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Ventilation in ARDS

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VENTILATION IN ARDS

Definition

"ARDS is a syndrome of inflammation and increased permeability associated with a constellation of clinical, radiologic and physiologic abnormalities unexplained by elevations in left atrial or pulmonary capillary pressure."

Published in an American-European Consensus Conference (AECC) statement in 1994.

Introduction

ARDS is the clinical manifestation of severe, acute lung injury. It is the result of a local or systemic event that initiates pulmonary endothelial and epithelial damage and subsequent increased permeability. The syndrome was first described in 1967 by Ashbaugh who had 12 patients with acute respiratory distress, cyanosis refractory to oxygen therapy, decreased lung compliance and diffuse infiltrates evident on chest x-ray.

The incidence is between 15 and 34 cases per 100000 people per year which doesn't sound like much but the prevalence amongst intensive care patients is 9%. And more relevant to us as anesthetists, is the prevalence amongst ventilated patients which is 36,9%. Therefore the likelihood that we as anesthetists are going to encounter this pathology, is high enough for us to need to know more about it than the average doctor.

The mortality rate from ARDS/ALI is about 40 to 50%, this figure has not fallen since 1994 according to a comprehensive review of major studies that assessed ARDS deaths. Most deaths are attributed to associated conditions such as sepsis and multi-system organ failure rather than hypoxaemia alone.

There is also short and long-term morbidity associated with these syndromes.
Short term morbidity leads to a prolonged stay in the ICU and prolonged ventilator dependence. Those that survive the illness have high rates of disability and a reduced health related quality of life as well as cognitive impairment.

Diagnostic Criteria for ARDS

- Identifiable associated condition
- Acute onset
- Pulmonary artery wedge pressure less than or equal to 18mmhg or absence of clinical evidence of left atrial hypertension.
- Acute lung injury is present if PaO2/ FiO_2 ratio is less than or equal to 300
- Acute respiratory distress syndrome is present if PaO_2/FiO_2 ratio is less than or equal to 200

(A normal person breathing room air (FiO_2 = 0.21) whose PaO_2 is 100mmHg would have a PaO_2/FiO_2 ratio of 500)

Pathogenesis

The American-European Consensus Conference defined two pathogenetic pathways leading to ARDS – a direct (pulmonary) insult that directly affects lung parenchyma and an indirect (extrapulmonary) insult that results from an acute systemic inflammatory response.

After a direct insult (most commonly pneumonia or gastric aspiration), pro-inflammatory cytokines (such asTNF, IL-1 and IL-8) are released in the lung and the pulmonary epithelium is the primary injured structure.

In extrapulmonary ARDS, the insult is indirect and pulmonary lesions are caused by circulating inflammatory mediators that are released from extra-pulmonary foci into the blood (eg sepsis, pancreatitis). The endothelial cell is the primary target for injury.

The cytokines recruit and activate neutrophils which release toxic oxygen radicals and proteases so that the end result of both pathways is diffuse alveolar-capillary damage. A protein rich fluid escapes from the intravascular space to the interstitial space and then to the alveoli. There is a decrease in the production and turnover of surfactant resulting in alveolar collapse. The pathology can be divided into three phases, each with its own histologic characteristics (while being clinically indistinguishable) however there is significant overlap between these stages.

1. Early/ exudative phase (Day 0-5) includes an interstitial and then intra-alveolar oedema with a protein rich exudate and the formation of hyaline membranes.

2. Late/ proliferative phase (days 5–10) Pulmonary oedema may resolve. Leukocytes are replaced by alveolar macrophages, there is a proliferation of type two epithelial cells, squamous metaplasia causing alveolar septal thickening, and early deposition of collagen.

3. Very late/ Fibrotic phase (After day 10). This is characterised by obliteration of normal lung architecture, diffuse fibrosis, and cyst formation. It does not occur in all patients and some patients achieve complete resolution of lung injury before progressing to this phase while others progress directly to develop fibrosis. Honeycombing may develop with severe fibrosis and a progressive pulmonary hypertension may also result. There is also evidence of impaired fibrinolysis in ARDS that leads to capillary thrombosis and microinfarction

Risk Factors

Direct Lung Injury	Indirect lung injury
Pneumonia	Sepsis
Gastric aspiration	Multiple trauma
Pulmonary contusion	Multiple Blood transfusions
Fat emboli	Cardiopulmonary Bypass
Inhalational injury	Burns
Near Drowning	Acute Pancreatitis
Reperfusion Pulmonary Oedema	Drug Overdose

Certain pre-existing conditions such as chronic lung disease and chronic alcoholism significantly increase the risk of developing ARDS.

Clinical Findings

The clinical picture is progressive. Tachypnea, tachycardia and respiratory alkalosis usually develop in the first 12 to 24 hours after the precipitating event and can occur before the appearance of infiltrates on a chest x-ray.

The inflammatory process and alveolar flooding lead to severe ventilation-perfusion mismatch since many alveoli are perfused but not ventilated resulting in severe hypoxia and reduced PaO_2/FiO_2 ratio. There is also a

marked reduction in lung compliance which increases the work of breathing. There is an increase in physiologic dead space and patients have to increase their minute ventilation to blow off CO_2. Pulmonary hypertension can develop and is due to hypoxic vasoconstriction as well as vascular compression by positive pressure ventilation.

The severe hypoxia, dead space and decreased lung compliance result in the development of respiratory failure – most patients within 48hrs of the onset of symptoms.

Lung Imaging

CXR – In the **exudative phase** bilateral diffuse, fluffy alveolar infiltrates are present (consistent with pulmonary oedema) which progress to diffuse, fluffy alveolar opacities. Although one can't reliably distinguish ARDS from cardiogenic pulmonary oedema on chest x-ray, patients with ARDS often lack cardiomegaly, pleural effusions and vascular redistribution.

- In the **proliferative phase** radiographic densities become less opaque and reticular opacities may be present.

- In the **fibrotic phase** CXR may have a honeycombing appearance.

CT Chest – In **exudative phase**: Bilateral alveolar opacities which are more pronounced in the dependant posterior lung zones. The anterior lung fields are relatively spared.

-In the **fibrotic** and **proliferative phase**: Bilateral reticular opacities, reduced lung volumes and occasionally large bullae.

Management

To date no specific pharmacologic interventions have proved effective for ARDS or ALI, therefore therapy is largely supportive and can be divided into nonventilatory supportive care and ventilatory support.

-Nonventilatory supportive care.

This includes:

1. Identifying the underlying cause and treating it aggressively

2. Initiating appropriate nutrition (enteral is preferred in most cases)

3. Maintaining an appropriate level of sedation to facilitate patient-ventilator synchrony and therefore limit patient discomfort while avoiding excessive and prolonged sedation and use of paralytic agents

4. Reducing Oxygen requirements – this can be done by treating fever, agitation, shivering and appropriate feeding.

5. Minimize the development of potential complications :

   Eg. nosocomial infections with careful hand washing, barrier nursing and use of aseptic techniques during insertion of central and arterial lines and other invasive procedures.

   Stress ulcer prophylaxis is indicated in all patients with ARDS to prevent gastro-intestinal bleeding as well as some form of DVT prophylaxis to prevent thromboembolism.

6. Fluid management is controversial – two studies suggested that limiting fluid retention in patients with ARDS leads to less pulmonary oedema and decreased mortality, but people have expressed concern that reducing intravascular volume may impair oxygen delivery to tissues and increase the risk of developing multiorgan failure which is already a leading cause of death in patients with ARDS. Fluid therapy should be goal directed and the development of oedema avoided. One recommendation is to restrict the use of crystalloid infusions to maintenance and medication and to supplement the intravascular volume with colloids.

7. Optimisation of Haemodynamics – Hypotension worsens V/Q mismatch by increasing both physiological dead-space and shunt. If the patient's haemodynamics don't improve with fluid resuscitation, inotropes (dobutamine or adrenalin) and /or vasopressors (noradrenalin or vasopressin) may be required to maintain perfusion pressures.

8. Optimisation of Haemoglobin – Transfusions are generally not considered necessary for Hb levels greater than 7 g/dL (TRICC study in 1999) but in patients with cardiac disease, ongoing bleeding or acute critical illness, a target Hb of 9 -10 g/dL is appropriate especially if there are signs of reduced oxygen delivery.

-Ventilatory Support

Nearly all patients with ARDS require mechanical ventilation and it represents the main therapeutic support to maintain acceptable pulmonary gas-exchange whilst treating the underlying disease.

But mechanical ventilation can potentiate or directly injure the lungs through a variety of mechanisms collectively referred to as ventilator induced lung injury (VILI). These mechanisms include :

1. Exposure to high inflation pressures (barotrauma)
2. Exposure to large tidal volumes resulting in overdistension of the lung (volutrauma)
3. Repetitive opening and closing of alveoli and the development of a high pressure at the interface of collapsed alveoli with open lung regions.(atelectrauma)
4. Mechanotransduction resulting in up-regulated cytokine release and a systemic inflammatory response (biotrauma) – this contributes to the development of multisystem or organ failure.

The lungs of patients with ALI or ARDS are particularly prone to ventilator associated lung injury because they are heterogeneously affected. As a result, some areas of the lung (usually dependant regions) are atelectatic, consolidated, less compliant and therefore less available for ventilation while other areas (usually non-dependant regions) appear and behave normally.

This understanding gave rise to the "baby-lung" concept. Because a markedly reduced volume of lung is available for ventilation in ARDS, functionally it is like having a baby-sized lung in an adult-sized body. Consequently, mechanical ventilation can result in barotrauma or volutrauma when pressures and volumes meant for the entire lung are forced into a small portion of functional lung. This understanding has been important in developing protective-ventilation strategies.

Lung-Protective Ventilation

Lung-protective ventilation involves strategies to reduce further lung injury in patients with ALI or ARDS. This includes limiting tidal volumes to 6ml/kg of ideal body weight (IBW), and limiting intra-pulmonary plateau pressures to less than 30cmH_2O.

A number of trials and meta-analyses have evaluated lung-protective ventilation using a variety of volume and pressure limited strategies as compared with conventional approaches – the conventional approach generally taken to be a tidal volume of 10 to 15ml/kg and a peep of 5cm. Three randomized trials done in the late 90's with sample sizes of 52 to 120 patients, did not find a difference in mortality between the treatment and control arms. A study done by Amato et al in 1998 used a higher positive end expiratory pressure (PEEP) and recruitment manoeuvres in conjunction with pressure and volume limited ventilation in the intervention group. This study demonstrated a significant reduction in 28 day mortality but there was no difference in mortality at hospital discharge and a high mortality rate (71%) in the control group may have accounted for the survival difference. But there was still a strong suggestion from this trial that ventilatory strategies could have an impact on mortality.

There became a need to carry out multi-centre clinical trials enrolling larger sample sizes in order to obtain statistically significant results. In 1994 the National Heart, lung and blood Institute (NHLBI) of the National Institutes of Health (NIH) formed a clinical network to carry out large trials of novel therapies for ARDS. This became known as ARDSNet. They conducted the largest trial of volume and pressure limited ventilation. This trial of 861 patients demonstrated a 9% absolute decrease in mortality (31% vs 40% P=0.007) when patients have reduced tidal volumes (6ml/kg of predicted body weight within a range of 4-8ml/kg PBW depending on plateau pressure and pH) and reduced pressures (less than 30cmH_2O). The trial was published in 2000 to a celebrated response but it didn't take long before controversies regarding this high profile trial emerged – one of the main criticisms being that control group did not represent the usual standard of care as tidal volumes of 12ml/kg IBW and pressures of 34cmH2O or more were used. Authors of a subsequent meta-analysis looking at 5 trials on the subject, concluded that there was no scientific basis for the use of a low tidal ventilation strategy in patients with ARDS or ALI. They also stated that the ARDSNet trial only served to show the harmful effect of high tidal ventilation (12ml/kg) associated with high airway pressures (34cmH_2O or more).

This meta-analysis was criticized as having methodological flaws and its findings have been contradicted by two subsequent meta-analyses. But there has been a growing appreciation that it is the limitation of intra-pulmonary pressures to <30cmH2O, rather than tidal volume limitation, that is responsible for most of the benefit seen in the ARDSNet trial.

Either way, the ARDSnet trial showed that a volume and pressure limited ventilation strategy resulted in a significant and sustained short term mortality benefit for patients with ARDS and this strategy should be used in all ICU's.

Consequences of Lung-protective ventilation

This strategy is not without side effects –

1. Elevated arterial carbon dioxide – referred to as permissive hypercapnia. Although acute hypercapnic respiratory acidosis has many potential side-effects, the extent to which a more controlled subacute elevation of carbon dioxide is harmful remains uncertain. Some evidence by Laffey et al in 2004 indicates that permissive hypercapnia is relatively benign. Renal compensation, whether intrinsic or by dialysis, will maintain the pH > 7.3 and bicarbonate or buffer administration is seldom needed. (Of note the ARDS investigators treated acidosis by increasing the respiratory rates, allowing bicarbonate infusions and increasing tidal volumes up to 8ml/kg). One contraindication includes patients with raised intracranial pressure who should be kept normocarbic.

2. Worsened oxygenation is another possible side effect (In the ARDSNet study patients in the intervention arm had reduced oxygenation in the first few days but improved survival)

3. Increased need for sedation or analgesia compared to patients receiving conventional ventilation - these agents can prolong the period of mechanical ventilation, lengthen ICU and hospital stay and lead to complications such as critical illness polyneuropathy. (However there was no significant difference in sedation or analgesia use between the interventional and control groups in the ARDSNet trial).

Other Possible Components of a Lung-Protective Ventilation Strategy (Open-Lung Strategy)

In addition to volume and pressure limitation, higher PEEP and the use of recruitment manoeuvres (i.e. an open-lung approach) may be important in a Lung-protective strategy.

Recruitment

Recruitment refers to the dynamic process of reopening collapsed alveoli by increasing transpulmonary pressure. This can be achieved by a variety of mechanisms such as a transient high continuous positive airway pressure (eg 40cmH2O for 40 seconds). The subsequent application of PEEP will then maintain the lung volume recruited. The optimal pressure, duration, and frequency of recruitment manoeuvres has not been defined and tested in clinical trials.

In ARDS, hypoxaemia is most often due to shunt which is due to two main causes:

- Consolidation / pulmonary oedema (non-recruitable)
- Collapse / atelectasis (recruitable)

The most recruitable form of ALI/ARDS is early, extrapulmonary lung injury while the least recruitable is late pulmonary lung injury.

The manoeuvres are also associated with adverse effects - transient oxygen desaturation and hypotension being the most common as well as barotrauma (eg pneumothorax), arrhythmia and bacterial translocation. One should be cautious in patients with hypovolaemia as the increase in intra-thoracic pressure impedes venous return and this can result in a dangerous fall in both RV and LV preload. One should also avoid performing these manoeuvres in patients with raised intra-cranial pressure (> 25cmH2O) as the increase in intra-thoracic pressure impedes jugular venous flow and may further raise ICP which could result in brain herniation.

Positive End Expiratory Pressure (PEEP)

Advantages of PEEP:

If a substantial portion of the lung is not aerated at end-expiration because of atelectasis, flooding and consolidation, this could result in excessive mechanical forces in aerated lung regions, between aerated and non-aerated lung regions or in bronchioles and alveoli that open and close with each breath resulting in ventilation induced injury. The proportion of non-aerated lung may be reduced by applying a positive end-expiratory pressure as this opens and stabilizes collapsible alveoli. PEEP also redistributes lung fluid from alveolar to interstitial spaces and therefore improves lung compliance and arterial oxygenation.

Disadvantages of PEEP:

PEEP is also associated with adverse effects namely circulatory depression and overdistension of normal lung regions. Although a higher PEEP may increase arterial oxygenation and allow lower levels of FiO2 to be used, it can impair venous return in hypovolaemic patients. This results in a reduced cardiac output which can cause an overall reduction in oxygen delivery.

Traditional Use of PEEP:

In the past most patients with ARDS have been treated with PEEP values of 5 to 12cmH2O - a range that reflected the physicians' attempts to balance the beneficial effects of PEEP with the adverse effects. But PEEP levels that exceed these traditional levels may decrease ventilator induced lung injury by further reducing the proportion of non-aerated lung.

What does the Literature Say?

The isolated effect of a higher PEEP and recruitment manoeuvres could not be determined in the small trial by Amato et al in 1998 but in 2004 the ARDSNet published the results of the ALVEOLI trial which looked at higher versus lower positive end-expiratory pressures in 549 patients with ARDS. All study patients received volume limited lung protective ventilation (6ml/kg IBW), the control group received a PEEP of 5 - 24cmH_2O and the intervention group a PEEP of 12 – 24cmH_2O. PEEP was set using a PEEP/FiO_2 table. The study was stopped early after enrollment of 549 of the 750 patients as there was no significant difference in hospital mortality or number of ventilator free days.

With all the known advantages of PEEP, why did the ARDSNet ALVEOLI trial fail to show benefit? One of the reasons is that as PEEP increases, plateau pressure also increases and excessive plateau pressure is associated with adverse outcome. So the benefit of the high PEEP in the interventional arm was offset by high plateau pressures and the harm of low PEEP was offset by the lower plateau pressures. As a result the trial is being repeated with the same PEEP strategy but keeping inflation pressure at or below 35cmH_2O in the high PEEP group.

What PEEP to use?

PEEP is beneficial, the question is how much? A commentary titled "Positive end-expiratory pressure in acute respiratory distress syndrome: should the 'open lung strategy' be replaced by a 'Protective lung strategy'" by Rouby et al in 2007 looked at the concept of "best PEEP". They stated

that PEEP is associated with alveolar recruitment and lung hyperinflation despite a low tidal volume and that the best PEEP should correspond to the best compromise between recruitment and distension.

How does the clinician determine the “best PEEP” for each patient? One strategy is to start patients with ARDS on a PEEP of 7cmH2O (this coincides with the lower inflection point on most pressure-volume curves). If the patient desaturates, a recruitment manoeuvre is performed – if this results in an improvement (seen as an improvement in oxygenation, lung mechanics – an increased tidal volume for the same PAWP in pressure control mode or a reduction in PAWP for the same tidal volume in pressure control mode - and a reduction in CO_2) – the lungs still have capacity for recruitment and the PEEP can be increased from 7 to say 10cmH_2O. If derecruitment occurs, the procedure can be repeated and the PEEP increased further. However, if there is no response to a recruitment manoeuvre, (ie. no improvement in oxygenation, lung mechanics and carbon dioxide) PEEP should not be increased as the lungs have no capacity for recruitment and are at risk of injury due to overdistension.

A Ventilatory Approach for the Clinician

Pressure or volume controlled ventilation – modes of ventilation offering full support are preffered to those offering partial support (eg SIMV / PSV)

Recruitment manoeuvres – performed prior to ventilation,
after disconnection from the ventilator and when derecruitment occurs (as described previously)

Tidal Volume – low – 6ml/Kg IBW
Peak airway pressure - < or equal to 35 - 40 cmH_20
Respiratory Rate – 12 - 20
I:E ratio – 1:1 to 1:3 (prolonging inspiratory time may give diseased units more time to open so that more lung is recruited.)
PEEP – start at 7cmH_2O and increase as previously recommended to obtain “best PEEP”
FiO_2 – lowest possible to ensure arterial oxygenation > 90%

Goals:
Arterial oxygenation: 55 – 80mmHg
Arterial carbon dioxide: 35 – 60mmHg
Arterial PH: 7.3
Arterial saturation > 90%

Refractory Hypoxaemia

A subset of patients with ARDS will not respond to the recommended ventilation strategy and will remain hypoxaemic. This group of patients may be amenable to rescue therapies – these alternative ventilatory approaches and adjunctive therapies have some evidence of short term physiological benefit but no consistent evidence for survival advantage when studied with large randomized trials. The current recommendation is that they are only used as rescue therapy for patients with ARDS or ALI with life-threatening hypoxaemia failing maximal conventional lung-protective ventilation.

Some of these include:

-Corticosteroids
-Prone Ventilation
-High Frequency Oscillatory Ventilation
-Airway Pressure Release Ventilation
-Nitric Oxide
-Extracorporeal Membrane Oxygenation

Corticosteroid Therapy

This topic has been covered in some depth by Dr Amod in her presentation -Steroids in ARDS. Since ARDS is caused by inflammatory injury to the lung, corticosteroids were thought to be useful as they inhibit cytokine synthesis, neutrophil activation and fibrogenesis.

This has been a controversial topic for some time with many conflicting reports in the literature. The largest RCT of corticosteroids in septic shock, the CORTICUS trial was published in 2008 and failed to show a benefit for steroid treatment in septic shock and ARDS. The trial has been criticized but there has been limited evidence otherwise to support the use of steroids. The literature has suggested that if steroid therapy is to be used, it should be commenced within 72hrs of the onset of ARDS at physiologic doses and for at least 7days as well as being tapered over at least 7 days to prevent rebound inflammation.

Prone Ventilation

Let’s think about mechanical ventilation: gas enters the lungs under positive pressure and takes the path of least resistance to the non-dependant areas of the lung that already have limited perfusion (remember West’s Zones). Mechanical ventilation thus augments the gravitational effects on blood flow

so that blood is increasingly distributed to the dependant lung which is receiving reduced ventilation – especially in the supine position. The dependant lung becomes progressively more atelectatic during mechanical ventilation but is well perfused resulting in an increasing shunt. The non-dependant lung becomes hyperinflated with reduced perfusion resulting in increasing physiological dead space. The zone of optimal V/Q matching is therefore reduced by mechanical ventilation and if ventilation is inappropriate, hypoxia or hypercarbia may result.

The prone position helps to limit V/Q mismatch as the large volume of lung tissue lying posteriorly in the chest (dependant in supine position) is able to expand more freely without the weight of mediastinal structures and abdominal contents compressing them thereby improving ventilation. Since the consolidation in ARDS is most severe in the dependant regions which have the best perfusion, improving ventilation in these regions reduces V/Q mismatching. It has also been found that perfusion remains prevalent in the posterior areas even in the prone position where they are no longer dependant.

Other potential physiologic benefits include:

- Improved respiratory mechanics – eg. improved FRC (reduced compression of lungs)
- Reduced and improved distribution of injurious mechanical forces.
- Improved mobilization of secretions

The literature has only been able to show that prone ventilation improves oxygenation but no study has shown that the prone position significantly reduces mortality.

Prone positioning also has its disadvantages, a study done by Geurin et al published in 2004 randomized 791 patients to supine or prone positioning for at least 8hrs a day and although it also demonstrated improved oxygenation without a survival benefit at 28 days, it revealed a significantly higher rate of adverse events in the prone group. These included bronchial intubation, endotracheal tube obstruction and pressure sores. Other documented adverse events include a higher rate of self-extubation and poor tolerance of enteral nutrition with more vomiting episodes and greater residual gastric volumes.

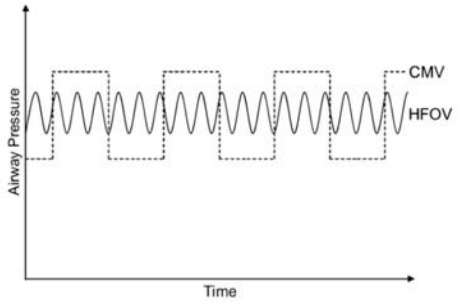
The criticism of this trial is that patients were only kept prone for 8 hours and were actually supine for the rest of the 24 hours which may have negated the benefits of proning. Further information is needed to determine

what duration and frequency of proning is most beneficial to reduce mortality. We also need to determine which group of patients respond to this treatment and how to effectively nurse patients who are in the prone position. It was suggested by Guerin in 2006 that patients who could benefit from prone positioning are those with the most severe ARDS and those with dorsal lung infiltrates.

High Frequency Ventilation (HFV)

There are three types of HFV – positive pressure, jet and oscillation. All of them use tidal volumes below that of anatomic dead space at high frequencies (up to 600 breaths per minute)

The physiologic benefits – reduced ventilator induced injury and less haemodynamic compromise have not been translated into improved survival rates in clinical trials. One of the concerns with HFV is the heavy sedation and frequent paralysis which patients require.



Pressure Time tracing for HFOV (solid line) as compared with Conventional Mechanical Ventilation (Dashed Line)

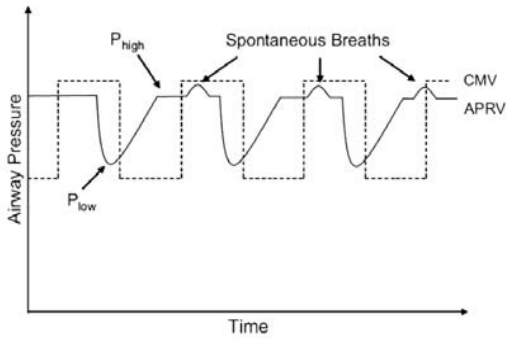
Airway Pressure Release Ventilation (APRV)

This is a mode of ventilation designed to allow patients to breathe spontaneously while receiving a continuous positive airway pressure with an intermittent pressure release phase lasting 0.4 -0.6 seconds every 4-6 seconds. A continuous airway pressure maintains adequate lung volumes and recruits alveoli while limiting barotrauma. Since ventilation results from the decrease in airway pressure, the risk of overdistension is minimized.

The patient is able to breathe spontaneously which enables diaphragmatic contractions, increasing the recruitment of atelectatic alveoli in the dependant juxtadiaphragmatic regions improving ventilation-perfusion

matching. Allowing patients to breath spontaneously may reduce the need for heavy sedation and paralysis.

The largest RCT by Varpula and colleagues compared APRV with synchronized intermittent ventilation with pressure control or pressure support in a single centre, the trial was terminated early for futility after recruiting 53 of 80 patients. Although inspiratory pressures were lower in the APRV group in the first week, there was no significant difference in ventilator free days or in mortality at 28days and at one year between the two groups.



Pressure-time tracing for APRV (solid line) as compared with Conventional Ventilation (dashed Line)

Extracorporeal Membrane Oxygenation (ECMO)

This provides both gas exchange and perfusion functions for patients with life-threatening ARDS and allows the lung to rest from mechanical ventilation. ECMO can be provided by veno-arterial or veno-veno bypass techniques, using artificial membranes to provide oxygen and remove carbon dioxide and extravascular fluid.

In adults, early studies showed no difference in outcome compared to conventional ventilation. More recently there has been some renewed interest but there is still no consensus regarding the use of ECMO in adults.

In children, its use has been supported by a multicentre (32 hospitals), retrospective cohort of 331 older children with respiratory failure despite ventilator support performed by the Paediatric Critical Care study group. The study showed a reduced mortality as a result of this disease from 47 to

26%. Therefore ECMO is a recognised form of treatment of life-threatening ARDS in children not responding to mechanical ventilation strategies.

Inhaled Nitric Oxide

Inhaled Nitric Oxide relaxes pulmonary vascular smooth muscle and reduces elevated pulmonary artery pressures. It improves arterial oxygenation by dilating vessels receiving better ventilation thereby improving matching of perfusion to ventilation. Again these physiologic benefits have not meant improvement in mortality. There is also significant rebound in pulmonary pressures after withdrawal of NO. The routine use of Nitric oxide in adults is not recommended however clinicians may still consider its use for life threatening hypoxaemia in conjunction with other supportive therapies but there is currently no evidence to support its use here either. The major place for its use is in neonatal ICU for treatment of pulmonary hypertension pre- and post-operatively in neonates with complex congenital cardiac lesions.

Conclusion

As I've mentioned before, mortality in patients with ARDS is still very high and has not fallen since 1994. This has been attributed to several possibilities, one possibility is that ARDS is defined as a broad syndrome and perhaps treatments need to be tailored to be subgroups of patients and tested. The other possibility is that effective therapies do exist (eg.lung-protective ventilation) but are not consistently implemented in all treatment facilities. In fact studies have shown that lung-protective strategies are often not employed even at hospitals that were involved in the ARDSNet study.

One of these studies entitled "Underuse of Lung Protective Ventilation: Analysis of potential factors to explain physician behaviour" by Kalhan et al in 2006 showed that physicians tended to reserve protective ventilation for patients with severe ARDS. This may be because of fears of the side effects of low tidal ventilation resulting in reluctance to use this strategy on less sick patients.

With the lack of conclusive evidence to support the many proposed pharmacological therapies, mechanical ventilation still remains the mainstay of therapy and the field in which most progress has been made over the years since ARDS was first described.

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