Management of hypoxia in Acute Respiratory Distress Syndrome (ARDS)

1.Purpose of guideline	1) To guide an escalation in therapy to patients with severe ARDS 2) To ensure oxygenation is optimized whilst minimizing lung injury
2. Responsibility	All medical and nursing staff providing care and treatment for patients with ARDS in DCCM
3. Guideline management principles and goals	The principle of this document is to minimize lung injury, optimize oxygenation, and maximize survival in patients who are mechanically ventilated for ARDS. As there is a broad spectrum of severity in this syndrome, a step-wise escalation in therapy, based on best evidence and the standard practice of the DCCM, will be presented.

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4. Diagnostic criteria

ARDS is a clinical diagnosis of exclusion. Differential diagnosis includes bilateral pneumonia (although ARDS can be triggered by this), cardiac pulmonary oedema, diffuse alveolar haemorrhage, inflammatory and autoimmune lung diseases. It is often the consequence of a triggering event, such as pneumonia, sepsis, trauma, pancreatitis, shock, transfusion related, and drug toxicity.

ARDS is defined based on the Berlin criteria, which is the international consensus for the diagnosis of ARDS and includes the following:

- Acute onset of symptoms, defined as within 7 days.
- Bilateral opacities on either chest x-ray or CT-scan.
- Not fully explained by cardiac failure, fluid overload. Having heart failure does not preclude the diagnosis per se.

The severity of ARDS is determined by the PaO2/FiO2 ratio as follows:

ARDS severity	**PaO2/FiO2**
Mild	26.7-40kPa
Moderate	13.3-26.6kPa
Severe	<13.3kPa
CPAP or PEEP ≥ 5mmH2O	

For guidance, a SpO2 of 90% is commonly correlated with a PaO2 of 8Kpa, which is the equivalent of 60mmHg.

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6. Process of Treatment

A) Diagnosis and treatment of underlying pathology	ARDS is commonly triggered by an underlying event, some of which can be treated (e.g. infection), or need to be managed (e.g. trauma). These need to identified and treated specifically.

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B) Commencing respiratory therapy

General resuscitation should be applied to all critically ill patients. This section will look at specific therapies in the management of ARDS.

In the awake patient with respiratory failure, high flow nasal prongs (HFNP) can be used in the first instance for the delivery of up to FiO2 of 1 and flow of 50L/min. Initial studies suggest that this may reduce intubation rates, with no suggestion of harm

Noninvasive ventilation

Noninvasive Ventilation is not recommended for ARDS as it is associated with high failure rate and possibly increased mortality rate. It should only be considered for patients where intubation is not appropriate due to treatment limitation or there is a specific indication, such as cardiogenic pulmonary oedema, OSA.

Intubation and ventilation

If appropriate for the patient, Intubation and ventilation should be considered if FiO2 >0.6, respiratory acidosis with pH <7.3, RR>40, persistent high respiratory muscle workload, aiming for SpO2 of ≥ 92%. Intubation should also be considered if the patient is deteriorating rapidly despite not meeting the above criteria.

The ventilation of the patient is based on the ARDSnet ventilator settings.

Recommended standard target parameters after intubation

Aim for SpO2 88-92%, permissive hypercapnia aiming for a pH>7.2-7.3 (once metabolic acidosis is accounted for).

Recommended ventilator settings

The default mode of ventilation is SIMV PRVC.

Vt of 6-8ml/kg of ideal body weight (IBW)

IBW male= 50kg + [0.91 x (height in cm – 152.4)]
IBW female= 45.5kg + [0.91 x (height in cm – 152.4)]

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IBW calculation guide

Height (cm)	Male IBW	Female IBW
150	48	43
160	57	52
170	66	62
180	75	71

PEEP of 10-15cmH2O Discuss with SMO if >15cmH2O required
RR <35
I:E ratio of 1:1-2
Plateau pressure (Pplat) <30cmH2O
Peak inspiratory pressure (PIP) < 30cmH2O if SIMV PRVC, <35cmH2O if SIMV VC mode

Sedation and muscle relaxation

Recommended regimen:

Propofol 200mg/hr
Diazepam 20mg loading dose, followed by 10mg q4-6h while paralysed
Vecuronium 4-8mg/hr for up to 48hrs
Morphine 5-10mg/hr or
Fentanyl 50-100mcg/hr

Deep sedation and muscle relaxants are likely to be required for the initial management of ARDS to ensure ventilator synchrony and lung protection. Cases of awareness have occurred in DCCM in this patient group and therefore Diazepam should be used when they are paralyzed. Muscle relaxation has been demonstrated to be safe for up to 48hrs in the treatment of ARDS, however prolonged use may result in critical illness myopathy and therefore use beyond 48hrs requires ongoing review and consideration of the risks and benefits.

Fluid therapy

In this group of patients, it is important to avoid fluid and sodium overload. While fluid resuscitation may be required for the acute phase in some pathologies that cause ARDS e.g. septic shock, trauma, fluid given should be judicious. Once the acute phase is over, fluid removal through ultrafiltration or diuretics should be considered to remove excessive sodium given during the acute phase to optimize oxygenation.

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When to call the duty SMO

Asking for help depends on your level of experience and competency. The following are situations where discussion with the SMO should be considered (note that the list is not exhaustive):

1. Where the registrar or senior nurse is concerned and would like SMO input **AT ANY POINT**
2. Where intubation of the patient is required or thought to be required
3. Where there is a deterioration of FiO2 requirement ≥ 0.2 to maintain target SpO2
4. Where nitric oxide, prone positioning or ECMO is thought to be required

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C) Refractory respiratory failure

Ongoing hypoxia despite optimized ventilator settings and sedation will require additional strategies. Escalation of therapy should be considered once the patient ventilation meets the criteria for severe ARDS. Using the recommended SpO2 target of 88-92%, the FiO2 required which is suggestive of severe ARDS is around 0.6-0.7. The next line of therapy is nitric oxide and this is usually used in conjunction with the prone position.

Inhaled Nitric oxide

Inhaled nitric oxide is an option that is used to improve oxygenation. While there is no evidence that this therapy improves mortality or duration of mechanical ventilation, it can give transient modest improvements to oxygenation. The risk is that of methaemoglobinaemia, haemorrhage and renal failure, but this occurs relatively rarely. The use of the nitric oxide must be used with the **Servo I** ventilator to allow for scavenging. The use of nitric oxide is at the discretion of specialists and the dose is around 10ppm. This can be roughly calculated by the flow of Nitric oxide divided by the minute volume. Currently, there is no method of nitric oxide dose monitoring within DCCM.

Prone position

Putting patients in the prone position with severe ARDS have shown to increase survival. In the DCCM, patients are put in the prone position for 8 hours, followed by 4 hours of rest in the supine position to achieve a total of 16 hours in prone position in a 24 hour period, balanced by regular rest period. A benzodiazepine should be part of the sedation regimen.

Relative contraindications to the prone position: body habitus, abdominal compartment syndrome, high ICP and facial trauma and surgery.

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Extracorporeal Membrane Oxygenation (ECMO)

The following is from CVICU ECMO guidelines, and can be found on the following link: https://static1.squarespace.com/static/5796f6f1725e2587d1b820e6/t/5c082a72cd83666ef1a822e0/1544039029716/CVICU+Indications+and+contraindications+for+ECMO.pdf

The role of ECMO in severe ARDS is that of a rescue therapy, when conventional mechanical ventilation fails. If the patient has a reversible condition and:

1) Refractory hypoxia with PaO2/FIO2 < 60-80 mmHg (< 8-11 kPa) despite maximum ventilatory support (PIP 30-35 cm H2O, PEEP 10-20 cm H2O) and non-ventilatory strategies (i.e., diuresis, prone ventilation, recruitment maneuvers, inhaled nitric oxide) to improve gas exchange, or
2) Refractory hypercapnia with PaCO2 > 80-100 mmHg (> 11-15 kPa) despite maximum ventilatory support (PIP ≥ 35 cm H2O, Pplateau ≥ 30 cm H2O, RR > 20).

Factors to consider

It may be appropriate to tolerate worse gas exchange if the patient has only been recently intubated and ventilated (e.g., < 12 hours).
It may be appropriate for patients with less severely impaired gas exchange to be considered for ECMO if they have been ventilated for a longer period (e.g., > 3 days) and have not responded.
Patients who are clearly deteriorating may be considered for ECMO despite less severely impaired gas exchange.

Contraindications
There are no absolute contraindications to ECMO for respiratory failure except irreversible lung disease (bridging to lung transplantation is not provided as a treatment option in New Zealand), and each patient must be considered on a case by case basis. The following are relative contraindications:
Prolonged mechanical ventilation (> 7 days) at high ventilatory pressures (PIP > 35 cm H2O) and/or high FIO2 (> 0.8)
Age > 65 years
Weight > 125 kg

- Chronic organ dysfunction. Conditions to consider include: renal failure, neurological dysfunction, chronic pulmonary disease, chronic cardiac disease, malignancy, and cirrhosis
- Severe septic shock with evidence of severely impaired tissue perfusion (e.g., cold mottled limbs, severe metabolic acidosis)
- Progressive disease inflammatory or autoimmune conditions

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Recommended stepwise escalation of therapy for hypoxaemia

Step	Action
1.	If spontaneously ventilating, use high flow nasal prongs
2.	Intubate and ventilate. Maintain paralysis for up to 2-3 days and diazepam as part of sedation plan. Consider NIV if there is limitation of therapy.
3.	Ventilator settings as per ARDSnet. Up titrated PEEP as tolerated up to 15cmH2O.
4.	Start nitric oxide after discussion with the duty Intensivist.
5.	Prone if FiO2 around 0.6-0.7 despite above optimization.
6.	Discuss with CVICU consultant on for consideration of ECMO by the duty Intensivist if failure of prone position, FiO2 >0.7
7.	At all points of deterioration: Rule out immediate reversible causes such as pneumothorax, mucus plugging

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Recommended stepwise de-escalation of therapies

Step	Action
1.	Wean nitric oxide if FiO2 is 0.5 by halving the flow. If FiO2 ≤ 0.6 after 1hr, stop nitric oxide.
2.	Stop proning the patient once the patient requires FiO2 of 0.4-0.5 while supine for at least 4hrs to achieve target parameters and nitric oxide is stopped.
3.	Stop muscle relaxation if consistently requiring FiO2 0.4-0.5 while supine
4.	Wean sedation once PEEP requirement ≤10cmH2O
5.	Consideration of a tracheostomy and wean as per weaning protocol. Removal of excessive sodium and fluid with diuretics or ultrafiltration.

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Appendix (for reference only)

ARDSnet PEEP increment recommendations, for reference for SMOs, **NOT TO FOLLOWED** as a routine.

Lower PEEP/higher FIO2

FiO2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO2

FiO2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

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