the use of prone positioning.

DISCUSSION OF MANAGEMENT OPTIONS

There are limited therapeutic options for ARDS and management is supportive, targeting the underlying cause.^{3,18} Mild ARDS can usually be managed with oxygen, physiotherapy, diuretics some patients requiring non-invasive ventilation.⁴ Moderate-Severe cases usually require mechanical ventilation.⁴ Mechanical ventilation should be initiated when PaO_2 falls below 8.3kPa on FiO_2 of 0.6, or if the PaCO_2 rises above 6kPa.¹¹ Unfortunately, mechanical ventilation itself can cause further damage

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to the lungs, commonly known as ventilator induced lung injury (VILI).³ The aim of ARDS management is to prevent iatrogenic lung injury whilst achieving adequate oxygenation and satisfactory clearance of carbon dioxide.¹

VILI usually occurs as a result from a combination of insults. The main reasons are barotrauma, volutrauma, atelectrauma and biotrauma.¹⁸ Barotrauma is due to the use of high pressures for ventilation. Volutrauma is caused by high volumes leading to alveolar overfilling and rupture and is decreased by using low tidal volumes.¹⁷ Atelectotrauma is damage to alveoli due to repeated inflation and deflation, when lung is recruited and de-recruited. It can be minimised using a high positive end-expiratory pressure (PEEP) preventing lung de-recruitment.¹⁷ Biotrauma is due to pro-inflammatory and toxic mediators in systemic circulation causing end-organ damage.¹⁷ Lung protective ventilation should be used for all patients with ARDS. This is a combination of low ventilatory pressures, high PEEP and low tidal volumes.^{1,16}

The use of low tidal volumes has been shown to reduce 28-day mortality from ARDS and reduce incidence of VILI.^{8,19} Use of low tidal volumes can cause hypercapnia and respiratory acidosis, but this is accepted in order to minimise the risk of VILI.⁴ It is often referred to as permissive hypercapnia.⁴ In ARDS, where possible, the pH should be maintained above 7.2, and if sustained below this for 24 hours then extracorporeal membrane oxygenation should be considered.¹⁸ Allowing patients to use breath-assisted modes of ventilation has been shown to reduce requirement of sedation, vasopressors and length of intensive care stay.²⁰

Improving alveoli recruitment improves lung compliance and oxygenation, reducing the pressures required for adequate ventilation and thereby reducing the incidence of both atelectrauma and VILI.^{18,21} The use of a high PEEP and prolonged inspiratory phase both help to maintain the patency of injured alveoli and improve recruitment of alveoli.^{4,8} A high PEEP of 15mmH₂O is standard in mechanical ventilation for ARDS.²²

In ARDS the ideal fluid management is to maintain intravascular volume as low as possible whilst simultaneously ensuring adequate organ perfusion.²¹ This conservative fluid management approach helps to reduce further pulmonary oedema and significantly reduce ARDS mortality.^{4,23}

The use of neuromuscular blockage in ARDS has been demonstrated to reduce ventilation pressures, pulmonary oxygen requirement and help prevent patient-ventilator asynchrony thus preventing VILI.¹⁷ Cisatracurium is the neuromuscular drug of choice in ARDS patients because it is neither hepatic or renally excreted and has some anti-inflammatory properties.¹⁷ Current evidence suggests that use of cisatracurium for 48 hours in moderate-severe ARDS reduces both the 90-day mortality rate and the length of stay on intensive care.⁸

There is currently little evidence surrounding the use of steroids, routine hemofiltration, inhaled nitrous oxide, anti-inflammatories and surfactant replacement in ARDS and they are not routinely used.^{4,5}

Prone positioning is when a patient is positioned face-down while mechanically ventilated.⁸ It leads to significantly better oxygenation than the conventional

supine ventilation in ARDS patients.⁸ Prone positioning was first attempted in 1974 and has been used for 40 years on intensive care units as a rescue therapy.^{6,24} It was initially thought prone positioning did not show any increase in mortality in multiple trials due to the prevalence of adverse effects.¹⁴ In 2013 prone positioning was found to have a beneficial reduction in mortality when used for prolonged periods in severe ARDS and the evidence base is continuing to grow.^{25,34} Prone positioning improves oxygenation by improving lung recruitment, ventilation-perfusion matching and alveolar gas exchange.^{5,11} It is particularly useful in patients who are difficult to oxygenate satisfactorily, and can reduce both the pressures and FiO₂ required for ventilation.⁵

The use of prone positioning in clinical practice is still low despite the increasing evidence base.²⁶ In a study researching why prone positioning was not offered to eligible patients the most common reason was when patients were perceived to be insufficiently hypoxemic to benefit.²⁶ It was found to still be widely viewed as a rescue therapy and is therefore not being fully utilised in intensive care units.²⁶

Prone positioning should be the first approach for persistent low hypoxaemia alongside neuromuscular blockage.⁸ For optimal benefit, patients should undergo prone positioning initiated within 48 hours of the onset and diagnosis of severe ARDS for sessions of at least 16 hours.^{8,25,27} Patients should then be returned to a supine position for 4 hours and reassessed. If after 4 hours in the supine position the PaO₂/FiO₂ is still less than 150mmHg with PEEP of at least 10cmH₂O and FiO₂ of less than 0.6, then prone positioning should be repeated.²⁵ Prone positioning should be stopped if PaO₂/FiO₂ is better than 150cmH₂O on a PEEP of 10cmH₂O and FiO₂ of less than 0.6, if their oxygenation is worse in the prone position than in the supine position, if there are any complications or if it has been 96 hours or longer since initiation of mechanical ventilation.^{2,8,18}

Prone positioning is contraindicated if the patient has any unstable fractures (especially spinal and long bone), haemodynamic instability, reduced cerebral perfusion or raised intracranial pressure, is within 15 weeks of abdominal or thoracic surgery, pregnant, if they have compartment syndrome or if they have had a recent deep vein thrombosis.^{8,25}

The 28-day mortality rate from ARDS is 32.8%. The use of prone positioning has been shown to reduce 28-day mortality from ARDS by 16.7% and 90-day by 17.4% if used for more than 12 hours per session.^{9,10,28,29} This reduction can be up to 26% for patients with severe ARDS.²⁵

Prone positioning is simple with experienced, trained staff.^{8,30} However, the process can be labour intensive and ideally requires 4 members of staff; 1 person to manage the airway, 2 people to move the patient and one person to lead the manoeuvre by checking lines and the patient's monitor.²⁴

The mechanism responsible for the improved oxygenation is incompletely understood.²⁵ Lungs are not symmetrical due to intrathoracic structures, the diaphragm and abdominal contents.⁹ Therefore, placing patients in the prone position allows previously compressed lung to be

recruited and this may be one mechanism for the observed improvement in oxygenation.^{9,31} Prone positioning has also been associated with reduced incidence of VILI because lower pressures are required to maintain the same levels of oxygenation.³⁰ Prone positioning also increases oxygen delivery to the bases of the lungs therefore facilitating consistent gas distribution throughout the lungs and improving the ventilation-perfusion relationship.¹⁹ It has also been shown to reduce the systemic concentration of pro-inflammatory cytokines after each session.⁶

Prone positioning is associated with an increased risk of pressure sores, facial oedema, raised intracranial pressure, corneal abrasions, conjunctivitis, unintended extubation, endotracheal tube obstruction and cardiac arrest, but these are mainly theoretical and complications seem to occur less frequently in trials than anticipated.^{8,26,33,34} Airway secretions usually increase due to postural drainage and lung recruitment and may require use of suction and occasionally bronchoscopy if the secretions cannot be controlled through normal suction procedures.²⁹ Prone positioning requires increased sedation and prevents early mobilisation of patients however, this seems to make little difference to the speed of recovery.³

The main two reasons for not trialling prone positioning in ventilated patients with severe ARDS were haemodynamic instability and hypoxaemia not severe enough to fit the guidelines for prone positioning.³² Prone positioning has been shown to be beneficial to cardiovascular physiology by reversing the pulmonary artery uncoupling and unloading of the right ventricle which is thought to contribute to the mortality benefit of prone positioning.³² Right ventricular failure has been shown to be a predictor in mortality from ARDS so patients who are haemodynamically unstable may benefit from prone positioning. More data is required to ensure there is a positive impact on mortality.³²

Extracorporeal membrane oxygenation (ECMO) is often used as a rescue therapy for intractable hypoxia due to severe ARDS.³⁴ However there is a high cost, it can only be offered at specialist centres and often requires long distance transportation of critically unwell patients. It is a complex intervention used to bypass the heart and lungs to facilitate recovery. There is currently a limited evidence base demonstrating improvement in outcomes and it has considerable complications. One paper reports that 16% of patients who died from severe ARDS following ECMO had trialled prone positioning prior to ECMO.³² It has been suggested that it may be a clinician assumption that the high cost, complicated ECMO is superior to the simple proven intervention of prone positioning, but may also be due to lack of familiarity and training, or concern over complications of prone positioning.³²

CONCLUSION

ARDS is an important cause of global mortality and a leading cause of death in intensive care units. Until recently there have been few trials providing strong evidence of any management options. In the last couple of years, reduced mortality from moderate-severe ARDS has been associated with the use of neuromuscular blockers, lung protective ventilation and early prone positioning.

There is a growing evidence base for the use of prone positioning early in the management of moderate-severe ARDS. It is important that eligible patients are identified early in the disease process to ensure they receive optimal benefit from the intervention. Prone positioning is one of the few management options shown to reduce mortality in ARDS.

There is currently ongoing research into other management options and the role of biomarkers to assess severity of ARDS. It has been proposed that ARDS may in fact be a broad term encompassing many different pathological conditions. Further research is required to attempt to deconstruct these conditions and establish optimal management for the subgroups within ARDS.

To ensure all patients receive optimal care it is important to keep up to date with the latest literature and evidence-base for the management of ARDS. It likely to be an area of medicine where the management options will rapidly evolve over the coming years.

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