The Newcastle upon Tyne Hospitals NHS Foundation Trust

Ventilation in Acute Respiratory Distress Syndrome (ARDS)

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1 Introduction

According to the Berlin Definition 'ARDS is a type of acute diffuse, inflammatory lung injury leading to increased pulmonary vascular permeability, increased lung weight, and loss of aerated lung tissue. The clinical hallmarks are hypoxemia and bilateral radiographic opacities, associated with increased venous admixture, increased physiological dead space, and decreased lung compliance.'[1]

2 Guideline scope

This document is an aide-memoire for management of patients with acute respiratory distress syndrome (ARDS). ARDS is a complex multifactorial disease process unsuitable for protocolised management. The following issues are discussed to augment clinical decision-making and aide management on a case by case basis.

3 Main Body of the guideline

3.1 Definition

The respiratory distress syndrome was first described in adult patients in the Lancet in 1967. There was recognition that the constellation of symptoms and signs associated with this condition result in a high mortality and a unifying diagnostic criterion was required. The condition was coined ARDS and a consensus definition was produced in 1994 and then further updated in 2012 with the Berlin definition.[1,2]

The diagnostic requirements for ARDS are:

1. Respiratory failure not fully explained by cardiac failure or fluid overload

2. Bilateral opacities on chest x-ray or CT imaging

3. Onset within 7 days of precipitant (table1) or new worsening symptoms

4. Minimum Positive End Expiratory Pressure (PEEP) of 5 cm H20 (delivered either noninvasively or invasively_

5. Impaired Oxygenation Pa02/Fi02 <300 mm Hg (<40kPa)

Severity of ARDS

Divided into Mild, Moderate and Severe ARDS based on the ratio of arterial blood partial pressure of oxygen (PaO_2) to the fraction inspired oxygen ($Fi0_2$) breathed by the patient: The P/F ratio or $Pa0_2/Fi0_2$ ratio.

- Mild $Pa0_2/Fi0_2$ 200 - 300 mm Hg (or 26.67-40kPa)
- Moderate $Pa0_2/Fi0_2$ 100 - 200 mm Hg (or 13.3-26.67kPa)
- Severe $Pa0_2/Fi0_2$ <100 mm Hg (or<13.3kPa)

Patient mortality and the duration of mechanical ventilation increases with the severity of ARDS from mild to moderate to severe disease. However, the Berlin definition of ARDS is not designed to be used for prognostication.

Table 1: Causes of ARDS [2]

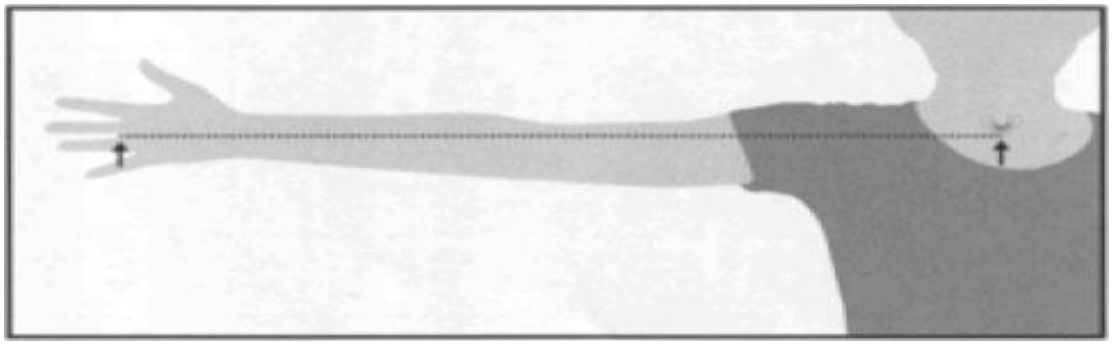
Pulmonary ARDS	**Extra- pulmonary ARDS**
Pneumonia • Viral • Bacterial • Fungal • Aspiration	Sepsis
Inhalational injury • Chemical • Burn • Drowning	Burns
Smoking	Pancreatitis
Non protective ventilation	Drug reaction
Chest trauma/contusion	Trauma
Thoracic surgery	Cardio pulmonary bypass
Vasculitis	Blood transfusion
Fat embolism	Non cardiogenic shock

3.2 General Respiratory Management

The general principles of ARDS ventilator management are to provide adequate oxygenation and ventilation whist avoiding the deleterious effects of invasive mechanical ventilation causing further ventilator induced lung injury. Mechanisms of

damage include volutrauma, barotrauma, alectetrauma, oxygen toxicity and biotrauma. The ARDSnet study published in 2000 showed that low tidal volume ventilation of 6ml/kg predicted body weight, plateau pressure <30 cmH20, tolerance of hypercapnia and the use of PEEP improved mortality in ARDS. This remains the most effective evidence based strategy in the management of ARDS patients.[3] Different ventilator modes have been tried in ARDS including oscillatory ventilation with mixed/negative results, but in general there is limited strong evidence to guide one mode over another and choice should be guided by clinical experience and emerging evidence.

3.3 Calculation of Tidal Volumes by Measurement of Demispan



The demispan of any patient likely to be ventilated for longer than 6 hours should be measured and documented on the bedside chart.

This allows for calculation of predicted ideal body weight using either the formulae below or the charts overleaf.

Male = [height in cm-152.4] x 0.91 + 50

Female = [height in cm-152.4] x 0.91 + 45.5

Females

Demispan(cm)	Height(cm)	Ideal Body Weight(kg)	**6ml/kg**	8ml/kg
60	141	35	**211**	282
62	144	38	**226**	301
64	147	40	**241**	321
66	149	43	**256**	341
68	152	45	**270**	360
70	155	48	**285**	380
72	157	50	**300**	400
74	160	52	**314**	419
76	163	55	**329**	439
78	165	57	**343**	459
80	168	60	**359**	478
82	171	62	**373**	498
84	174	65	**388**	518
86	176	67	**403**	537
88	179	70	**418**	557
90	182	72	**432**	577

Males

Demispan(cm)	Height(cm)	Ideal Body Weight(kg)	**6ml/kg**	8ml/kg
70	156	53	**319**	425
72	159	56	**334**	445
74	161	58	**349**	466
76	164	61	**364**	486
78	167	63	**380**	506
80	170	66	**395**	527
82	173	68	**410**	547
84	175	71	**426**	567
86	179	73	**441**	588
88	181	76	**456**	608
90	184	79	**471**	629
92	187	81	**487**	649
94	190	84	**502**	669
96	192	86	**517**	690
98	195	89	**533**	710
100	198	91	**548**	731

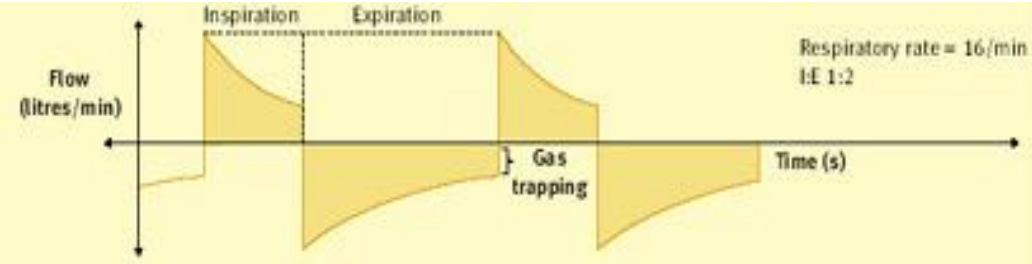
3.4 Pressure Control versus Volume Control Ventilation (PCV v VCV)

PCV offers the advantage of a decelerating flow pattern, potential improved patient-ventilator synchrony and avoidance of high transpulmonary pressures with changes in compliance. The aim is to limit peak & plateau inflation pressures to 35 & 30cm/H_20 if possible and to deliver tidal volumes of 6ml/kg ideal body weight.

Volume controlled ventilation allows easier control of tidal volumes but less control over pressures. In practice, tidal volume limited pressure control ventilatory modes are becoming more available. There is no evidence that one mode offers a survival advantage over another, the key is maintaining the appropriate low tidal volumes and plateau pressures. [4]

3.5 Inverse Ratio Ventilation (I:E ratio > 1:1)

Usually, when setting the frequency or inspiratory time (Tinsp), the I:E ratio should be 1:2 to eliminate the possibility of gas trapping (see below).



In inverse ratio ventilation, the effect of a prolonged inspiratory time is to increase mean intrathoracic pressure for a given level of PEEP and peak inflation pressure. In theory this this allows more time for lung units with long time constants to fill and may recruit alveoli, improving oxygenation. The risk of this strategy is gas trapping with associated haemodynamic instability and alveolar distension. [4] PEEP may deliver similar effects with less risk of dynamic hyperinflation, although there is no evidence of different clinical outcomes.

3.6 Prone Ventilation

Prone positioning has been used in ARDS for many years to improve oxygenation, this improvement in oxygenation had not translated into a survival benefit in early trials. More recently, the PROSEVA Study Group published a trial in 2013 of 466 patients with severe ARDS on an $Fi0_2$ of greater than 60%. This trial compared proning for at least 16 hours a day compared to standard care. There was a significant reduction in mortality in the proning group with no difference in complication rates relating to proning itself between the two groups.[5] Of note the trial was performed predominantly in French ICUs who used proning regularly for 5 years prior to the trial and hence may have additional experience that had a positive impact on the trial.

Proning is an accepted technique, which according to recent epidemiological data is underused, that has been shown to have a survival benefit in severe ARDS.[5] It should be considered when patient fulfil the criteria e.g. Severe ARDS ($Pa0_2$:$Fi0_2$ ratio of <150 mm Hg with an $Fi0_2$ of ≥0.6) with at least a PEEP of 5 cm of water, and

optimised tidal volumes of approximately 6 ml per kilogram of predicted body weight. If referring the patient for ECMO due to hypoxia it is likely they will ask if a trial of proning has been considered. See prone ventilation NUTH guideline for more details on this topic.

3.7 Sedation and Neuromuscular paralysis

This can reduce work of breathing and metabolic demands, and may be required to facilitate prone ventilation, although neuromuscular paralysis is not essential (see guideline number 1.10). The ACURASYS trial published in 2010 compared 48 hours of neuromuscular blockade using cisatracurium versus placebo in patients with early serve ARDS with a Pa02/Fi02 ratio of less than 150 mm Hg. The 90-day adjusted mortality was lower with neuromuscular blockade and this group also had an increase in ventilator free days. It also confirmed no increase in ICU acquired muscle weakness in the cisatracurium group. However, the trial was small and there was no difference in crude mortality data, only adjusted mortality. In summary, this trial showed that neuromuscular blockade in this context is safe and could be beneficial within the first 48 hours during severe ARDS.[6]

3.8 Fluid Balance

A high positive fluid balance is associated with poor outcomes including increased mortality in ARDS. It is unclear if this reflects sicker patients receiving more fluid, or more fluid causing poorer outcomes. Achieving the best oxygen delivery with least amount of fluid and vasoactive drugs may be a better strategy than liberal fluid resuscitation without vasoactives. As patients gain hemodynamic stability diuretics or Heamofiltration may be used to achieve a sensible fluid balance.

3.9 Positive End Expiratory Pressure (PEEP)

As a general guide, PEEP is generally altered according to the adequacy of the oxygenation of the patient (see table below). This may be changed according to individual patient requirements.

FiO2 (%)	PEEP (cmH2O)
30	5
40	5 to 8
50	8 to 10
60	10
70	10 to 14
80	14
90	14 to 18
100	18 to 24

3.10 Lung Recruitment Strategies

There is no firm evidence base to “prove” the benefit of any single strategy, or even that recruitment manoeuvres (RM) produce anything more than a transient improvement in oxygenation. Late (fibroproliferative) ARDS or consolidated (e.g. pneumonic) lung is less likely to respond to RM than early ARDS, but no pre-recruitment measurements accurately predict an individual response to RM. A recent RCT published in JAMA in 2017 compared lung recruitment manoeuvre and PEEP titration according to the best respiratory-system compliance versus low PEEP in 1000 patients with moderate to severe ARDS. The intervention group with RM had a higher 6-month mortality and an increased risk of haemodynamic instability, barotrauma and pneumothorax requiring drainage.[7] Considering this new evidence careful thought should be given to the use of recruitment manoeuvres. In general, preventing derecruitment of expanded lung may be more beneficial than overexpansion of alveoli.

The following are general principles of recruitment manoeuvres

1: *Target oxygenation goals for ARDS*

Typically, an adequate response to RM is defined as an increase in $Pa0_2$ of > 15% above initial values, although alterations in combined cardiovascular and respiratory function is a more meaningful measure of response in practice.

Generally aim for PaO2 7.5-10.5kPa (or $Sp0_2$ >88%-90%). Aim to keep $Fi0_2$ below 0.6 if possible.

2: *Recruit available lung (collapsed alveoli)*

Appropriately experienced medical staff should supervise these manoeuvres.

If the patient remains cardiovascularly stable, there are various options for recruitment manoeuvres. Examples are:

- Increase CPAP or PEEP to 15-20cm/H_20, and increase peak inflation pressure to 45cm/ H20. Maintain these settings for 3-5 minutes, then reduce ventilation parameters to initial peak values & increased PEEP.

- An inspiratory pause of ~ 40 seconds with a CPAP level of 40cm/ H_20

- Raise PEEP by 20cm/ H_20 over current level, with Peak inflation pressure a further 20 cm/ H_20 above this for 2 minutes.

Typically, after a RM, PEEP is left higher than pre-RM values, with Peak pressure set according to tidal volumes.

Ensure adequate volume resuscitation for recruitment manoeuvres. (hypovolaemic patients may become very hypotensive with high intrathoracic pressures). Vasoactive drugs may need to be increased during this manoeuvre.

Manual hyperinflation e.g. disconnection from the ventilator and use of hand ventilation via a c-circuit is not routinely indicated. It can generate high airway

pressures (up to 70-80 cm/ H20) and high tidal volumes. Disconnecting the ventilator circuit for manual hyperinflation will cause rapid alveolar collapse due to loss of PEEP. Occasionally, manual hyperinflation may be useful for physiotherapy/secretion management. Discuss with senior staff before use.

3: *Retain recruited lung and reduce ongoing damage*

Maintain high PEEP levels (15-20cm/H_20) and use low tidal volume ventilation (6ml/kg ideal body weight- see table 2). If high peak pressures (>35cm/H_20) are required to achieve these tidal volumes, consider reduction to 4ml/kg tidal volume. There is no strong current evidence that PEEP levels of 10-15cm/H_2O result in different outcomes compared to lower PEEP. Several strategies for determining optimal PEEP have been described, none have been proven to be superior. These include using PEEP tables targeting oxygenation, using incremental PEEP targeting plateau pressure or using decremental PEEP post recruitment manoeuvres. [4]

Notes: raising CPAP/PEEP above 10cm/H_20 will recruit much of collapsed lung. Further stepwise recruitment continues in some individuals even up to PEEP values of 50cm/H_20. However, PEEP levels greater than 20 cm/ H_20 should be discussed with senior medical staff.

4: *Permissive Hypercapnia*

A respiratory acidosis due to a high $PaC0_2$ (permissive hypercapnia) is likely to develop and may in fact be beneficial. This is usually acceptable unless there are specific contraindications such as raised intracranial pressure, if so the balance of risks and benefits of treatment goals must be considered and discussion with a senior clinician is mandatory. A pH above 7.15 is unlikely to cause problems. Use 8.4% bicarbonate solution to keep pH above 7.15 if required. A respiratory rate of up to 35bpm may also be needed to maintain adequate minute volumes, although dangerous amounts of gas trapping and dynamic hyperinflation may become significant at higher respiratory rates.

3.11 Non Invasive Ventilation

Patients with hypoxaemic respiratory failure receive less benefit from NIV than those with hypercapnic respiratory failure. NIV has a limited role to play in the management of ALI/ARDS.

3.12 Other treatments

Inhaled nitric oxide and corticosteroids have been used for patients with ARDS. Initiation of those therapies should only occur after discussion with an Intensive Care Consultant.

High frequency oscillation is no longer recommended in adult patients but is still used in the paediatric population.

3.13 Extracorporeal membrane oxygenation (ECMO)

Veno-venous ECMO has increasingly been used in the management of acute reversible severe ARDS. This has been informed by the CESAR trial and the experience of treating H1N1 influenza in New Zealand and Australia in 2009. The benefit of ECMO is that oxygenation can be provided when the lungs fail preventing hypoxic brain and organ injury whilst also affording the lungs rest, utilising low tidal volumes, potentially allowing recovery to take place. ECMO should be considered in patients with a $Pa0_2$:$Fi0_2$ ratio of < 100mmHg (<13.3kPa), pH <7.2 and a Murray (lung injury) score over 3 (see table 4). ECMO services in the UK tend to follow the inclusion and exclusion criteria used in the CESAR trial protocol and outlined in table 3. Other exclusion criteria suggested include; advanced cancer, ARDS secondary to bone marrow transplant and pulmonary fibrosis. [9]

The CESAR Trial published in 2009 randomised 180 patients with severe but reversible ARDS to ECMO vs conventional ventilation. The inclusion criteria and exclusion criteria are found in the table below. The patients who were randomised to receive ECMO and who received care in an ECMO centre had improved 6-month survival without disability. It is important to note that 20% of the patients who arrived at the ECMO centre did not actually receive ECMO but instead conventional ventilation. Conventional ventilation was not protocolised and thus may not have been strictly adhered to, but broadly included protective ventilatory strategies, proning, diuresis and supportive care. These results suggest that ECMO is an important treatment option for refractory acute severe ARDS, however the benefit seen may reflect expert clinical management in an ECMO centre rather than simply ECMO itself. [8]

Table 3: The CESAR Trial Inclusion Criteria

Patient Inclusion Criteria	**Patient Exclusion Criteria**
Adult patients (18-65 years)	Duration of high pressure and/or high FiO2 ventilation >7 days
Severe, but potentially reversible, respiratory failure	Intra-cranial bleeding
Murray score ≥ 3.0, or uncompensated hypercapnoea with a pH <7.20	Any other contra-indication to limited heparinisation
	Patients who are moribund and have any contra-indication to continuation of active treatment

Murray score

The Murray score is a lung injury score developed in 1988 as part of an expanded definition of ARDS prior to the Berlin Definition. This scoring system utilises four variables, each variable is given a score between 0 and 4, and the total score of all the variables is divided by four to give a lung injury score (see table 4). The lung injury score or 'Murray Score' can be used as one of several clinical factors to guide when patients should be discussed with an ECMO centre if appropriate. A Murray score of 1 -2.5 suggests moderate lung injury, a score >2.5 suggests severe lung injury. [2]

A Murray score above 3 was used in the CESAR trial as an inclusion criteria for accepting adult patients with ARDS for veno-venous Extra Corporeal Membrane Oxygenation (vvECMO). Leicester Hospitals who co-ordinate the national ECMO service for ARDS via Glenfield hospital quote the CESAR trial criteria as their criteria for ECMO. However, early referral is recommended before a patient reaches a Murray score of 3 in those expected to continue to deteriorate.

Table 4: Murray Score Calculation

	0	**1**	**2**	**3**	**4**
PEEP cm/H_2O	5	6-8	9-11	12-14	15+
CXR (number of affected quadrants)	0	1	2	3	4
Compliance ml/cm/H_2O	>80	60-79	40-59	20-39	<20
PaO_2/FiO_2 ratio (mmHg and kPa)	>300mm Hg >40kPa	225-299 mmHg 30-40kPa	175-224 mmHg 23.2-30kPa	100-174 mmHg 30-23.2kPa	<100 mmHg <13.3kPa

To Calculate the Murray Score add up the points for each aspect (PEEP, CXR, compliance and PaO_2/FiO_2 ratio), then divide by four.

ECMO referral via Leicester Hospitals

- A dedicated phone line with call conferencing facility for all Adult ECMO referrals has been set up.
- Most calls will be answered within 30 seconds by trained call handling staff.
- Call 0300 300 3200 to contact the Leicester ECMO Team for immediate advice & support.
- To inform them of the suitability for ECMO they will request information such as; demographics; clinical status; physiological parameters; ventilator settings; height and weight; biochemical/laboratory results; microbiology; radiology and echo findings; drugs; present and past medical history; baseline level of function; and social history including smoking and alcohol.
- Leicester ECMO Team provide a retrieval service where they will put the patient on ECMO at the referring hospital and then transfer them back to Leicester.
- If Leicester do not have an ECMO bed available they will co-ordinate an available bed in the country where possible.
- Despite the Freeman Hospital in Newcastle Trust providing ECMO for cardiac and transplant patients they are not funded to provide vvECMO for patients with primary respiratory failure.

4 Training, Implementation, Resource Implications

This document aims to support the standard training processes in place across the critical care units in NUTH with regards to invasive ventilation in patients with ARDS.

5 Monitoring Section

This document contains standards which staff can use to audit processes against.

6 Evidence Review and Evaluation

A literature search was performed and discussion occurred amongst senior ICM clinicians from the RVI and FRH Critical Care Units in compiling this document.

7 References

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