

Supplemental Material

Appendix 1

Apnoea Testing on veno-arterial extracorporeal membrane oxygenation (ECMO)

Protocol (See Figure 2)

Preconditions

- Ensure pre-conditions are satisfied for clinical brain death testing
 - Consider neuromuscular stimulation
 - Consider opiate and benzodiazepine reversal agents
 - Consider high spinal injury

Other brain stem reflexes

- Complete other brain stem reflexes according to Australian and New Zealand Intensive Care Society (ANZICS) guideline

Baseline oxygenation and circuit setting titration

- Check baseline arterial blood gas (from right radial artery if peripheral VA-ECMO) to ensure patient oxygen saturations (SaO_2) $\geq 88\%$ and document baseline pH and partial pressure of carbon dioxide (PaCO_2). If PaCO_2 is chronically elevated, then calculate maximum target by adding on 20mmHg.

Patient oxygenation and ventilator monitoring for apnoea test

- Administer continuous flow of oxygen via a bag valve mask (BVM). Attach an end tidal carbon dioxide (ETCO_2) monitor and positive end expiratory valve (PEEP valve), set at 10 cmH₂O
- Include a capnometer in the circuit to detect ventilatory waveform
- Dedicate a staff member to observe and report ventilator effort with patient torso exposed

Commence apnoea test (reduce clearance of PaCO_2)

- Set inspired oxygen on fresh gas flow (FGF) to 1.0
- Reduce FGF by 50% (caution if FGF: ECMO flow < 0.5)
- Continuously observe for patient desaturation

- Monitor for signs of patient ventilatory effort

Ensure safe circuit oxygenation and adequate hypercapnia

- Measure arterial blood gas from post-oxygenator blood returning to the patient to ensure $\text{SaO}_2 \geq 88\%$; if not, titrate FGF upwards until this target is met. (*ensure adequate circuit oxygenation*)
 - If $\text{SaO}_2 < 88\%$, increase FGF to the lowest value that achieves the desired patient oxygen saturation
- Measure patient's arterial blood gas via the right arm to ensure $\text{SaO}_2 \geq 88\%$ (*adequate upper body perfusion*)
 - If $\text{SaO}_2 < 88\%$ despite up titration in FGF,
 - Consider increase in PEEP
 - Consider increasing ECMO blood flow to improve oxygen delivery (beware of access insufficiency)
 - Consider 1-2 rescue (lung) breaths

Ensure adequate PaCO_2 for test completion

- Continue to observe for signs of patient ventilatory effort
- Check post-oxygenator gas to ensure $\text{PaCO}_2 > 60\text{mmHg}$
- Recheck patient's arterial blood gas after **five (5) minutes** or earlier if haemodynamic instability or desaturation $<88\%$ occur.
 - If PaCO_2 has not risen adequately, either wait longer if PaCO_2 beginning to rise or reduce FGF further (small decrements if $\text{FGF:ECMO blood flow} < 0.5$)
 - Repeat post-oxygenator (VA-ECMO) immediately then patient arterial blood gases after two minutes on new settings
 - Consider reducing FGF settings in increments of 10%. For each FGF changes, check post-oxygenator gas immediately to ensure adequate oxygenation and then check arterial blood gases at 2 minutes.

Note: FGF should NOT be reduced below 10% of ECMO blood flow – this may result in low saturations in post-oxygenator blood

Endpoints for apnoea testing

1. Patient's blood gas and post-oxygenator gas show a rise in PaCO₂ >60mmHg (or 20% increase from baseline) with fall in pH < 7.30 :
Consistent with brain death
2. Development of hypoxia (arterial) and inadequate rise in PaCO₂ with FGF at minimum flow tolerated by patient: **apnoea testing is not possible**
3. Haemodynamic instability (mean arterial pressure [MAP] < 60 mmHg) that is unsupportable with inotropes: **apnoea testing is not possible**
4. Respiratory effort noted: **not brain dead**