Organ donor management

For any potential organ donor, active management can dramatically increase the chances of successful donation of all of their organs and helps to maximise the graft function and survival.

The physiological changes following brain stem death can result in cardiovascular instability and a multiple organ dysfunction syndrome. This can be prevented and treated thus maximising the number of organs that can be retrieved from an individual, each of which should go on to dramatically improve the life of a recipient. It has been said that following brain stem death, you are no longer treating the donor but instead are treating multiple recipients.

For the purposes of these guidelines, it will be assumed that brainstem death has been confirmed and that consent for all suitable organs to be donated has been given. The donor should be actively managed based on the initial assumption that they will be able to donate their heart, lungs, kidneys, liver and possibly additional organs. All of the four major organs require assessment for suitability, whilst simultaneously, optimal perfusion is maintained together with minimal iatrogenic injury. This latter aspect extends to the pre-emptive minimisation of the injury induced by ex-vivo cold ischaemia.

In the management of an organ donor antagonistic and competing interests may develop, most frequently with regard to the administration of intravenous fluids or high doses of vasoactive drugs. For example, optimising renal perfusion may require administration of fluids, and yet the same fluid bolus may increase extravascular lung water and diminish gas exchange. Consequently, cardiac output monitoring should be initiated (if not already in place) and an early assessment of lung donor suitability should be made, as in cases where the lungs are clearly unsuitable, a more liberal fluid balance strategy may be appropriate.

The following references may be helpful:

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Wood, K. E. and J. McCartney (2007). "Management of the potential organ donor." Transplantation Reviews 21(4): 204-218. http://www.sciencedirect.com/science/article/B75B4-4PV1MCN-9/2/1edbb52213982172b7d4ee999909df4d

Van Raemdonck, D., A. Neyrinck, et al. (2009). "Lung Donor Selection and Management." Proc Am Thorac Soc 6(1): 28-38. http://pats.atsjournals.org/cgi/content/abstract/6/1/28

Initial checklist of monitoring, physiological targets and investigations

	Parameter	Method / rationale and notes
Airway	Check endotracheal / tracheostomy tube is patent ☐	If available check for normal inspiratory and expiratory flow profiles on ventilator
	The distal tip of the tube is located in the lower trachea ☐	Recent CXR. If not available then request a new CXR. Have the film reviewed by a senior clinician for any new lung infiltrates and any other abnormalities / diagnoses.
	Cuff pressure is ~30cmH_2O ☐	Cuff pressure manometer. Cuff leaks result in lung de-recruitment and increase the risk of passive aspiration. High pressures cause local mucosal injury.
	Check for proximal endotracheal secretions ☐	Collect any secretions present and send for urgent microscopy with gram stain. Request culture and sensitivities. **Consider** antibiotics. If secretions are viscous / difficult to suction **consider** nebulising hypertonic saline (5%-7%) [1] / bronchoscopy.
Breathing	Perform recruitment manoeuvre on the ventilator ☐ and set PEEP at a level to retain the recruited lung ☐. E.g. an inspiratory hold at 35cmH_2O for 60-90 secs with PEEP set in the range 5-10cmH_2O. If recruitment has been successful then there should be an increase in the expiratory tidal volume for the same inspiratory pressure set (or a decrease in plateau pressure for the same set tidal volume).	This is always needed following apnoea testing. If unfamiliar with recruitment manoeuvres, ask for help. Watch for cardiovascular decompensation. If this occurs consider whether the patient may be hypovolaemic (see circulation section below). Transient desaturation is often seen with recruitment manoeuvres and is of no concern.
	Set the ventilator to deliver 100% oxygen ☐ and transiently set to volume control ventilation (or volume targeted pressure control) and set the tidal volume to 8ml/kg ☐. Please ensure rate and I:E ratio set appropriately ☐. Following these tests modify ventilator settings ☐ (see later section).	After 15mins take an arterial blood gas* ☐. Measured PaO_2 Suitable lungs should achieve a PaO_2 >40kPa (300mmHg) [diffusion test]. Measured peak / plateau pressure A tidal volume of 8ml/kg should be achieved with a peak / plateau pressure of <30cmH_2O [compliance test].

Initial checklist of monitoring, physiological targets and investigations - continued

	Parameter	Method / rationale and notes
Circulation	If not already in place institute continuous 3 lead ECG, CVP, invasive arterial pressure and cardiac output monitoring. Ideal targets: **Sinus rhythm 60-100 bpm** ☐ **CVP 4-12mmHg** ☐ **Cardiac index (CI)) ≥2.0 l/min/m^2** ☐ **Mean arterial pressure (MAP) 60-80mmHg** ☐ **Central venous oxygen saturation** **($ScvO_2$) ≥70%** ☐ [Please record hourly observations and all therapies on chart]	Following brain stem death patients may develop dysrhythmias, hypovolaemia (e.g. diabetes insipidus), cardiac dysfunction (e.g. reversible global myocardial depression), hypertension (e.g. catecholamine storm) and hypotension (e.g. a mixture of the above +/- vasoplegia). Continuous and complete monitoring of the cardiovascular system is essential. Use whichever method of cardiac output monitoring you are most familiar with. **If you are not achieving these targets institute immediate therapy as per guidelines** (see later).
	Perform a 12 lead ECG ☐ to fully assess for rhythm and diagnose any abnormality. If available, compare to a recent ECG performed prior to brain stem death ☐.	Look for conduction abnormalities, signs of hypertrophy and acute or previous ischaemia / infarction. Acute strain patterns may represent reversible pathology.
	If available, request a echocardiogram	This is to exclude any structural heart disease including, valves, hypertrophic / thinned myocardium, regional wall abnormalities etc.

* when taking the ABG if not already done within the last 12 hours take blood for FBC, clotting studies, group and save, renal, liver and bone biochemistry and troponin (+/- additional samples for virology and tissue typing).

Additional routine care issues and targets

	Parameter	Method / rationale and notes
Temperature	Maintain temperature at 35.5-37.5°C ☐	Hypothermia secondary to brain stem death is more common than hyperthermia. Actively warm / cool as appropriate.
Fluid balance	Neutral to negative (unless grossly hypovolaemic)	Optimal intravascular volume for perfusion vs. minimisation of extravascular lung water. Avoid maintenance fluids. **Consider** balanced crystalloid replacement of last hours urine output.
Glycaemic control	Blood sugar 4.0-8.0mmol/l ☐ Measure at least 2 hourly ☐ In addition, **insulin** may play a role in cellular protection and therefore is recommended (even in those donors with normoglycaemia) **at an infusion rate of 1iu/hr** ☐.	**Consider** instigating (or continuing) low dose / low volume enteral feeding ☐ [multiple potential benefits including sodium and water balance, splanchnic perfusion, glycaemic control etc]. **Alternatively, consider** continuous infusion of 20% or 50% dextrose (25 or 10mls/hr respectively) to avoid hypoglycaemia ☐.
Electrolytes	Na^+ 135-150mmol'l ☐ K^+ 3.5-5.0mmol/l ☐ Mg^{2+} >0.8mmol/l Ca^{2+} 1.0-1.3mmol/l (ionised) ☐ or 2.0-2.6mmol/l (total) corrected for albumin ☐ PO_4^{3-}>0/8mmol/l ☐	Actively manage as necessary. Of note Na^+ >150 mmol/l is associated with significant hepatic graft dysfunction.
Patient position	Maintain 30-45° head of bed elevation ☐. Consider side-back-side rotation.	To reduce passive aspiration and increase FRC.
DVT prophylaxis	In not already in place fit TED stockings ☐ +/- calf compressors ☐	
Review medications	Stop all unnecessary drugs ☐	

Organ specific therapies and physiological targets

	Targets	**Rationale / therapeutic suggestions**
Lungs	PaO_2 >8kPa on minimum FiO_2	Minimise absorption atelectais and oxygen toxicity
	$PaCO_2$ 5.0-6.5kPa (or higher as long as pH>7.30)	Minimise ventilatory requirement and thereby minimise ventilator induce lung injury. (Mild permissive hypercapnia may be advantageous.)
	Tidal volume 6-8ml/kg (ideal body weight)	Minimise ventilator induce lung injury.
	Peak / plateau pressures <30cmH_2O	Minimise ventilator induce lung injury.
	At least 2 hourly clinical assessment of lung recruitability and retention of recruited units. Look for deteriorating saturations / increasing oxygen requirements and deteriorating dynamic lung compliance (reduced expiratory tidal volume achieved for set pressure / increase in inspiratory pressure to achieve same expiratory tidal volume)	Optimal PEEP set. Consider recruitment manoeuvre followed by decremental trial to find best PEEP setting. Consider sigh breaths or periodic prolonged inspiratory holds. Only suction if clinically indicated by signs of secretions within the proximal bronchial tree and always consider the need for re-recruitment afterwards. (Clinical signs of secretions within the proximal tracheobronchial tree include classic “upper airway secretion” crepitations on auscultation, an irregular or diminished flow profile (expiratory more common than inspiratory) and progressive deterioration in compliance and / or gas exchange. In the latter case, suction prior to the recruitment manoeuvre.) Do not disconnect from the ventilator unless absolutely necessary. If unavoidable, perform a recruitment manoeuvre immediately after re connection. DO NOT perform manual hyperinflation manoeuvres with a Water’s circuit or equivalent.
	Reduce / minimise extravascular lung water	Minimum IV fluids to achieve adequate preload (see below) Consider trial of frusemide infusion at 0.5-10mg/hr to achieve 100-200ml negative fluid balance per hour Consider nebulised salbutamol 2.5mg 2 hourly to increase alveolar fluid clearance rate [2].

Organ specific therapies and physiological targets - continued

	Targets	Rationale / therapeutic suggestions
Cardiovascular	Sinus rhythm 60-100 bpm	Bradycardia may result from brainstem compression. Consider short acting positive chronotrope e.g. isoprenaline, dobutamine, salbutamol etc For sinus tachycardia consider the differential diagnosis and treat the cause. If associated with hypertension consider short acting β-blockade with esmolol. If associated with hypotension consider hypovolaemia, myocardial depression and vasoplegia.
	Preload / intravascular volume [3] CVP 4-12mmHg Systolic / pulse pressure variation <15% Stroke volume variation <15% Increase in aortic blood flow with passive leg raising <10%	**If** the patient has a MAP of 60-80mmHg with no vasoactive drug support then monitor preload parameters for trend information. **If** the patient has a MAP of <60mmg **or** is requiring vasopressors to achieve a MAP of 60-80mmHg **AND** 1 (or more) preload parameters indicates hypovolaemia **then** administer a 3-5ml/kg fluid bolus (balanced crystalloid or colloid) as rapidly as possible. Record the pre and post fluid bolus stroke volume / cardiac output. An increase of ≥15% indicates a positive response to the fluid challenge. If positive, consider whether to repeat the challenge and when to review this decision. If <15% then consider myocardial depression and vasoplegia
	Myocardial contractility Cardiac index (CI)) ≥2.0 l/min/m^2	**If** the CI is low **AND** there is no evidence of hypovolaemia **AND / OR** no response to a fluid challenge **THEN** commence: T_3 (tri-iodothyronine) [first line inotrope] 4µg bolus then 3 µg/hr infusion OR T_4 (thyroxine) 20 µg bolus then 10 µg/hr infusion **If** this fails to achieve the target CI **THEN** commence: Dobutamine at 2.5 µg//kg/hr and increase as necessary up to a maximum of 10 µg//kg/hr NOTE low dose dobutamine may be beneficial at low doses in ameliorating ex-vivo, cold ischaemic injury [4] but high doses may deplete high energy phosphates

Organ specific therapies and physiological targets - continued

	Targets	Rationale / therapeutic suggestions
Cardiovascular	Afterload / perfusion pressure MAP 60-80mmHg	**If** MAP <60mmHg and preload and myocardial contractility have been optimised / treated **then** commence [first line vasopressor AND "hormonal resuscitation therapy]: Vasopressin 1ui bolus then 0.5-4iu/hr. OR Teripressin 1.3 µg//kg/hr [5]. (This can be simplified to 2mg made up to 48mls. Give 2 ml bolus then infuse @ 2mls per hour.) **If** this fails to achieve a MAP of 60-80mmHg **then** add in noradrenaline (norephinephrine) OR dopamine. **If** the patient appears to exhibit noradrenaline "resistance" defined as a dose >0.2 µg//kg/hr **then consider** a trial dose of hydrocortisone 50-100mg (in addition to the methylprednisolone already administered). The rationale for this approach is based on the mineralocorticoid effects of hydrocortisone [6] (methylpredisolone has no mineralocorticoid action). If successful in facilitating a ≥15% dose reduction in noradrenaline consider either a hydrocortisone infusion at 10mg/kr or repeated 50mg boluses at 4-6 hourly intervals. If MAP >80mmHg then consider esmolol (loading dose then infusion) AND / OR glycerine trinitrate (up to 40mg/hr) to achieve target MAP (and maintain heart rate >40bpm). The use of very short acting drugs is recommended as there is a significant risk of brain stem dead patients rapidly developing a rebound hypotensive state.
	Measures of global oxygen supply demand balance $ScvO_2$ ≥70% [Hb] >8g/dL	Having optimised / treated heart rate / rhythm, preload, contractility and afterload, the adequacy of oxygen delivery can be judged by monitoring the $ScvO_2$. If this is low, it suggests that either delivery is suboptimal and / or consumption is high. Re-consider the 4 cardiovascular variables above AND consider haemoglobin concentration. If [Hb] is low or suboptimal then considered packed RBC transfusion. If may be of value to increase [Hb] above this threshold to mitigate against blood loss during organ retrieval. Please discuss this with the retrieval teams as there maybe negative consequences of blood transfusion on graft function.

Organ specific therapies and physiological targets - continued

	Targets	Rationale / therapeutic suggestions
Renal	Urine output 0.5-2.5 ml/kg/hr	Cardiovascular optimisation should achieve this. Watch for polyuria / diabetes insipidus. If occurs, ensure adequate intravascular volume replacement (with 5% dextrose) and commence vasopressin / terlipressin / DDAVP therapy. Monitor and correct Na^+. Low dose dobutamine 2.5 µg/kg/min [4] OR dopamine 4 µg/kg/min [7] may be useful in mitigating against cold ischaemic injury.
Liver	Normal bilirubin / ALT / ALP / γGT / pT (INR) / fibrinogen / lactate / glucose	Cardiovascular optimisation should achieve this. If available consider measuring indocyanine green (ICG) clearance [8]

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